KMCH Touch

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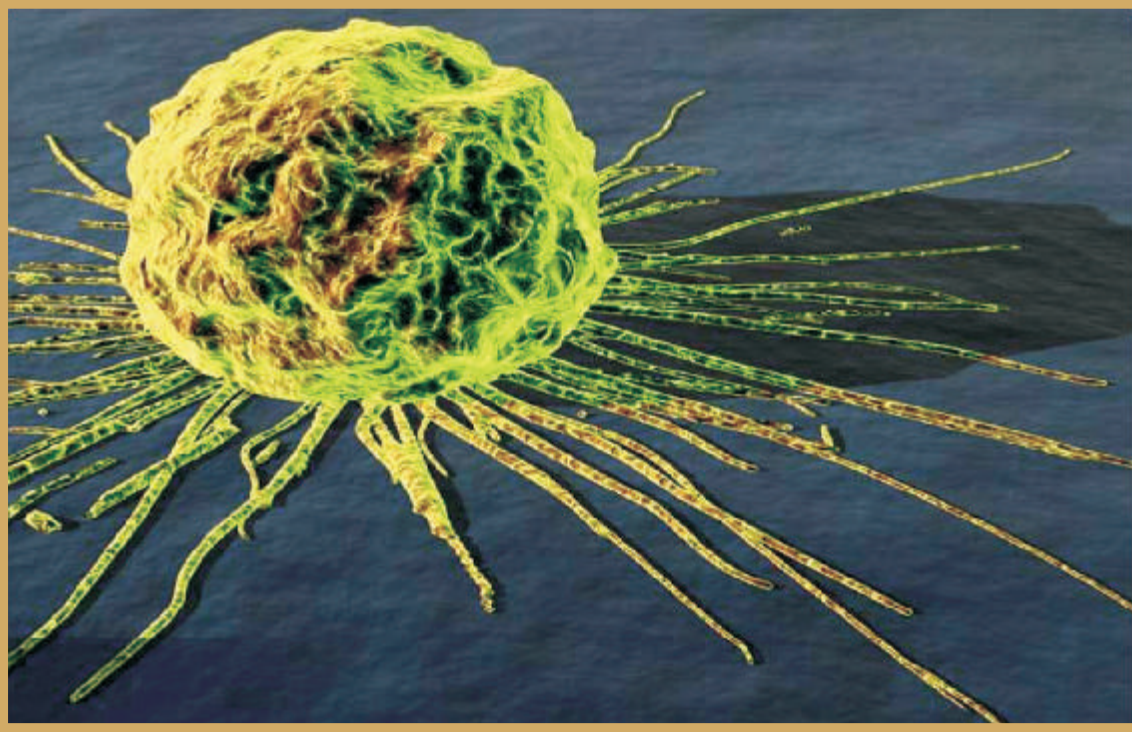
QUARTERLY NEWS JOURNAL OF KOVAI MEDICAL CENTER AND HOSPITAL

Special Anniversary Issue

FOCUS ON ONCOLOGY



Upcoming Event

KMCH Spine Conference -2011
Date : 31st July, 2011

KMCH Anaesthesia Update -2011
Date : 4th September, 2011

CHAIRMAN'S DESK

Health Care services in India and in the world are going through tremendous changes because of changing natures of diseases and how those are tackled with improved technologies and novel treatment modalities. India is in the transition status of poverty to affluence. We have population of increased life expectancy with various medical problems. Changing food habits, poor quality environment and bad living conditions have enormous impact on health conditions of our Indian population.

Diabetes, Hypertension, Ischemic heart diseases and now Cancer of various kinds are increasingly afflicting Indians. India has now big responsibility of not only taking care of poverty but also has to take care of these conditions. Governments of India and Tamilnadu have taken steps to tackle these problems. We, in the private sector have also social responsibility to assist in these areas especially cancer awareness, detection and treatment programs.

KMCH after realizing the need of the nation embarked on ambitious project of "Cancer." Our project is called "Comprehensive Cancer Care." It includes cancer awareness, cancer detection and cancer treatment. The cost of the project is Rs.250 crores. The Comprehensive Cancer Center will have 200 beds hospital facility and state of the art equipments to treat cancer and cancer related ailments.

The major equipments and facilities are

1. Varian Triology Linear Accelerator
2. Brachy therapy units
3. PET scan
4. SPECT scan
5. 3T MRI scan
6. 500 Slice CT scan
7. Bi-Plan Cath lab
8. Digital Mammogram
9. Bone marrow transplant suites
10. Radio-active isotopes treatment suites for thyroid diseases
11. 7 separate operation theatres for Cancer Center
12. 200 beds hospital with special suites for cancer patients with rehabilitation facilities.

KMCH Comprehensive Cancer Care Center is specially designed to cater all kinds of cancer with latest equipments with well trained experts. Dr.V.Kannan is the director of Comprehensive Cancer Care Center. We have assembled experts in various areas of cancer treatments and they are supported by best radiation physicists, nuclear physicists and technologists. We are fortune enough to have these many experts in this area of Tamilnadu. We can say boldly that KMCH has one of the finest facilities for treatment of cancers in India and the world. We assure that we will maintain the decorum and the quality of care for all sections of people of India at affordable cost.

With regards

Dr. Nalla G Palaniswami
Chairman

THE EDITORIAL BOARD

Linus Pauling, a two-time Nobel Laureate once said: "Everyone should know that the 'War on Cancer' is largely a fraud"

Perhaps nothing strikes at the very heart of an individual quite like hearing the word "cancer". And while survival rates have increased in recent years, there's still no denying cancer is becoming the number one killer of the human species.

We all know that cancer is growing at an alarming rate in India. In fact, cancer has become one of the 10 leading causes of death in India. Over 700,000 new cases of cancer and 300,00 deaths occur annually due to cancer.

Nearly 15,00,000 patients require facilities for diagnosis, treatment and follow up at a given time. Data from population-based registries under National Cancer Registry Program indicate that the leading sites of cancer are oral cavity, lungs, esophagus and stomach amongst men and cervix, breast and oral cavity amongst women. According to an Indian study published in Asian Pacific Journal of Cancer Prevention in 2010, the total cancer cases are 979,786 cases in 2010; tobacco-related cancers for males are estimated to be 190,244, while the number of cancer cases related to digestive system is estimated to be 190,030. For head and neck cancers, the estimates are 172,643 cases. Gynaecology related cancers are estimated to go up from 153,850 in 2010 to 182,602 in 2020.

Among males and females, cancer of breast alone is expected to cross the figure of 100,000 by the year 2020. The Cancer Registry has been collecting all essential data pertaining to cancer patients, in the resident population of the respective areas. The registry then analyzes the data and produces a report, which is presented to the Indian Council of Medical Research.

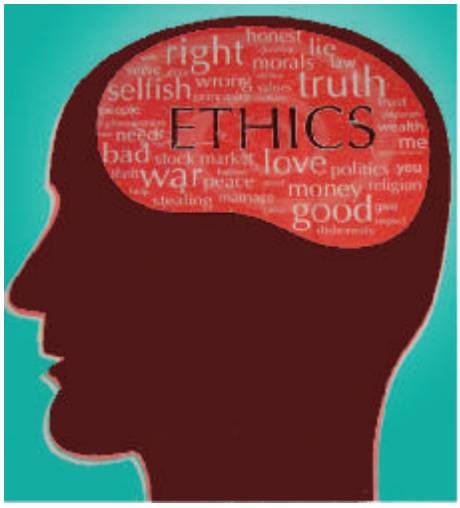
In order to extend the assessment of cancer patient care, Hospital Based Cancer Registries were also started in Bangalore, Chennai and Mumbai in 1984. Recently, even large multi-specialty hospitals with oncology services in private sector were suggested to contribute data to the Registry.

Keeping all this in mind, the Editorial Board thought it was pertinent to stress on Cancer and Oncology services offered by KMCH by dedicating this issue of KMCH Touch to cancer-related information. Here at KMCH, we have a full-fledged team of doctors and nuclear medicine specialists offering exclusive oncology services supported by state-of-the-art technology. The doctors involved in the oncology team have been trained in some of the best centers in India and abroad, and are highly experienced in their respective areas of specialization.

The Editorial Board would like to thank the Chairman for letting us go overboard on this issue! We also sincerely acknowledge all the doctors who have contributed their valuable time and expertise to this issue in spite of their hectic schedules. The release of this issue of KMCH Touch also coincides with the 21st Anniversary of KMCH. We hope this 'Special Anniversary Issue' makes good reading, being informative and useful.

OF ETHOS

Dr. Aarthi Kannan
(D/o. Dr. V. Kannan, Director, Comprehensive Cancer Center, KMCH)



Albert Einstein hit the nail on the head when he said: "Relativity applies to physics, not ethics."

In all the questions and answers of life, the most puzzling one is of ethics. We're cornered by the concepts of right and wrong from various people, various cultures and we rarely get an idea of what it's all about.

By a good 21 to 22 years of age, the fun and frolic still remains but an unknown sense of responsibility looms over. In a profession like medicine, how critical are basic ethics? And how does money affect it?

An architect friend of mine had come across a bunch of students celebrating a day off at a regular hangout, and casually asked them, "Where do you see yourself five years down the line?" They gave a rather amusing reply, "We see ourselves as 'rich'." How ambitious, how hopeful, he thought. Youngsters have great potential, but many of them are invariably misled to think that life is about earning and chilling out. When they discover it is not easy, quite a few are tempted to look towards means of easy money.

The road to comfort is anything but straight

You need a good, respectable role model; so when you're confused about right and wrong, you'll know where to look; but that's not easy to find; they're rare. It must dawn on the youth community, especially a community of aspiring-doctors that responsibility to humanity is far beyond self. Look at the larger picture…money is not all that it's blown up to be. It's merely a tool to pay off our bills and we must keep it where it's supposed to be.

Another oncologist friend, in response to my question: "Don't you think what you've said is idealistic; too difficult to follow in actual life?" He replies, "It's difficult only when you fight with yourself."

What is the role of ethics in medicine?

"Of utmost importance, it is, in the practice of medicine. We aren't dealing with still-life objects. It's a question of life and death many times. We ought to keep in mind that every life is to be valued priceless, and which cannot be compromised", says Oncologist Dr. Kannan, who believes that good ethics take a birth at an academic level. One never really knows what's ethical or unethical. Yet another idealistic article by a budding doc. Yes? No?

Well. Becoming a doctor isn't a cakewalk. Being one is a challenge by itself. Am I hearing a loud 'yes'? To live up to that pride, we've to qualify for a fourth dimension called 'ethics', beyond all our academic subjects. To swim up the current, what we need is a simple set of codes and rules in daily practice. That's where ethics steps in.

A senior oncologist in Mumbai says, "For ethical practice, we need to know our subject and learn with utmost sincerity and effort from M.B.B.S. level itself. Money is what we all seek to support our lives; but money should only be an effect and not the cause of what we work for. If it becomes the cause, then we'd chase it anyhow; which is when we'd lose quality in our work."

To all my fellow students

Ethics regarding our field has been an eye-opener to me. Many senior professors and doctors have stressed on it all this while, but age has kept us frolicking. It's fun to have fun, and it is essential that we enjoy life as kids at heart, but let a little sense of thought always prevail. After all, we don't want The Hippocrates' oath to become the hypocrite's oath. Good education translates into good ethics. The time is now.

Guess which organ or tissue in body that does not get cancer?
It is only the NAIL and HAIR.

RADIATION THERAPY IN HEAD AND NECK CARCINOMA: CONVENTIONAL 2D TO 3D-CRT, IMRT-IGRT AND BEYOND

Dr. V. Kannan, Dr. C.V. Eswar
Department of Oncology

Radiotherapy is an effective treatment modality for cancer and > 50% of cancer patients require radiotherapy treatment. With advances in computer technology and imaging for 3-dimensional (3-D) volume determination with CT and MRI scans 2-dimensional (2-D) treatment has evolved into 3-D treatment.

Developments in engineering has led to advances in radiation treatment technology like dual energy linear accelerator with dynamic jaws, multileaf collimation (MLC), microMLC and online portal imaging facility with fluro and cone beam kV and MV CT scans. Electronic network has integrated the 3-D images, computerized 3-D planning system and linear accelerator to deliver optimal radiation doses to the 3-D target volume with intensity modulation of the mega voltage beams called Intensity Modulated Radiation Therapy (IMRT).

IMRT uses inverse treatment planning technique and computer aided optimization to generate intensity modulated beam profiles. It develops a treatment plan that fulfills as closely as possible the specified criteria namely conformal dose distribution around the tumour with steeply decreasing dose gradients at the transition to adjacent normal tissues. IMRT delivery requires MLC in dynamic mode or multi segment step-and-shoot mode or tomotherapy beam over 360 degrees modulated by slit beam MLC.

The need to continuously improve tumour control while reducing normal tissue complication is an important challenge in head and neck cancer. Xerostomia is a severe complication resulting from unavoidable irradiation of parotid salivary glands during curative radiation therapy of nasopharynx, oropharynx, skull base and higher neck nodal tumours.

Conventional radiation by use of parallel opposing fields leads to delivery of > 40-45 Gy to both parotids causing a fall in serous saliva secretion and xerostomia. IMRT has been shown to reduce the dose to the parotid glands without compromising tumoricidal dose to head and neck tumours.

Dose-response relationship for parotid gland secretion has shown that a mean dose of < 26 Gy does not result in significant xerostomia (Chao 2001, 2004, Eisbruch 1999, 2003, Blanco 2005) and with IMRT this end point is easily achievable. Radiotherapy can also lead to permanent sensory neuronal hearing loss due to cochlear damage. CT/MRI inner ear localization and dose reduction with IMRT is feasible to preserve hearing.

IMRT allows us to escalate the dose with acceptable toxicity. IMRT also helps us to avoid complex conventional setups such as matching photon fields with electrons for neck nodes to minimise spinal cord toxicity.

The recent RTOG studies in head and neck cancer have used a single phase treatment with (SIB) simultaneous integrated boost helping to reduce overall treatment time and further improve local control. IMRT in nasopharynx using dose painting was evaluated in hypofractionated schedule of 2.34 Gy per fraction (Bakst et al, 2011). The local control and survival were similar to conventional fraction IMRT but brain radiation toxicity was found to be elevated. The authors therefore recommend only IMRT with conventional fractionation.

In oropharynx carcinoma 41 patients treated with IMRT and chemotherapy were compared to 71 patients treated with conventional RT and chemotherapy (Lee et al, 2006). Three-year overall survival was 82% in IMRT and 76% in CRT group. Between the 2 groups in 20 months, the xerostomia of grade 2 was > 67% in CRT group and 12% in IMRT group.

Dysphagia and aspiration after chemo-radiation were studied in 26 patients (Eisbruch, 2004) with head and neck cancer. Pharyngeal constrictors, glottic and supraglottic region radiation damage was identified as the causative factor. Sparing of these structures from high-dose was feasible with dysphagia-optimized IMRT.

The first case of IMRT in India published in the year 2001 (Kannan et al) was a case of sphenoid sinus carcinoma treated to a dose of 70 Gy with concurrent chemotherapy. Patient had no evidence of disease at two-year follow-up. A total of 36 children with nasopharyngeal carcinoma were treated at Tata Memorial hospital, Mumbai with 3D CRT and IMRT (Laskar et al, 2008). The results revealed that with IMRT treatment the tolerance and compliance were better. Nangia et al (2010) using RTOG guidelines for selective nodal irradiation treated 83 head and neck cancer patients with IMRT. The 3-year overall survival and locoregional relapse free survival were 81.7% and

60.8%. Grade II xerostomia was observed in 36.1%.

In head and neck tumours we quite often see rapid changes in the tumour volume due to good early response with radiotherapy. Also oral mucositis with poor intake can cause weight loss altering the patient anatomy and these changes can significantly change the treated volume from the planned one. Tracking the reduction in target volumes during IMRT called adaptive IMRT was studied by investigators in treatment of laryngo-hypopharyngeal tumours (Gregoire 2006, Geets 2006). Before and during treatment in weeks 2, 3, 4 and 5 CT, MRI and FDG-PET were done and GTV was found to decrease significantly. This can potentially decrease dose to non-target tissue and morbidity.

There have been great strides in the field of (IGRT) image guided radio-therapy in the last 5 years. The increasing conformal dose distribution with small volume with rapid fall-off in isodoses demands this more precise target positioning during treatment. Factors that can affect the positional uncertainty in target and sensitive critical normal tissues are errors in 3-D target delineation, patient position, internal organ motion and tumour volume changes during a course of 6-8 weeks fractionated radiotherapy.

Varian Trilogy Linear Accelerator at KMCH

Systematic or treatment preparation errors may be introduced if patient condition during 3-D simulation is different than at treatment and this also includes errors in 3-D target and organ at risk (OAR) delineation. A random or treatment execution error can occur due to daily treatment setup errors or due to organ motion. Patient positioning error is greatly overcome by electronic portal imaging device with state-of-art amorphous silicon type.

Technology has progressed from 2-D portal images to online 3-D CT images (IGRT). Online CT portal images favor precise position of the treatment target (patient) to match the isodose (van Herk 2005, Pouliot 2005). This can be achieved by remote control adjustment of the treatment couch to match the 3-D isodose or by online 3-D planning prior to each treatment.

The advent of CT planning has made practice of radiotherapy more precise but it also demands good CT/MRI/PET imaging and good clinician understanding of the CT anatomy. Target delineation errors remain constant during the course of radiation and will have a large impact on target dose (Rasch et al, 2005). Major sources of delineation variation are visibility of target and its extension. Addition of other imaging modalities to CT scan like MRI and PET scans was found to improve better delineation of structures of interest (Rasch et al, 1997; Geets et al 2004).

Rapid advances in imaging have resulted in functional imaging like MRSI, PET and SPECT which have been integrated with anatomical volume to create functional volume for concentrating higher 3-D dose to abnormal functional volume. PET-CT scanner has higher sensitivity and specificity than either technique alone.

It provides images of anatomy and function for more accurate tumour volume delineation and for creation of morphological and biological target volume. Planning results of FDG-PET voxel based IMRT (vIMRT) and PET contour based IMRT were compared in 15 patients (Vanderstraeten, 2006). In the vIMRT dose peaks were created inside the PTV following the distribution of PET voxel intensity value, which can assist in biological focused dose escalation.

New approaches in precision curative radiotherapy, 4D-RT and SBRT, are more commonly employed in sites other than head and neck carcinoma. Precision online volume image guided IMRT with biological optimization (bIMRT) is the future of radiation oncology. Randomized phase 3 trials are expected to confirm the results of the early prospective data of toxicity reduction published till date.

CASE PRESENTATION : PRIMARY ORBITAL LYMPHOMA

Dr. V. Kannan, Dr. Sarada Krishnamurthy, Dr. C. V. Eswar
Department of Oncology

This 71-year old lady presented with left orbital swelling and redness in April 2011 (Fig. 1). She had a biopsy of the lesion and the pathology was reported as a low grade B cell lymphoma of the orbit. The immuno-histochemistry results showed CD20+, CD25+, CD5+, CD3-ve and CD10-ve. MRI scan reported a lobulated lesion in the superior and lateral aspect of left orbit with homogenous post contrast enhancement with no clear plane from the superior rectus muscle. PET CT confirmed a metabolically active left orbital extraconal soft tissue thickening extending to the retro-orbital region up to the optic foramen with no significant uptake elsewhere. After tumour board discussion it was decided to proceed with radiotherapy as definitive treatment.

For radiotherapy, a head and neck thermoplastic immobilisation mask was prepared followed by planning CT scan and MRI scan. Her PET scan images were fused with MRI and CT images (Fig. 2). The treatment planning volume (GTV, CTV and PTV) and organs to be protected were created on the PET and MRI images and transferred to CT images for beam planning. An IMRT rapid arc plan was done for the PTV. Following QA checks on the linear accelerator, treatment was delivered with IMRT rapid arc to the left orbit(Fig. 3). She had rapid tumour regression by 8 fractions and adaptive radiotherapy was done by repeating the planning CT scan and treatment was continued. The total dose delivered was 30Gy in 15 fractions. There was a near complete response at the end of treatment and further follow-up with imaging is planned.

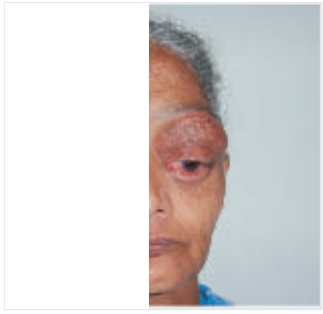


Fig.1 Pre - treatment - Left sided orbital mass

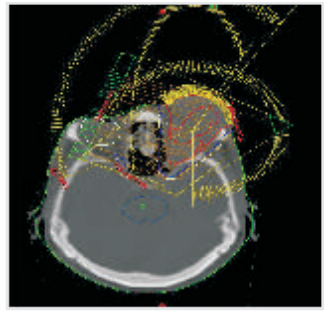


Fig.3 IMRT Rapid Arc Plan

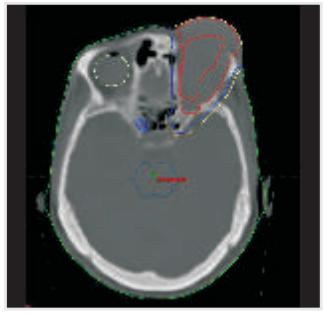
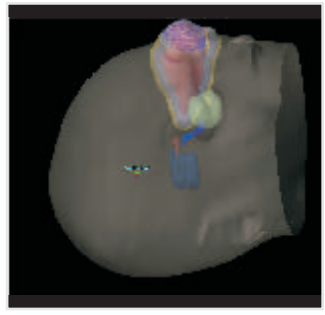
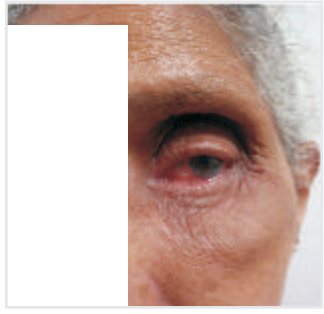


Fig.2 MRI-CT-PET fused: GTV, CTV, PTV



3-D volumes and OAR



Post- treatment – near complete response

Discussion

The orbit is a rare site of presentation of non-Hodgkin's lymphoma (NHL). Primary orbit lymphoma (POL) represents 1% of all NHLs and 8% of extranodal NHLs . Bilateral involvement occurs in 10-15% of cases of POL . The majority of patients at the time of diagnosis are over 65 . The common manifestation of the disease is a slow growing orbital mass that can be either asymptomatic or depending on the location of the tumour associated with proptosis, ocular dysmotility, periorbital swelling, blurring of vision and chemosis. The most frequent histology of POL is indolent NHL such as extranodal marginal B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) . Less common pathology is diffuse large B cell lymphoma

The management of localised POL consists of radiation treatment encompassing the entire orbit delivering a dose of 25 to 30 Gy. This can achieve a local control rate of >95%. For patients with advanced disease, sequential chemo-radiation treatment is preferred .

Conclusion

This is a rare case of localised POL which demonstrates a near complete response to definitive radiation therapy using IMRT - thus offering maximum therapeutic benefit with least toxicity to the patient.

TARGETED CANCER THERAPY – THE FUTURE OF MEDICAL ONCOLOGY

Dr. Sarada Krishnamurthy, Dr. V. Kannan
Department of Oncology

Cancer may be thought of as a fatal wound in which genetic and epigenetic aberrations occur. These aberrations elaborate a host of proteins into a tangled myriad of interactions and in turn, these interactions set the stage for the initiation and progression of tumour growth. Tumours have six distinct and essential alterations in their cell physiology that collectively dictate their malignant phenotype potential. These processes include: oncogene addiction (self-sufficiency in growth signals), loss of tumour suppressors (insensitivity to growth-inhibitory signals), anti-apoptosis (evasion of programmed cellular death), aberrant cell cycle (limitless replication potential), sustained angiogenesis, and lastly, invasion/metastasis.

Up until the turn of the 21st century, the crux of cancer therapy primarily focused on the removal of a tumour and then the attack of rapidly dividing cancer cells. What came in with the new millennium was 'targeted cancer therapy' – a breath of fresh air for the modern day oncologist. Targeted agents are designed to interfere with a specific molecular target that is believed to have a critical role in the growth and progression of a tumour, selective for cancer cells than for normal cells, thus causing less damage to normal cells, reducing unwanted side effects, and thus overall, improving the quality of life for the patient.

Historically, the first target for this novel approach was the estrogen receptor involved in tumour genesis of breast cancer. When estrogen binds to the intracellular estrogen receptor, the hormone-receptor complex activates the expression of certain genes that are involved in cell growth and proliferation. By interfering with estrogen's ability to stimulate the growth of cancerous cells, a newer approach to the management of breast cancer embarked. This has been the model and platform for other drugs that interfere with estrogens. Amongst them are: tamoxifen (a selective estrogen receptor modulator), fulvestrant (which binds to the estrogen receptor and decreases intracellular estrogen levels) and aromatase inhibitors such as anastrazole, exemestane, and letrozole. The ushering in of the new millennium opened wide a new spectrum of drugs that could target specific mutations. The most historically significant and memorable one is the 'wonder drug' Gleevec (Imatinib Mesylate). Gleevec made its appearance on the front cover of TIME magazine on 30 May 2001 (Fig.1) and thus, its debut into the public forum. It has since revolutionized the approach to treating dreadful diseases such as chronic myelogenous leukemia and gastrointestinal stromal tumour. The mutant kinase fusion protein called BCR-ABL displays an activation of the Abl kinase, which drives chronic myelogenous leukemia. Imatinib effectively blocks all the kinase, thus demonstrating major clinical responses. The 'Her 'receptor has been the target for the monoclonal antibody called traztuzumab, which is used in the treatment of Her-2 positive breast cancers. The Her proteins regulate cell growth, survival, adhesion, migration, and differentiation functions that are amplified or weakened in cancer cells. Rituximab is a chimeric monoclonal antibody against the protein CD20, and is used in the treatment of many lymphomas, leukemias, transplant rejection and certain autoimmune disorders.

Drug	Class of drug/action	Use
Imatinib	Tyrosine kinase inhibitor	CML, GIST
Desatinib	Tyrosine kinase inhibitor	CML
Nilotinib	Tyrosine kinase inhibitor	CML
Traztuzumab	Her-2 binder	Breast cancer
Lapatanib	Multi targeted tyrosine kinase inhibitor	Breast cancer
Geftinib	EGFR inhibitor	Luna cancer
Erlotinib	EGFR inhibitor	Lung, pancreatic cancers
Cetuximab	EGFR inhibitor	Head, neck & colorectal cancers
Evorolimus	mTOR inhibitor	Renal cell cancer

Fig. 1

Signal transduction inhibitors

Proteasome inhibitors induce apoptosis in certain cancer cells. The introduction of bortezomib in the treatment of multiple myeloma has revolutionized the entire approach to this disease. From an era in which remission rates were considered rare, long lasting remissions are now achieved with the use of this agent in conjunction with drugs such as thalidomide and lenali-domide, which are angiogenesis inhibitors. Targeted cancer therapies are not without limitations. The development of tumour resistance to these agents is a distinct reality. With the advances in genetic sequencing, scientists have been able to solve some of these puzzles. As we enter a new era of novel therapeutic strategies, we gain a new sense of appreciation and hope as the concepts that were once a vision, have now been turned into reality.

"EARLY FOR CURE; LATE FOR CHRONIC"

Dr. N. Sudhakar
Department of Oncology

One of the deadliest diseases of this century is cancer. According to reports by W.H.O., one out of three women and one out of four men are prone to getting cancer in the world.

Now with such alarming figures the task of hospitals and doctors has become very challenging. But with the advancement of technology its cure has become possible provided the disease is diagnosed in its early phase. Today the use of modern technology has brought the cure rate of cancer to almost 70-80%.

Early detection is the key to stemming the disease at the bud. We can begin with responsibility towards our health and well being. It is critical that we bear in mind that early detection is the key to tackling this adversary.

'Early Detection is Your Best Weapon against Cancer'

Here are two of the most important weapons we have against cancer; these are prevention and early detection. If we cannot prevent cancer, we need to understand that early detection is your very best weapon against cancer. The current understanding of the cancer disease process is that if detected 'Early', it can be 'Cured' and if detected 'Late' it can be considered as a 'Chronic' disease, and not incurable.

Early Detection For Women

Breast Cancer: Women should undergo a mammogram annually starting at the age of 40. Women should also set a schedule of visit to their regular doctor for a clinical breast exam. Women aged 40 and above should have an annual clinical breast exam. Beginning at the age of 20, women should perform a monthly breast self-exam. Be willing to report immediately to the doctor when there are changes in the breasts.

Talk with your doctor about elevated risk factors for breast cancer such as a family history of breast cancer, past breast cancer, or a genetic predisposition to cancer.

Cervical Cancer : A regular Pap test annually, or every 2 years for the newer liquid-based Pap test should be done by all women. Women ages 30 or above, who have had 3 normal annual Pap test can now get tested every 2 to 3 years instead of annually.

Recommendations for more frequent tests are administered by the doctor if patient is HIV+ or the immune system is weak. Ask your doctor about the HPV/DNA test. Women over 70 years could stop having annual Pap tests. Hysterectomy patients usually don't have to take the tests, unless the reason was a treatment for cervical cancer.

For endometrium cancer, report any vaginal spotting or bleeding to your doctor if patient is menopausal. If there is a risk of hereditary nonpolyposis colon cancer (HNPCC) after the age of 35, an annual endometrial biopsy is necessary.

Early Detection for Men

Prostate Cancer: A PSA test is annually given to all men and a digital rectal exam beginning at 50 years old. At the age of 45, men are already at high risk for prostate cancer and should start annual testing. African-American men and men with a close blood relative who had prostate cancer are at high risk for prostate cancer at a young age.

Early Detection For Both Men and Women

Colorectal Cancer – Both men and women at age of 50 or older should do one of the following early detection screenings:

- Yearly stool occult blood test (FOBT), or
- Flexible sigmoidoscopy every 5 years
- Combination of FOBT annually + flexible sigmoidoscopy every 5 years,
- Double contrast barium enema every 5 years
- Colonoscopy after 1 decade

An individual is at an elevated risk of developing colon cancer if he has a history of colon cancer, or polyps or inflammatory bowel disease, or a family history any of these. If this is the case, that person begins a regular screenings and exams at an early age, and he may have to do them more often. Some people are at a higher risk for developing certain kinds of cancer.

High risk people need to have tests done more often and beginning at an earlier age. The higher is the possibility to survive when cancer is detected earlier. Organ preservation in early stage cancers is a reality in this modern state of the art treatments particularly in breast, anal canal and head and neck cancers.

Advanced disease is sometimes curable but definitely treatable. Though most cancers in India and other developing countries are diagnosed at quite an advanced stage with all modern gadgets and technology advancements hope still lingers among cancer patients. A few examples of cases treated at

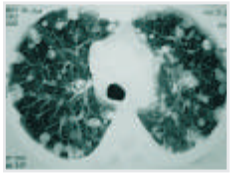
our Comprehensive Cancer Centre demonstrate this reality.

CASE #1

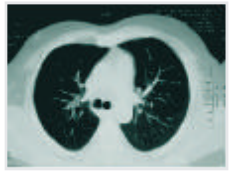
Mr B, aged 50yrs, complaints of dyspnoea, cough for 3 months.

On evaluation: CT chest shows multiple lung secondaries, CT abdomen and tumour markers are normal. CT guided biopsy of lung lesion was taken, HPE – Adeno-carcinoma.

PET Showing Complete Response



Pre-chemotherapy



Post-chemotherapy

Taken up for palliative chemo with Gem + cis. Symptomatic improvement from 2nd cycle Completed 6 cycles.Imaging with PET-CT revealed complete response. Patient is asymptomatic till date with a follow up of 8 months.

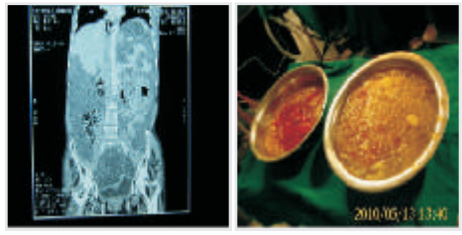
CASE #2

Mrs A , 67yrs old

Complaints of abdominal distension and weight loss for one year duration. No comorbids.

On evaluation: CT abdomen and pelvis showed pseudomyxoma peritonei with an ovarian mass, Chest X-ray was normal

diagnosed as Ovarian Carcinoma with Pseudomyxoma peritoneii.



Taken up for laparotomy – total hysterectomy with bilateral salpingo-oopherectomy and peritonectomy were done. Planned for adjuvant chemotherapy along with intraperitoneal chemotherapy. Completed a total of 6 cycles.

Intraperitoneal chemotherapy in progress

Dr Sugarbaker model is a classical example for team effort including Surgeon, Gynaecologist, Oncologist.

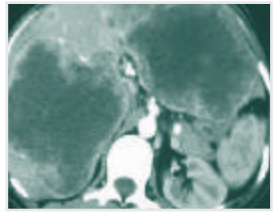
General condition improved after treatment. CT abdomen showed non-progressive disease after 12 months of follow up.

Intraoperative and early postoperative chemotheapy are practiced in select centres worldwide to avoid infective complications. Ours is one among them. In this predo-minantly peritoneal disease, intraperitoneal chemotherapy has the best response.

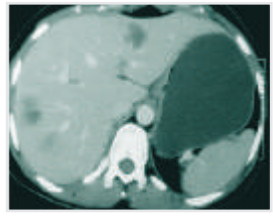
CASE #3

Mrs S, aged 50yrs Cancer Left breast – Metastatic disease, liver, lung, brain secondaries

WBRT given, Her2neu 3 +



Pre-chemoimmuno therapy



Post-chemoimmuno therapy

Treated with Inj Herceptin a monoclonal antibody to Her2neu along with Taxanes.

Remarkable response was seen and her general condition improved, though the liver and lung secondary showed only a partial response. She survived for 18 months. Since monoclonal antibody was used, there was less side effects.

Of the 3 cases of metastatic disease presented here, 2 were in a moribund condition with extensive lung secondaries. As per the existing guidelines, we would have been justified in offering them palliative (hospice) care alone.

Unfortunately, some of the symptoms of disseminated disease, like breathlessness, cannot be alleviated by a purely symptomatic approach aimed at treating the symptom rather than the cause. These conditions require specific therapy aimed at halting the progress of the disease causing the symptoms.

With the advent of newer molecules with greater efficacy and lesser toxicity with state of the art supportive care, these patients stand a better chance to achieve a better quality of life with improved survival.

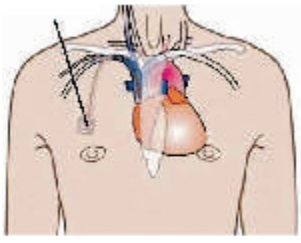
TOTALLY IMPLANTABLE VENOUS ACCESS SYSTEM (TIVAS)

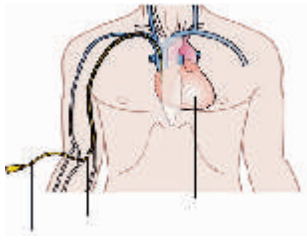
Dr. M. Bhuvaneswaran, Dr. Sarada Krishnamurthy

TIVAS is a totally implantable vascular access device designed to provide rep-eated access to the vascular system for the delivery of drugs, intravenous fluids, parenteral nutrition and blood products. They can also be used to draw of blood samples.

There are many brands available in the market like Microport, Bardport, PowerPort (power injectable), Passport, Infuse-a-Port, Medi-Port, and Lifesite (for hemodialysis patients). The most commonly used type in KMCH is the 'Port-a-cath' (Smiths Medical Co). The infraclavicular fossa is a satisfactory site, though the upper arm can be used as well. Port site selection should allow for good port stability, should not interfere with mobility or cause pressure points. Ports can be placed in the subclavian or jugular veins or the basilic vein by a cut-down under local anaesthesia. Ideally, the catheter terminates in the superior vena cava, just upstream of the right atrium.

Implantable port

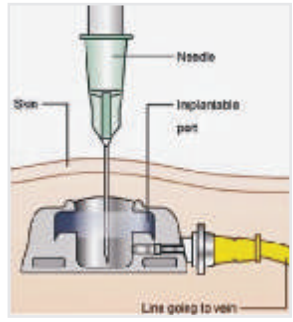




Heart PICC line enters body here

This position allows infused agents to be spread throughout the body quickly and efficiently.

How does it work?



A port consists of a reservoir compartment (the portal) that has a silicone bubble for needle insertion (the septum), with an attached plastic tube (the catheter). The device is surgically inserted under the skin in the upper chest or in the arm and appears as a bump under the skin. It requires no special maintenance and is completely internal so activities like swimming and bathing are not a problem.

The septum is made of a special self-sealing silicone rubber; it can be punctured hundreds of times before it weakens significantly. After each use, a heparin lock is made by injecting a small amount of heparinized saline into the device. The port can be left accessed for as long as required. The port is covered in a dressing to protect the site from infection and to secure the needle in position. If a port is used infrequently, it may be necessary to access the port, flushing it with saline and injecting a new heparin lock every month is done to prevent clotting between uses.

We routinely use this device at KMCH in cancer patients who need postoperative chemotherapy as and when needed. Most often, we place the ports in the infraclavicular fossa with the catheter tunnelled to the internal jugular vein.

THE CANCEROUS MIND

Dr. S. Paranthaman Sethupathi
Department of Psychiatry

Cancer kills.....

We all know this. But we are oblivious to the emotional and psychological trauma that this disease causes to the patient and his family. The initial diagnosis comes as a huge blow. It leaves the patient and the family with a huge question:

"WHY ME? WHY US?"

By virtue of being a more socially grouped community than our Western counterparts, Indians tend to be more cohesive in their emotions. Firstly, the patient goes through the 'denial' phase and then the 'acceptance' phase. The initial stage is usually met with anger, irritability and sometimes, complete denial. The patient would never have smoked, drank an ounce of alcohol, be a vegetarian and the most pious man, hence making it impossible for them to believe that such a horrid disease could affect them. Then comes the acceptance phase which is more likely to cause depression. Depression is a disabling illness that affects about 15% to 25% of cancer patients. Important issues in the life of any person with cancer may include the following:

- Fear of death
- Interruption of life plans
- Changes in body image and self- esteem
- Changes in social role and lifestyle
- Money and legal concerns

Sadness and grief are normal reactions to the crises faced during cancer, and will be experienced at times by all people. Because sadness is common, it is important to distinguish between normal levels of sadness and depression. An important part of cancer care is the recognition of depression that needs to be treated. People with cancer are three times more likely than the general population to develop depression. Greater the pain, more likely the depression. The consequences of untreated depression can be severe. A recent meta-analysis of 25 previous studies found that depressed patients (not just cancer patients) are three times more likely than non-depressed patients not to comply with treatment. Estimates of cancer patients who take their own lives range from twice the incidence of the general population to ten times. There are many misconceptions about cancer and how people cope with it, such as the following:

- All people with cancer are depressed
- Depression in a person with cancer is normal
- Treatment does not help the depression
- Everyone with cancer faces suffering and a painful death

"I'll throw myself out of the window if I have to go for chemotherapy one more time," sounds perfectly appropriate coming from a person who has been through far too much, already. As a result, many physicians do not assess for depression, or assume that because depression is a normal reaction to cancer, it does not merit treatment.

Over the years, psychiatry has advanced by leaps and bounds. Treatment of depressive or anxiety symptoms associated with cancer can be done with minimal interference of chemotherapy medications. Other than medications, a lot can be done for the patient and the family with psychotherapy and counseling. There are multiple relaxation techniques that a good psychologist and occupational therapist can offer to reduce the emotional distress for the patient and also the family unit. We at KMCH provide these psychiatric therapies as a part of the Comprehensive Cancer Care package.

Awareness for the physicians to look for the illness is the primary step in diagnosing and treating depression or anxiety associated with cancer.

The cancerous mind is DEFINITELY treatable.

Tobacco use is the single largest preventable cause of cancer in the world. The three men who appeared in the Marlboro advertisements – Wayne McLaren, David McLean and Dick Hammer – all died of lung cancer!!!!

BONE MARROW TRANSPLANTATION - A LIFE SAVING APPLIED ART

Dr. Rajasekar Thirugnanam
Department of Oncology

Comprehensive Cancer Care Center is in its finishing stages in KMCH and it is apt that the present issue of the Journal from KMCH has been dedicated to cancer care. The Hematology Department is slowly taking shape and as part of this department a two-bedded bone marrow transplant unit is also being set up. I take this opportunity to introduce and discuss bone marrow transplantation.

BONE MARROW TRANSPLANTATION

Hematopoietic stem cell transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cell into a recipient. The first successful hematopoietic cell transplants in humans were performed by infusion of hematopoietic progenitor and stem cells derived from the marrow of identical twins (syngeneic transplant). Application of transplant therapy broadened with the use of hematopoietic cells obtained from either related or unrelated donors (allogeneic transplant) suitably matched at the human leukocyte antigens (HLA), or even with a patient's own hematopoietic cells (autologous transplant). Although the term bone marrow transplantation (BMT) is historically applied to the field, hematopoietic cell transplantation (HCT) may be more appropriate because stem and progenitor cells are needed for prompt and complete engraftment in the clinical arena, and their source may be not only marrow but peripheral blood (PB), umbilical cord blood (UCB), or even fetal liver.

Stem cell transplantation is a medical procedure in the fields of hematology and oncology, most often performed for people with diseases of the blood, bone marrow, or certain cancers. It remains a risky procedure with many possible complications including risk to life and has traditionally been reserved for patients with life-threatening diseases. The use of cell- and immune-based therapies to treat hematologic disorders has come of age. Over the last 50 years hematopoietic cell transplantation has evolved into curative therapy for a variety of marrow failure states, hematologic malignancies, immune deficiencies, and inborn errors of metabolism.

Dr. E. Donnal Thomas (left) receives the 1990 Nobel Prize in Medicine

History

Georges Mathé, a French oncologist, performed the first bone marrow transplant in 1959 on five Yugoslavian nuclear workers whose bone marrow had been damaged by irradiation caused by a Criticality accident at the Vinca Nuclear Institute, but all of these transplants were rejected. Stem cell transplantation was pioneered using bone-marrow-derived stem cells by a team at the Fred Hutchinson Cancer Research Center from the 1950s through the 1970s led by E. Donnall Thomas, whose work was later recognized with a Nobel Prize in Physiology or Medicine. Thomas' work showed that bone marrow cells infused intravenously could repopulate the bone marrow and produce new blood cells. His work also reduced the likelihood of developing a life-threatening complication called graft-versus-host disease. The first physician to perform a successful human bone marrow transplant on a disease other than cancer was Robert Good at the University of Minnesota in 1968.

Types of Transplants

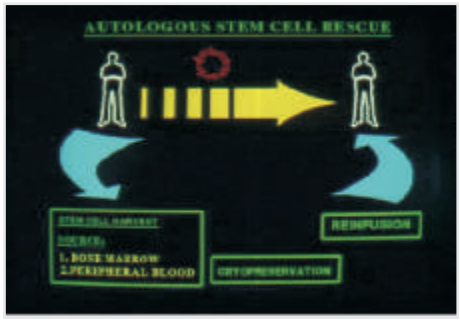
There are two types of marrow transplants: augologous and allogeneic, depending on the source of stem cells. Syngeneic transplant is a type of allogeneic transplant, where the donor is an identical twin.

Autologous transplant

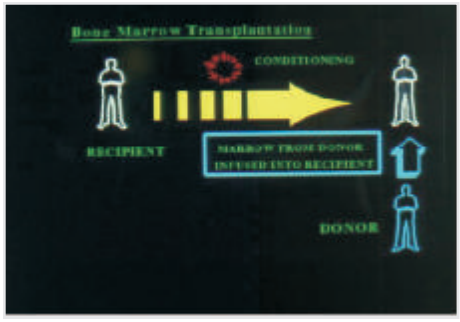
Autologous hematopoietic cell transplantation is most commonly used to reestablish hematopoiesis after high-dose cancer chemotherapy or radiation therapy. This approach permits the use of anti tumour agents in doses much higher than can be provided in a conventional therapy setting. Autologous HCT is most useful in circumstances where a correlation exists between increased therapy dose and tumor response, and where the dose-limiting feature of therapy is hematopoietic suppression.

Allogeneic Transplant

Allogeneic HSCT involves two people: the (healthy) donor and the (patient) recipient. Allogeneic HSC donors must have a tissue (HLA) type that matches the recipient. Matching is performed on the basis of variability at three or more loci of the (HLA) gene, and a perfect match at these loci is



AUTOLOGOUS BMT



ALLOGENEIC BMT

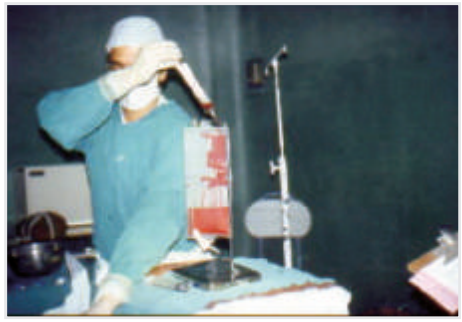
preferred. Even if there is a good match at these critical alleles, the recipient will require immunosuppressive medications to mitigate graft-versus-host disease. Allogeneic transplant donors may be related (usually a HLA matched sibling), syngeneic (a monozygotic or 'identical' twin of the patient) or unrelated (donor who is not related with a very close degree of HLA matching).

Transplant procedure

Since this is a risky procedure, the patient is comprehensively evaluated for co-morbidities and only a fit patient is taken for this procedure.

Stem cell collection

Hematologists performing BM harvest on a donor



BM harvest being collected

Stem cell source can be from the bone marrow or peripheral blood. Bone marrow harvest is performed in the operation theatre under anaesthesia, by inserting bone marrow aspiration needles into the iliac bone several times and aspirating the marrow.

To obtain stem cells from the peripheral blood the same have to be first mobilized from the bone marrow with colony stimulating factor injections to the donor, usually for 4 days and then collecting the stem cells from peripheral blood with the help of an apharesis machines.

BONE MARROW TRANSPLANT PROCEDURE

Preparative Regimen

Cobe spectra

Hemonetics

A patient admitted to the bone marrow transplant unit will first undergo several days of chemotherapy and/or radiation, which destroys bone marrow and cancerous cells and makes room for the new bone marrow. This is called the conditioning or preparative regimen. The exact regimen of chemotherapy and/or radiation varies according to the disease being treated and the "protocol" or preferred treatment plan of the facility where the BMT is being performed.

Prior to conditioning, a small flexible tube called a catheter (sometimes called a "Hickman®" or central venous line) will be inserted into a large vein in the patient's chest just above the heart. This tube enables the medical staff to administer drugs and blood products to the patient painlessly, and to withdraw hundreds of blood samples required during the course of treatment without inserting needles into the patient's arms or hands.

The dosage of chemotherapy and/or radiation given to patients during conditioning is much stronger than dosages administered to patients with the same disease who are not undergoing a BMT. Patients may become weak, irritable and nauseous. Most BMT centers administer anti-nausea medications to minimize discomfort.

The Transplant

A day or two following the chemotherapy and/or radiation treatment, the transplant will occur. The bone marrow is infused into the patient intravenously in much the same way that any blood product is given. The transplant is not a surgical procedure. It takes place in the patient's room, not an operating room.

Patients are checked frequently for signs of fever, chills, hives and chest pains while the bone marrow is being infused. When the transplant is completed, the days and weeks of waiting begin.

Engraftment

The two to four weeks immediately following

transplant are the most critical. The high-dose chemotherapy and/or radiation given to the patient during conditioning will have destroyed the patient's bone marrow, crippling the body's "immune" or defense system. As the patient waits for the transplanted bone marrow to migrate to the cavities of the large bones, set up housekeeping or "engraft," and begin producing normal blood cells, he or she will be very susceptible to infection and excessive bleeding. Multiple antibiotics and blood transfusions will be administered to the patient to help prevent and fight infection. Transfusions of platelets will be given to prevent bleeding. Allogeneic patients will receive additional medications to prevent and control graft-versus-host disease.

Extraordinary precautions will be taken to minimize the patient's exposure to viruses and bacteria. Visitors and hospital personnel will wash their hands with antiseptic soap and, in some cases, wear protective gowns, gloves and/or masks while in the patient's room. Fresh fruits, vegetables, plants and cut flowers will be prohibited in the patient's room since they often carry fungi and bacteria that pose a risk of infection. When leaving the room, the patient may wear a mask, gown and gloves as a barrier against bacteria and virus, and as a reminder to others that he or she is susceptible to infection. Blood samples will be taken daily to determine whether or not engraftment has occurred and to monitor organ function. When the transplanted bone marrow finally engrafts and begins producing normal blood cells, the patient will gradually be taken off the antibiotics, and blood and platelet transfusions will generally no longer be required. Once the bone marrow is producing a sufficient number of healthy red blood cells, white blood cells and platelets, the patient will be discharged from the hospital, provided no other complications have developed. BMT patients typically spend eight to twelve weeks in the hospital.

Course in hospital

A bone marrow transplant is a physically, emotionally, and psychologically taxing procedure for both the patient and family. A patient needs and should seek as much help as possible to cope with the experience. "Toughing it out" on your own is not the smartest way to cope with the transplant experience.

The bone marrow transplant is a debilitating experience, similar to the symptoms of a severe case of the flu - nausea, vomiting, fever, diarrhoea, extreme weakness, except that this persists not for days, but for several weeks. That approximates what a BMT patient experiences during hospitalization.

Complications can develop after a bone marrow transplant such as infection, bleeding, graft-versus-host disease, or liver disease, which can create additional discomfort. The pain, however, is usually controllable by medication. In addition, mouth sores can develop that make eating and swallowing uncomfortable and frequently these patients need to start on total parenteral nutrition.

Life after transplant

It can take as long as a year for the new bone marrow to function normally. Patients are closely monitored during this time to identify any infections or complications that may develop.

Life after transplant can be both exhilarating and worrisome. On the one hand, it's exciting to be alive after being so close to death. Most patients find their quality of life improved after transplant.

Nonetheless, there is always the worry that relapse will occur. Furthermore, innocent statements or events can sometimes conjure up unpleasant memories of the transplant experience long after the patient has recovered. It can take a long time for the patient to come to grips with these difficulties.

Is it worth it?

Yes! For most patients contemplating a bone marrow transplant, the alternative is near-certain death. Despite the fact that the transplant can be a trying experience, most find that the pleasure that comes from being alive and healthy after the transplant is well worth the effort.

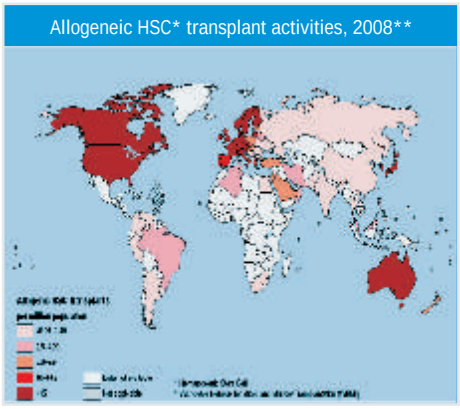
Scenario in India

With a population of over a billion and practice of consanguineous marriage, there is a huge demand for allogeneic transplant for hematological malignances as well as inherited conditions like hemoglobin-opathies and enzyme deficiencies. However the number of tertiary care centers with bone marrow transplant units is grossly inadequate as is evident from the picture below. Clearly some initiatives need to be taken.

REQUIREMENTS FOR A BMT UNIT

A near sterile environment is an absolute necessity and includes sterility of the room and whatever that enters the room, including air, water, supplies, food for patient and the personnel.

BMT rooms have to be of Class 100A standard with less than 100 particles of more than 0.3 microns size in the air and less than



1 colony forming unit of bacterial or fungal growth in a 4 inch diameter petri dish. Point-of-use, high-efficiency (>99%) particulate air (HEPA) filters capable of removing particles >0.3 µm in diameter is a necessity in these rooms. Rooms should have directed airflow so that air enters at one side of the room and is exhausted at the opposite side, with a minimum of 12 air changes per hour and should be well sealed (e.g., around windows and electrical outlets), to provide consistent positive pressure in the HSCT recipient's room.

Consistent pressure differentials should be maintained between patients' rooms and the hallways or anterooms at >2.5 Pascals. Water for the patient to drink needs to be sterile water from the pharmacy and for the patient's toilet needs and cleaning the unit needs to be boiled cooled, filtered and UV sterilized. The various supplies to BMT need to be outer wrapped, surface sterilized, disposable as far as possible and the Linen autoclaved. Food for patients needs to be pressure-cooked.

It is our sincere aim that the BMT unit in KMCH will conform to all the above requirements and with the co-operation and well wishes of one and all; quality service would be rendered to the patients.

SKIN TUMOURS

Dr. Jeevan Kumar
Department of Dermatology

Skin cancer can be found early and both doctors and patients play important roles in finding skin cancer. If you have any of the following symptoms, consult your doctor.

- Any change on the skin, especially in the size or colour of a mole or other darkly pigmented growth or spot, or a new growth
- Scaliness, oozing, bleeding, or change in the appearance of a bump or nodule
- The spread of pigmentation beyond its border such as dark colouring that spreads past the edge of a mole or mark
- A change in sensation, itchiness, tenderness or pain

The exact incidence in India is not known. But non-melanoma skin cancer is known to be uncommon in Asians. It has been noted that the incidence of all varieties of skin cancers is lower among Indians due to the protective effects of melanin. Skin cancer arises when skin cells lose the ability to divide and grow normally. Healthy skin cells normally divide in an orderly way to replace dead cells and grow new skin. Abnormal cells grow out of control and form a tumour. A tumour is considered benign (not cancerous) if it is limited to a few cell layers and does not invade surrounding tissues. But if the tumour spreads or has the potential to spread to surrounding tissues or organs, it is considered malignant, or cancerous. A pre-malignant or pre-cancerous lesion is an abnormality in a tissue area, which is just a step away from cancer. Not all pre-malignant lesions change to cancer, but most have greater potential for doing so than normal tissues. There are many varieties of pre-malignant lesions, but the most important one, especially for the Indian population is leukoplakia . Risk factors for skin cancers include:

- Unprotected and/or excessive exposure to ultraviolet (UV) radiation
- Fair complexion
- Occupational exposures to coal tar, pitch, creosote, arsenic compounds, or radium
- Family history of multiple or atypical moles

Xeroderma pigmentosum (XP)

This very rare inherited condition reduces the skin's ability to repair damage to DNA caused by sun exposure. People with this disorder often develop many skin cancers starting in childhood.

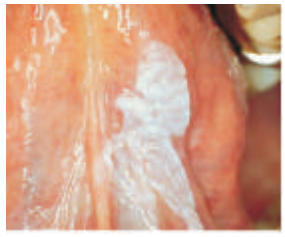
Basal cell nevos syndrome (Gorlin syndrome)

In this rare congenital condition, people develop many basal cell cancers over their lifetimes. Affected people may also have abnormalities of the jaw and other bones, eyes, and nervous tissue. In

families with this syndrome, those affected often begin developing basal cell cancers when they are young under age 20.

Some of the precancerous skin conditions are:

Leukoplakia: Clinical term used to describe patches of keratosis. It is visible as adherent white patches on the mucous membranes of the oral cavity, including the tongue, but also other areas of the urinary tract and the genitals. Leukoplakia is primarily caused by the use of tobacco.

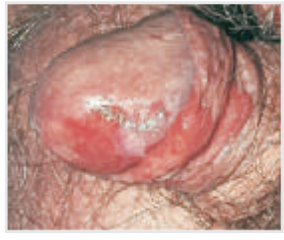


Leukoplakia of tongue

Actinic or solar keratosis: These are common asymptotic lesions seen mostly on sun-exposed areas of fair skinned people. They are especially seen in those who 'burn' easily or tan poorly. Commonly seen on the back of the hands, the face, upper chest, upper back and lower lip.

Bowen's disease: This is actually a cancer located totally within the top layer of the skin called the epidermis, and favours the sun exposed areas of the face, neck and extremities

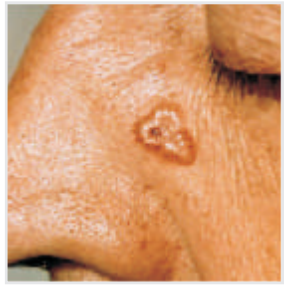
Erythroplasia of Queyrat: a dark red, velvety, flat or slightly raised hard patch on the glans penis (the bulbous tip of the penis) or on the inner side of the prepuce (the retractile top skin of the penis). It may at times produce a discharge and become painful.



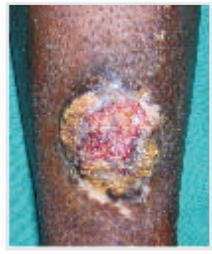
There are a number of different types of skin cancers depending on the type of skin cell from which they arise. Each kind of skin cancer has its own distinctive appearance. Common skin cancers are as follows:

- Basal cell carcinoma
- Squamous cell carcinoma
- Malignant melanoma

Basal cell carcinoma is the most common and least serious kind of skin cancer. That's because it grows slowly and rarely spreads. When seen under a microscope, these cancers share features with the cells in the lowest layer of the epidermis, called the basal cell layer. They usually develop on sun-exposed areas, especially the head and neck. Basal cell carcinoma is found almost exclusively in middle-aged or older people.



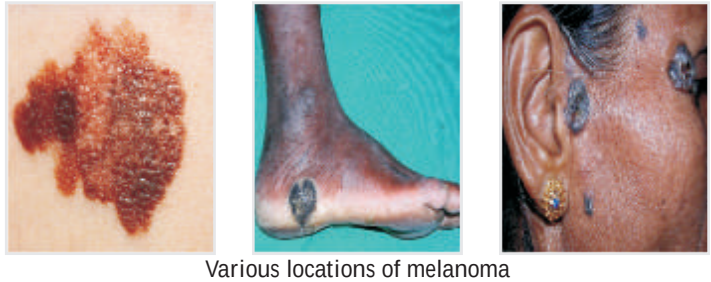
Basal cell carcinoma



Squamous cell carcinoma

Squamous cell carcinoma is more serious because it does spread to vital organs inside the body.. At first cancer cells tend to spread only as far as the nearest lymph nodes structures, which filter out and trap the cancer cells. If spread has occurred, the affected lymph nodes can be removed before cancer spreads to vital organs. They commonly appear on sun-exposed areas of the body such as the face, ears, neck, lips, and backs of the hands. They can also develop in scars or skin ulcers elsewhere. They sometimes start in actinic keratoses Less often, they form in the skin of the genital area. Squamous cell carcinomas tend to be more aggressive than basal cell cancers.

Malignant melanoma is the most serious kind of skin cancer because it may spread quickly from the skin through the lymph nodes or blood, to internal organs. Cancers that develop from melanocytes, the pigment-making cells of the skin Melanocytes can also form benign growths called moles.



Various locations of melanoma

Fortunately, most basal cell and squamous cell carcinomas can be cured with fairly minor surgery or other types of chemotherapy or radiotherapy treatments

Follow-up care

If patients have completed treatment, their doctors will still want to watch you closely and would recommend that you examine your skin once a month and protect yourself from the sun. Family members and friends can also be asked to watch for new lesions in areas that are hard to see. Patients should have follow-up examinations as advised by your doctor.

WHOLE-BODY IMAGING IN ONCOLOGY

Dr. Pankaj Mehta
Department of Diagnostic & Interventional Radiology

One in 15 individuals is expected to die of cancer. Early cancer detection and accurate staging are crucial for assessing prognosis and planning individually optimized treatment strategies.

In this context, whole-body imaging (WBI) provides vital information for decision-making. This is important because final decision to proceed with either curative or palliative treatment is frequently based on the information available from imaging studies that accurately identify the spread of disease.

Staging comprises tumour detection, precise anatomical localization and its local growth pattern (T-Stage) as well as assessment of local and distant lymphatic (N-Stage) and hematogeneous tumour spread (M-Stage).

Wholebody imaging is therefore an indispensable tool in oncology. Till a few years ago, nuclear medicine alone offered the possibility to examine the whole-body, by conventional scintigraphy or single photon emission computed tomography (SPECT), however, these modalities have a very poor spatial resolution.

Innovations in cross-sectional and Multiplanar imaging in the recent past have brought a paradigm shift in the way cancer can be assessed and staged through multislice CT, 3 Tesla MRI and the fusion of SPECT or PET with these modalities.

Thus, the high spatial resolution that is offered by MRI and CT can not only be used directly for evaluating cancer but can also be fused with PET or SPECT data, thereby eliminating the disadvantage of low spatial resolution of nuclear medicine scans.

COMPUTED TOMOGRAPHY (CT)

Over the last 10 years, spiral CT has gone through enormous technical advances and has made whole-body imaging within one single examination feasible. By providing high-resolution cross-sectional images of the whole body within a few seconds, CT has today become an indispensable tool for the current practice of oncologic radiology. It plays an important role in diagnosis, staging and follow of the disease process.

The impact of MDCT (Multi Detector Computed Tomography) is due to its superior temporal and spatial resolution. The isotropic imaging capability has transformed CT from an axial imaging modality to true volume imaging tool with multiplanar (imaging in any plane) and 3 dimensional imaging capability.

The increased temporal resolution (imaging resolution with respect to time) enable imaging in multiple phases like arterial, venous, delayed phases and thereby extracting maximum information regarding the tumour and its blood supply. This is very crucial to whole body oncology imaging where information with respect to local tumour staging and whole body spread is needed.

CT suffers from the disadvantage that it utilizes radiation to image the patient. Significant research is going on to keep the radiation to as low as possible.

Another disadvantage with CT is that the malignant potential of a mass cannot be predicted in all cases. CT diagnosis basically

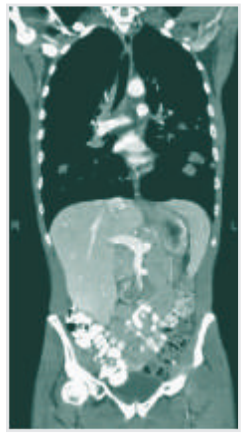


Fig .1 Whole body CT – coronal reformat

rely on morphological criteria, which may not always be appropriate to discriminate between benign and malignant lesions. The limited specificity of CT still remains a fundamental problem in oncology, e.g. for characterizing small lymph-nodes or for discriminating recurrent tumour from treatment related scar tissue. Follow-up examinations at regular intervals have to be performed in many cases to simply monitor changes of lesion size.

At Kovai Medical Center and Hospital (KMCH), and for the first time in India, a new 500 slice equivalent MDCT caters to the needs and has a special dose reduction software (a new low-dose computed tomography technique called adaptive statistical iterative reconstruction-ASIR) whereby CT can be performed with 30 to 65% lower dose than a conventional MDCT.

Functional information is needed to overcome this limitation and the advent of PET-CTand Whole Body MRI is contributing to remove the dilemma in this area.

KMCH offers PET-CT services through its Nuclear Medicine Department and has a state of art PET-CT machine. A detailed article on the PET-CT and other nuclear medicine facilities is available in this issue for further reading.

MAGNETIC RESONANCE IMAGING (MRI)

Compared to CT, MRI has the distinct advantage to provide high-resolution anatomical detail with superior soft tissue contrast without using radiation.

Mass lesions can be characterized by assessing the characteristic signal pattern on different MR sequences, for example, T1 and T2 weighted sequences, Inversion Recovery (IR), Diffusion-Weighted Imaging (DWI) and Dynamic Contrast-Enhanced (DCE) MR sequences. The spatial relationship of the tumour to the surrounding normal tissues can be visualized with high soft tissue contrast and local tumour spread can be identified. Whole Body MRI (WB-MRI) can therefore play an important part for evaluating the primary tumour and its local spread in addition to its distant spread.

The lack of X-ray exposure is favorable for offering dynamic imaging studies (which involves repeated scanning of the same area for a period of 1-2 minutes) as well frequent follow-up examinations for metastases screening even in young individuals.

The combination of an automated table movement, high performance gradients and parallel imaging technology enables high-resolution whole-body MRI with a total examination time of approximately 35-45 minutes.

Different solid tumours are characterized by a different yet predictable metastatic pattern dominated by specific sites of initial spread. The employment of disease-specific examination protocols can be based on this concept. For example, an examination protocol for prostate cancer should consider preferentially the pelvis and whole-body bone marrow, whereas a protocol for colorectal carcinomas should consider the pelvis and the liver.

KMCH was the first to install the state of the art 3Tesla MRI, Magnetom Skyra, in Asia. The machine has the shortest and widest bore (patient tunnel length and diameter) in the industry and this results in removing the element of claustrophobia (fear of closed spaces) which many patients face in other machines.

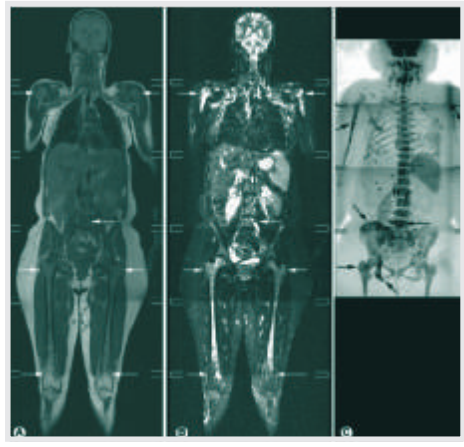


Fig. 2 Whole body MRI : A) Coronal T1WI, B) coronal Inversion recovery, C) WB- diffusion

With the Total Imaging Matrix (TIM) coil system and parallel imaging capabilities and robust gradients, it is well suited for whole body imaging with whole body diffusion studies in addition to the routine and higher end sequences. It can also perform body MR spectroscopy (2D and 3D MRS), dynamic contrast enhanced studies and body perfusion.

Hepato-biliary imaging with multiphase contrast exams and MR cholangio-pancreaticography are being performed in less than 30 minutes with extremely high resolution images.

The ability to image brain tumours with high resolution 3D sequences coupled with MRS, diffusion/perfusion studies and diffusion tractography (imaging white matter tracts) is at the cutting edge of today's MR technology and these are routinely performed for all brain tumour cases. The diffusion tractography results help the surgeon to plan their approach to minimize neurological deficits during biopsies and surgical resection.

TUMOUR ENTITIES

In order to screen for multifocal tumour growth or distant tumour spread, wholebody cross-sectional imaging is now considered a routine imaging strategy. The diagnostic approach, however, strongly depends on the tumour type. For example in renal cell carcinoma, the diagnostic accuracy of CT and MRI are equivalent, while FDG-PET is in most cases of no value. MRI is most sensitive for early detection of bone marrow disease, while CT allows detecting even subtle lung abnormalities. FDG-PET/CT is most appropriate to evaluate patients with carcinoma of unknown primary.

Lung cancer

Lung cancer is one of the leading causes of death in males worldwide. Smaller lesions may represent earlier stage disease, but unfortunately, the disease is often in an advanced stage when detected. MDCT and FDG-PET/CT plays an important role for staging and follow-up. MRI has yet no definite role in routine for early detection or staging of lung cancer, but clinical studies comparing MRI and CT are currently being widely performed.

Prostate cancer

Prostate cancer is one of the most common malignancy in men. High resolution MRI including MRS has been proven to be most accurate for predicting extra-capsular extension and seminal vesicle invasion. MRS is increasingly used to guide biopsy to

increase yield and thereby avoiding unnecessary repeat biopsies. Early detection of lymph node is a still major challenge for imaging. MRI diffusion studies with ADC mapping has helped to a large extent in this grey area. Lymph node imaging with ultra small super-paramagnetic iron oxide (USPIO) enhanced MRI is another important break-through which is waiting for FDA approval in this area .

Spectroscopy is an excellent tool for follow up of prostate lesions and whole body diffusion is a very sensitive tool for metastases screening in the bone marrow.

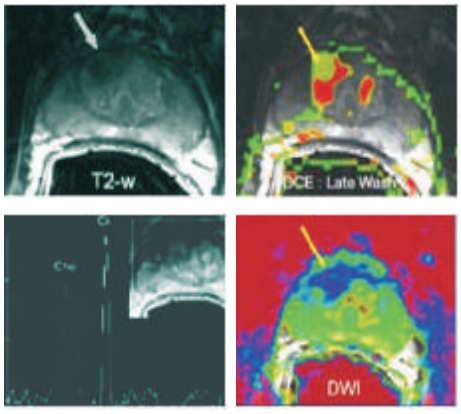


Fig. 3 Top left T2WI, top middle – dynamic contrast, top right MRS and bottom – Diffusion weighted image of prostate. Lesion in anterior aspect (arrow)

CT still lacks of sensitivity and specificity in prostate imaging. Since prostate cancer is FDG-negative in most cases, PET is not useful in prostate imaging for local or regional staging.

PET/CT, however, has been successfully applied for the detection of bone metastases and has been proven to be more accurate than conventional scintigraphy and single photon emission computed tomography (SPECT).

Whole body MRI helps to detect skeletal metastases by whole body diffusion and T2-weighted STIR sequences and has proved to be more sensitive than bone scintigraphy.

Breast cancer

Breast cancer is the leading cause of cancer death in women.

Magnetic resonance imaging (MRI) is highly sensitive for cancer staging, problem-solving, post treatment surveillance, and other indications. It can detect primary breast cancers and additional foci of cancer that are occult to standard imaging. A more detailed article is available in this issue for further reading.

Colorectal cancer

Colorectal cancer is also a common malignancy and is associated with significant morbidity and mortality. The aim of local staging is to classify the patients into different treatment groups. At the time of diagnosis, a significant number of the patients have already developed liver metastases, and another sizable percentage will develop it during the course of the disease. Prior to resection with curative intention, metastases to distant lymph nodes and organs as well as peritoneal carcinomatosis have to be excluded. Abdominal and pelvic CT and MRI have been proven as a highly accurate for staging of rectal cancer.

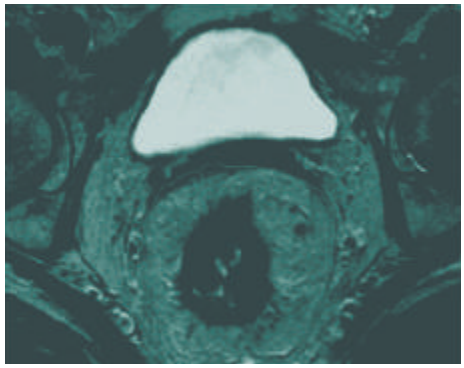


Fig. 4 MRI of rectal cancer. Mesorectal fascia outlined in red

Multiple myeloma

Early involvement of bone marrow by multiple myeloma can be assessed very well using MRI. The whole-body MRI examination protocol in patients with multiple myeloma was being performed by T1-weighted as well as T2-weighted STIR sequences. Now the coupling of diffusion weighted imaging of the axial skeleton with inversion recovery sequences has increased the sensitivity of MRI for picking up disease. Additional axial imaging may be necessary only in individual patients depending on the findings, e.g. in case of extensive extramedullary tumour spread, pathological fractures or organ involvement. Whole-body lowdose CT allows to screen for osteolytic foci and has the advantage of considerable reduced imaging time compared to whole-body MRI. As the lesions are FDG-negative, PET/CT has not found any application in this area.

Metastases

Bone metastases: They are important sequelae of various solid malignancies with a pattern of multifocal involvement being most common. In 80% of the cases, breast, prostate, bronchial, thyroid and renal cell carcinoma are the primary tumours. Recent studies have proven that the accuracy of coronal WB-Diffusion weighted imaging for the detection of skeletal metastases may even be superior compared to conventional skeletal scintigraphy. Often this is coupled with STIR imaging in coronal plane.

T1 weighted imaging is also added because osteoblastic lesion may be overlooked on STIR sequences due to the low contrast of metastases compared to fat-suppressed bone marrow. Regarding hematological malignancies, MRI plays an essential role for

detection, assessment of spread as well as evaluation of therapy response, e.g. in multiple myeloma where FDG-PET is negative.

Lymph node metastases: The specificity of CT and MRI is limited due to ambiguity of the applied morphologic criteria particularly in case of small lymph nodes. Recently contrast enhanced MRI using ultra small super-paramagnetic iron oxide (USPIO) has shown a 95-100% sensitivity and specificity profile for imaging lymph node involvement in prostatic cancer. This technique is being applied to other entities as well and is a subject of active research. FDG-PET/CT is still the most important modality for the detection of lymph node metastases in a variety of FDG-positive tumours.

Organ metastases: A clinical study with patients with advanced melanoma comparing whole-bodyCT, MRI and PET/CT has proven the feasibility and clinical potential of high-resolution WB-MRI.

With regards to brain, liver and bone metastases, MRI of these organs is on principle more sensitive than CT and FDGPET. The capability to detect small metastases depends considerably on the applied MRI technique specially if performed on higher field strength (1.5 tesla and above) magnets. Even small metastases can be detected within a wholebody examination, even in moving organs like the liver.

Metastases to the lung are frequent sequelae of different tumours and sub-millimeter MDCT is so far the method of choice for detecting small lung nodules.

With expanding therapeutic options in oncology comes a need to evaluate the cancer in a more detailed manner, with respect to loco-regional spread and distant spread.

Whole body imaging with MDCT, MRI and FDG PET/CT is playing an increasingly important role in cancer imaging. The techniques, many times, are complementary and together can provide the oncologist with comprehensive information, which is needed to plan and execute a treatment regime.

Whole body diffusion weighted imaging (WB-DWI) MRI is particularly under extensive trials as both MDCT and FDG PET/CT have radiation concerns.

3T MRI at KMCH

STATE OF THE ART IN BREAST IMAGING

Dr. R. Rupa
Department of Diagnostic and Interventional Radiology

Breast cancer in India is currently the most common cancer in females and has surpassed the incidence of cervical cancer which was the commonest cancer in the past. In India the incidence of breast cancer is 1 in every 30 women as against one in 8 in US. However the incidence of death is 1 in every 2 persons diagnosed as against 1 in 5 in US.

This is primarily because of fact that there is lack of awareness of breast cancer screening and Indian women present to the clinician only in the advanced stage of malignancy. Also in India, there is an increasing trend of breast cancer occurring in a younger population between 30 and 40 years and most of them are aggressive.

Screening

Screening is a systematic evaluation of a 'normal' individual to see if there is any underlying cancer. A 'normal' individual implies one who does not have any symptoms or signs of cancer, and one who is living a normal life.

Most tumours tend to produce symptoms when they are fairly advanced which decreases the chance of survival despite treatment.

Screening of the breast involves the following:

Breast Self Examination

This includes regular and systematic palpation of the breast by a woman herself to assess for any abnormality. Between the age of 20 and 40 years, a woman must regularly do a BSE, and must be evaluated by a clinician, atleast once every few years.

Mammography

Mammography will be advised by a clinician yearly, after a woman crosses 40 years of age. If mammography is normal, screening continues every year.

Mammography plays a critical part in diagnosing breast cancer. Mammograms have been shown to lower the risk of dying from breast cancer by 35% in women over the age of 50. Leading experts, the National Cancer Institute, the American Cancer Society, and the American College of Radiology now recommend annual mammograms for women over 40.

Some women wonder about the risks of radiation exposure due to mammography. Modern-day mammography only involves a tiny amount of radiation — even less than a standard chest x-ray.

Techniques of Mammography

Mammography can be performed in either conventional screen-film technique or through the advanced digital mammographic technique.

Digital mammography has many potential advantages over conventional screen-film techniques, especially in terms of image display, processing speed, and image transmission. Manipulation of images with interactive windowing and filtration can enhance certain structures and improve lesion conspicuity. Most importantly, it delivers only about three-fourths of the radiation that film-screen mammograms deliver. In addition digital images can be stored more easily.

With digital mammography, the images are recorded directly into a computer. The image can then be viewed on a computer screen and specific areas can be enlarged or highlighted. If there is a suspicious area, we can use the computer to take a closer look.

Many studies have shown that film-screen and digital mammography are equally accurate in screening for breast cancer. The Digital Mammographic Imaging Screening Trial (DMIST), found that digital mammography was a better screening tool than film-screen mammography for patients who are under age 50, those who have very dense or extremely dense breast tissue.

The Department of diagnostic and interventional radiology in Kovai Medical Center and Hospital is equipped with the state of the art full field direct digital mammography system – MAMMOMAT INSPIRATION (Siemens). Two of the most important advantages to the Mammomat Inspiration lie in its ability to produce excellent image quality and individualized dose.

The Opdose technique will automatically select the best anode/filter combination for the individual breast characteristics and is designed to minimize a patient's radiation dose and exposure time.

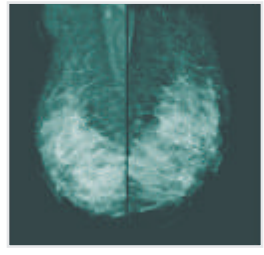


Fig. 1 (A & B) Digital mammogram of 60 year old patient in MLO view showing pleomorphic micro calcification in left breast

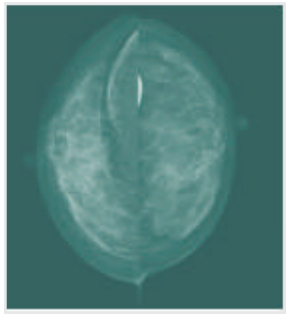


Fig. 2(A&B) CC view of the same patient showing the pleomorphic calcification in the inner quadrant of right breast

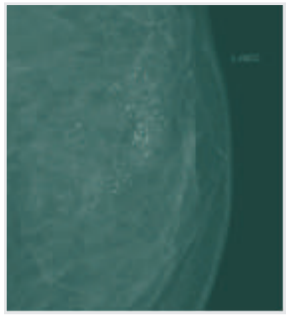


Fig. 3 Magnification view of the abnormality clearly depicting the pleomorphism of the calcification

The intelligent Opcomp function applies compression until the breast is no longer soft and pliable. The compression paddle will stop at the point of optimal compression. This is extremely comfortable and less painful for the patient as it eliminates the excessive inadvertent compression done manually by the technologist. (Fig: 1,2,3).

The system also has the most advanced fully automated Stereotactic biopsy unit. The combination of digital mammography with stereotactic biopsy has the potential advantage of significant reduction in the procedure time for mammographic biopsies. As mammography guided biopsy involves compression of breast, reduction in the procedure time significantly decreases the discomfort of the patient. Moreover since the system is fully automated it has got a high precision in hitting the target exactly. Hence even pre-clinical lesions like calcium deposits and tiny masses or architectural distortions which are detected only by mammography can be biopsied to obtain an accurate diagnosis very easily.

Advantages of Stereotactic biopsy :

- Less invasive than surgical biopsy, leaves little or no scarring, no pain, less cost and can be performed in less than an hour
- Excellent way to evaluate calcium deposits or tiny masses that are not visible on ultrasound
- No breast defect remains and, unlike surgery, stereotactic needle biopsy does not distort the breast tissue and make it difficult to read future mammograms
- Recovery time is brief and patients can soon resume their usual activities

Sonomammography

Ultrasound provides real-time imaging, does not use any ionizing radiation. It helps to detect lesions in dense breasts and to differentiate solid and cystic lesions. It is also a good tool for guiding minimally invasive procedures such as biopsies and aspirations. For most women 30 years of age and older, a mammogram will be used together with ultrasound. For women under age 30, ultrasound alone is often sufficient to determine whether an area of concern needs a biopsy or not.

MR Mammography

Breast MRI is used in various aspects – screening, characterising and staging of the lesion and monitoring the response to treatment. It is not recommended as a routine screening tool for all women. However, it is recommended in addition to conventional mammography, for screening women who are at high risk for breast cancer, usually due to a strong family history and/or a mutation in genes such as BRCA1 or BRCA2. It is the modality of choice in patients with breast implants.

It is currently widely used in characterising lesions by its morphology and enhancement kinetics, to assess the extent of lesions, to diagnose multiple lesions in a diagnosed case of malignancy which will alter the treatment plan, to detect occult breast malignancy in patients with axillary lymph node enlargement. It also helps in differentiating scar tissue and tumour recurrence in post operative patients.

MR imaging of breast is the modality of choice in monitoring the response to chemotherapy as the imaging not only provides the morphological information like reduction in size of the lesion, but also provides information regarding the tumour aggressiveness and metabolite in terms of decrease in diffusion restriction and drop in choline content in spectroscopy respectively.

The department of diagnostic and interventional radiology in Kovai Medical and Center and Hospital is equipped with state of the art 3 Tesla MRI – MAGNETOM SKYRA (Siemens). It has a dedicated 4 channel breast coil for performing breast MRI.

The advanced imaging techniques like dynamic contrast enhanced techniques can be done with good spatial and temporal resolution. Using the higher field strength, advanced imaging techniques like diffusion weighted imaging and spectroscopy can be obtained with much better image quality in less time as compared to lower Tesla machines. Diffusion weighted imaging increases the specificity for breast lesions,

for differentiation of benign versus malignant lesion. Breast spectroscopy helps in quantification of metabolite and is used in effective therapy monitoring and lesion differentiation. Motion artifact compensation techniques are also available which generate excellent images even in case of severe movement.(Fig 4,5,6,7). Breast cancer cannot be prevented but can definitely be cured by early diagnosis through appropriate screening techniques like mammography which will provide good survival benefit.

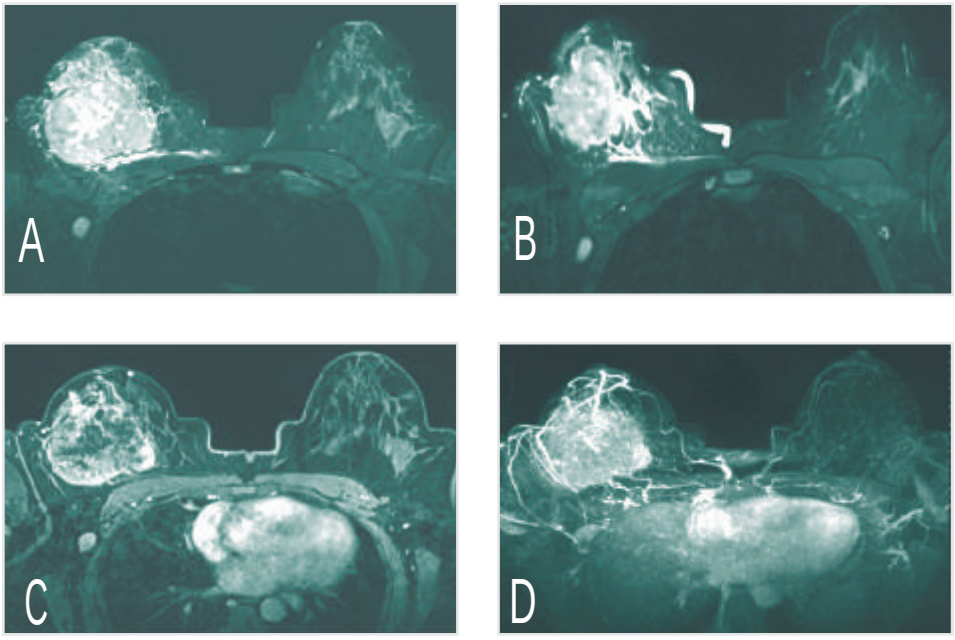


Fig. 4 Pre chemotherapy MR images of a 44 year old female patient

Image A & B – STIR sequence showing a large mass in the right breast with right axillary lymph node

Image C – Post contrast dynamic image showing enhancement of the mass and the lymph node

Image D - Post contrast MIP image showing tumour vascularity

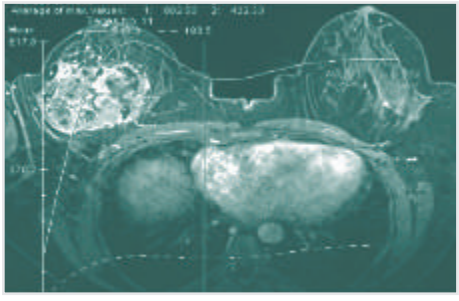
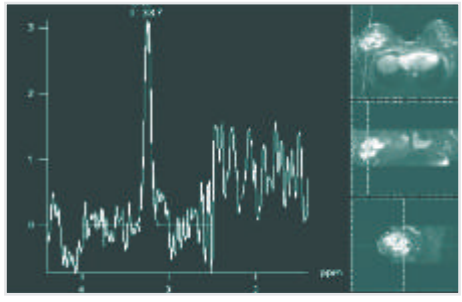


Fig. 5 Enhancement kinetics of the lesion showing rapid enhancement with wash out – Type 3 curve suggesting malignancy



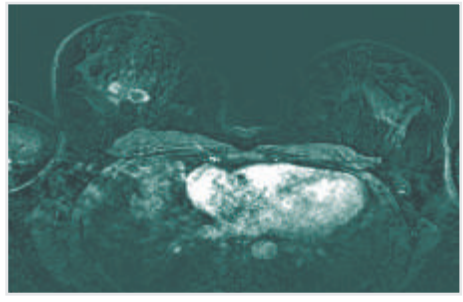


Fig. 6 Spectroscopy of the right breast lesion showing elevated choline peak

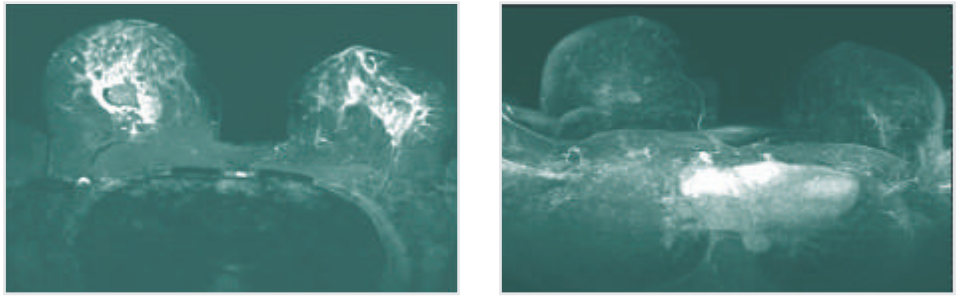
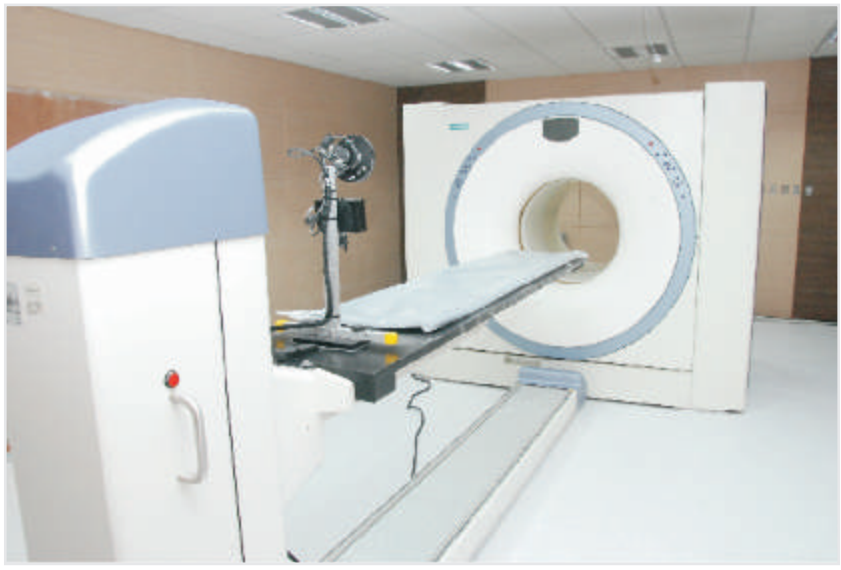


Fig. 7 Post chemotherapy images of the same patient- Image A: STIR sequence showing significant reduction in size of the lesion and axillary lymph node. Image B: post contrast dynamic image showing very minimal enhancement of the residual lesion. Image C: Post contrast MIP images showing minimal vascularity of the lesion

NUCLEAR MEDICINE – A GUIDING LIGHT IN ONCOLOGY

Dr. Ajit Shinto, Dr. K.K. Kamaleshwaran
Department of Nuclear Medicine and PET

As KMCH steps into the realms of state-of-the-art comprehensive cancer care, and in keeping with the vision of providing the most advanced diagnostic and therapeutic options for the patient, we are fortunate to have a world class facility in the Department of Nuclear Medicine and PET, boasting of technological innovations, equipment and personnel which are equivalent to, if not better than any department in the country.



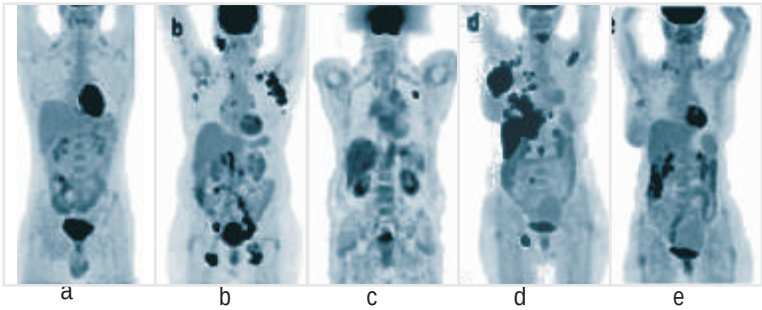
PET - CT scanner at KMCH

Nuclear Medicine

The field of Nuclear Medicine is not exactly a new one and has been serving the medical fraternity in a wide variety of clinical dilemmas, not restricted to oncology, for over 5 decades. Essentially, it is a diagnostic imaging modality, akin to radiology, with a few niche therapeutic applications. The basic difference between Nuclear Medicine vis-a-vis radiology, is that the former relies in alteration of function or 'pathophysiology' to make a diagnosis, while radiological imaging like CT, X-ray, MRI or USG relies in an alteration of structure, or 'patho-anatomy' in arriving at a diagnosis. Thus, they are both complementary to each other and not directly competitive. The study of organ function or to visualise what is happening at a cellular level externally, without entering the body and disturbing the process, is easier said than done. Drawing on our knowledge of pathophysiology, we know that different disease processes affect any given organ differently, i.e., Ischemia is different from malignancy, is different from infection, which is different from trauma etc. Also, any given organ can have multiple physiological functions. Keeping these two points in mind, we can give a disease specific diagnosis if we know what disease process we are looking to rule in or rule out and how it affects the organ in question. Thus the diagnostic test will depend on the organ to be studied and more specifically the molecular or physiological pathway under review. Nuclear Medicine is served by active biomolecules or pharmaceuticals that undergo the physiology in question inside the body and the kinetics of which will be altered in a specific way by the disease process. This change can be detected ex-vivo, by simply tagging these active molecules to a radioactive atom (a passive tag) that gives out signals in the form of gamma rays which can be detected by externally placed detectors. Thus we have a molecule to study the physiology, combined with a tag to detect the kinetics outside and a detector assembly (Gamma Camera) to analyse the data and form images. Any deviation from normal can be identified and the pattern matched with different disease processes. Nuclear Medicine is a very safe field, with usual radiation exposures to the patient equivalent to or much lesser than routine X-ray procedures.

FDG PET-CT Scan

PET is one of the most advanced types of scan in Nuclear Medicine, using the same basic principle. FDG is a glucose analogue, (and is the active component), which has F18 as its passive radioactive tag. When we inject F18 labelled FDG into a patient intravenously and image after about one hour, we get a whole body distribution of glucose or a 'glucose map'. Based on the pathophysiological basis of cancer, we know that a malignant cell differs from a normal cell in a lot ways, but a few cellular characteristics are utilised here. As there is an increased demand of glucose, the malignant cell instantly upregulates the number of GLUT receptors (which help to trap glucose) on its surface. Additionally it produces more enzymes in the HMP shunt pathway (helping to break down glucose and generate energy) and also decreases the enzymes that drive glucose out of the HMP pathway. Thus we have increased trapping and metabolism of glucose (or FDG, when used) and logically on an FDG PET scan, such cells will pick up and retain more glucose or FDG, helping us to pick



a b c d e

Whole body FDG PET images demonstrating:

a) Normal scan
b) Lymphoma with involvement of multiple Lymph node groups
c) Malignant solitary pulmonary nodule
d) Metastatic LABC
e) Same case post 4 cycles chemotherapy

up sites of cancer and its metastasis. What additionally helps us is that FDG unlike glucose, is not totally metabolised, so FDG once picked up by a cell is trapped inside the HMP shunt pathway (metabolically trapped) and can be imaged over hours if needed, giving it widespread clinical applicability. FDG-PET has revolutionised cancer care and has established itself in the work up, management and follow up protocols of numerous malignancies (NCCN, NHS, ASCO guidelines etc).

Thus the modality is routinely used as a single step whole body evaluation for staging, restaging, assessing response to therapy, recurrence evaluation in follow up of various cancers or even metastases of unknown origins.

Furthermore, technological innovation has led to the marriage of PET with a CT in the same machine giving us double the information with negligible additional time, cost or radiation exposure. Thus the latest generation of PET-CT machines, like the one we have at KMCH, are capable of a whole body functional image, a whole body contrast enhanced CT anatomical image and fusing the two, to give a one stop whole body imaging solution with very high sensitivity and specificity.

We are emboldened to even venture out into the realm of 3D and 4D PET-CT enabled Radiation Therapy planning, which helps to anatomically carve out and target higher radiation dose to functionally hypermetabolic areas within tumours with negligible doses to ametabolic/normal tissues and even PET-CT guided biopsies to sample from the most metabolically active sites. At present most of the clinicians use an FDG PET-CT at some stage in their work-up or management of oncology cases.

Life beyond PET-CT

F18 FDG has often been called the 'molecule of the century' due to its revolutionary contribution to oncology and is the actual resurrector of Nuclear Medicine, enabling it to ride this present wave of popularity. However, at this juncture, it is prudent to observe that Nuclear Medicine has a lot of applications beyond PET-CT and also beyond oncology. It does play a significant role in endocrinology, nephrology, cardiology, orthopaedics, paediatrics and numerous other fields; elaboration of which would be outside the scope of this essay. We hope to introduce various other forms of radio-nuclide therapy, such as bone pain palliation therapy with P-32/SM-153, refractory lymphoma therapy with radiolabelled antibodies, radio-peptide therapy for various tumours, MIBG therapy for neuroendocrine tumours, all of which share the significant advantages of molecular targeted therapy which are, minimal side effects, repeated usage and no toxicity.

KMCH has introduced a state-of-the-art Nuclear Medicine facility which is the first and only one of its kind in Coimbatore and surrounding areas having the latest diagnostic equipment - SPECT-CT (Symbia T from Siemens with a diagnostic CT), PET-CT (Siemens Biograph with a 6-slice diagnostic CT), isolation therapy ward and we hope to make this modality easily accessible, affordable and inexpendable in your clinical practice.

Nuclear Medicine for the layman: FAQ

What is Nuclear Medicine?

It is a branch of medical imaging helping in diagnosing disease at a very early stage.

Why is it called Nuclear Medicine?

Because it uses radiation in extremely small quantities as a tracer attached to other active bio-molecules that help to study the function of a cell or an organ.

How is it different from radiology?

Radiology relies on alteration in structure for diagnosis, while Nuclear Medicine relies on change in function of the organ or cell.

Is it safe?

It is an extremely safe field with radiation exposures similar to, or lesser than, standard X-ray testing. Even new-born children can be submitted to these tests if indicated.

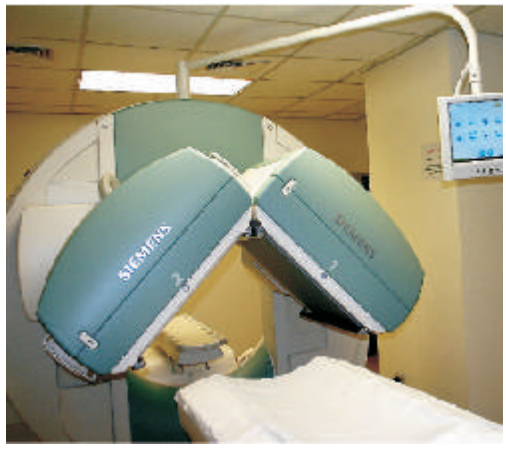
Are there any side effects?

There are no significant radiation or non-radiation related side effects.

Is it only diagnostic or is there therapy also?

We offer targeted, molecular based therapy for specific indications like thyroid cancer, bone tumours, liver tumours, blood cancer etc.

Are there any specific precautions?



SPECT-CT enabled Gamma camera at KMCH

There are no specific precautions. Fasting might be required in a few cases like cardiac, gall bladder imaging or PET-CT. All the tests are OPD based, requiring no admissions.

What is PET?

It is one of the latest scans, which help in finding out cancer at the earliest stage and its spread, as a single step evaluation for the whole body. It is extremely safe, cost effective and prevents multiple scans for different areas of the body.

Why is it called PET-CT?

Because a whole body PET scan (giving functional image of cancer) is coupled with a whole body CT scan, enabling a one stop comprehensive imaging solution with maximum information, at minimal additional cost, radiation and time loss.

What are the facilities available in the Department of Nuclear Medicine and PET at KMCH?

The department at KMCH is equipped with what is currently the best available diagnostic machines in the world in the form of a SPECT-CT enabled gamma camera, an LSO based PET-CT with diagnostic 6 slice CT, a 4 bedded isolation therapy ward for the most advanced forms of therapy and well qualified, experienced doctors and technologists with national and international standing.

MALIGNANT BRAIN TUMOURS

Dr. K. Madeswaran
Department of Neurosurgery

Introduction

Intracranial malignancies cause a variety of deleterious effects on the brain. The presence of cerebral oedema, malignant infiltration of normal brain tissue and bulk displacement of vital structures may lead to loss of normal brain function. White matter invasion by malignant tumours may result in destruction and disruption of fiber bundles. A wide variety of primary malignant tumours occur in brain. The most common primary malignant tumours are gliomas. The types are Astrocytoma, Oligodendroglioma and ependymoma. Medulloblastomas are common in childhood. World Health Organization (WHO) describes four grades of malignancy from 1 to 4 based on cellularity, nuclear atypia, vascularisation, mitotic figures and presence of necrosis. WHO grading system helps neurosurgeons to predict prognosis and has an impact on therapy.

Treatment

Generally, malignant tumours are treated by three modalities, Neurosurgical excision, Radiation therapy and Systemic chemo-therapy.

Neurosurgical excision

The goal of surgery is to perform radial resection with boundaries free of tumour cells. In reality it is not possible to perform such radical resections in every case despite improvements in magnification (micro-scope), increasing knowledge in micro-neuroanatomy, neuronavigation and intraoperative imaging. But it is accepted that quantum of resection alone has definite impact on prognosis.

Radiation therapy

Radiation therapy plays a major role in the treatment of radiosensitive primary malignant tumours and brain secondaries. External beam radiation therapy in its various forms is used in treating radiosensitive tumours. Radio surgery has found limited role in recurrent malignant tumours.

Systemic chemotherapy

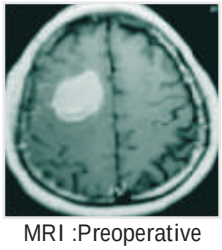
Nitrosourea based and compounds are the major group of substances used in treatment

of malignant brain tumours. At present, a combination of radiation and concomitant chemotherapy with temezolamide is accepted as effective in treating Glioblastomas.

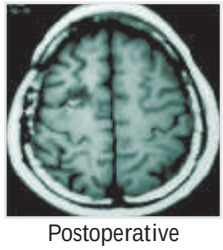
Astrocytomas (WHO Grade II)

Astrocytomas are slow growing, well-differentiated tumours with diffuse infiltration into the surrounding brain tissue. They mostly arise in cerebral hemispheres and present with seizures. Complete resection is impossible. Hence they tend to recur and progress to higher grade.

Grade II astrocytomas are treated by surgical resection. Inclusion of intraoperative imaging, electro physiological monitoring and awake craniotomies with functional mapping will increase the extent of resection.



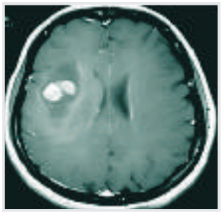
MRI :Preoperative



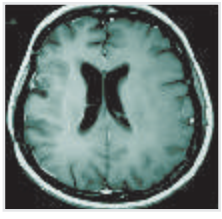
Postoperative

Anaplastic Astrocytoma (WHO Grade III)

These tumours also infiltrate the surrounding brain. Histologically, they show increased cellularity, cellular atypia and higher mitotic activity. They are most commonly located in the cerebral hemispheres and present with mass effect or seizures. The treatment approach is surgical resection, radiation therapy and chemotherapy. The reported survival is between 2 to 3 years.



MRI : Preoperative



Postoperative
(18 months)

Glioblastoma (Grade IV)

Glioblastomas are the most malignant of glial tumours. The incidence is 10-15% of all intracranial tumours or 50 - 60% of all glial tumours. They may develop de novo or from an already exiting astrocytoma. The peak incidence is between 50 to 70 years. Histologically, all characteristics of malignancy such as high mitotic activity, nuclear atypia and high cellularity with areas of necrosis are found.

The treatment approach to glioblastoma is radical microsurgical resection followed by combined radiation and chemotherapy protocol is the gold standard. The overall prognosis is poor with median survival time of about 14 months.

Oligodendroglioma

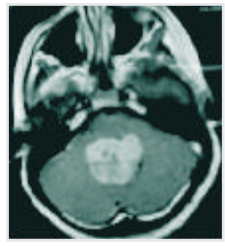
Like low-grade astrocytomas, Oligodendrogliomas infiltrate into the surrounding brain tissue. They are localised mainly to cerebral hemispheres with predisposition for the frontal lobes. The peak incidence is in the fifth decade. Microcalicifications are the histological hallmark of these tumours. The treatment of choice is surgical resection with no clear benefits from radiation therapy or chemotherapy.

Ependymoma

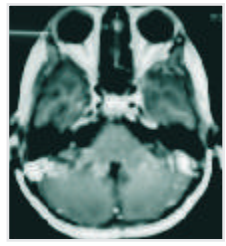
Ependymomas arise along the ventricular system. Infratentorial location is more common in children. WHO classifications describe variants of Grade II ependymomas: cellular ependymoma papillary ependymoma, clear cell ependymoma and tonycytic ependymoma with no difference in the biology or clinical course. The treatment modality of choice is surgical resection. Radiation therapy is recommended for recurrences.

Medulloblastomas

Medulloblastomas is the most common malignant tumours in children and accounts for 30% of all paediatric brain tumours. Medulloblastomy is the most common PNET tumour of brain. They are classified as WHO Grade IV tumours. Favourable outcomes depend on quantity of the resection. The surgical resection is followed by radiation therapy.



MRI : Preoperative

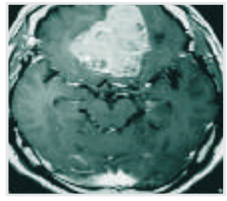


Postoperative
(4 years)

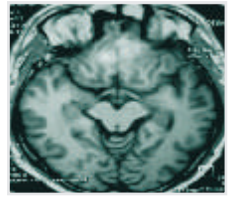
Stereotactic biopsy

The major indication for stereotactic biopsy of cerebral tumours is to obtain material for pathological diagnosis and additionally to aspirate fluid from a cyst. In general if the patient's general condition permits, the preferred treatment is craniotomy and radical excision. Stereotactic biopsy is preferred if the tumour is deep seated or in patients where surgical resection threaten eloquent areas of the brain.

Esthesioneuroblastoma



MRI : Preoperative



Postoperative

It is a neuroectodermal tumour arising from olfactory epithelium. They grow into paranasal sinuses, orbits, entering cranial cavity through cribriform plate of ethmiods. They often spread to cervical lymph nodes.

Treatment is radical resection followed by radiotherapy.

Conclusion

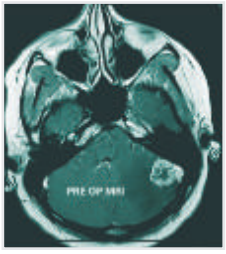
Radical excision of primary malignant tumours is safe. The excision can be more radical in eloquent areas of brain with use of neuronavigation, physiological monitoring and intraoperative MRI (iMRI).

On an average, we operate around 10 brain tumour cases in a month. We usually perform craniotomy, radical excision of malignant intra-axial tumours. In patients with tumours in eloquent areas, the excisions have to be less radical to prevent or reduce morbidity.

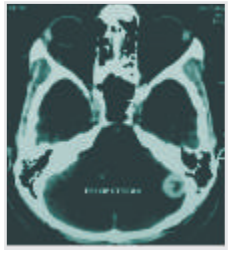
We also take up stereotactic biopsy (pinhole surgery) for confirmation of diagnosis in selected cases. The goal of treatment in primary malignant tumour is to prolong survival, less morbidity with good quality of life.

COMPREHENSIVE ONCOLOGY CARE FOR CARCINOMA OF THE RECTUM WITH BRAIN METASTASIS

Dr. Suresh Jayabalan[1], Dr. Sarada Krishnamurthy[2], Dr. Paulvannan S[3], Dr. Kannan V[4], Dr. Paranthaman Sethupathy B[5], Dr. Rajendran K[6]
1 Neurovascular & Skullbase Spinal Surgeon, 2 Medical Oncologist, 3 Surgical Gastroenterologist, 4 Radiation Oncologist, 5 Psychiatrist, 6 Neuro-anaesthetist



MRI:Preoperative



CT:Preoperative

Back round

This is a 36-year old lady who presented with recent onset of occipital headache, nausea and giddiness. She was diagnosed with a T3N2 rectal carcinoma and a high pre-operative CEA level in late 2009. She underwent neoadjuvant chemoradiation therapy, which was followed by low anterior resection of the rectum with total mesorectal excision. She developed a post-op anastomotic leak, which was managed with a Hartman's procedure. She then underwent adjuvant chemotherapy with plans for reversal of the colostomy.

Presentation

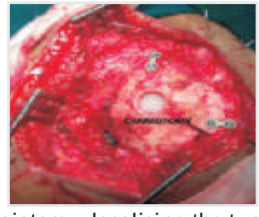
In July 2009, her CEA level rose and she presented with elevated intracranial pressure (ICP) features of headache and nausea. Clinically she had mild left 'finger-nose' incordination. PET Scan showed multiple metastases – including left cerebellum, lungs and bones. The cerebellar lesion was at the junction of transverse sinus and sigmoid sinus. The 4th ventricle was squashed due to brain edema mass effect. Her case was presented at our tumour board with the recommendation to proceed with brain tumour resection followed by whole brain radiation and systemic chemotherapy.

Management of Brain Metastasis

The patient underwent left retromastoid suboccipital craniotomy exposing the junction of the both sinuses. Total excision of the lesion was achieved with micro-neurosurgical techniques. The cerebellum became lax and the dura was closed. The suboccipital bone was replaced with plates and screws. Postoperatively, the patient recovered from her original symptoms and now awaits radiation and systemic chemotherapy.

Brain metastases occur from many primary tumours of the body. They present with ICP symptoms such as headache, vomiting and altered conscious level. Depending on the location of the tumour, the patient may present with focal neurological deficits, such as paralysis or seizure disorder. Up to 3 brain metastases can be surgically managed.

Here, a single cerebellar lesion was totally excised and referred for further management. It is rare to find comprehensive cancer care at a single institution. A multi-disciplinary approach to complex cases, as was done at our institution, is beneficial to patients for better care, comfort and outcome.



Craniotomy, localising the tumour

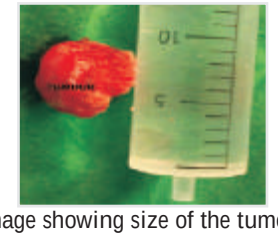
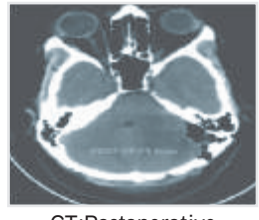


Image showing size of the tumour



CT:Postoperative

BONE TUMOURS

Dr. Bhaskaran
Department of Orthopaedic Surgery

Introduction

Bone tumours include both benign and malignant lesions. Malignant lesions can either be primary or secondary. The commonest malignant lesions are secondaries (metastatic) followed by multiple myeloma and osteosarcoma. The primary sources of bone secondaries are from Bronchus, Breast, Prostate, Thyroid and Kidney.

Detailed history, thorough clinical examinations and relevant investigations are important in diagnosing; assessing the nature and spread of tumour and then planning appropriate treatment (palliative or curative treatment). Multidisciplinary team approach comprising surgeons, oncologists, radiologists, pathologists and supportive staff are needed to provide better patient care.

Normally the presenting symptoms are pain which is continuous or worsening in nature, loss of weight or appetite, fever and unable to weight bear or difficulty in using limbs. High suspicion should be sought in case of sudden increase in pain or size of an already existing tumour. Relevant history such as haemoptysis, malena, haematemesis, haematuria, swallowing and breathing difficulties should be elicited to get information about the source of a primary tumour.

KMCH EXPERIENCE

CASE #1: Telangiectatic Osteosarcoma

A 9-year old boy fell down heavily while he was on a holiday and fractured his distal femur. He was given an above knee plaster locally and was then transferred after a couple of weeks to his native place. He developed increasing pain over the next two weeks at the fracture site (4 weeks after injury) and was reviewed in our clinic. X ray of his femur showed permeative pattern of bone destruction with new bone formation. Subsequent biopsy of his lesion confirmed telangiectatic osteosarcoma while the MRI scan of thigh and CT scan of his chest showed pulmonary metastasis with dissemination of tumour to proximal femur. He was totally asymptomatic before the fracture and until up to four weeks after the fracture has happened. Retrospective review of his X ray, which was taken at the time of fracture, demonstrated no obvious osteolytic lesion in the distal femur.

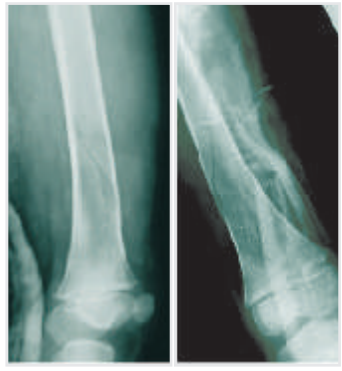


Fig. 1 Initial normal X-Ray

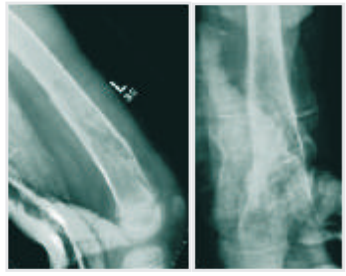


Fig. 2 X-ray 4 weeks later – lytic lesion visible

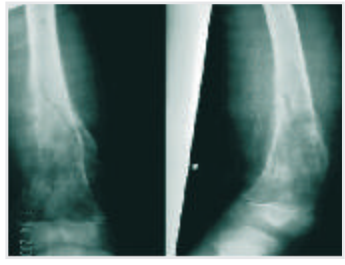


Fig. 3 & 4 Lytic lesion worsening

Telangiectatic osteosarcoma is a rare subtype of osteosarcoma and represents nearly 2% of all osteosarcomas. It seems to occur more commonly in the distal femur, proximal tibia and humerus. The incidence peaks in early to mid-adolescence and is not commonly encountered in very young and pre-adolescent patients. Normally it presents with a very short history. Osteosarcomas usually present with pain at night that precedes the tumour by weeks or even months. Sometimes there may be only a history of fatigue, a slight limp or history of trauma. The following criteria are essential to diagnose telangiectatic osteosarcoma:

1. Lytic destructive lesion with no appreciable area of sclerosis in roentgenogram
2. Cystic cavity with septa or a bag of blood in gross specimen
3. Histological features of aneurysmal bone cyst showing spaces separated by septa with very anaplastic cells

Controversy exists over prognosis for telangiectatic osteosarcoma in comparison to conventional osteosarcoma. Recent literature reports have shown an improved prognosis, which is believed to be due to early identification and advent of neoadjuvant chemotherapy. This patient did not have any symptoms suggestive of malignancy before and up to four weeks after the fracture. The initial X ray (Fig. 1) did not show any lytic lesion but X ray taken four weeks later showed a destructive lesion (Fig. 2) which deteriorated very quickly over the next couple of months (Fig. 3, 4).

CT scan of his chest demonstrated pulmonary metastasis and MRI

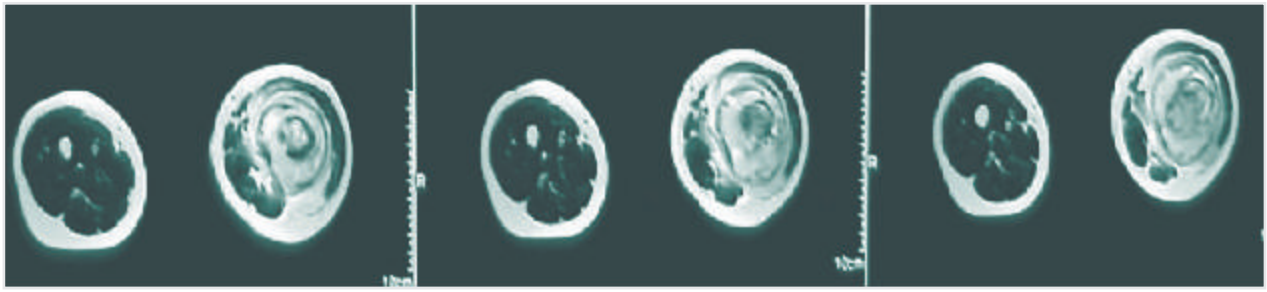


Fig. 5 MRI showing metastasis in femur

scan of thigh showed tumour in both the proximal and distal femur (Fig. 5). To our knowledge, this rare variety of telangiectatic osteosarcoma with this sort of presentation has not been reported in the English literature.

We should be aware of this possibility of rare presentation of Telangiectatic Osteosarcoma when seeing preadolescent patients with increasing pain following a fracture. The prognosis can be improved with early diagnosis and neoadjuvant chemotherapy.

CASE #2: Bone secondaries

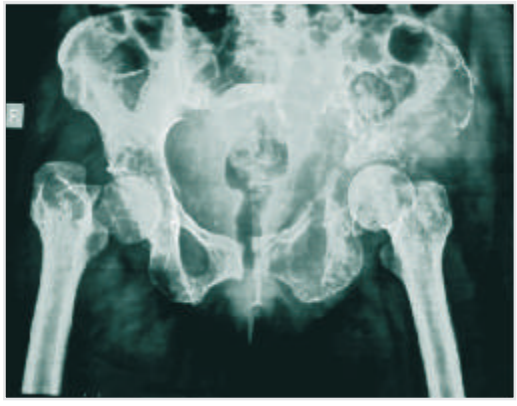


Fig. 6 Pelvic metastasis

A 43-year old woman presented with bone secondaries after having had two years of native treatment for carcinoma of the right breast. She had metastasis to spine, brain, lung, and pelvis with pathological fracture of right hip (Fig. 6).

MRI scan of her spine showed extensive metastasis with compression fracture of L1 and L5 with cord compression. After a multidisciplinary meeting decision was taken to offer her a palliative treatment in the form of hemiarthro-plasty of right hip and followed by radiotherapy to her brain and painful bone metastasis. She underwent

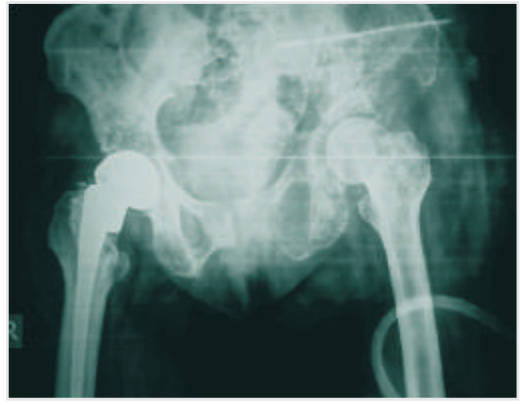


Fig. 7 Postoperative (hemiarthroplasty) X-Ray

surgery (Fig. 7) followed by radiotherapy to her brain and hip. Her pain was under control and was able to stand up with support after being handicapped a very long time. The aim of treatment in a patient with bone metastasis is to provide a quality of life during her remaining life by controlling pain, preventing fractures and making them mobile and independent. In this case, the severe pain was from her pathological fracture of hip and she was bedridden for long time that can lead to multiple complications such as bed sore, urinary tract infection, depression and poor quality of life. After her hip surgery (cemented hemiarthroplasty) (Fig. 7) she was able to sit and stand up after long time. She and her family were happy with the outcome. With good team approach and hospital facilities, appropriate treatment can provide an improved quality of life during their last days of life.

Conclusion

Outcomes in tumour patients can be improved by having high suspicion if there is continuous or worsening pain following a fracture. Quality life of patients with metastasis can be improved by multidisciplinary approach and adequate facilities to provide a required treatment.

SPINE TUMORS - AN OVERVIEW

Dr. P. E. Sreedharan Namboothiri, Dr. R.M. Neelgar
Department of Orthopaedic & Spine Surgery

Introduction

Spine tumours can be either from metastasis or primary malignancies. About 20-40% are benign spine tumours. Of all the primary benign bone tumours, 8% occur in spine and sacrum. In patients older than 21 years, 70% of spine tumours are malignant. Benign lesions are typically located in posterior elements and most (76%) anterior lesions are malignant.

Patients with spine tumours may present with persistent diffuse or localized pain with sleep disturbance, radiculopathy or spinal cord or root pressure symptoms. In case of thoracic lesions, bilateral radicular pain in corset-like pattern may be seen. Rapidly progressive symptoms indicate a malignant lesion.

Primary Spinal tumours

1. Anterior elements:

   Benign: eosinophilic granuloma, giant cell tumour, hemangioma, aneurysmal bone cyst Malignant: Chordoma, multiple myeloma, metastasis

2. Posterior elements:

   Benign: Osteoid osteoma, Osteoblastoma, Osteochondroma

3. Adjacent vertebrae:

   Benign: Aneurysmal bone cyst, Osteoblastoma

   Malignant: Chordoma, Chondrosarcoma

4. Multiple noncontiguous:

   Multiple myeloma, Metastasis

Metastatic spine tumours

Metastatic disease involves the spine in 50-85% of patients with malignancy, mostly affecting vertebral bodies of lumbar spine, followed by thoracic, cervical, and sacral region. Metastases are common from breast, lung, prostate, kidney, gastrointestinal tract, and thyroid. Breast and prostate cancer have high propensity to spread to spine due to interconnection of epidural venous plexus with the pelvic and mammary veins. Lymphoma is another tumour that commonly affects spine. In patients who develop neurological deterioration and paraparesis, only 25-35% regain lost function and complete paraplegics will not regain the lost function regardless of treatment. Rapid onset of symptoms over less than 24 hours is also a poor prognostic sign for neurological recovery in contrast to slow onset of symptoms.

DeWald's classification helps in the planning of treatment for spinal metastasis:

Class 1: Destruction without collapse but with pain a) < 50% destruction, b) > 50% destruction c) pedicle destruction

Class 2: Addition of moderate deformity and collapse with immune competence

Class 3: Immunocompromised with collapse and deformity

Class 4: Paralysis, collapse and deformity with immune competence

Class 5: Immune incompetence, deformity, collapse, paralysis

Investigations for Spinal Tumors:

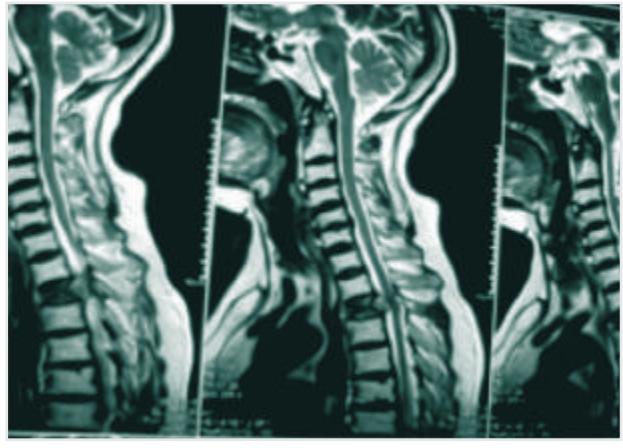


Fig. 1 D2 Isolated vertebral metastasis with collapse and cord compression

X rays are normal in the initial stages as 30 to 50% of the trabeculae are to be destroyed for a lytic lesion to be seen in the conventional radiography. The typical 'winking owl' sign in the AP spine radiograph is due to the destruction of the pedicle outline by tumour and indicates a very advanced stage of vertebral involvement.

Bone scan using Tc 99m pyrophosphate and diphosphonate compounds are sensitive to screen the whole skeletal system. They

detect osteoblastic new bone deposition. The sensitivity is better with Single-photon emission tomography (SPECT) and positron emission tomography (PET). Possibilities of false positivity and negativity are to be kept in mind.

MRI helps to quantify the size of the tumour, exact location and any skip lesion along the whole spinal column. It can detect lesions above 3 mm in diameter. The T1 and T2 'Short Tau Inversion Recovery' (STIR) sequences are particularly useful to evaluate spinal tumour. Gadolinium- diethylene triamine pentaacetic acid when used as an intravenous paramagnetic contrast agent is very useful for detecting extradural and intradural extramedullary tumours. The level of the spinal lesion seen in MRI may not correlate with clinical sensory level due to edema, vascular involvement or neuroanatomical peculiarities.

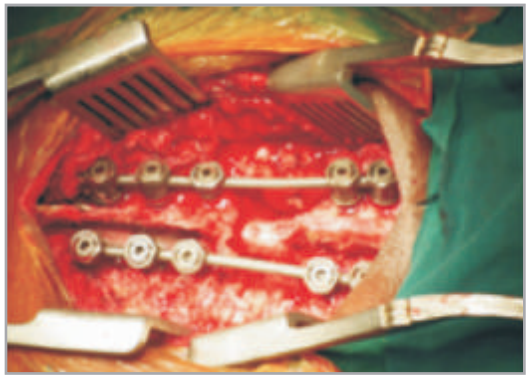


Fig. 2 Total spondylectomy- D2 tumour intraoperative photograph

CT scans are specifically useful for evaluation of cortical erosions, fracture and matrix ossification and calcification. CT lung is an essential staging tool. Radiation risk is to be assessed in each case.

Biopsy has to be done by the expert, final treating surgeon and should be through the most direct route.

Classification-Enneking (Benign Tumors):

Stage 1- Latent tumours like osteoid osteoma, eosinophilic granuloma, osteochondroma, and haemangioma does not require treatment, if at all planning for surgery intralesional excision is required with or without adjuvants eg.liquid nitrogen, phenol, or PMMA

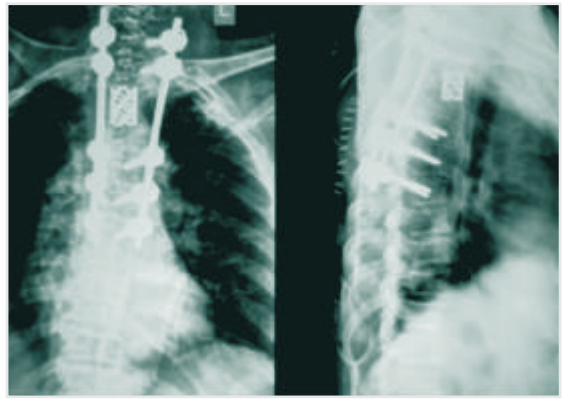


Fig. 3 D2 tumour - post operative x-rays

Stage 2 - Active and symptomatic- require en bloc excision like osteoid osteoma, osteoblastoma, eosinophilic granuloma, aggressive haemangioma, osteochondroma, aneurismal bone cyst

Stage 3 - Aggressive lesion benign tumours like giant cell tumours and osteoblastoma are locally aggressive having tendency to recur require wide excision of tumor with a cuff of normal tissue.

Enneking Classification (Malignant Tumors).

I Low grade

II High grade

III Regional or distant metastasis

If intracompartmental denoted A and extracompartmental by B. Marginal or wide excision is possible and radical excision is impossible in spine.

Treatment of Vertebral Column Tumors

1. Tumor excision, debridement and spinal fusion.
2. Radiotherapy
3. Chemotherapy

Principles to be followed in surgery of spinal tumours are:

In cervical and thoracic region spinal cord should be preserved. Some of the roots could be resected. In thoracic spine laminectomy will not provide safe access to anterior column so costotransversectomy or thoracotomy is a reasonable option

Sacral tumours require wide excision and complex reconstruction with combined approach to stabilize the ilia to the distal lumbar spine,

resection of sacral nerve roots affects continence. In cervical and thoracic spine laminectomy in immature spine create instability. Impending instability-more than 50% collapse of vertebral body, translation, segmental kyphosis > 20* above normal, involvement of anterior and posterior columns. Because most of these tumours arise from advanced cancer from another organ, the goal of spinal treatment is usually to:

- Control the severe pain that often occurs with these tumours (e.g. by removing pressure on the nerve roots)
- Preserve neurological function (e.g. by removing the pressure on the spinal cord)
- Fix structural instability in the spine

DeWald 1b and 1c are considered for surgery, Class 2 has good risk for surgery and Class 3 has greater risk for surgery. Class 4 is a relative surgical emergency and Class 5 are not considered for good operative risk. In any case, Quality of Life (QoL) is the concern. In general, if the patient is expected to live more than 3 months, spinal reconstruction is to be considered. Surgical reconstruction is recommended when >50% vertebral body destruction is identified or in presence of involvement of one or both pedicles because of risk of later fracture and deformity.

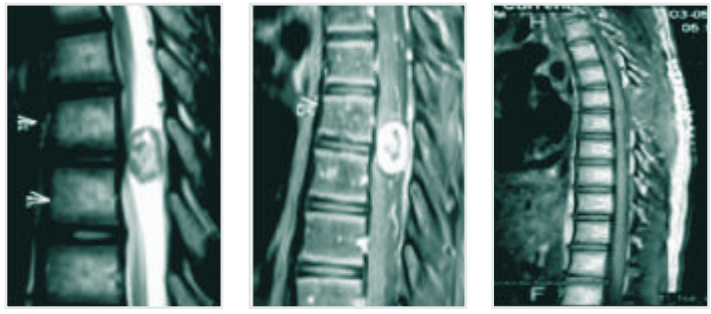
For most metastasis irradiation is mostly required for palliation. Instability is relative contraindication for irradiation because of collapse and progression of deformity that can occur due to necrosis of tissue. Surgery is indicated in cases of requirement of tissue diagnosis, isolated lesion, fracture causing instability, pain or spinal canal compromise, radio resistant tumours (gastro and kidney), recurrent tumours in previous irradiated site, progressing neurology, and potential instability.

Intradural-Extramedullary Tumors

Intradural-Extramedullary (inside the dura) tumours grow within the spinal canal (under the membrane that covers the spinal cord) but outside of the nerves. Usually these tumours are benign and slow growing. However, they can cause symptoms of pain and weakness.

Most of these spinal tumours are meningiomas that occur in the membranes surrounding the spinal cord and are usually benign but may be malignant. These tumours are more common in middle age and elderly women.

Nerve sheath tumours (Schwannomas and neurofibromas) that arise from the nerve roots that come off the spinal cord. Again, this type of tumour is usually benign and slow growing, and it may be years before any neurological problems occur.



Intradural Tumor MRI (T2) | Intradural Tumor MRI(STIR) | Intradural Tumor Post Operative MRI showing the complete removal

Fig. 4 Schwannoma in a 18 year boy

Intramedullary Tumours

Intramedullary tumours grow from inside the spinal cord or inside the individual nerves and often arise from the cells that provide physical support and insulation for the nervous system (glial cells). These tumours occur most often in the cervical spine (neck). They tend to be benign, but surgery to remove the tumour may be difficult.

The two most common types of intramedullary tumours are astrocytomas and ependymomas. These types of tumours are usually surgically removed.

The goal of treatment is usually to:

- Totally remove the tumour
- Preserve neurological function

The spinal cord and nerves are highly sensitive and avoiding damage to these structures is a critical part of surgery. Monitoring techniques may be used throughout the surgery to determine the function of the spinal cord as the tumours are being removed (e.g. SSEP).

If the tumour cannot be completely removed (e.g. if it adheres to many spinal nerves), post-operative radiation therapy may improve outcome in some cases. If the tumour is metastatic, chemotherapy may also be helpful.

Following the surgery, it may take some time for the nerves to fully heal. Usually rehabilitation and time significantly helps improve a patient's neurological function.

HEAD & NECK SURGICAL ONCOLOGY SERVICE AT KMCH

Dr. M. Dhiwakar

Department of Ear Nose Throat – Head & Neck Surgery

A full-fledged Head & Neck Surgery programme has been recently commenced at KMCH. This programme offers comprehensive and world class surgical treatment for benign and malignant diseases affecting the thyroid and parathyroid, neck, oral cavity, oropharynx, larynx, hypopharynx, salivary glands, paranasal sinuses and skull base. Innovative and novel surgical approaches are adopted in removing tumours that involve no or small incisions.

Various anatomical regions of Neck

This improves the cosmetic outcome, reduces pain and facilitates early speech, swallowing and discharge from hospital. Such procedures include selective neck dissection, minimal access thyroidectomy and parathyroidectomy and endoscopic resection of skull base tumours. Transoral laser microsurgery equipment is also being done. Since the program commenced 6 months ago, more than 30 major resections have been performed. A few examples are illustrated here.

Endoscopic skull base surgery

A 32-year old gentleman had presented with nasal bleeding and obstruction 18 months ago due to squamous cell carcinoma involving the paranasal sinuses. Treatment was given in the form of chemoradiation. Unfortunately, the tumour came back to involve the ethmoid sinuses in the region between the eyes and base of the brain (Fig. 1).

Endoscopy showed the tumour filling the nasal cavity. An entirely endoscopic transnasal approach was undertaken to achieve tumour resection. High definition video monitor and powered instruments were used to facilitate visualization, access, dissection and removal. Tumour was carefully removed from the critical areas of the undersurface of the brain, frontal sinus and orbit. The bony covering of the eyeball socket was involved by tumour, and it was therefore removed. The patient made an excellent recovery and was discharged from the hospital in 2 days. The postoperative cavity had no evidence of gross tumour.

Surgery for thyroid cancer

A 35-year old lady presented with a lump in her neck for several years. Fine needle biopsy showed papillary thyroid cancer and CT scan showed a large tumour arising from the left thyroid lobe that had spread to several lymph nodes in the neck (Fig. 2).

The thyroid gland along with the lymph nodes in the central and lateral compartments of the neck were dissected and removed (Fig. 3). In the process, all critical structures, such as the recurrent laryngeal nerve that is responsible for voice, parathyroid glands that regulate calcium levels in the blood, spinal accessory nerve that supplies the shoulder, and jugular vein were preserved (Fig. 4).

The patient made a rapid recovery and was discharged home within 5 days with no problems. The patient then underwent radio-iodine treatment. She has an excellent chance of cure.

Surgery for cancer of the mouth

Patient 1: A 60-year old lady presented with a painful growth in her mouth that involved the right cheek (Fig. 5).

Biopsy confirmed this to be cancer (squamous cell). Surgery was

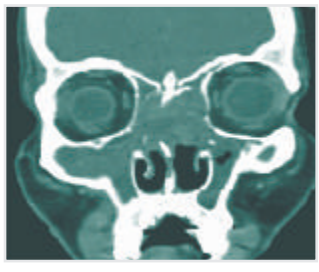


Fig. 1 CT Scan showing recurrent tumour

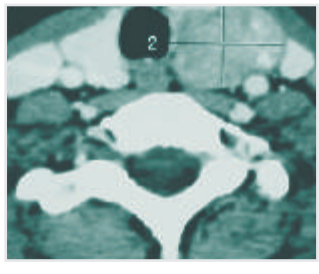


Fig. 2 CT scan showing tumour from left lobe of thyroid

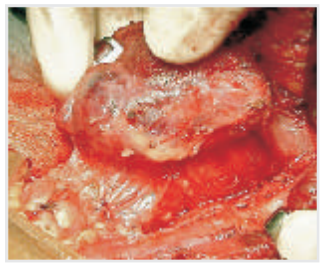


Fig. 3 Resection of left lobe of thyroid with nodes

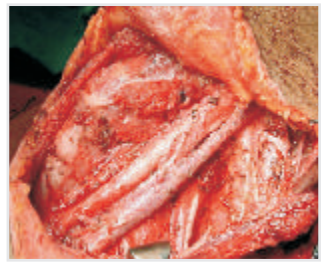
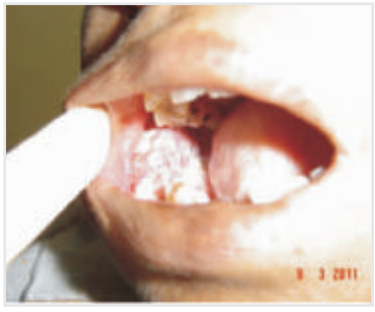


Fig. 4 After resection, preserved structures



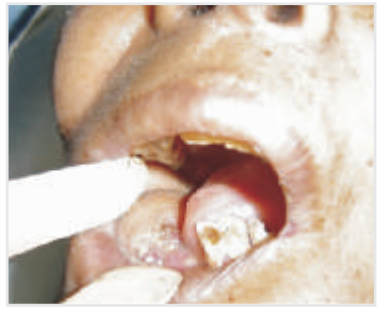


Fig. 5 & 7 Carcinoma of right cheek – before & after treatment

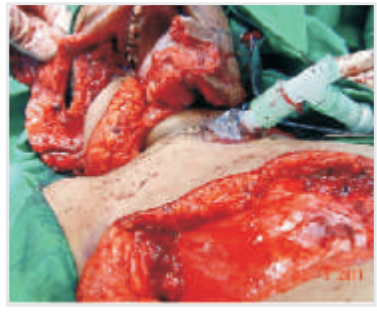


Fig. 6 Reconstruction in progress

undertaken to remove the tumour with a wide margin, along with a portion of the mandible and neck lymph nodes. The defect was reconstructed with skin and muscle of the right chest wall a pectoralis major flap . (Fig. 6). The patient made a good postoperative recovery and went home in 1 week. She is able to breathe, talk, chew and swallow normally without any problem (Fig. 7). With postoperative radiotherapy, she has a good chance of cure.

Patient 2: A 45-year old lady presented with a painful ulcer deep inside her mouth that caused severe inability to open her mouth.

Biopsy revealed cancer (squamous cell). It was invading the mandible and floor of mouth. The tumour was removed along with the underlying muscle, part of mandible and lymph nodes in the neck (Fig. 8). Similar to the above patient, the defect was reconstructed with a pectoralis major flap. The patient made a good recovery and went home in 1 week. Due to the extensive disease, she would require postoperative chemoradiation.

Surgery for parotid cancer

A 50-year old lady presented with a painful lump in front of her left ear that on fine needle biopsy revealed cancer involving the parotid (salivary) gland. CT scan showed that it had spread to the neck lymph nodes. In the process of removing the tumour, it was apparent that the facial nerve that moves the face was invaded by cancer. It was therefore sacrificed along with the whole parotid gland and left neck lymph nodes (Fig. 9).

Dr. Nambi, Consultant Plastic Surgeon, used an adjacent nerve to bridge and repair the sacrificed nerve. The patient recovered well and is awaiting radiation therapy.

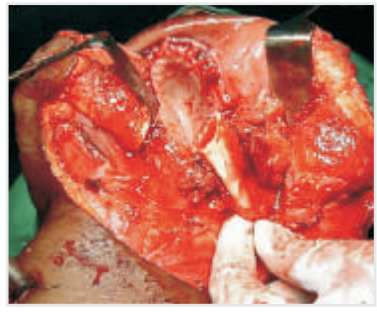


Fig. 8 Resection of oral tumour

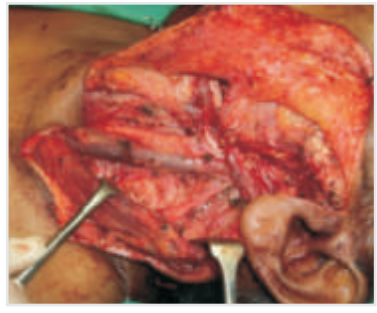


Fig. 9 After radical parotidectomy

World's first documented cancer case was in 1500 B.C. in ancient Egypt, while today cancer is the second leading cause of death in the world

MICROVASCULAR RECONSTRUCTION OF THE HEAD & NECK

Dr. Nambi Ilango
Department of Plastic & Reconstructive Surgery

The role of a plastic or reconstructive surgeon in an oncological team is often underestimated. These specialists are a valuable asset to the team. Large defects following removal of head and neck tumours often need repair by transfer of tissue such as skin, muscle and bone from elsewhere in the body. This involves harvesting the tissue along with its supplying blood vessels (pedicle). This tissue is then transferred to repair the head and neck defect. The blood vessels of the neck are sutured to the pedicle to provide nourishment for the free flap. This intricate and challenging procedure is undertaken under the microscope and sutures thinner than the human hair are used. Free tissue transfer ensures that almost completely normal form and functions are restored. This is made possible due to the pliability of the transferred tissue and bony support where indicated. The majority of patients return to normal appearance, speech, chewing and swallowing. The microvascular reconstructive program for head and neck defects at KMCH offers the full range of free tissue transfers with outcomes that are comparable to the best centers in the world. Some examples of microvascular reconstruction of head and neck oncological defects performed at KMCH are illustrated here.

Pharyngo – Oesophageal reconstruction with Jejunal free flap

A 65-year old gentleman was operated for papillary thyroid carcinoma involving the trachea and oesophagus. The entire thyroid gland, neck nodes and voice box (larynx) were removed along with the upper part of the food pipe (cervical esophagus). The airway was established by an end tracheostomy. The continuity of the digestive tract was restored with a segment of jejunum with its blood vessels which were connected to the neck vessels by microvascular anastomosis. In this case the, jejunal vessels were connected with the left superior thyroid artery and the external jugular vein (Figs – 1a to 1d).

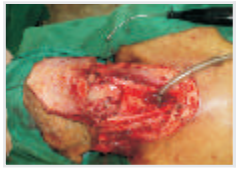


Fig. 1a

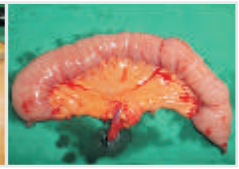


Fig. 1b

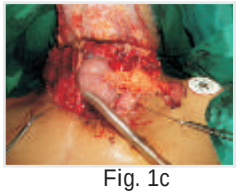


Fig. 1c

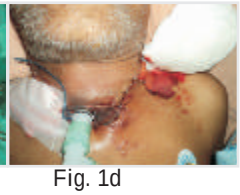


Fig. 1d

Tongue and floor of the mouth reconstruction with Anterolateral thigh free flap

A 72-year old gentleman was operated for carcinoma of the tongue involving the right margin and floor of the mouth. The resultant defect involving the right half of the tongue, right side floor of the mouth, anterior and lateral alveolus and part of the pharynx were reconstructed using anterolateral thigh flap. The flap pedicle was anastomosed with right superior thyroid artery and right internal jugular vein using an end to side anastomosis (Figs – 2a to 2f).

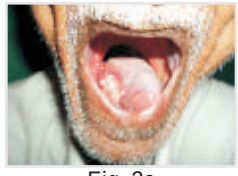


Fig. 2a

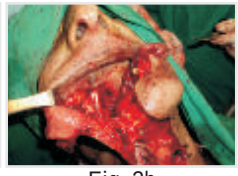


Fig. 2b

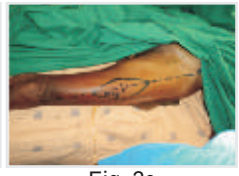


Fig. 2c

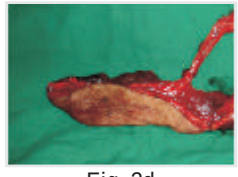


Fig. 2d

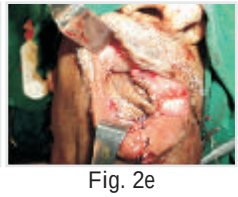


Fig. 2e

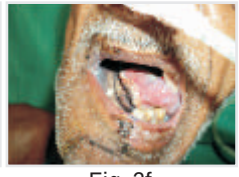


Fig. 2f

Buccal mucosa and alveolar reconstruction with Radial artery forearm free flap

A 75-year old female was operated for carcinoma of the left buccal mucosa, involving the adjacent lower jaw and the upper jaw. Because of this, the patient presented with trismus. The post excision defect involving the above mentioned areas were reconstructed with radial artery forearm flap. Micro vascular anastomosis of the flap blood vessels was done with left facial artery and a tributary of the left internal jugular vein (Figs – 3a to 3f).

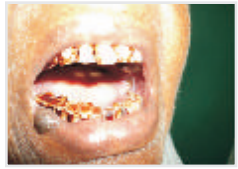


Fig. 3a

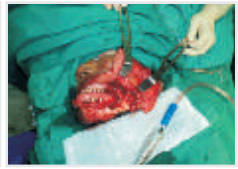


Fig. 3b

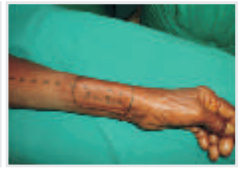


Fig. 3c

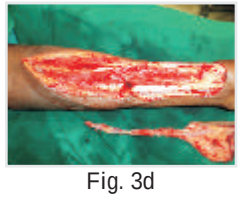


Fig. 3d

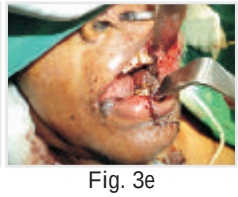


Fig. 3e

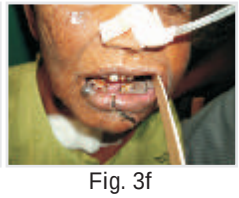


Fig. 3f

BASAL CELL CARCINOMA – LEFT INFRA – ORBITAL REGION

Dr. Nambi Ilango
Department of Plastic & Reconstructive Surgery

An 85-year old lady presented with history of pigmented lesion in her left infra-orbital region since last 5 years. There was increase in size of the lesion with itching since last 3 months. A clinical diagnosis of basal cell carcinoma was made which was confirmed by biopsy. She was managed with wide local excision and reconstruction with Mustarde's flap.


Fig. 1 Preoperative view

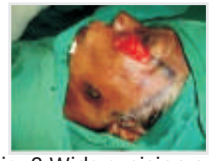


Fig. 2 Wide excision and outline of Mustarde's flap

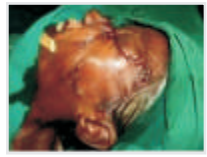


Fig. 3 After reconstruction with flap

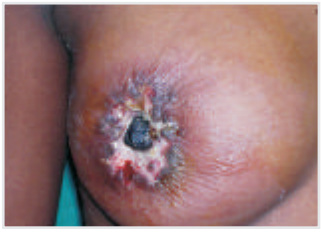

Fig. 4 Postoperative view

Breast Cancer

Dr. K.S. Rajkumar
Department of Surgery

Introduction

It is the 2nd most common female cancer. It accounts for 32% of all female cancers. 2,11,300 new cases were diagnosed yearly and it is still rising. It accounts for 40,000 deaths yearly.


Infiltrating Carcinoma with nipple destruction

Risk factors for breast cancer

Factors Important in Populations

Early menarche and late menopause
Nulliparity
Age at first birth
Breast-feeding
Exogenous hormone use or exposure
Alcohol consumption

Factors Important in Individual Patients

Gender (female > > male)
Age (steady increase with age)
Family history (mothers, sisters, daughters)

History of previous breast cancer (non-invasive or invasive, ipsilateral or contralateral)

Histologic Risk Factors

Proliferative breast disease
Atypical ductal hyperplasia (ADH)
Atypical lobular hyperplasia (ALH)
Lobular carcinoma in situ (LCIS)

Classification of Breast Cancer

Noninvasive Epithelial Cancers

Lobular carcinoma in situ (LCIS)

Ductal carcinoma in situ (DCIS) or intraductal carcinoma

Papillary, cribriform, solid, and comedo types

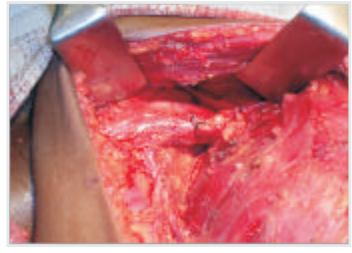
Invasive Epithelial Cancers

American Joint Committee on Cancer Staging System for Breast Cancer

Stage 1	–	T1, N0, M0
Stage IIA	–	T0/T1, N1, M0
		T2, N0, M0
Stage IIB	–	T2, N1, M0
		T3, N0,M0
Stage IIIA	–	T0/T1/T2, N2, M0
		T3, N1/N2, M0
Stage IIIB	–	T4,N0/N1/N2, M0
Stage IIIC	–	Any T, N3, M0
Stage IV	–	Any T, any N, M1

KMCH EXPERIENCE - Carcinoma Breast Management

We have done a total of 102 operations for Breast Carcinoma so far in the last 8 years in this hospital. Varieties of surgery ranges from Simple Mastectomy (10%), Toilet Mastectomy (4%), Simple Mastectomy with axillary clearance (68%) and Radical Mastectomy (12%). We were not able to convince even one patient for a breast


Axillary vessels skeletonised in node dissection

conservation surgery. Regarding the types of cancer - majority were Infiltrating duct carcinoma (71%) although we had other types like Lobular carcinoma, Inflammatory carcinoma, Scirrhous carcinoma and Medullary carcinoma. No patient requested for breast reconstruction even though there were many young patients, the main reason being cost. A dedicated team like any other breast unit in the western countries is ideal to manage breast cancers, and counsel patients for breast conservation and/or reconstruction as and when indicated.

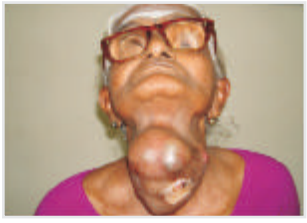
THYROID CANCER

Dr. K. S. Rajkumar
Department of Surgery

Introduction

The burden of thyroid disease in the general population is enormous. Thyroid disorders are the most common among all the endocrine diseases in India. In studies from western literature as many as 50% of people in the community have microscopic nodules, 3.5% have occult papillary carcinoma, 15% have palpable goitres, 10% demonstrate an abnormal thyroid-stimulating hormone level, and 5% of women have overt hypothyroidism or hyperthyroidism.

Thyroid nodules


Large malignant tumour of thyroid with skin involvement

Thyroid nodules may be benign (simple non toxic or multinodular goitre, follicular adenomas and cysts) or malignant (papillary carcinoma, follicular carcinomas and medullary carcinoma). They are more common in females and prevalence mainly depends on age, sex, iodine intake, diet (goitrogens), therapeutic and environmental radiation exposure. Although the vast majority are benign lesions, about 5% may actually represent thyroid cancer.

Thyroid malignancies

Thyroid tumours are the most common endocrine neoplasms. 5-10% of all thyroid nodules coming to medical attention are carcinomas. The diagnosis can be established by a thorough medical history, clinical examination, imaging & FNAC of the nodule.

Risk factors for thyroid malignancy

Malignancy is more common in children and adults >60. Equal incidence is seen in both male & female. The only well-established risk factor for differentiated thyroid cancer is external head and neck radiation, especially during infancy. Papillary thyroid carcinoma may occur in: Rare inherited syndromes (Familial adenomatous polyposis, Gardner's syndrome, Cowden's disease)

Patient's Age and Gender

Classification & Incidence of thyroid cancer

Tumours of follicular cell origin:

Differentiated

- Papillary – 75%
- Follicular – 10%
- Hurthle cell – 5%

Undifferentiated

- Anaplastic – 5%

Tumours of parafollicular cell:

- Medullary – 5%

Other: Lymphoma - <1%

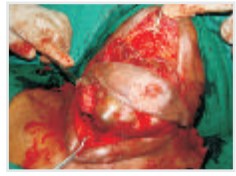
Clinical presentation

Most patients are euthyroid and present with a thyroid nodule. Symptoms such as dysphagia, dyspnea and hoarseness usually indicate advanced disease. Ipsilateral cervical lymph nodes may also be present.

Diagnosis

It includes good history, physical examination, USG neck, FNAC, Thyroid function tests & Radioiodine uptake scan.

Treatment


Dissection of tumour including excision of excess skin


Postoperative picture

The primary treatment of Papillary thyroid cancer is surgical resection. For lesions < 1cm, lobectomy with isthumusectomy is favoured. For lesions > 2cm, total thyroidectomy is favoured. Patients with history of exposure to radiation should be offered total thyroidectomy. Complete neck dissection is offered for medullary & Hurthley cell cancer. Postoperative radioactive iodine (RAI) ablation is offered for all patients with well-differentiated cancer & older than 45 years.

Prognosis

Both papillary & follicular cancer have good prognosis with 20-year survival rate of 90% & 70% respectively. Most important prognostic factor is age. Bad prognostic factors include tumours > 4cm, metastatic disease, extension beyond gland & tall columnar cells on histopathology.

THYROID CANCER SURGERIES AT KMCH

Out of 233 Thyroid surgeries we have performed in this hospital, 32 were for cancer. 27 of them were Papillary carcinoma, 3 were Follicular carcinoma, 1 was Medullary carcinoma and 1 was Anaplastic Carcinoma. We have done Total Thyroidectomy for all malignant cases even though literature says Hemithyroidectomy can be

done for 1 cm lesion involving only one lobe. For the majority of the patients only Total Thyroidectomy was done and a few required unilteral or bilateral neck dissection. For 4 patients after the Hemi-thyroidectomy when the histology came as carcinoma, I took them back to theatre and removed the other lobe of thyroid. Fortunately we never had any mortality or any other major complications for any of these patients, although few needed post op ventilation and ICU stay. 6 patients had unilateral vocal cord palsy, which recovered over a period of time with speech therapy. 3 patients had permanent hypocalcemia who were put on regular calcium. About 30 patients with Papillary and Follicular carcinoma were sent for postoperative I131 scan and radio-iodine ablation therapy. Out of these, 28 needed only a single ablation therapy and 2 needed more than 2 ablations. All these patients were subjected through 6 monthly and followed by yearly radio-iodine uptake scan as per the international protocol and they are being regularly followed here by Dr. Velayutham, Endocrinologist. Now that we have our own Oncology department, we should get more malignant cases in the future and the Nuclear medicine department, which is going to start functioning soon, would be of great help for our patients.

MEDIASTINAL TUMOURS

Introduction

Historically, in adults, the most common type of mediastinal tumour or cyst found is the neurogenic tumour (21%), followed by thymic tumours (19%), lymphomas (13%), and germ cell tumours (10%). In adults, only approximately 1-2% of neurogenic tumours are malignant. In patients younger than 20 years or older than 40 years, approximately one third of mediastinal tumours are malignant, while in patients aged 20-40 years, roughly half are malignant.

Any discussion of masses and tumours of the mediastinum requires delineation of the boundaries of that area. Most commonly, the mediastinum is subdivided into 3 spaces or compartments: anterior, middle, posterior. The anterior compartment extends from the posterior surface of the sternum to the anterior surface of the pericardium and great vessels. The middle compartment, or middle mediastinum, is located between the posterior limit of the anterior compartment and the anterior longitudinal spinal ligament. The posterior mediastinum is the area posterior to the heart and trachea and includes the paravertebral sulci.

Pathophysiology

Tumors and cysts of the mediastinum can produce abnormal effects at both systemic and local levels.

Local pathophysiology

Malignant mediastinal tumours can produce abnormalities by invasion of local structures. Pathophysiologic changes that can be produced by invasion of specific structures are obstructive pneumonia and hemoptysis; dysphagia; superior vena cava syndrome; pleural effusion; and various neurologic abnormalities such as vocal cord paralysis, Horner syndrome, paraplegia, diaphragmatic paralysis, and pain in the distribution of specific sensory nerves.

Systemic pathophysiology

Certain mediastinal tumours can produce systemic abnormalities, mostly due to bioactive substances produced by specific neoplasms. The most common of these is neuroblastoma, ganglioneuroma and ganglioneuroblastoma, which produce excess amounts of the catecholamines, epinephrine, and norepinephrine. Autonomic nerve tumours are also capable of producing excess amounts of vasoactive intestinal peptide. Some neurosarcomas have been associated with the production of an insulin-like substance that, in turn, can produce hypoglycemia.

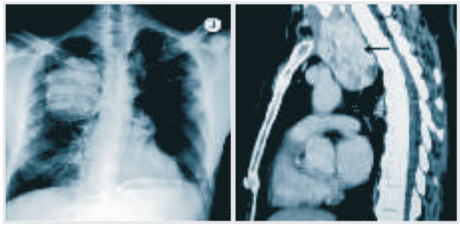
Presentation

Many mediastinal tumours and cysts produce no symptoms and are found incidentally during chest radiographs or other imaging studies of the thorax performed for another reason. Symptoms are present in approximately one third of patients. Respiratory symptoms: persistent cough, dyspnea, stridor, and obstructive pneumonia Constitutional symptoms: weight loss, fever, malaise, and vague chest pain. Invasion of the chest wall or pleura, persistent pleural effusions, invasion of nearby nerves within the thorax can produce local and referred pain, hoarseness from recurrent nerve paralysis, diaphragmatic paralysis from phrenic nerve paralysis, Horner syndrome from autonomic nerve invasion, and even motor paralysis from direct spinal cord involvement, pain in the shoulder or upper extremity from invasion of

the brachial plexus, superior vena cava syndrome due to venous obstruction. Functioning mediastinal pheochromocytomas produce an excess of circulating catecholamines. The hallmark clinical finding in individuals with these neoplasms is malignant hypertension as they are most often resistant to standard antihypertensive therapy.

Imaging Studies

- Chest radiography
- CT scan of the chest and mediastinum
- Magnetic resonance imaging
- Radionuclide scanning
- Echocardiography and ultrasonography
- Positron emission tomography
- Arteriography / MRI angiography



Chest X-Ray of mediastinal tumour

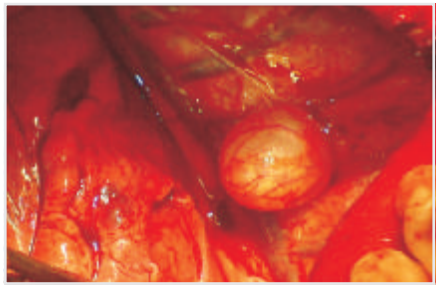
CT Scan of mediastinal tumour (arrow)

Diagnostic Procedures

- Transthoracic needle biopsy
- Cervical mediastinoscopy
- Anterior mediastinotomy
- Posterior mediastinotomy
- Video-assisted thoracic surgery (VATS)
- Sternotomy and thoracotomy

Histologic Types

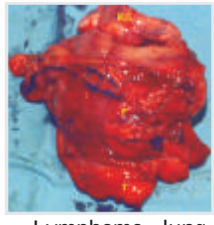
Various benign and malignant neurogenic tumours occur in the mediastinum, essentially the posterior mediastinum. These are the commonest types: Malignant



Mediastinal tumour

schwannoma, Neuroblastoma, Ganglioneuroblastoma, Melanotic progonoma, Askin tumor, Mediastinal paragangliomas and pheochromocytomas.

Treatment



Lymphoma - lung

Malignant schwannoma and neurofibrosarcoma Surgical resection is the primary mode of therapy. Radiation therapy may be used pos toperatively to control residual disease, but the benefit of this is unknown. No known chemotherapeutic regimens are effective against these tumours. Ganglio-neuroma and Melanotic progonoma Treatment is surgical in nature.

Neuroblastoma and Ganglioneuroblastoma

Patients at INSS stages 1 and 2 are considered candidates for resection. For patients with more advanced disease (INSS stage 3, 4, or 4S), a combination of surgery and chemotherapy is recommended. Intense chemotherapy with whole-body irradiation or myeloablative chemotherapy is administered, followed by autologous bone marrow transplant.

Askin tumour

Surgical resection followed by irradiation and chemotherapy is recommended in all cases.

Surgery

VATS resection is now commonplace for these benign tumours. Shorter hospital stay and more rapid return to work have been demonstrated with this method. When surgical resection of malignant neoplasms of the mediastinum is the primary treatment, bloc resection of the tumour should be performed whenever possible. Regional lymphadenectomy should accompany surgical resection of neuroblastomas. Tumours or cysts located in the anterior mediastinum are generally approached through a median sternotomy. This approach is used for tumours of the thymus. Those located in the posterior or middle mediastinum and paravertebral sulci, such as most neurogenic tumours and foregut cysts, are approached through a VATS incision or a posterolateral thoracotomy incision. Standard single-lumen endotracheal intubation is appropriate for resections performed via the median sternotomy approach. Use of a double-lumen endotracheal tube for single-lung ventilation is preferable for those procedures performed through a thoracotomy incision and for all procedures performed using VATS.

Outcome and Prognosis

Prognosis after resection of a mediastinal tumour varies widely depending on the type of lesion resected. Prognosis after treatment of malignant mediastinal tumours depends on the type of lesion, its biological behaviour, and the extent of the disease present.

Neuroblastoma

The overall survival rate for thoracic neuroblastomas is greater than 70% at 5 years and greater than 60% at 10 years.

Ganglioneuroblastoma

Has a better prognosis because a large percentage of them manifest as an asymptomatic solitary mass and can be completely resected in many cases. A skin or peripheral neuroectodermal tumour: Survival is commonly less than 1 year, and long-term survival, even with aggressive therapy, is rare.

Malignant nerve sheath tumours

Long-term survival rate approaches 50% for this neoplasm; however, individuals with associated von Recklinghausen disease have a high incidence of local or distant recurrence within 2 years.

Future and Controversies

Numerous exciting advances have been made in areas of diagnostic imaging, biologic analysis, and therapy. Emerging diagnostic modalities such as PET scans and other radionuclide studies may be able to assist in the diagnosis of specific neoplasms and in post-therapy surveillance for recurrent disease. Numerous biological markers have been identified for many tumours and will play a vital role in better identifying individual neoplasms so that treatment can be optimized. Use of VATS technology has entered the armamentarium of the thoracic surgeon with respect to the treatment of numerous mediastinal diseases. This modality is already used commonly for biopsy of masses and lymph nodes. It has also been commonly used for resection of various mediastinal cysts, mediastinal parathyroid adenomas, and localized benign tumours of the posterior mediastinum such as ganglio-neuromas. Robotic resection has also been used for general thoracic surgical procedures, including thymectomy and extirpations of benign mediastinal masses. Its use may be limited by lack of appropriate instrumentation.

OESOPHAGEAL CANCER

Dr. A. Ganesan
Department of Surgery

Worldwide, oesophageal cancer is the eighth most common cancer and sixth leading cause of cancer death. In India it is the fourth commonest cancer in men and 5th common one in women. Oesophageal cancer accounts for 6% of cancers in India. There are two common histological types, squamous cell carcinoma and adeno-carcinoma. In Europe and America incidence of adenocarcinoma of the oesophagus is rising at epidemic proportion presumably due to GERD and Barrett's oesophagus. In Europe and America adenocarcinoma is the commonest oesophageal malignancy, in contrast to Africa and Asia where squamous cell carcinoma is the commonest. Proposed aetiology is mainly environmental in origin. Factors proposed as the causation of squamous cell carcinoma includes alcohol consumption, smoking, betel nut and tobacco chewing, pickled food, smoked food and processed meat. Protective factors include fruits, vegetables turmeric and other antioxidants. Reflux oesophagitis especially bile reflux and Barrett's oesophagus are the causative factors for adenocarcinoma.

Clinical manifestations

Oesophageal cancer is asymptomatic in its early stages. Dysphagia occurs only when > 60% of the circumference is involved. Weight loss associated with dysphagia is a strong predictor of oesophageal cancer. Sometimes odynophagia may be an early symptom. Late features include cervical lympadenopathy, jaundice, hepatomegaly, pleural effusion, Horner's syndrome, cough, stridor, and haemoptysis.

Diagnosis

Diagnosis is by endoscopy and biopsy. Sometimes this can be missed on the first attempt. Chemo-endoscopy with dye spray technique is useful in screening for early cancers and precursor lesions. Barium swallow can also be diagnostic but it is being used very little nowadays.

Staging

CT scan of chest and abdomen is useful to assess metastatic disease, invasion of adjacent organs and mediastinal or abdominal lympadenopathy. Endoscopic USS is the current modality of choice to assess the depth of invasion of the tumour and paraoesophgeal, perigastric and celiac lymph nodes. Bronchoscope is done for upper thoracic oesophageal tumours to rule out invasion of bronchus. Endo bronchial USS is useful in some doubtful cases of bronchial invasion. PET scan may be useful in doubtful case of metastatic disease. Currently PET Scan is recommended for the assessment of response to neoadjuvant chemotherapy.

Management

Management depends on the stage and location of the tumour. Surgery offers cure in

early stages of this disease. Cancers of the cervical oesophagus is generally treated by concurrent chemoradiation because of high morbidity associated with surgery. For operable cancers in the rest of the locations radical surgery with lympadenectomy is the treatment of choice if the patient is fit for a major operation. Role of neoadjuvant treatment in clearly resectable oesophageal cancer is debatable. Neoadjuvant chemotherapy or chemoradiotherapy is advisable in patients with bulky disease with borderline operability. For medically unfit patients radical radiotherapy is offered. For metastatic and locally advanced tumours self-expanding metallic stent provides good palliation of dysphagia.

Surgical approaches

Open approaches

Ivor Lewis approach: Laparotomy followed by right thoracotomy provides good exposure for lower thoracic and mid-thoracic oesophageal tumours and allows one to perform two stage lymphadenectomy. Mceven's three-stage approach: Laparotomy and thoracotomy followed by a cervical incision. It is done for upper thoracic tumours and can be combined with cervical lymphadenectomy. It is an option in mid and lower thoracic tumours if the surgeon wishes to avoid an intrathoracic anastamosis and consequences of a leak in the mediastinum. Left thoraco-abdominal is attractive where we don't need to change the position of the patient during surgery but it gives only limited exposure of the oesophagus. It is advisable only for selective OG junction tumours. Transhiatal approach: This approach does a blind oesophagectomy without lymphadenectomy. It is not an oncologically sound principle in my opinion. This technique was popularized by Orringer, where he justifies this approach because all his patients undergo pre-operative chemotherapy.

Minimally invasive approaches

Laparoscopic and thoracoscopic with cervical anastomosis: this is similar to Mceven's three-stage procedure. Laparoscopic and thoracoscopic with thoracic anastomosis is similar to Ivor Lewis approach. Laparoscopic and Transhiatal: This is different to blind open transhiatal approach as the dissection is done under laparoscopic view. Hybrid Minimally Invasive Esophagectomy (HMIE): Here part of the surgery is done by minimally invasive approach and part is done by open method.

Is there any benefit for minimally invasive oesophagectomy?

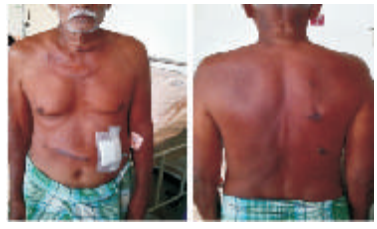
There is no RCT so far. A meta-analysis of 12 studies was reported in 2010. According to this study, 672 open oesophagectomies were compared with 612 minimally invasive oesophagectomies (MIE).

- There was no significant difference in 30-day mortality; however, MIE had lower blood loss, shorter hospital stay, and reduced total morbidity and respiratory complications. For all other outcomes, there was no significant difference between the two groups.

- In conclusion minimally invasive oesophagectomy is a safe alternative to the open technique. Patients undergoing MIE may benefit from shorter hospital stay, and lower respiratory complications and total morbidity compared with open oesophagectomy. Multicenter, prospective large randomized controlled trials are required to confirm these findings.

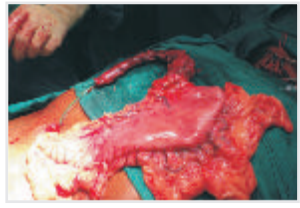
CASE # 1

A 65-year old man presented with a history of dysphagia and weight loss. Upper GI endoscopy showed tumour in the midthoracic oesophagus starting at 25 cm. CT scan showed the tumour was operable. EUS confirmed CT findings. Biopsy showed squamous cell carcinoma. Patient underwent thoracoscopic mobili-sation of oesophagus with mediastinal lymphadenectomy followed by laparoscopic gastric mobilisation with lymphadenectomy and cervical pull through a gastric tube. Patient recovered well with no complications and was discharged on the 8th postoperative day. Final histology showed it was a T3 tumour with 4 out of 23 lymph nodes positive. Patient could complete only 4 cycles of chemotherapy. Patient is doing well 5 months after surgery.



Postoperative picture showing thoracoscopic and laparoscopic port sites

CASE # 2



Oesophagogastrectomy in progress

A 67-year old lady presented with a history of dysphagia. Endoscopy showed mid-thoracic growth and biopsy showed squamous cell carcinoma. CT scan showed the tumour was operable. Patient underwent same procedure like the case # 1. Patient had a complication from dislodged feeding tube requiring re-operation. Histology showed T3 N0 squamous cell carcinoma. Patient is doing well 4 months after surgery Oesophago-gastrectomy in progress.

CANCER OF THE STOMACH: CURRENT CONCEPTS

Dr. M. Rangarajan
Department of Surgery

INCIDENCE

In India, the incidence of cancer stomach in males is 5.6% and 2.5% in females, according to a survey of six Indian cities (Indian Cancer Registry-consolidated report 1990-1996). South India has the highest incidence of carcinoma of the stomach in India for males (12.6%) and females (5.5%). Within India itself cancer rates vary dramatically. The ICMR guidelines state that the incidence of stomach cancer is 57 per 1 lakh in India's northeast, compared with the rates as low as 5 per 1 lakh in other regions. The stomach remained as the leading site of cancer in males in Chennai and Bangalore, followed by Mumbai, Delhi, and Bhopal.

Other studies have proved that patients of Asian descent with gastric carcinoma have better overall and cancer specific survival rates from gastric carcinoma. They also exhibit different clinical features. These data reflect differences in epidemiology between gastric carcinoma in the East and West and are consistent with the hypothesis that gastric carcinoma in Asians is biologically different from gastric carcinoma in non-Asians.

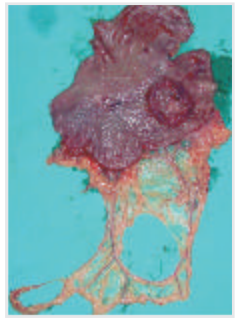
Over the last 45 years, the death rate is declining thanks to early detection, better understanding of the disease and advances in technology.

ETIOLOGY

1. Spicy food
2. Polycyclic hydrocarbons in grilled and barbecued meat
3. High intake of animal fat and salt
4. Protein malnutrition
5. Excess alcohol and smoking
6. Dietary nitrates
7. Refluxed bile acids

RISK FACTORS

1. Atrophic gastritis
2. Pernicious anemia
3. Previous partial gastrectomy
4. Adenomatous polyps (38% risk)
5. Blood group A
6. Chronic gastric ulcer (4% risk)
7. H.Pylori infection
8. Advanced age
9. Male gender
10. Chronic atrophic gastritis
11. Intestinal metaplasia
12. Menetrier's disease (giant hypertrophic gastritis)


Total gastrectomy specimen

The most important is atrophic gastritis. In pernicious anemia, there is a 5-fold increase in incidence of atrophic gastritis. This progresses to intestinal metaplasia, dysplasia and carcinoma-in-situ. Most of the above-mentioned etiological factors give rise to atrophic gastritis by damaging the gastric mucosa.

CLINICAL FEATURES

In the early period, there are no symptoms. Tumours of the inlet and outlet of the stomach produce mild dyspeptic symptoms initially and obstruction later (vomiting of undigested food after eating, ball rolling movements, relative constipation, dehydration, anemia and occasionally epigastric distension or lump). Tumours of the body give rise to vague epigastric discomfort, anorexia or may remain silent to the end. The most common symptoms are epigastric pain, indigestion, anorexia, weight loss, hemetemisis, melena, dysphagia, abdominal lump, diarrhoea and steatorrhea. Tumours of the cardioesophageal junction produce dysphagia, tumours of the body usually produce vague symptoms since it does not interfere with the physiology or mechanics of the stomach. Left supraclavicular node enlargement ('Virchows node'), umbilical nodule ('Sister Joseph nodule') or anterior rectal deposits ('Bloomer shelf') are signs of incurable disease.

INVESTIGATIONS

The most useful initial investigation is upper GI endoscopy and biopsy, though modern double-contrast studies have an accuracy of 99%. As use of endoscopy increases, early diagnosis of gastric cancer increases, so the proportion of curative resections and 5-year survival rates increases, concomitantly. USG and CECT scan of the abdomen are done to assess evidence of metastasis, lymph node

status and involvement of neighbouring organs. Endoscopic ultrasound can also be used to assess the T stage and perigastric lymph nodal status.

SCREENING

The basic idea of screening is to pick up the disease early and provide curative surgery, especially in prevalent countries like Japan. The Japanese have proved that screening significantly decreases mortality of gastric cancer. The use of upper gastrointestinal surveys and 'gastrocamera' have made early detection possible. Screening in Japan has increased the yield of mucosal or submucosal lesions from 3.8% in 1955 to 34.5% in 1966, with a corresponding survival rate of 90.9%. Mass screening is not cost-effective in areas with low incidence of gastric cancer. In such situations, high-risk groups must first be identified and then screened.

Diagnostic Laparoscopy

In countries besides Japan, the presentation of gastric cancer is usually late and at diagnosis, a significant proportion of patients have inoperable tumours. Today, it is unreasonable to offer a patient an exploratory laparotomy for diagnosis alone and find out the tumour is unresectable. Diagnostic laparoscopy has established itself as an accurate diagnostic tool for gastric cancer. At present, it fulfils two important roles for patients with gastric cancer: (i) it spares patients the trauma of undergoing an exploratory laparotomy and, (ii) identifies patients with locally advanced disease for neo-adjuvant therapy.

It increases staging and prognostic accuracy, identifying operable and curable patients and patients suitable for oncological treatment. Overall staging accuracy of diagnostic laparoscopy is almost twice as high as that of USG and CT scan (72% vs. 38%). Diagnostic laparoscopy can lead to a change in the preoperative stage in 58% of patients. Upstaging is more common than downstaging, thereby sparing the patient of laparotomy. It can serve as a screening tool for high-risk patients. So, diagnostic laparoscopy is a simple, low morbidity procedure and may be suggested for all cases undergoing laparotomy for curative gastrectomy.

TREATMENT

Surgery provides the only possibility of a cure, radical gastrectomy being the procedure of choice. The principal strategy is adequate resection of the primary tumour (5cm clearance) and complete removal of regional lymphatic system. The commonly practiced gastrectomies for cancer are distal radical, proximal radical and total gastrectomy. Depending on the individual case - omentum, spleen, distal oesophagus, proximal duodenum and parts of pancreas or transverse colon can be resected. Gastrectomy can be palliative or curative.

D2 Dissection complete

The extent of lymph node dissection to be done combined with curative resection (according to Japanese Research Society for Gastric Cancer):

D1: Removal of perigastric nodes (groups 1-6)

D2: Left gastric, hepatic and celiac nodes (groups 7-9) + D1

D3: Splenic, hepatoduodenal and retropancreatic nodes (group 10-13) + D2

D4: Superior mesenteric, midcolic, paraaortic, infradiaphragmatic and hiatal nodes (group 14-18) + D3

Curative surgery

The following criteria have to be fulfilled for curative resection :

1. No distant metastasis (Virchow's node, lung, liver, bone and peritoneal metastasis)
2. Serosa is not involved by tumour
3. At least 5cm tumour-free margins
4. Resection level exceeds the level of nodal clearance
5. Safe and well functioning reconstruction

In the event of fixity to surrounding structures, if it can be removed en bloc, this still amounts to curative resection. Pancreas and spleen are to be preserved as it increases morbidity without altering prognosis.

Palliative surgery

When cure is not possible, palliation is indicated. Symptoms that require palliation are pain, vomiting, dysphagia, bleeding and malaise. Palliative gastrectomy, if possible, should be done. It involves total or partial resection of stomach without nodal clearance. In unresectable tumours, Tanners anterior gastrojejunostomy is done

to palliate vomiting. Dysphagia is palliated with intubation or laser lumenisation. Enteral nutrition is accomplished by feeding gastrostomy or jejunostomy. All of these procedures can be performed laparoscopically.

Laparoscopic Gastrectomy

The original work for laparoscopic resection was carried out by Ohgami et al at Keio University in Japan. Laparoscopy-assisted resection and Billroth I reconstruction for early cancer of antrum was first done by Japanese surgeon Kitano in 1992. Dr. Goh first performed the laparoscopic Billroth II gastrectomy for ulcer disease in 1992 and Dr. Azagra in Belgium performed the first laparoscopic gastrectomy for cancer in June 1993. Since then there are several reports of laparoscopic gastrectomy performed for gastric cancer including hand-assisted, laparoscopic assisted as well as total laparoscopic procedures. The most important issues in laparoscopic gastrectomy for cancer are oncologic clearance, port site metastasis and benefits over open gastrectomy. These issues now have been resolved by several prospective randomised trials.

Technically, laparoscopic gastrectomy for cancer is safe, meets oncologic clearance criteria and there is no evidence for increased port-site metastasis. Uyama et al reported in the year 2000 on laparoscopic distal gastrectomy with D2 lymph node dissection for advanced stage gastric cancer located in the middle or lower third of the stomach. There are few reports of laparoscopic operation for advanced stage proximal gastric cancer.

Recently, the conventional open surgical procedures for advanced stage proximal gastric cancer have diversified. Many Japanese gastric surgeons select from three types of gastrectomies for advanced stage proximal gastric cancer, according to the stage of the cancer:

Type I (function-preserving) gastrectomy is total or proximal gastrectomy with preservation of the spleen and pancreas.

Type II (function-preserving) is total or proximal gastrectomy with preservation of the pancreas, but combined with splenectomy.

Type III (radical) is total gastrectomy combined with distal pancreatico-splenectomy.

Among the various types of function – preserving gastrectomy and limited gastrectomies performed in an attempt to improve postoperative quality of life for early gastric cancer, laparoscopic gastrectomy with preservation of the vagus nerve is one of the noteworthy procedures. In Japan, it is increasingly being preferred for early gastric carcinoma due to the following advantages:

(i) lower incidences of postoperative diarrhoea and gallstone formation

(ii) Maintenance of pancreatic function

(iii) Minimal postoperative pain

(iv) Quicker mobilization

(v) Shorter hospitalisation

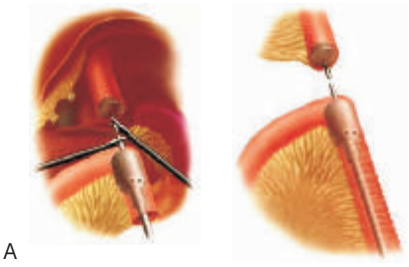
(vi) Improved cosmesis

Now, laparoscopic gastrectomy with its various modifications is emerging as the treatment of choice in resectable gastric cancer and other laparoscopic gastric procedure to provide palliation in unresectable gastric cancers.

When comparing open versus laparoscopic gastrectomies, the following issues have to be addressed. They are operative parameters like blood loss, time and cost; patient parameters like pain, length of hospital stay and return to activity; oncological considerations like extent of resection, lymph node dissection, recurrence rate and survival rate. Some comparative studies conclude that there is a tendency for less extensive lymph node dissection in the laparoscopic group, but for the same level of dissection a similar number of nodes was found.

Palliative Laparoscopic Surgery

The use of laparoscopy for palliation is much less controversial than for curative surgery, as oncologic clearance is not attempted. Patients with incurable or unresectable gastric cancer benefit from minimally invasive palliative surgery because of reduced morbidity and reduced hospital stay. Palliative surgery can be resection, bypass or enteral feeding. Limited gastrectomy is done to palliate symptoms like bleeding. For inoperable cancers involving the outlet with obstruction, palliation is achieved by laparoscopic anterior gastrojejunostomy. Compared with open procedures, these patients benefit from shorter hospital stay, lower blood loss, less pain, similar or shorter operative time, satisfactory palliation and similar results. When even bypass is not feasible, a feeding gastrostomy or jejunostomy for enteral feeding is done. Several laparoscopic techniques have been described – whatever technique is chosen, the results are satisfactory



A B

Side-to-Side Oesophagojejunal Anastomosis (A – laparoscopic; B – open)

KMCH EXPERIENCE

We prefer laparoscopic distal radical and total gastrectomy with D2 lymphadenectomy for all early and resectable gastric cancers. Oesophagogastrectomy is done for tumours of the cardia and reconstruction by oesophagogastrostomy performed within the mediastinum. We performed D2 lymphadenectomy in all cases of gastric cancer. Mean numbers of lymph nodes harvested were 22.5 and major complications rate were 5.75% (duodenal blow-out in 1, duodenal stump bleed in 1, chylorrhea in 1, and anastomotic leak in 2 patients). The conversion rate and 30 days postoperative mortality were 0%. Compared to open gastrectomy series, patients who underwent laparoscopic gastrectomy had a shorter hospital stay, decreased complication rate, decreased postoperative pain and rapid return to normal activity.

About 25 years after the introduction of therapeutic laparoscopy, its role in gastric surgery is becoming accepted. Laparoscopic gastrectomy with its various modifications accompanied by lymph node dissection for early gastric carcinoma is technically feasible, safe and oncologically correct. It has many advantages over conventional open surgical techniques. Although operative duration is currently long, laparoscopic gastrectomy is beneficial for early-stage gastric malignancies. More comparative studies have to be done to prove beyond doubt that laparoscopic gastrectomy for cancer stomach is superior to the open procedure.

At present time, techniques and equipment are available to perform most of the resections and reconstructive procedures. These advanced procedures are being done only by expert laparoscopic surgeons, but will become more common in future due to better understanding of technical and oncological impact of minimally invasive techniques, training and education.

LIVER TUMOURS

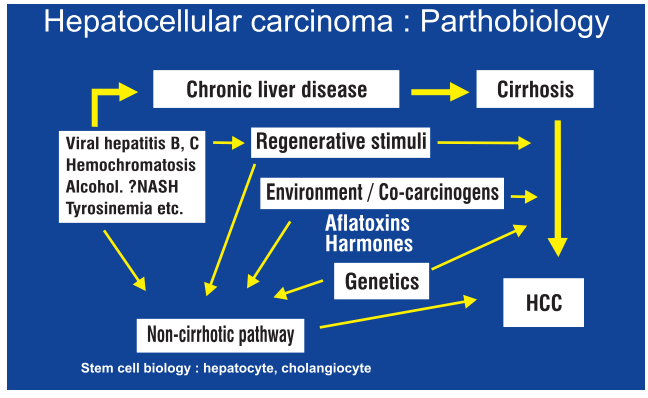
Dr. S. Paulvannan
Department of Surgery

Background

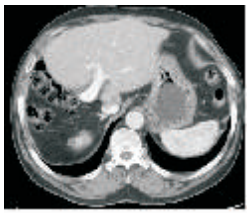
Hepatocellular carcinoma (HCC) is the common primary malignancy of the liver and occurs predominantly in patients with chronic liver disease and cirrhosis.. HCC is now the third leading cause of cancer deaths worldwide, with over 500,000 people affected. The presentation of HCC is now increasingly recognized at a much earlier stage due to the routine screening of patients with known cirrhosis, using cross-sectional imaging studies and serum AFP levels.Incidental on a routine/surveillance USS/CT, anorexia, weight loss, RUQ discomfort, signs of CLD, paraneoplastic syndromes and as an emergency with a ruptured tumour.

Assessment

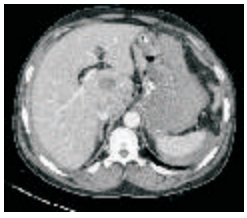
Triple phase CT scan: Highly accurate in the diagnosis and characterization of HCC with a sensitivity of 68% (95% CI 55–80) and a specificity of 93% (95% CI 89–96). Classic CT findings of HCC include a hypervascular pattern with arterial enhancement and rapid washout during the portal venous phase. Other features include visualization of a tumour capsule, demonstration of an internal mosaic resulting from variable attenuation within the tumour, and portal vein branch invasion. CT volumetry is very useful in measuring the FLR (Future Liver Remnant). MRI: An excellent method to characterize HCC with a sensitivity of 81% (95% CI 70–91) and a specificity of 85% (95% CI 77–93).



To biopsy or not?



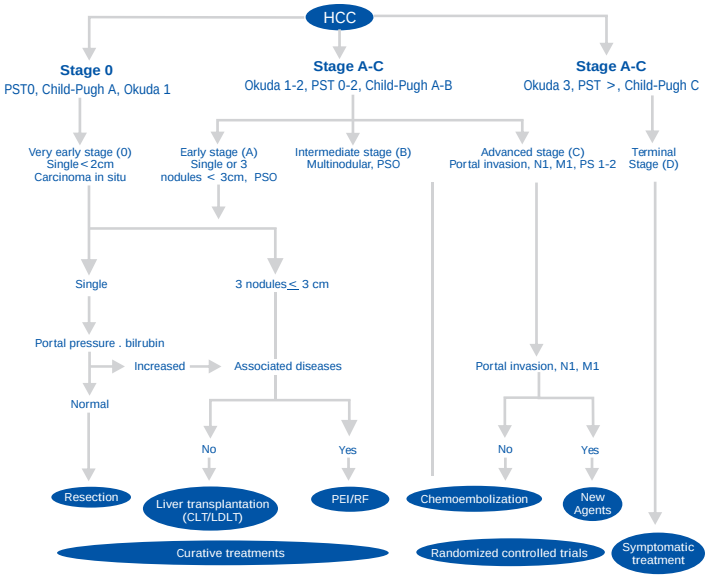
Post-hepatectomy image



Ruptured caudate lobe HCC

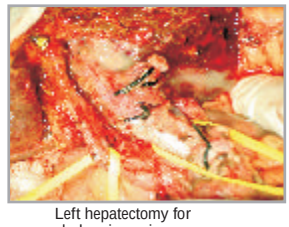
The decision to biopsy a lesion suspected of being HCC is the subject of ongoing controversy. Procedure related morbidity, needle tract seedling and false negative result should be balanced against the benefit of confirmation of HCC. Biopsy is not indicated in patients with typical imaging features on the background of CLD and a raised AFP. In lesions less than 1 cm, close follow up with no biopsy is recommended. Biopsy of the FLR is very useful to exclude cirrhosis prior to a major liver resection. It is indicated in lesions of 1 to 2 cm size and prior to initiating palliative procedures.

Selection of patients for surgery

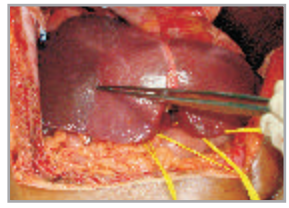


Surgical resection of HCC

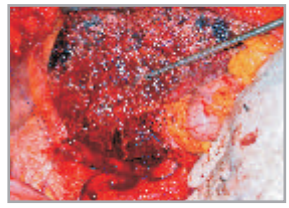
Better understanding of liver anatomy, advances in the technique of liver resection, better patient selection, expert anaesthetic management with a low CVP anaesthesia, improved postoperative care and high volume centers have resulted in a dramatic reduction in preoperative morbidity and mortality. Liver resection is the operation of choice for patients with tumours less than 5 cm in the absence of cirrhosis. These patients can often tolerate resection of up to 50% of the total liver volume with the operative mortality rate of less than 5% and a morbidity rate of 20% with 5-year survival rates of up to 74%. In non-cirrhotics, up to 80% of the liver can be removed safely. Most of the complications are managed non-operatively.



Left hepatectomy for cholangiocarcinoma



Line of demarcation to ascertain level of resection



Completed extended right hepatectomy

Pathologic characteristics associated with a higher rate of recurrence include tumour at the resection margin, cirrhosis, vascular invasion, advanced tumour grade, number of tumour nodules, microvascular portal vein thrombosis, a preresection serum AFP level of greater than 10,000 ng/mL, large intraoperative transfusion requirements, preoperative AST greater than twice normal, and diagnosis of hepatitis C.

Liver transplantation

Compared with resection for hepatocellular carcinoma, orthotopic liver transplantation (OLT) offers several potential advantages. Complete hepatectomy eliminates the possibility of local recurrence at the resection margin and removes the cirrhotic liver. Liver transplantation also eliminates concerns about the capacity of the postresection liver remnant to provide adequate liver volume. Milan criteria patients with established cirrhosis and a single hepatocellular carcinoma ($\leq$5 cm in diameter) or up to 3 hepatocellular carcinomas (all $\leq$3 cm in diameter) have a 4-year overall survival rate of 85% and a tumour-free survival rate of 92%.

Additional strategies:

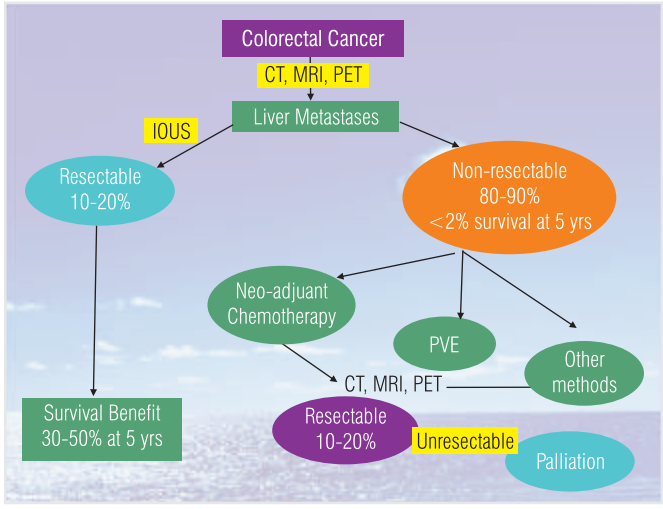
Living donor liver transplantation (LDLT) and split liver transplant. These techniques expand the organ pool and appear to offer equivalent survival to whole organ transplant. They have also been used in patients undergoing transplantation whose tumour burden exceeds the Milan criteria.

Nonsurgical therapies

TACE (Transcatheter Arterial ChemoEmbolization), TheraSphere (150 Gray brachytherapy), a variety of hormonal and biologic agents like Tamoxifen, antiandrogens (eg, cyproterone, ketoconazole), Interferon, Interleukin 2 (IL-2), Octreotide and recently, the novel agent, Sorafenib.

Ablative therapies

As a bridge to transplant by reducing the risk of tumour progression or as a palliative procedure to extend disease-free survival. Ablative procedures, including PEI (Percutaneous Ethanol Injection), RFA (Radio Frequency Ablation) and cryotherapy can be performed percutaneously, laparoscopically, or using an open surgical approach.



CHOLANGIOCARCINOMA

Hilar cholangiocarcinoma (Klatskin tumour) is an uncommon neoplasm arising from the biliary confluence or the right or left hepatic ducts. Treatment for hilar cholangiocarcinoma has remained challenging because of the lack of effective adjuvant treatment and the locally advanced nature of the tumour at presentation. Unlike intrahepatic or distal cholangiocarcinoma, which can be treated with hepatic resection or Whipple's operation respectively, surgical management of hilar cholangiocarcinoma has evolved since its original description. In the last 20 years, surgical management of hilar cholangiocarcinoma has evolved due to improvements in pre-operative imaging and an enhanced appreciation of tumour growth characteristics. This has resulted in the recognition that liver resection is necessary to manage both direct hepatic invasion and the longitudinal intraductal extension that typically characterize hilar cholangio-carcinoma.

Pre-operative assessment:

Hilar cholangiocarcinoma is suspected when the USS shows a dilated IHBR and collapsed CBD and GB. CT scan is the next step and MRCP remains the investigation of choice to assess the extent of the tumour. Preoperative PTC guided biliary drainage is essential to improve the function and Portal Venous Embolization (PVE) is required in selected cases to increase the volume and function of FLR. Staging laparoscopy is done in all cases to exclude any occult metastases.

Surgery

The “no-touch” surgical resection aiming at achieving negative resection margins and radical resection includes a major hepatectomy based on the extent, PV involvement and liver atrophy, caudate lobe resection, hepatoduodenal lymphadenectomy with or without portal vein resection. The resectability rate was highly variable, ranging between 28 and 95%, and curative resection rates ranged between 14 and 95%. The 5-year survival rate varies from 25 to 40%. Unfortunately, the early experience with OLT had been disappointing.

Conclusion

Surgical resection remains the mainstay of treatment of hilar cholangiocarcinoma. Negative resection margins enhanced by major hepatic resections are associated with improved outcome. Preresectional management with biliary drainage, portal vein embolization and staging laparoscopy should be considered in selected patients. Additional evidence is needed to fully define the role of orthotopic liver transplantation. Improvements in adjuvant therapy are necessary for improving long-term outcome.

LIVER SECONDARIES

The words “liver metastases” generally mean a very poor prognosis. Most patients die within 12 months if untreated and survival beyond 5 years is unheard off. Mean survival is between 12-24 months with chemotherapy. However, long-term survival and cure after liver resection is possible in selected patients with liver metastases from Colorectal, renal, adrenal and NETs. The absolute contraindication for liver resection is unresectable extrahepatic disease and metastatic peri portal node. Therapeutic strategies for the “mariginal cases” include chemotherapeutic downsizing, PVE, two-stage hepatectomy, combining in situ RFA and vascular resection. Published the literature from high volume centers around the world have shown a 5 year survival of 35-40%.

KMCH EXPERIENCE

Liver surgeries are done routinely mainly for malignant and also for some benign conditions. Cases are evaluated thoroughly and all the treatment options as well as the risks associated are explained to the patients. Major liver resections are done by open method and minor/segmental resections are done laparoscopically. With the good team of specialists involved in the care of these patients, it is not surprising that KMCH is becoming a high volume center for liver and pancreatic cancer surgeries.

PANCREATIC TUMOURS

Dr. S. Paulvannan
Department of Surgery

Introduction

The pancreas is the tenth most common site of new cancers and pancreatic cancer is the fourth leading cause of cancer deaths among men and women, responsible for 6% of all cancer-related deaths. It is notoriously difficult to diagnose in its early stages.

Etiology

The predisposing factors include smoking, obesity and dietary factors, diabetes mellitus, chronic pancreatitis, heriditary pancreatitis and genetic factors.

Prognosis

The collective median survival time for all patients is 4-6 months. 60-70% of patients have locally advanced or metastatic disease at presentation and 10-20% of patients are medically unfit to undergo curative resection. In patients who undergo curative resection, median survival ranges from 12-19 months and 5-year survival is 20-30%.

Symptoms and signs

Initial symptoms are often nonspecific and subtle in onset. Symptoms include anorexia, nausea, fatigue, epigastric or back pain, significant weight loss and recent onset of diabetes. The most characteristic sign of pancreatic carcinoma of the head of pancreas is painless obstructive jaundice, often preceded by pruritus. Examination reveals jaundice, palpable liver with distended gallbladder. In distal tumours, the tumour may be palpable. Presence of ascitis and left supraclavicular node usually indicate metastatic disease.

Assessment

General: CHG, RBS, Creatinine, LFT, PT, Na, K, Cardio-respiratory assessment

Diagnosis and Staging: USS, Triple phase spiral CT, MRI, EUS, PET-CT, Staging laparoscopy and tumour markers (CA19-9, CEA)

Approach Considerations

After a thorough preoperative workup, the surgical approach can be tailored to the location, size, and locally invasive characteristics of the tumour. There is consensus on the fact that surgery is the primary mode of treatment for pancreatic cancer.

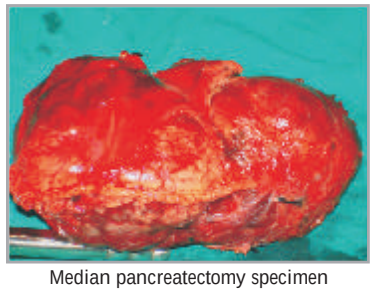
Curative resections include Whipple's pancreaticoduodenectomy with or without sparing of the pylorus, total pancreatectomy; and distal pancreatectomy. Each procedure has its own set of preoperative complications and risks, which are taken into account and discussed with the patient when considering the resection.

At initial presentation, only 20% of patients present with early disease suitable for curative resection (Stage I, II) and the rest present with locally advanced disease (Stage III) and/or distant metastases (Stage IV). Extrapancreatic disease, invasion of the superior mesenteric, celiac, and hepatic arteries precludes a curative resection.

Historically, vascular involvement has been considered a contraindication to curative resection. However, the invasion of the superior mesenteric or portal vein is no longer an absolute contraindication and it is agreed that venous involvement is a function of tumour location rather than an indicator of aggressive tumour biology.

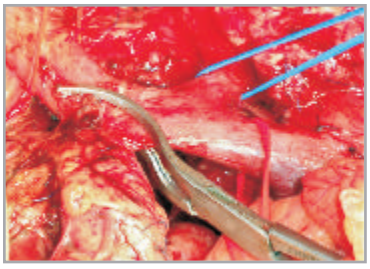
Pancreaticoduodenectomy (Whipple Procedure)

Patients who will most likely benefit from this procedure have a tumour located in the head of the pancreas or the periampullary region as well as cholangiocarcinoma (bile duct cancer), and duodenal tumours. The standard operation involves removal of pancreatic head, duodenum, gallbladder, and the antrum of the stomach, with surgical drainage of the distal pancreatic duct and biliary system, usually accomplished through Roux-en-y anastomosis to the jejunum. The primary reason for removing so much of the intraabdominal structures is that they all share a common blood supply. This surgery carries an overall mortality rate of 3-5% and 20-30% morbidity rate. The complications include pancreatic anastomotic leak (5-20%) with resultant sepsis and bleeding and delayed gastric emptying(25%).


Median pancreatectomy specimen

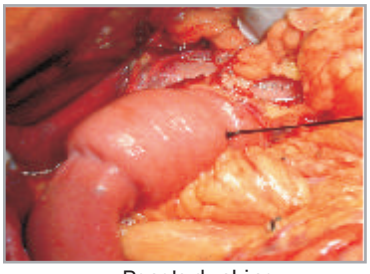
Preoperative ERCP and biliary drainage is found to be associated with

increased post operative infective complications in randomised trials and is not recommended routinely. PPPD (Pylorus Preserving PD) is a modification to prevent DGE and in fact found to have no superiority over the standard PD. Extended lymphadenectomy and total pancreatectomy are advocated to improve the survival and unfortunately associated with increased mortality and morbidity without survival benefit. Tumours involving the SMV or PV can be resected partially or completely and reconstruction is done using native veins (ie, internal jugular, greater saphenous, or splenic) or prosthetic grafts. There are no differences in median hospital stay, morbidity, mortality, tumour size, margin and nodal positivity and survival. Various modifications to the pancreatic anastomoses have been practiced to reduce pancreatic leak and Peng's dunking pancreaticojejunostomy followed by a duct-to-mucosa anastomosis are the favorites in our unit. Laparoscopic Whipple's resection is also feasible with comparable results.

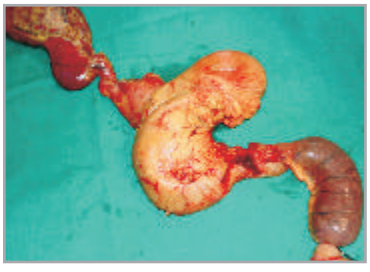


Pancreatic head tumour involving portal vein

Distal Pancreatectomy (DP)



Peng's dunking pancreaticojejunostomy

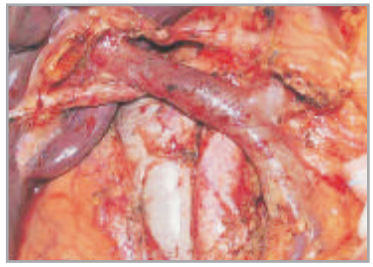


Resected specimen

This procedure has a lower mortality rate (2%) than the standard Whipple procedure. Essentially, DP may be an effective procedure for tumours located in the body and tail of the pancreas. Unfortunately, masses located in this area present later than the periampullary tumours and hence have a higher unrespectability rate. The procedure involves isolation of the distal portion of the pancreas containing the tumor, followed by resection of that segment, with oversewing of the distal pancreatic duct. Complications involve pancreatic stump leak, hemorrhage, and endocrine insufficiency.

Total Pancreatectomy

This procedure is rarely performed and has the highest associated mortality rate (8.3%). It is only indicated for multifocal tumours or large tumours involving the neck of the pancreas. The complications include brittle diabetes and pancreatic exocrine deficiency.



Radical dissection of Whipple's operation showing the complete anatomy

Palliative Therapy

Pain Narcotics, EUS guided neurolysis of the celiac ganglia, radiation therapy

Jaundice

Endoscopic placement of plastic or metal stents or by choledocho-jejunostomy or cholecystojejunostomy.

Duodenal obstruction

Gastrojejunostomy or an endoscopic duodenal stenting.

Chemotherapy

Gemcitabine based chemotherapy (GEMCAP trial and FOLFRINOX trials).

Adjuvant Therapy

Several studies (GITSG, ESPAC, CONKO) suggested the possibility that chemotherapy, with or without radiation therapy, would significantly improve median survivals following surgical resection of operable disease. Adjuvant therapy with gemcitabine is now accepted as standard therapy for surgically resected pancreatic cancer.

Neoadjuvant therapy

The use of chemotherapy and/or radiation therapy in the neoadjuvant setting has been a source of controversy. Several trials conducted at M.D. Anderson Cancer Center have shown median survival as high as 25 months.

No form of neoadjuvant therapy in pancreatic carcinoma is regarded as a standard form of therapy and this remains an area for clinical trial study.

Cystic Neoplasms Of Pancreas

These constitute 10% of pancreatic neoplasms, and are being detected with increasing frequency. Many of the lesions are small and asymptomatic and may be associated with pancreatitis or have malignant potential. Preoperative imaging using CT and MRCP and determination of cyst pathology using EUS is essential as the biological behaviour is vastly different. The management is complex and evolving.

Types

Among these neoplasms, (SCN) serous cystadenomas (32 to 39 %), (MCN) mucinous cystic neoplasms (10 to 45 %), and (IPMN) intraductal papillary mucinous neoplasms (21 to 33 %) represent the majority of the cases encountered in our practice.

Treatment

Serous cystadenomas does not have any malignant potential and doesn't need resection. Mucinous cystic neoplasms and IPMNs (main duct and >3cm sized branch duct) have a high malignant potential and need resection. In the absence of invasive disease, prognosis is excellent after appropriate surgery.

PANCREATIC RESECTION WORK AT KMCH

Pancreatic tumours are managed routinely at KMCH with excellent results. About 80% of the resections are for cancer and the remaining resections are for cystic neoplasms, NETs, solid pseudopapillary tumour and trauma. There was no surgical mortality in the last 3 years and morbidity is around 20%, wound infection being the commonest. Pancreatic leak rate is 15% and all of them were biochemical grade A leaks and managed conservatively with no change in the clinical course. All the patients had R0 resection and selected patients are offered adjuvant chemotherapy. During the follow up (3 to 36 months), 20% have recurrence or distant metastases requiring palliative chemotherapy. The multi disciplinary approach to the management of these cases has resulted in excellent results. As a high volume centre, the results are on par with the major centres around the world.

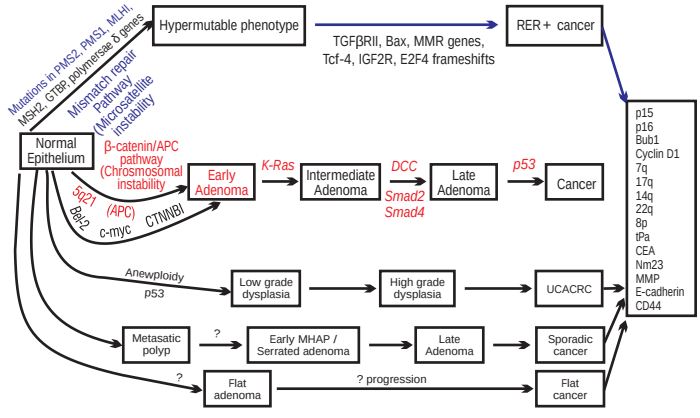
COLORECTAL CANCER

Dr. A. Ganesan
Department of Surgery

Worldwide, colorectal cancer is the fourth most common cancer in men and the third most common cancer in women. The reported incidence in India is around 5 per 100000 populations (Chennai registry-GLOBOCAN 2008) in contrast to 25-45 per 100000 in western countries. A study by American Cancer society finds that incidence of colorectal cancer rate between 1983 and 2002 have increased in 27 out of 51 developing countries including India. The proposed reason is industrialisation and western diet.

About 75 % colorectal cancers are sporadic in nature where there is no family history of CRC, while 20% are familial in the sense that there is a family history but there is no identifiable gene mutation. 5% are hereditary where there is germ line mutation either in the APC gene in case of FAP accounting for 1% or in MMR genes in case of HNPCC accounting for 4 % of colorectal cancers. Colorectal cancer is a genetic disease but not necessarily inherited.

Pathways of colorectal cancer development



Signs and symptoms

Most colorectal cancers are asymptomatic. When they do produce symptoms, here are some of them:

- Rectal bleeding with a change in bowel habit to looser stools and/or increased frequency of defecation persistent for 6 weeks
- Change in bowel habit as above without rectal bleeding and persistent for 6 weeks
- Rectal bleeding persistently without anal symptoms
- A definite palpable right sided abdominal mass
- A definite palpable rectal mass
- Unexplained iron deficiency anaemia

Diagnosis

Most rectal cancers are within the reach of the examiners finger.

Colonoscopy is the gold standard and is useful in diagnosis and prevention of CRC. It is proven that adenomatous polyps are the precursors for CRC, and if this adenoma can be removed during a colonoscopy, it prevents the future development of CRC. Virtual colonoscopy or a barium enema can be considered for those who refuses colonoscopy or if the colonoscopy is incomplete. In future, identification faecal DNA might make it simpler.

Staging

Staging is done by way of high resolution CT scan of chest and abdomen. For Rectal cancers MRI of the rectum is mandatory. It gives accurate local staging. ERUS can be done in early tumours where a local excision is contemplated.

Management

Colorectal cancers are curable in their early stages. Surgery is the first line management. Surgery depends on the site of tumour in the colon. The surgery has to be radical with lymphadenectomy. Adherent organs can be resected en bloc if this can be done without a major problem. Presence of liver metastasis and pulmonary metastasis is not contraindication unless the disease is widespread.

Adjuvant treatment

Dukes A or T1-2 N0: As the risk of local or systemic recurrence is low after a good radical surgery, adjuvant chemotherapy is not beneficial.

Dukes B T3 N0: adjuvant chemotherapy is indicated in selective groups.

Dukes C Any T N1-2: The risk of recurrence is high around 50% and adjuvant chemotherapy is beneficial in reducing the risk of recurrence.

Immunotherapy

Metastatic CRC patients without KRAS mutation will benefit from anti-EGFR therapy like cetuximab and panitumumab. Patients with KRAS mutant tumours (around 40%) do not benefit from expensive anti-EGFR therapy.

Rectal cancer management

Accurate local staging by MRI will help to decide the management. T1, T2 early T3/N1 tumours are treated by surgery. Surgery is performed in the TME plane with preservation of autonomic nerves. With the latest advance in technology sphincter preservation is possible in most instances of rectal cancers avoiding a permanent stoma.

Preoperative short course radiotherapy for 5 days is considered in select cases. Late T3 or T4 tumours, N2 tumours are treated by concurrent long course chemoradiation followed by surgery. Patients are selected for postoperative adjuvant therapy on similar lines to colon cancers.

Survival

In general colorectal cancers carry better prognosis than most cancers.

Stage	5 year survival
Dukes A	90-93%
Dukes B	60-78%
Dukes C	20-50%
Dukes D	6%

Laparoscopic resection

Laparoscopic colectomy (Fig. 1-6) was first started in 1990. Initial results were not encouraging because surgeons were not experienced and the technology was limited. Improvement in technology and enthusiasm from surgical community had resurrected the interest. Laparoscopic surgery is associated with less pain, earlier recovery, shorter hospital stay and less wound related complications. Several

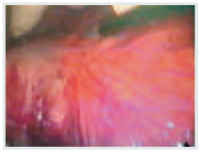


Fig 1. Transection of the hepatocolic ligament

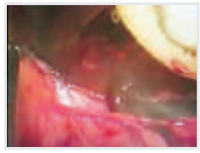


Fig 2. Transection of the white line

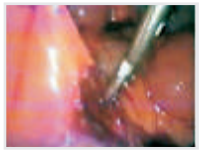


Fig. 3 Making the window of the iliacecal mesentery for division of the

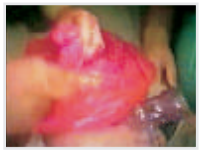


Fig. 4 The dissected colon is going to resect under wound protection of plastic bag

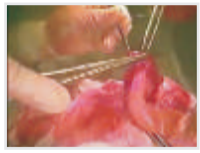


Fig. 5 Anastomosis after colon resection

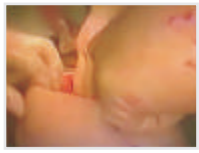


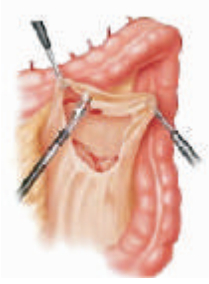
Fig. 6 Preparation before wound closure

randomised trials were conducted across Europe and America.

Name of Trial	Country of Origin	Laparoscopic (LAC)	Open (OC)
CLASICC trial 1996-2002	27 UK centres 2:1 randomisation	526	268
CLASICC trial 1997-2003	6 European Countries	534	542
COSTG trial 1994-2001	48 Institution across America	435	437
Lacv et al	Spain	111	108

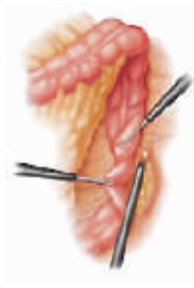
Landmark trials

First three trials showed there was no difference in the disease free or overall survival between both groups. The 4th trial had actually shown a better oncological outcome in the laparoscopic group. (LAC was independently associated with reduced risk of tumour relapse (hazard ratio 0·39, 95% CI 0·19—0·82), death from any cause (0·48, 0·23—1·01), and death from a cancer-related cause (0·38, 0·16—0·91) compared with OC. This superiority of LAC was due to differences in patients with stage III tumours).



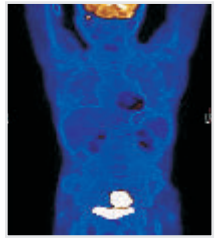
Cochrane review 2008: Long-term results of laparoscopic colorectal cancer resection

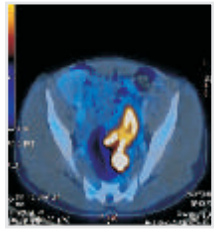
Out of 32 reported trials, 12 randomised controlled trials, involving 3346 patients were analysed. This concluded Laparoscopic surgery for colon cancer is a safe procedure that is associated with a survival rate equal to survival after open surgery. The procedure can therefore be offered routinely to patients in hospitals where surgeons with sufficient experience in laparoscopic colon surgery are available.



NICE Guidelines 2006

Laparoscopic resection should be given as a potential alternative to open resection for individuals with colorectal cancer when performed by appropriately trained surgeons.

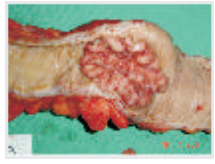




PET Scan

CASE #1

A 32-year old male presented with a 3-month history of rectal bleeding. Rectal examination showed a circumferential tumour within easy reach of finger. Colonoscopy and biopsy confirmed adenocarcinoma at 5cm from anal verge. CT and PET scan showed no metastatic disease. MRI showed the tumour as early T3. The patient underwent laparoscopic low anterior resection and covering ileostomy. Patient recovered well. Ileostomy was closed 1 month later. Patient is doing well without any recurrence 16 months after surgery



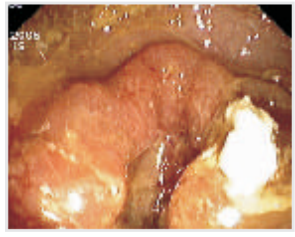
Resected specimen

CASE # 2

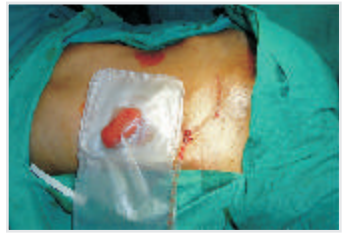
A 67-year old male doctor presented with rectal bleeding and altered bowel habit. Colonoscopy showed a tumour at 12 cm. CT scan showed solitary liver metastasis and a possible lung metastasis. He underwent laparoscopic anterior resection and recovered well. He had completed his chemotherapy. He is waiting to undergo hepatic and lung resection.

CASE #3

A 68-year old male presented with anaemia and bleeding per rectum

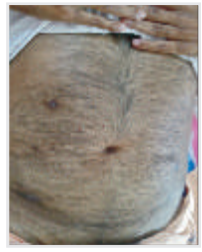


Colonoscopic view of the tumour



Postoperative picture showing temporary ileostomy and small incision to extract specimen

for 1 month. Per rectal examination showed a tumour at 6cm from anal verge. CT scan showed T2 rectal tumour and locally advanced tumour in transverse colon and a tumour in the ascending colon. Standard treatment would be a pan-proctocolectomy and ileostomy, but the patient vehemently opposed the idea of a stoma. So a Laparoscopic assisted panpro-ctocolectomy and double stapled ileal-pouch-anal anastomosis was performed. Patient is doing well 4 months after surgery. In conclusion at KMCH we offer state of the art care at all levels of the management of colorectal cancers including minimally invasive surgery comparable to any centre in the world.



3 months postoperative scar – hardly visible

EARLY COLONIC CANCER CURED BY ADVANCED ENDOSCOPIC TECHNIQUE

Dr. M. Ganesh
Department of Medical Gastroenterology

Introduction

The incidence of cancer is on the rise in India. Various technologies are now being invented to diagnose treat and fight against cancer. Gastrointestinal tract is one of the commonest sites for malignancy. In some cases, early cancer arising in the GI tract can be removed by advanced endoscopic technique EMR (endoscopic mucosal resection).

What causes cancer?

The colonic inner lining (mucosa) slowly grows abnormally and turns into cancer over a period of time. These early colonic mucosal over-growths are called polyps and they are the precursor for majority of the cancer. About 2/3rd of the polyps are adenomas and they have a malignant potential. The excess growth can vary from a very small size to large size. The colonic polyps are detected during routine surveillance and they are removed by endoscopic methods.

The polyps are divided broadly into two types :

- Pedunculated (polyp attached to the inner colonic lumen by a stalk) hanging like a pendulum.
- Sessile (without a stalk and directly arises from the colonic mucosa)

Pedunculated polyps are removed by endoscopic snare techniques. But sessile polyps are always difficult to remove, especially large sessile ones. In my 12 years experience as a consultant Interventional endoscopist, we have done many complicated EMRs of the gastrointestinal tract. Here we discuss a case of endoscopic removal of a very large sessile lower rectal polyp, which had turned into early cancer proved by biopsy.

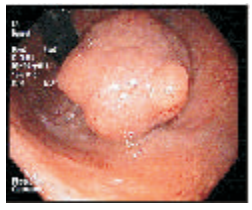


Fig. 1 Endoscopic view of low rectal polyp

A 70-year old gentleman presented with recurrent per rectal bleeding for the past 6 months. Flexible colonoscopy revealed a 3cm large sessile polyp (Fig. 1) located 4 cm from anal verge. Biopsy of the polyp showed villous adenoma with high-grade dysplasia, and the possibility of an underlying malignant (cancer) transformation was strongly suspected. We decided to attempt endoscopic excision of the tumour.

Any sessile polyp more than 2 cm in diameter is difficult to remove by endoscopic technique and it carries the risk of perforation and bleeding complication from the GI tract. It needs expertise and technical skills to perform these procedures. EMR is a novel endoscopic technique, which was used to remove the polyp completely (Fig. 2 & 3).

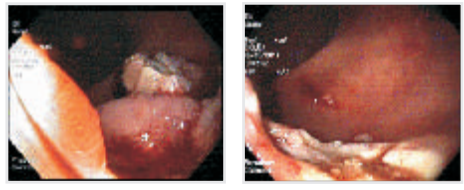


Fig. 2 & 3 Completion of endoscopic polypectomy

In this technique the flat polyp is lifted out from the underlying layers using saline/ xylocaine and the entire polyp is removed endoscopically. The resected specimen, as suspected, showed cancer involving only mucosa (inner lining of the colonic wall) considered as 'intramucosal' early colonic cancer. There was no infiltration detected to the deeper layers. The tumour was also removed with a clear margin of 5mm, almost similar to a surgical resection. The procedure was completed in 25 minutes. He was discharged immediately following the procedure without any complications. He is doing fine after 2 months follow up.

OVARIAN CANCER

Dr. Athima Pathak
Department of Obstetrics & Gynaecology

Ovarian cancer is the second most common gynaecologic cancer. It caused nearly 14,000 deaths in 2010 alone. It has a 47% survival rate, up from 38% in the late 1970s. During that time, the overall five-year survival rate for all cancers improved more significantly: 68% for the general population diagnosed in 2001, up from 50% in the 1970s.

Signs and symptoms

The signs and symptoms of ovarian cancer are most of the times absent, and when they exist they may be subtle and nonspecific. Most women with ovarian cancer report one or more symptoms such as: abdominal pain or discomfort, abdominal mass, bloating, back pain, urinary urgency, constipation, ascites, tiredness and a range of other non-specific symptoms, as well as more specific symptoms such as pelvic pain, abnormal vaginal bleeding or involuntary weight loss.

Causes

In most cases, the exact cause of ovarian cancer remains unknown. The risk of developing ovarian cancer appears to be affected by several factors:

1. Older women, and in those who have a first or second degree relative with the disease, have an increased risk
2. Hereditary caused by mutations in specific genes (BRCA1, BRCA2, genes for hereditary non-polyposis colorectal cancer)
3. Infertility
4. Endometriosis
5. Those who have never been pregnant
6. Use of estrogen replacement therapy

Hormones

Women who used oral contraceptives for 10 years had about a 60% reduction in risk of ovarian cancer. The ovaries contain eggs and secrete the hormones that control the reproductive cycle. Removing the ovaries and the fallopian tubes greatly reduces the amount of the hormones estrogen and progesterone circulating in your body. This can halt or slow breast and ovarian cancers that need these hormones to grow. The link to the use of fertility medication, such as Clomiphene citrate, has been controversial.

Diagnosis

Diagnosis of ovarian cancer starts with a physical exmination (including a pelvic examination), a blood test (for CA-125). In addition, serum alpha-fetoprotein (AFP) and lactate dehydrogenase (LDH) should be measured in young girls and adolescents with suspected ovarian tumours because the younger the patient, the greater the likelihood of a malignant germ cell tumor. A complete blood count (CBC) and serum electrolyte test should be obtained in all patients. The new test approved by the FDA in 2011, OVA1 improves ovarian cancer detection over CA125 blood test and clinical assessment.

Pelvic imaging with CT scan and transvaginal ultrasound are essential. For very young patients, MRI may be preferred to rectal and vaginal examination. The diagnosis must be confirmed with surgery to inspect the abdominal cavity via diagnostic laparoscopy, take biopsies and look for cancer cells in the abdominal fluid.

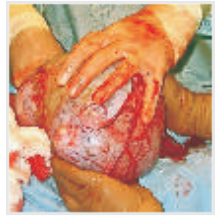
Classification

Ovarian cancer is classified according to the histology of the tumour, obtained in a pathology report. Histology dictates many aspects of clinical treatment, management, and prognosis.

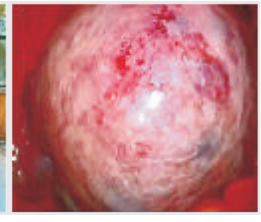
1. Epithelial carcinoma: commonest, types are serous tumour, endometrioid tumour and mucinous cystadenocarcinoma.
2. Sex cord-stromal tumour, including estrogen-producing granulosa cell tumour and virilizing Sertoli-Leydig cell tumour or arrhenoblastoma.
3. Germ cell tumours.
4. Mixed tumours, containing elements of more than one of the above classes of tumour histology.
5. Secondary cancer, common primary cancers are breast cancer and gastrointestinal cancer (Krukenberg cancer).

Management

Treatment usually involves chemotherapy and surgery, and sometimes radiotherapy. Surgical treatment may be sufficient for malignant tumours that are well-differe-ntiated and confined to the ovary. Addition of chemotherapy may be required for more aggressive tumours that are confined to the



Malignant ovarian cyst



Laparoscopic view of ovarian tumour

ovary. For patients with advanced disease a combination of surgical reduction with a combination chemotherapy regimen is standard. Borderline tumours, even following spread outside of the ovary, are managed well with surgery, and chemotherapy is not seen as useful.

Surgery is the preferred treatment and is frequently necessary to obtain a tissue specimen for differential diagnosis via its histology. Improved survival is attributed to more accurate staging of the disease and a higher rate of aggressive surgical excision of tumour in the abdomen by gynaecologic oncologists as opposed to general gynaecologists and general surgeons.

The type of surgery depends upon how widespread the cancer is when diagnosed, as well as the presumed type and grade of cancer.

The options are: unilateral oophorectomy, bilateral oophorectomy, salpingectomy, and hysterectomy. For Stage 1 disease, especially in young females who wish to preserve their fertility, a unilateral salpingo-oophorectomy is ideal. In advanced malignancy, where complete resection is not feasible, tumour debulking surgery is done. Minimally invasive surgical techniques may facilitate the safe removal of very large (greater than 10 cm) tumours with fewer complications of surgery.

Prognosis

Ovarian cancer usually has a poor prognosis. It is disproportionately deadly because it lacks any clear early detection or screening test, meaning that most cases are not diagnosed until they have reached advanced stages.

More than 60% of women presenting with this cancer already have stage III or stage IV cancer, when it has already spread beyond the ovaries. The five-year survival rate for all stages of ovarian cancer is 45.5%. For cases where a diagnosis is made early in the disease, when the cancer is still confined to the primary site, the five-year survival rate is 92.7%.

CASE

Mrs.B a 55-year old P2 L2 admitted with increasing size of abdomen for 9 Months. She attained menopause 4 years ago.

No post-menopausal bleeding.

Abdominal examination revealed a large mass of about 32 wks of gravid uterus size, firm, mobile and non-tender.

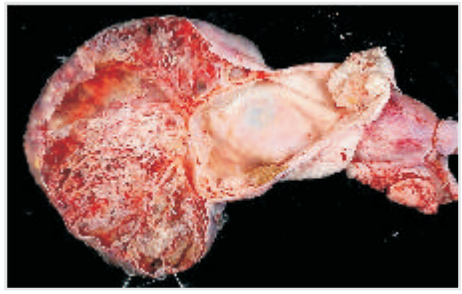
Vaginal examination revealed the vault to be atrophic, cervix was high up, uterus size could not be made out, a large mass was felt occupying the entire pelvis.

CA 125: 489.9

FNAC: peritoneal fluid was positive for malignant cells.

PAP Smear: normal.

USG: a large multiloculated cystic mass lesion occupying the entire abdomen with few septation showing internal vascularity; mural nodule noted; cystic areas packed with few internal echoes; uterus and ovaries were not assessed.



Resected specimen of ovarian tumour

Treatment

Laprotomy, total abdominal hysterectomy, bilateral salpingo-oopherectomy, peritonectomy, omentectomy, bilateral external iliac lymphadenectomy, and para-arotic node removal.

Histopatholigical examiniation: bilateral papillary serous cystadenocarcinoma, well-differentiated type with predominant cystadenoma component with evidence of stromal invasion, capsular breach and Psammamatous calcification. So patient was planned for adjuvant chemotherapy.

CANCER CERVIX

Epidemiology

Worldwide, cervical cancer is 12th most deadly cancer in women. It affects about 16 per 100,000 women per year and kills about 9 per 100,000 per year. Approximately 80% of cervical cancers occur in developing countries.

Signs and symptoms

The early stages of cervical cancer may be completely asymptomatic. Vaginal bleeding, contact bleeding or (rarely) a vaginal mass may indicate the presence of malignancy. Also, moderate pain during sexual intercourse and vaginal discharge are symptoms of cervical cancer. In advanced disease, metastases may be present in the abdomen, lungs or elsewhere. Symptoms of advanced cervical cancer may include: loss of appetite, weight loss, fatigue, pelvic pain, back pain, leg pain, single swollen leg, heavy bleeding from the vagina, leaking of urine or faeces from the vagina and bone fractures.

Causes

Human papillomavirus (HPV) infection with high-risk types has been shown to be a

necessary factor in the development of cervical cancer. HPV DNA may be detected in virtually all cases of cervical cancer. Not all of the causes of cervical cancer are known.

Screening

The widespread introduction of the Papanicolaou test for cervical cancer screening has been credited with dramatically reducing the incidence and mortality of cervical cancer in developed countries. If pre-malignant disease or cervical cancer is detected early, it can be monitored or treated relatively non-invasively, with little impairment of fertility. Screening is typically recommended starting three years or more after first sex, or starting at age 21 to 25.

Recommendations for how often a Pap smear should be done vary from once a year to once every five years, in the absence of abnormal results. Guidelines vary on how long to continue screening, but well screened women who have not had abnormal smears can stop screening about age 60 to 70. New technologies like 'liquid based cytology' commissioned by NICE has now been incorporated within the screening programme. Although it was probably intended to improve on the accuracy of the Pap test, its main advantage has been to reduce the number of inadequate smears from 9% to 1%. The HPV test is a newer technique for cervical cancer triage that detects the presence of human papillo-mavirus infection in the cervix. It is more sensitive than the Pap smear, but less specific and its role in routine screening is still evolving.

Treatment

Stage IA : hysterectomy

Stage IB & IIA : radical hysterectomy OR radiotherapy

Stage IIB & IVA : radiotherapy and cisplatin based hemo-therapy.

Stage IVB : combination of hycamtin + cisplatin

Prognosis

Prognosis depends on the stage of the cancer. With treatment, the 5-year relative survival rate for the earliest stage of invasive cervical cancer is 92%, and the overall (all stages combined) 5-year survival rate is about 72%. With treatment, 80 to 90% of women with stage I cancer and 50 to 65% of those with stage II cancer are alive 5 years after diagnosis. Only 25 to 35% of women with stage III cancer and 15% or fewer of those with stage IV cancer are alive after 5 years. As the cancer metastasizes to other parts of the body, prognosis drops dramatically because treatment of local lesions is generally more effective than whole body treatments such as chemo-therapy.

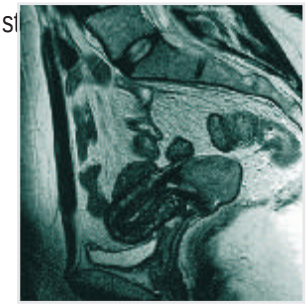
CASE

Mrs.K a 61-year old lady admitted with complaints of postmenopausal bleeding for 2 days. She attained menopause 10 years back. She got married at the age of 27 years and is a nulligravida.

P/V: Cervix is high up, feels firm, posterior fornix has restricted mobility, hard mass in the posterior fornix.

Pap smear: high-grade squamous intra-epithelial lesion.

Endometrial curettings: adenocarcimoma – moderately differentiated type possibly arising from the endocervix, infiltrating into deeper st



MRI showing cancer cervix

Resected specimen of cancer cervix

CA 125: 127.9

USG: Cystic lesion size 5.9 x 4.6 x 4.1cm with solid component and internal vascularity; another small cystic lesion 2.8 x 1.5cm noted adjacent to ovaries; ovaries are not separately seen.

Physical examination: Thin built, not ana emic, afebrile, no pedal edema, soft abdomen.

MRI: A 6 x 7cm growth in the endocervix, continuous into the endometrium of the uterus, adherent to the anterior rectal wall, minimal invasion in the pouch of Douglas, no abdominal nodes, liver is normal.

Treatment: Wertheim's hysterectomy

Uterine artery was transected at the level of the ureter thus preserving the branch to the ureter. Cardinal ligament was not divided near the lateral wall but instead was divided at about its mid position near the ureteral dissection. The anterior vesicouterine ligament is divided, but posterior vesicouterine is preserved. Small margin of vagina was excised as well.

RENAL CELL CARCINOMA

Dr. P. B. Barani Kumar, Dr. Kuppurajan
Department of Urology

Epidemiology

The incidence of renal cell cancer (RCC) has been rising steadily. Nearly 51190 new diagnoses and 12890 deaths reported in the United States alone in 2007. It is more common in men than women: the male-to-female ratio is 1.6:1 and has been decreasing over the last decade. Blacks have a slightly higher rate of RCC than whites. In Europe the incidence of RCC has doubled in the period from 1975 to 2005. RCC accounted for 3777 deaths in the UK in 2006; male 2372, female 1820.

Classification

- Clear cell renal cell carcinoma
- Papillary renal cell carcinoma
- Chromophobe renal cell carcinoma
- Collecting duct carcinoma

Risk factors

- Cigarette smoking
- Obesity
- Hypertension
- Family history
- Occupational exposure to cadmium
- Dialysis patients with acquired cystic disease of kidney (30 times greater risk)
- von Hippel-Lindau disease, hereditary leiomyoma RCC Syndrome and Birt-Hogg-Dubé Syndrome
- Sickle cell trait
- Hysterectomy

Symptoms

Unfortunately, RCC symptoms usually do not appear until the disease has progressed. In fact, it is usually detected "accidentally" when another symptom or condition is being investigated. Symptoms of RCC include:

- Blood in the urine
- Abdominal mass
- Pain in the flanks or lower back
- Unintentional weight loss
- Fatigue
- Unexplained fever
- Unexplained anaemia

Diagnosis

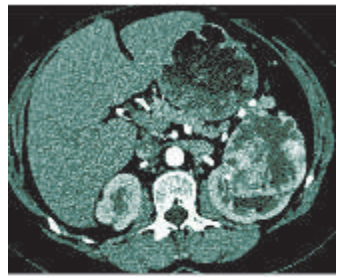
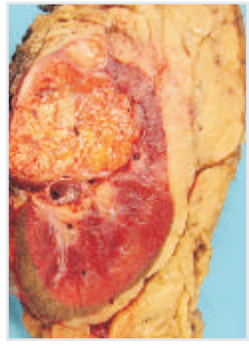


Fig. 1 CT Scan of RCC–right kidney

A palpable mass or the finding of a mass on an X-ray done for another reason are usually what leads a physician to suspect kidney cancer. The first step in diagnosing RCC is through various imaging tests and blood test. Ultrasound, CT scan (Fig. 1), MRI, and intravenous pyelogram (IVP) are all imaging methods that may be used to help diagnose kidney cancer. Ultimately, it is a kidney biopsy that will confirm the presence or absence of cancer and what type it is. A kidney biopsy can be done through a fine needle aspiration biopsy technique. If cancer is found, more tests may need to be done to determine if the kidney cancer has spread to nearby tissues and organs. This is called staging.

Treatment Options

Surgery to remove all or part of the kidney is standard treatment for renal cell carcinoma. People with early stage RCC are the best candidates for surgery, but those who have a later stage of the disease may not be healthy enough to withstand surgery.


Resected specimen of RCC

Radiation therapy is most often used only for palliation. Chemotherapy is not commonly used in treating renal cell carcinoma. It is often used along with immunotherapy or when immunotherapy is not effective. Immunotherapy, also called biologic therapy, is a treatment option for many types of kidney cancer include interferon or interleukin-2. Several targeted therapy drugs have been approved for use in some patients with kidney cancer. These drugs block and

prevent the growth and spreading of malignant cells. They do this by attacking the cells directly or preventing the growth of blood vessels that provide tumours nourishment to grow.

Surgical Treatment

Nephron-Sparing Nephrectomy

Organ preserving approach is the order of the day for most of the malignancies now. In RCC, radical nephrectomy has been the gold standard surgery until now. But now with increasing number of incidentally diagnosed renal mass lesions by ultrasound or CT done for other conditions, the concept of Nephron Sparing Surgery (NSS) has gained importance. Since there is an increase in incidence of diabetes and hypertension, which may affect the kidney it is better to preserve as much functioning parenchyma as possible. NSS as treatment of choice was described by Czerny in 1890. Now the interest in NSS has increased because of advanced renal imaging, improved method of preventing ischemic renal injury, increased incidence of incidental tumour and good long term results.

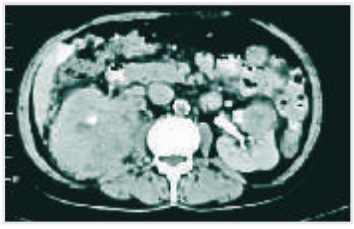


Fig. 2a Bilateral RCC (absolute indication)

Fig. 2b Unilateral RCC < 4cm size (elective indication)

Indications

a) Absolute indication in which patient will become anephric following surgery like bilateral RCC (Fig. 2a) or tumour in a solitary kidney (Fig. 2c)

b) Relative indication in pre-existing renal diseases like stone disease, chronic pyelonephritis or VUR

c) Diabetes, hypertension, nephro-sclerosis and von Hipple Lindau Disease

d) Elective indication include patient with unilateral tumour and good functioning opposite kidney. Usually done for exophytic tumours which are < 4 cm or in patients who are good candidates for surveillance (Fig. 2b)

Contraindications

Patients with multiple tumours, with features of regional metastasis, tumour > 4 cm and centrally located tumour. But now size criteria has expanded and data is available even for tumours with size > 4 cm which show good long-term survival benefit.

Evaluation

All the patients require local staging using contrast CT with vascular reconstruction or MRI. Metastatic evaluation with chest CT and Bone scan can be done.

Technique

Nephron sparing surgery can be done by both open surgical method and minimal invasive method. The basic steps are complete mobilization of the kidney with pernephic fat attached to the tumour (Fig. 3 a,b,d), renal arterial control and infusion of mannitol before renal artery clamping and cooling of kidney by either surface cooling with ice slush (Fig. 3c) or intra-arterial cooling or intra-pelvic cooling and resection of tumour with a 1-cm margin.

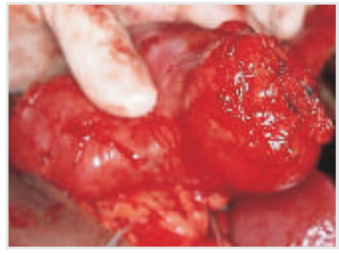


Fig. 3a exophytic mass lesion

Fig. 3b Surface cooling with ice slush

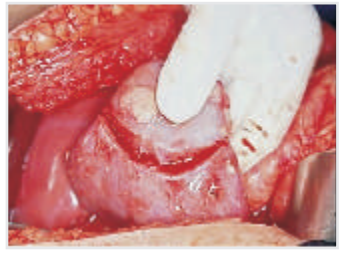


Fig 3c: Excision of mass with 1 cm margin

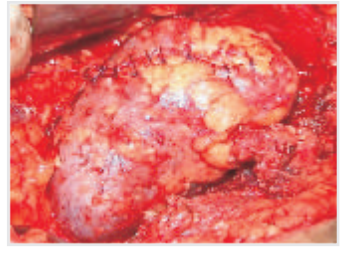


Fig 3d: after parenchymal closure

In minimally invasive approach there is always a concern about haemostasis , vascular control and negative margin status without direct tactile input. Now with the advent of vessel sealing devise, intra-arterial renal cooling and better minimally invasive instruments and robots available to do this, the results can be replicated as in open surgery.

Advantage

NSS has the advantage of preservation of maximal renal parenchymal tissue, which might avoid development of end stage renal disease. After taking into consideration various factors like surgical time, vessel clamping time, hypothermia, infusion of mannitol in patients with absolute indication, the raise in serum creatinine was from 1.4 +_ 0.5 mg/dl to 1.8 +_ 0.8 mg/dl. It has a great advantage preserving the renal parenchyma in patients who are prone to develop bilateral RCC.

Disadvantage

The main disadvantage is the development of local recurrence, (incidence of 0 – 10 %:) the reason being tumour multifocality rather than incomplete resection. Overall incidence of multifocality is 6.5-28% (Novick et al). Interestingly, the risk of multifocality in tumour < 4 cm is only 5%. Normal resection margin was considered as 1cm, present studies have shown that recurrence was independent of width margin around the tumour, now it is proposed that margin of 5 mm is sufficient but frozen section is mandatory.

Patients undergoing NSS with > 50% reduction in functioning parenchyma are at risk of hyperfiltration injury with development of proteinuria, focal segmental glomerulosclerosis and progressive renal failure. Efforts to prevent the damaging effects of renal hyperfiltration primary focus are on low protein diet and ACE inhibitors. The optimal time for initiating the regimen is not clear and it may be best to implement this therapy as early as possible to obviate the maladaptive responses that can lead to progressive sclerosis and renal failure.

Complications of Surgery

No surgery is without complications. The chance of intraoperative or postoperative bleeding is about 0- 5 %. In case of postoperative bleeding, it can be controlled by angio-embolisation, though rarely these patients may need completion nephrectomy. Urine leak or fistula can rarely occur, which can be averted by proper closure of the calyx. Rarely acute renal insufficiency may occur, usually in patients with bilateral RCC or solitary kidney with tumours undergoing NSS.

Follow up

Most important aspect of NSS is follow-up, if we feel that a particular patient is not fit for surveillance, ideally NSS should not be attempted. In T1 (< 2.5cm) disease, patient's yearly physical examination with blood test and radiological imaging are not required in view of low risk of recurrence. In T2 (> 2.5 cm) disease, patients will need yearly physical examination, blood test, chest x-ray and CT scan every 2 years.

Discussion

Nephron sparing surgery is widely accepted treatment option in solitary kidney with RCC, bilateral RCC and patients with RCC and renal impairment, but this technique has also been accepted for RCC < 4 cm with normal contralateral kidney. Several studies have showed comparable cancer specific survival rate for lower stage disease with NSS and radical nephrectomy. A study from Cleveland Clinic has shown no postoperative tumour recurrence and cancer-specific 5-year survival rate was 100% in T1-2 stage RCC. Butler noted cancer specific 5-year survival in radical nephrectomy and NSS was 97% and 100% respectively. Now, the organ conserving approach is being propagated for RCC, size criteria of < 4 cm for elective indication is expanded to 7 cm and some are claiming similar cancer free survival rates after elective NSS and radical nephrectomy. Randomized prospective studies are required to prove the result, until then 4 cm criteria holds good.

Other relative issues like location of tumour in case selection for NSS has to be addressed. Most surgeons would prefer to avoid NSS for centrally located tumours due to technical difficulty and doubts about clearance. Various studies have proved that there are no biological differences between centrally and peripherally located tumours, both NSS and radical nephrectomy produce the same result in these tumours.

The primary advantage of elective NSS is preservation of renal function and the very real possibility that lesions might be benign. Frank et al has demonstrated that statistically significant increased renal insufficiency occurs after radical nephrectomy compared to NSS. Analysis of cost and morbidity after taking into consideration of minimally invasive surgery is comparable for both radical nephrectomy and NSS. Interestingly, reports suggest that quality of life and psychological adaptation are better for elective nephron sparing surgery than for radical nephrectomy.

NSS is ideal in patients with Von Hippel- Landau, where the tumours tend to recur and multifocal disease is common. These patients require resection of both solid and cystic components. After NSS, they require close observation because they may develop local recurrence with need for repeat surgery. Nephron sparing surgery can

be considered curative in tumours < 4cm with good cancer free survival rate.

Laparoscopic Radical Nephrectomy

Following the first laparoscopic nephrectomy in 1990, this procedure rapidly became an accepted alternative for the surgical management of T1 renal tumours. At present, laparoscopic radical nephrectomy (LRN) is considered the standard of care for management of T1 RCC not amenable to nephron-sparing surgery. Over time, minimally invasive approaches have been extended towards treatment of larger lesions with several groups reporting equivalent oncologic outcomes for stage T2 and even T3 lesions (Fig. 4 a,b,c).

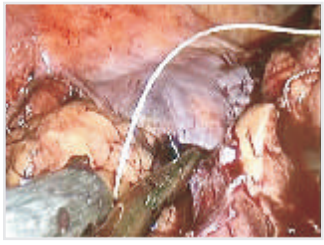


Fig. 4a Dissection of Gerota's fascia

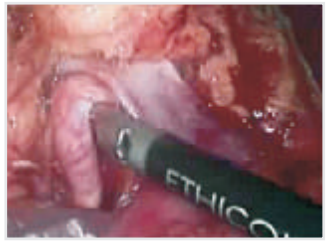


Fig. 4b Isolation of renal pedicle

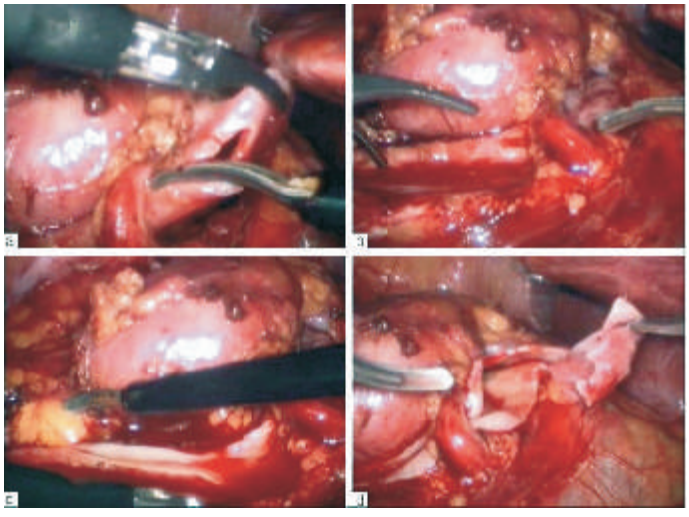


Fig. 4c Steps of laparoscopic nephrectomy

The standard advantages of laparoscopy over open surgical approaches are well known. Intraoperative blood loss, length of hospital stay, analgesic requirements, and time of convalescence have all been shown to be lower for laparoscopic surgery, without sacrificing oncologic efficacy. For these reasons, LRN has become the standard of care for renal masses <7 cm in size. Now, series demonstrating LRN for larger, locally advanced tumours (T2 and greater) are being reported.LRN uses a minimally invasive approach to perform exactly the same procedure that is done in open radical nephrectomy. The operation involves removal of the kidney along with Gerota's fascia. If the adrenal gland is involved, it can be removed as well. The operation also often includes removal of the lymph nodes that are around the kidney.

Candidates

There are a number of important patient and tumour parameters that are critical in deciding the type of treatment that is best for kidney cancer. The decision on a proper strategy for the treatment of kidney cancer is challenging and should be made by each patient in conjunction with an urologist.

- Considerations are numerous but include:
- Size and general radiographic appearance of the mass
- Local anatomy of the mass
- Overall age and health condition of the patient
- Number of lesions in the kidney
- Patient personal preference
- Overall kidney function

Advantages / Disadvantages

As LRN, by definition, uses a laparoscopic approach, patients get all the benefits of a minimally invasive procedure. Blood loss is significantly less with laparoscopic radical nephrectomy compared to open radical nephrectomy. Pain is also significantly less with LRN. The decreased blood loss, pain, and trauma to the body also result in faster overall recovery from the operation. With LRN, patients return to full activity in less than half the time it takes to recover from open radical nephrectomy.

As LRN is a relatively new and somewhat technically challenging operation, it is not offered at all centers. A disadvantage of the procedure is that only few doctors offer this procedure to their patients, so the procedure is not available to all patients.

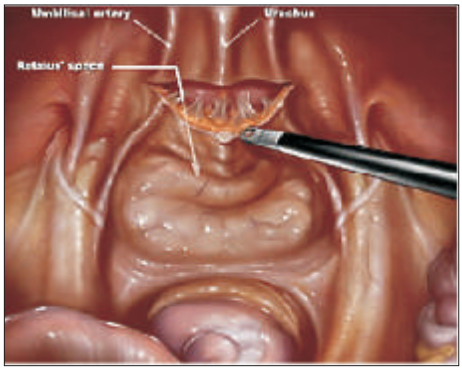
KMCH EXPERIENCE

The department of urology has now started to perform NSS and LRN in our cancer patients, offering all the benefits. Our complication rates match international standards. Initially, experience was gained by performing laparoscopic nephrectomies for benign diseases, including donor nephrectomies in a transplant setting.

Laparoscopic Radical Prostatectomy

Currently, open radical prostatectomy for prostate cancer is still the 'gold standard'. Laparoscopic radical prostatectomy (LRP) is a modern form of radical prostatectomy that may replace the open technique in future. Contrasted with the open form of the surgery, laparoscopic radical prostatectomy does not make a large incision. The laparoscopic and open forms of radical prostatectomy physically remove the entire prostate and reconstruct the urethra directly to the bladder.

Laparoscopic radical prostatectomy and open radical pro-statectomy differ in how they access the deep pelvis and generate operative views. In contrast to open radical pro-statectomy, the laparoscopic radical prostate-ctomy makes no use of retractors and does not require that the abdominal wall to be stretched for the duration of the operation.



Laparoscopic anatomy of Pelvis

Less bleeding means a more stable operative course and less need for transfusions; this in turn means less risk of such complications as allergic reactions and infections. It means less anaemia, fatigue, and cardiovascular complications. There is also very little pain because of the minimal nature of the physical access. One of the main benefits of the procedure is rapid discharge after surgery by the next day. The procedure takes at least five hours and as long as eight hours for the average urologist, without a bilateral lymph node dissection, compared to 2.5–3 hours when done by an open technique with an incision, with a completed lymph node dissection.

Progression of laparoscopic radical prostatectomy

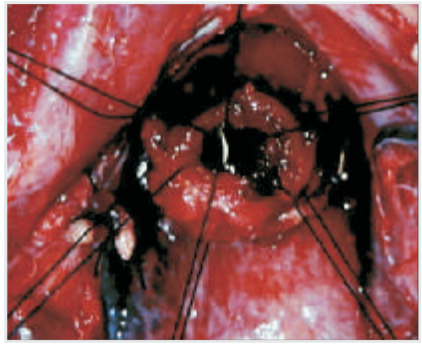
The first successful laparoscopic radical prostatectomies were performed by Schuessler in 1992 and 1997. Unfortunately, the technique did not gain widespread acceptance because of its extreme technical difficulty and because it offered no advantage over the criterion standard of open radical retropubic prostatectomy. The initial series reported operative times that ranged from 8 to 11 hours and a mean hospital stay of 7 days. The laparoscopic approach gained new attention when 2 French groups published their experience with laparoscopic radical prostatectomy in 1999 and 2000.

They reported modifications to the original technique, resulting in operative times that ranged from 4 to 5 hours and had a mean blood loss of 402 ml. The authors also reported a decreased mean hospital stay, due predominantly to earlier removal of the Foley catheter.

Even in the hands of these skilled laparoscopists, nerve-sparing dissection and construction of the urethrovesical anastomosis were demanding.

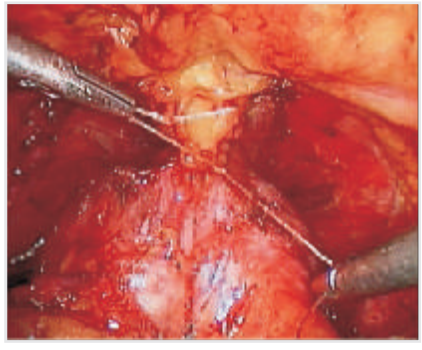
With advances in medical technology, improved optics, and the widespread use of new laparoscopic instrumentation such as ultrasonic cutting and coagulating devices (eg, Harmonic scalpel), laparoscopic radical prostatectomy began to gain acceptance and was increasingly performed in several high-volume centers worldwide. However, the technical demands of laparoscopic radical prostatectomy prevented its widespread use by the average urologist and thus limited penetration.

Laparoscopic Transperitoneal Approach (Montsouris technique)



The widely used trans peritoneal approach is described by French urologists Guillonneau and Vallancien.

Laparoscopic Extraperitoneal Approach



The laparoscopic extra peritoneal approach was first described by Raboy, from Staten Island University Hospital, New York, as a simulation of the open retroperitoneal appro-ach to the prostate.

UNKNOWN PRIMARY CANCER – PATHOLOGIST'S APPROACH AND IMPLICATIONS IN TREATMENT

Dr. K.H. Kantharaju
Department of Pathology

Since last year, we treated five unusual cases presenting with cancer at metastatic sites. Two patients (middle-aged lady and elderly male) presented with lymph node swellings in neck and biopsy revealed metastatic adenocarcinoma and poorly differentiated carcinoma respectively, but primary site was not found. Third patient was a middle-aged lady presented with swelling in right axilla and biopsy revealed metastatic adenocarcinoma (possibly from breast origin, but no primary lesion found in the breast).

Fourth case was elderly male who presented with multiple lesions in liver and core biopsy revealed metastatic adenocarcinoma, with no evidence of any primary lesion in spite of further investigations. Fifth case was elderly male who presented with left inguinal lymph node swelling and biopsy & immunohistochemistry (IHC) study revealed metastatic transitional cell carcinoma, where as no primary lesion found elsewhere in the body. These types of cases that present with metastasis and where the primary site remains unknown till death are termed as Unknown Primary Cancer (UPC).

What is 'Unknown Primary Cancer'?

As doctors are aware, most cancer patients present with primary lesion with or without spread to other distant sites (metastasis). However, about 10 to 15% of patients initially present with metastatic disease alone and primary lesion was not found in spite of extensive investigations. These cases are labeled as Unknown Primary Cancers (UPC). This entity does not represent one clearly defined cancer but encompasses a multitude of clinical presentations and pathologies. The usual sites that are involved in UPC are:

1. Lymph nodes -11% (including cervical, supraclavicular, axillary, inguinal or abdominal)
2. Solid organs (like liver -24%, lung/pleura – 12%, bones – 08%, brain -02%, others-08%, multiple sites – 26%)
3. Serous cavities

The median survival of UPC patients in the past was only four months, but there are subgroups of patients with much longer survival times. Recently, five favourable sites have been recognized which include:

1. Women with isolated Axillary Adenocarcinoma (from breast)
2. Women with peritoneal deposits of Papillary Serous Adenocarcinoma (from ovary or peritoneum)
3. Young men with extragonadal germ cell syndrome (from Germ Cell Tumors of Testis)
4. Men with blastic bone metastasis and tumour staining/ elevated serum levels of S. PSA (Prostatic Specific Antigen)
5. Isolated neck nodes involved with Squamous Cell Carcinoma (Head and neck as primary)

Other UPC subsets are less understood including poorly differentiated neuroendocrine carcinomas and UPCs presenting at a single site. Although these favorable subsets comprise 20% of all UPCs, specific treatment result in greatly improved outcomes. The other 80% of UPC form an unfavorable subset (usually adenocarcinomas) has been improved with broad spectrum antineoplastic agents. The newer combinations are the state of art therapies for these patients, but recent biologic insight has resulted in a less empiric and more site-specific therapeutic approach.

Thus, identification of specific type of cancer in UPC is very crucial before starting any treatment. Diagnostic cellular pathology has improved remarkably in the last decade. IHC is now able to reliably pinpoint the specific lineage of these neoplasms that are difficult to diagnose by routine Hematoxylin and Eosin (H&E) light microscopy.

Pathologic Evaluation of UPC

The pathologic approach to metastasis with UPC is step-wise and uses the clinical context, morphology and where necessary, IHC. IHC has revolutionized our ability to type and subtype tumours and for adenocarcinomas, to predict their likely primary site. Pathologist should be aware of age, clinical context of individual case including age, gender, metastatic site and staging information.

A stepwise pathologic approach will be described. First, is there a lesion present and if so, is it malignant? Second, what broad type of cancer is it – Carcinoma (broadly including Germ cell tumor), Melanoma, Lymphoma or Sarcoma?. Third, if it is carcinoma, then what subtype is it – Adenocarcinoma, Squamous / transitional cell carcinoma or neuroendocrine type? Fourth, if it is adenocarcinoma, can we predict where the tumour originated?

Most UPCs are in fact carcinomas of unknown primary site. The

relative frequency of Carcinoma subtypes – 80 to 90% Adenocarcinomas, 5 to 10% Squamous(and transitional) cell carcinomas, and 5% neuroendocrine carcinomas. Most of the rare cases of UPC in childhood are embryonal (small round blue cell) tumours.

Pathologic samples submitted in UPC

Solid organ metastases are commonly sampled by needle core biopsy; lymph nodes and superficial masses are assessed on fine needle aspiration cytology (FNAC) and occasionally requires excision biopsy; and serous effusions are evaluated by effusion cytology. Specimen will be usually small and used carefully and proceed to ancillary investigations (like IHC) in a step-wise manner. In core biopsies, metastatic tumour is often focally seen and might miss the tumour as well.

In these cases, deeper sections, known as levels will be taken. Broad distinction of tumours is often possible on morphology (H&E secions), because tumours resemble the tissue from which they originate. Confirmation of morphologic diagnosis and further sub-typing is done by Immunohistochemistry study, which is very well established in recent times. First set of IHC evaluations should be done only after seeing the tumour in initial H&E sections.

Role of IHC in UPCs

IHC is the demonstration of specific proteins (antigen) on a section of tissue or cells. This is achieved using a specific antibody, which reacts with the antigen and highlighted by colouring agent. The resulting staining is usually crisp and brown/red in colour. Most antibodies are named for their antigens. IHC is often assumed as straight forward, but is potentially variable and subject to variations. Therefore it is important to ensure best practice in both technical performance and microscopic interpretation. IHC staining should always be used in a panel and interpreted in the morphological and clinical context.

At the cellular level, IHC staining may be nuclear, cytoplasmic and/or membranous and it is important to know the expected pattern. The staining intensity may range from weak to moderate to strong. There is often significant heterogeneity of staining within a tumour, which can be a problem in small sized core biopsies. In view of moderate sensitivity and specificity of tumour markers, tumour heterogeneity and technical and interpretive variation, it is always important to use antibodies in panels along with controls. The results of IHC panels are usefully represented in the form of IHC data tables.

First line IHC panel generally include an epithelial marker (AE1/3 or Pancytokeratin), a melanocytic marker (eg, S-100), and a lymphoid marker (eg,CLA). Positivity with any of these markers will generally lead to a second IHC panel to confirm the diagnosis and provide tumour sub-typing. If the tumour is negative for first line markers, then Vimentin (to r/o sarcoma), germ cell tumour markers and CLA negative hematolymphoid markers should be used.

Basic IHC panel presented as Data Table

CLA	S-100	AE 1/3 or Pancytokeratin	Diagnosis	Action
+	--	--	Lymphoma	Subtyping
--	+	--	Melanoma	Further IHC confirmation (HMB- 45, Melan - A)
--	--	+	Carcinoma	Further subtyping
--	--	--	Sarcoma/ rare tumor	Further IHC workup
+	+	+	Rare tumor	Further IHC workup

In carcinoma (including germ cell tumour), specific IHC marker study done for subtyping:

1. Squamous cell carcinoma- CK 5/6, p63
2. Transitional cell carcinoma- CK7/20, Uroplakin 3
3. Adenocarcinoma – EMA, CK 7/20 (further IHC done to predict specific site)
4. Neuroendocrine Carcinoma – Chromogranin, Synaptophysin, NSE
5. Germ cell tumours – PLAP, OCT4, HCG, AFP, CD30

Adenocarcinomas are not only the most common cancers overall, they also make up at least 60% and possibly up to 90% of UPCs. One autopsy study (Pentheroudakis et al) revealed incidence of adenocarcinoma at primary site as follows :

Lung – 27%, Pancreas – 19%, Bowel – 11%, Kidney/Adrenals – 06%, Liver/Bile duct – 06%, Stomach – 05%, Ovary/ Uterus – 03 %, Prostate – 02 % and others – 21%.

In Adenocarcinomas, site-specific markers should be used to know the possible primary site. Many IHC markers have been established with good reliability.

Prostate	–	PSA, PAP
Lung	–	TTF-1, CK 7 +
Breast	–	GCDFP-15, Mammoglobin, ER
Colon	–	CDX2, CK20, CK7-ve
Ovary	–	CA125, Mesothelin, WT1
Liver	–	Hepatocellular carcinoma – Hepar 1, canalicular pCEA
Kidney	–	Renal Cell Carcinoma – RCC, CD10
Thyroid	–	TTF-1, Thyroglobulin
Adrenal	–	Adrenocortical Carcinoma – Melan - A, Inhibin

Upper GI and pancreatobiliary tumours are the hardest to predict using IHC although some markers are shared (eg CDX2).

In Sarcomas –Vimentin, Desmin, Actin, Myo D1, Myogenin, S-100, CD34, c-kit (CD - 117), CD-99, etc are used to identify the specific lineage (like muscle, nerve, vascular, GIST, Ewings / PNET etc).

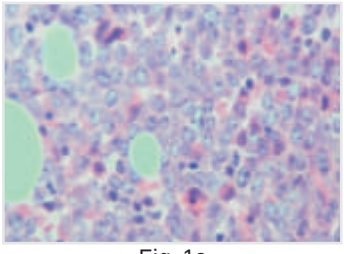


Fig. 1a

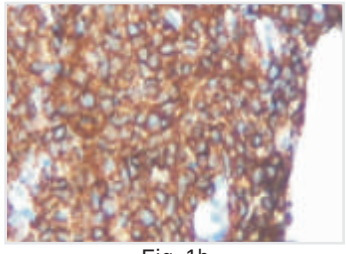


Fig. 1b

Fig. 1a Bone marrow biopsy - diffuse infiltration by large cells (on H&E)
Fig. 1b CD 20 + on IHC, final diagnosis was Non Hodgkin's Lymphoma – Diffuse Large B Cell (DLBCL) type.

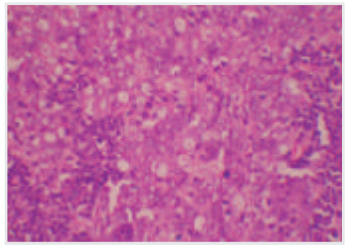


Fig. 2a

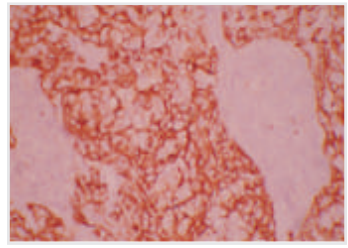


Fig. 2b

Fig. 2a Cervical Lymph node - diffuse infiltration by large cells (on H&E)
Fig. 2b IHC shows poorly differentiated carcinoma (Pancytokeratin marker positivity)

In Lymphomas, B-cell (CD 20,CD 79a,CD 19 etc), T-cell (CD 3) and other lineage markers (CD15, CD 30,etc) are used for sub typing.

At present, many basic questions regarding the pathobiology and pathophysiology of these tumours remain unanswered. There is no direct evidence that molecular genetic abnormalities in these tumours differ from those seen in metastatic cancers of known primary site.

Molecular profiling is a new technology that may facilitate identification of the tissue of origin and decrease the need for empiric treatment in future patients. UPC colon cancer profile can be identified and these patients respond well to current regimens for metastatic colorectal cancer.

Basic understanding of the molecular mechanisms responsible for the genesis, growth and metastasis of neoplastic cells will eventually lead to more effective therapy for many cancer patients, including those with UPC. Improved identification of the tissue of origin, as well as the incorporation of new-targeted agents into therapy, will continue to improve the treatment for patients with UPC. With the recent launching of Oncology Services at KMCH, Pathology department is also embarking on special laboratory techniques and IHC is one among them, which aids in planning the ideal treatment for specific type of cancer.

Take Control of Your Health and Reduce Your Cancer Risk

- Stay away from tobacco
- Maintain a healthy weight
- Get moving with regular physical activity
- Eat healthy with plenty of fruits and vegetables
- Avoid alcohol
- Know yourself, your family history and your risks
- Have regular check-ups and cancer screening tests

"THEY'RE ONCOLICIOUS!"

Dr. Aarthi Kannan, Dr. Sarada Krishnamurthy

(As told by the daughters of two prominent oncologists)

Edward Abbey once said, "Growth for the sake of growth is the ideology of the cancer cell".

You can always fight against something whose reason you know by eliminating the cause of the effect. But how on earth does one fight against something that has no apparent reason? Or something that has a reason that is beyond the scope of our current understanding?

We must have been about seven or eight years old when we became really curious about cancer. For our level of understanding, cancer was explained as something that simply grows. We imagined small round lumps – some big, some small and many, of course very oddly shaped. The fundamental question at that age was: "What's so bad about growing, daddy? We grow! Your beard grows, too!" The answer to that question was the simplified truth – "It's different. That lump is a very bad growth. It's kind of like a little monster inside of someone that'll eat them up".

"So you remove that monster and kill it?" we would ask. "Well, yes. That's how we fight it." With that answered, we thought our fathers were superheroes in the war against this evil.

Medical school wasn't far away.

With the introduction of Guyton and Robbins, a whole new world was unleashed. Guyton's Physiology explained cancer to us as an uncontrolled, undifferentiated growth of cells. It also introduced to young minds the concept of 'apoptosis', a process that keeps cancer cells in check – a form of programmed cell death, by which old or damaged cells die of their own accord.Robbins opened up a whole new world to us through 'neoplasia'. It was all about oncogenes and everything that triggered them, and all the mechanisms that put the 'tumour suppressor genes' to sleep! What happens when genes become confused (mutated) are that they start spilling out abnormal proteins and doing abnormal things. Hence, cells grow faster than the body can feed or handle it. After that, it is all about the war of cancer cells against the normal body cells.

Wow! So much for cancer!

We grew up watching and learning about those cute little molecular pathways, and diagrams of macrophages eating up cancer cells, of old cells agreeably shrinking and dying by apoptosis, hearing a little bit about Ubiqitin, a little bit of RB 13q14, a dash of targeted therapy and radiation therapy, and a pinch about the vinca plants.

This takes us straight back to the old days, when oncologists like our dads started off, but did not have fancy super specialization degrees or fellowships. They knew little about molecular pathways, for back then, these things were not even discovered. They had a very foggy idea about cancer. Yet, they did all they could with what they had. Physical examination, X-Rays and CT scans were sufficient for that time and age.

At the smallest of opportunities, with the least of technology and incredibly high levels of clinical acumen, they treated cancer. We've grown up watching these great doctors comforting patients, removing their fears, wiping their tears, giving them words of advice and solace – all the while mustering up the courage to fight cancer together as a team of patient and doctor. After many treatments, some patients would go home and come back with smiles and sweets as their doctors had given them a second life. Some went home, only to come back with tears, as the cancer had come right back! And others, never made it back as they had met their ultimate destiny.

From a day and age where there were no cancer manuals or far and few teachers to be mentored from, we salute our fathers, who represent the pioneers of an exciting field with a promising future. Without physicians like them, who have dedicated their academic and professional lives to the cause of fighting cancer, the world of oncology would indeed be a drab one!!! As the future of oncology, we do indeed have very, very large shoes to fill!

Dr. Aarthi Kannan – now an intern at Somaiya Medical College, Mumbai. She is the daughter of Dr. V. Kannan – Director of the Comprehensive Cancer Care Center, KMCH

Dr. Sarada Krishnamurthy – is a consultant in Medical Oncology & Haematology at KMCH and is the daughter of Dr. Muthuswamy Krishnamurthy, MD, FACP – retired HOD and Program Director of Medical oncology & Haematology at New York Methodist Hospital, NY, USA; Clinical Associate Professor of Medicine at Weill Medical College – Cornell University, NY, USA; Adjunct Professor of Medicine at St. George's University of Medicine

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- Endo Urological & Laparoscopic Procedures
- ENT Surgery
- Fertility/Reproductive Medicine
- General Surgery
- Haematology
- Head & Neck Surgery
- Interventional Cardiology
- Interventional Gastroenterology
- Interventional Pulmonology
- Interventional & Diagnostic Radiology
- Intensive Care Medicine
- Laparoscopic Surgery
- Master Health Checkup
- Nephrology
- Neurology
- Neonatology
- Neurosurgery
- Nuclear Medicine
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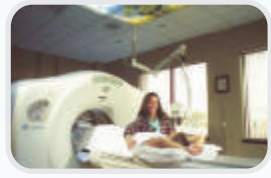

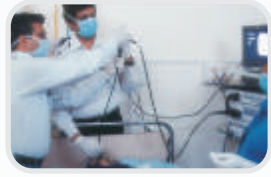

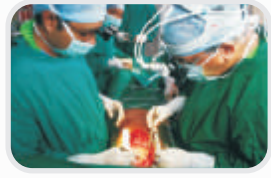

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Post Box No. 3209, Avanashi Road, Coimbatore - 641 014
Phone : 0422 - 3083800, 4323800, 801, 802, Fax : 0422 2627782, www.kmchhospitals.com
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Post Box No. 3209, Avanashi Road, Coimbatore - 641 014
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