



Fostering a culture of innovation and excellence



ONCOLOGY:

New Challenges, New Strategies

IN THIS ISSUE

THE WAY WE DO IT AT FORTIS

Coming Together of Oncology in Delhi NCR: The Fortis Way

Page No. 08

CLINICAL RESEARCH

Study on Autologous Dendritic Cell Immunotherapy for use in Refractory Prostate, Ovarian, Colorectal and Lung Cancer

Page No. 44

SPECIAL FEATURES

- Radio-theranostics
- IORT
- HIPEC

Page No. 10

CONTENTS

INSPIRATION

Message from Dr Vinod Raina	04
Message from Dr Sandeep Nayak	04

FROM THE EDITORIAL TEAM

Message from the Editorial Team	
---------------------------------	--

THE WAY WE DO IT AT FORTIS

Coming Together of Oncology in		
Delhi NCR : The Fortis Way		08

SPECIAL FEATURE

Strides in Oncology	
How is Comprehensive Genomic Profiling Being Currently Used in Oncology Clinics?	
Radio-theranostics: How Tiny Radioactive Molecules are Personalising Cancer Care	
Intra-operative Radiotherapy – A Leap Towards Lesser, Faster, Better	
HIPEC in Ovarian Cancer: A Promising Approach 17	
Innovations in Surgical Oncology	
RABIT (Robotic-assisted Breast-Axillo Insufflation Thyroidectomy): Our Experience	
Sentinel Lymph Node Mapping In Endometrial Cancer Staging- Minimal Access Robot-Assisted Surgical Approach	
MR-LINAC: A Cutting Edge Radiation Technology for Cancer Patients 25	
Pain Management and Palliative Care	
Psycho-oncology	

CLINICAL CONVERSATIONS

Innovative Reconstruction for a Complex	
Resection: Offbeat Case	30
Retroperitoneal 10 kg Recurrent Lipo Sarcoma	31
Intraoperative Radiation Therapy (IORT) -	
Winning Combination of Technology and	
Teamwork	32
Colonic Cancer with Lynch Syndrome	33

Neuroendocrine Carcinoma of Cervix - A Case Report	37
Unsuspected Low Grade Endometrial	
Stromal Sarcoma - Clues to Improve	
Preoperative Diagnosis	39
Simultaneous Surgical Management of	
Malignancy and Coronary Heart Disease:	
Our Meritorious Experience	41

TRIVIA

 42

CLINICAL RESEARCH

Study on Autologous Dendritic Cell	
Immunotherapy for use in Refractory	
Prostate, Ovarian, Colorectal and Lung	
Cancer	4
Phase IV Study on Regorafenib in patient	
with Metastatic Colorectal Cancer (mCRC)	4
A Phase III Comparison Study between SB12	
(proposed Eculizumab biosimilar) and	
Soliris [®] in Subjects with Paroxysmal	
Nocturnal Hemoglobinuria 4	5

ONCO CONNECT

Case	1	 47
Case	2	 48

LEARNINGS FROM COVID-19

The Second-vs First-wave of COVID-19: More of the Same or a Lot Worse? A Comparison of Mortality between the Two Waves in Patients Admitted to Intensive Care Units in Nine Hospitals in Western Maharashtra	50
Hydroxychloroquine Pre-exposure Prophylaxis Provides No Protection Against COVID-19 Among Health Care Workers: A Cross-sectional Study in a Tertiary Care	
Hospital in North India	51
Answers to the Crossword	52



INSPIRATION



Message from Dr Vinod Raina, Chair- Onco Sciences, Fortis Cancer Institute, Fortis Memorial, Gurugram



Dear Colleagues,

As the result of the outbreak of COVID in March 2020, hospitals globally saw a tremendous fall in visits of cancer patients. Even patients who were in the middle of treatment, stopped visiting. We had to contact critically ill patients to coax them to at least continue and complete their cancer treatment. The initial mortality and morbidity of cancer reported by the media in India was indeed very scary; this continued till July 2020, further accentuated by the horrifying news of wide spread, bed and oxygen shortages. After the brief lull of 3-4 months, patients started reporting back, before we again saw the massive second outbreak. We saw relative calm till November 2021 when the third wave hit us. It seems we are recovering now and the benefits of vaccination are becoming apparent. The overall impact on cancer mortality and morbidity has been very severe and painful. Of course, during active COVID infection we do avoid chemotherapy, surgery as well as radiotherapy, unless it is very urgent in some cancers like leukemia etc.

In the recovery phase, now since the last fortnight, we are seeing many cancer patients returning to hospital but some unfortunately in a very advanced stage, particularly common cancers like breast, lung and Gl. Patients have undergone serious trauma and their common questions are whether vaccination is to be taken during cancer treatment and whether it will be deleterious for cancer patients. Doctors do not have any clear cut answers as there are no trials so far on these issues. But from our clinical experience of the past two years, it seems that those who have had at least two doses of vaccination are deriving huge clinical benefits; there seem to be no deleterious effect on cancer treatment due to vaccination.

What will be the long term impact of COVID on CANCER and of CANCER on COVID will be known only in the long run. My gut feeling is that the worst is behind us and those who do not have active infection should come forward for cancer treatment without any further delay and fear as well as resume their screening tests.

Message from Dr Sandeep Nayak, Chair-Oncology Speciality Council and Director- Surgical Oncology, Fortis Cancer Institute, Bengaluru



Dear Colleagues,

It is an honour and privilege to write on behalf of the Fortis Oncology Speciality Council. The formation of the Council was to connect all the Oncologists in the system and use the collective intelligence to improve the working and outcomes for the patients. The Council has managed to start a Pan Fortis Multi-disciplinary Tumour Board to discuss the complicated cancer cases and find solutions for them. We have also had several meetings to fine tune the functioning of Oncology care delivery across the network.

This issue of **Clinical Connect** is dedicated to Oncology. We, the Oncologists of Fortis, are united under the umbrella of Fortis Cancer Institute (FCI) and all the members of this family have worked hard to deliver high quality of care and have strived for academic excellence.

Our organisation has some of the finest clinicians that the country, as well as the world has known. Many have made significant contribution to the development of clinical science by developing unique surgical techniques, participating in newer clinical trials, etc. Many of our centres are recognised teaching hospitals for postdoctoral as well as fellowship training programmes.

Through **Clinical Connect** we hope to share and celebrate many of the achievements that we as an organisation have achieved. I hope you will all find the articles a good read.



FROM THE EDITORIAL TEAM



Message from the Editorial Team



Dr Ritu Garg Head – SBU, Fortis Memorial Research Institute

The COVID-19 epidemic has tested healthcare systems around the world. Oncology patients especially faced an unparalleled challenge as they struggled against all odds to fight the disease progression and continue treatment. Cancer screening and early detection has been most impacted which has left a visible impact with more patients coming with advanced stage cancer.

Despite all the challenges in last two years, our clinicians have worked endlessly and tirelessly to deliver best outcomes to their patients. The team of clinicians at Fortis provide an evidence-based multidisciplinary diagnostic, consultative and treatment services for patients with cancer and is backed by a transdisciplinary and multi-modality approach in the field of adult and paediatric oncology.

February is marked as World Cancer Awareness month and this special edition focuses on innovations in Oncology practices, current clinical research projects, path breaking case studies, advancement in digital technology, robotics in surgery, Genomic Profiling, Radiotheranostics, Intra-operative Radiotherapy, HIPEC and more which are key driving factors for the future of oncology. We have umpteen inspiring patient stories which encourages us all to continuously evolve, be on cutting edge and walk with them in their journey. Psycho Oncology is an important pillar and integral part of Cancer treatment. Our group of hospitals not only focuseson the physical challenges of the patients but also runs a psycho oncology programme which, in these COVID times, holds even greater value for cancer pat ients and their attendants.

We look forward to your suggestions on this issue on Oncology and also your feedback on the upcoming editions.





THE WAY WE DO IT AT FORTIS



Coming Together of Oncology in Delhi NCR: The Fortis Way



Dr Shubham Garg Senior Consultant - Surgical Oncology, Fortis Hospital, Noida

Treating cancer is never a one-man job. It is a team effort that requires clinicians across multiple specialities to stand together and get counted for. The Departments of Oncology at Fortis Hospitals across Delhi NCR hosted the three-day 4th Annual Conference of Delhi NCR Oncology Forum in a hybrid format from December 3-5, 2021, in Noida, Uttar Pradesh. The event was webcast live on an online platform. The theme was 'Evidence, Technology and Consensus (ETC) in Oncology.'

The highlight of the conference was the organising team constituted by all the leading Oncology clinicians from the Fortis Network in Delhi NCR, with every single Oncology clinician contributing towards curating the scientific programme.

Day 1 and Day 2 of the event focussed on 'Evidence' and 'Consensus' in a virtual only mode, having two simultaneous halls generating 16 hours of scientific content. It involved faculty of national and international repute and had interesting debates and passionate discussions. There were around 450 registrations with almost 250 simultaneous logins at the peak time. Gynae-oncology and Breast Cancer were the most well attended sessions. Day 3 focused on 'Technology in Oncology,' and included panel discussions with leading faculty from Delhi NCR participating in the physical meeting. The highlight of the event was a talk by Dr Ananya Chaudhary from Manchester on MR based LINAC system. It was followed up by a healthy discussion on the radiation practices with the technological advances with tomotherapy.

The event was not about gathering a big crowd. The event was not about getting a lot of international speakers. The event was about showcasing the collective strength of Fortis Oncology in Delhi NCR. And I think we nailed it.









SPECIAL FEATURE

Newer Developments in Oncology

- Strides in Oncology Dr Nitesh Rohtagi
 How is Comprehensive Genomic Profiling Being Currently Used in
 - Oncology Clinics? Dr Niti Raizada
 - Radio-theranostics: How Tiny Radioactive Molecules are
 Personalising Cancer Care Dr Ishita B Sen
 - Intra-operative Radiotherapy A Leap Towards Lesser, Faster, Better - Dr Nisha Vishnu, Dr Sandeep Nayak
 - HIPEC in Ovarian Cancer: A Promising Approach - Dr Rashmi Rekha Bora, Dr Rama Joshi
 - Innovations in Surgical Oncology - Dr Hitesh R Singhavi, Dr Anil Heroor
 - RABIT (Robotic-assisted Breast-Axillo Insufflation Thyroidectomy): Our Experience
 Dr Abhilasha Sadhoo, Dr Sandeep Nayak
 - Sentinel Lymph Node Mapping In Endometrial Cancer Staging- Minimal Access Robot-Assisted Surgical
 - Approach Dr Tarini Sonwani, Dr Rama Joshi
 - MR-LINAC: A Cutting Edge Radiation Technology for Cancer Patients - Dr Anil Kumar Anand
 - Pain Management and Palliative Care -Dr Kailash Kothari
 - Psycho-oncology Dr Samir Parikh



Strides in Oncology



Dr Nitesh Rohtagi Senior Director – Medical Oncology Fortis Memorial Research Institute, Gurguram

In the history of mankind, Year 2021 will be remembered as the year when healthcare both failed and succeeded, at the same time. While the COVID-19 pandemic was at the epicentre, the stories that will be remembered and repeated will be of how individual teams reacted to the situation and treated their patients against all odds.

Oncology or cancer medicine, was no different. Despite all the challenges 2021 posed, the year saw some big advances being made in both technology and the art and science of Oncology.

Some of the key developments

- The American Society of Clinical Oncology focuses on cancer disparities and health equity. In August 2020, it updated its policy statement and identified four key focus areas: ensuring equitable access to high-quality care, ensuring equitable research, addressing structural barriers, and increasing awareness and action.
- Molecular profiling in gastrointestinal cancers including oesophageal, stomach pancreas, gall bladder and colorectal

cancers set a new standard of care in early and advanced diseases where the role of both immunotherapy and targeted therapy was consolidated and benchmarks were set for future research.

- Aspirin usage was linked to longterm reduction in cancer risk in patients with hereditary cancer predisposition.
- 4. Immunotherapy before surgery in early stage triple negative breast cancer, the most virulent type, was established for the first time. Similarly, the role of a new class of drugs – the CDK 4/6 and PARPi – was established in reducing the risk of recurrence in high risk postoperative breast cancer patients.
- Patients with lung cancer also saw benefits of post-surgical administration of targeted therapy with osimertinib.
- Hepatocellular carcinoma saw new treatment options after almost a decade with combination of immunotherapy

using atezolizumab and targeted therapy with bevacizumab.

- CAR T cell treatment improved survival for majority of patients with relapsed or refractory mantle cell lymphomas.
- We saw huge developments in the integration of Artificial Intelligence and Deep Learning in cancer research.
- 9. Obesity reduction is probably the most important action to reduce incidence of cancer.
- 10. COVID-19 will be remembered as a catalyst in research with positive impact on Oncology outcomes. This was a result of decentralisation and global acceptance of virtual collaborations. Further, new trial designs focusing on timeliness and optimisation will be the key.

The advances in all branches of Oncology will continue to offer new and promising diagnostic and treatment options for oncology patients.





How is Comprehensive Genomic Profiling Being Currently Used in Oncology Clinics?



Dr Niti Raizada Director - Medical Oncology and Haemato-Oncology Fortis Hospitals, Bengaluru

Gone are the days when Oncologists would treat their patients with the same kind of treatment approach and therapy for the same malignancies. With generic treatment, some showed favourable response to the treatment whereas some showed no response at all and in some cases, the tumour used to become aggressive despite the treatment.

Research has shown that carcinogenesis is the process of multiple genomic events and multiple genetic alterations. Quite a few genomic parameters have become standard of care for the successful treatment of cancer nowadays, such as ras- raf pathways, EFGR/ALK/ROS etc. But we need more information in a consolidated manner to customise or personalise treatment.

In reality, we are entering a world of bio-informatics, where there is unlimited data to assess. This includes genomics, epigenetics, microbiomics, transcriptomics, metabolomics and proteomics to name a few...and so 'multi-omics' is the fast becoming the key word! As we are getting more into the era of precision and personalised oncology, next-generation sequencing is becoming an indispensable tool in the clinical practice for the assessment of biomarkers with less tissue and in a short time. Here comes the concept of Comprehensive Genomic Profiling or CGP or CMP (Comprehensive Molecular Profiling).

How is CGP implementation changing our clinical practice?

One gets all the results from a single assay and in less time, whether it is:

- 1. Driver mutations or the mutational landscape of a cancer
- 2. Passenger/bystander mutations
- 3. Actionable mutations or even undruggable mutations

- 4. Pathways of resistance
- 5. Genomic signatures like TMB and MSI - largely known as 'pan tumour markers' for immunotherapy etc.
- 6. CGP informed targeted therapies and immunotherapy also helps to lessen the drug-related toxicity and add value in improving quality of life of our patients.

We should adopt the change in terms of clinical practice, for optimal treatment outcomes.

The CGP derived insights will also be an indispensable tool in the battle against cancer, and in the coming age, Oncologists will have more and more genomically informed data for the comprehensive management of cancer.





Radio-theranostics: How Tiny Radioactive Molecules are Personalising Cancer Care



Dr Ishita B Sen Senior Director - Nuclear Medicine Fortis Memorial Research Institute, Gurugram

The term 'theranostics' is an integration of the words 'therapeutics' and 'diagnostics.' Theranostic agents are paired agents, one an imaging agent that 'sees' the lesion and the other, a companion therapeutic agent that 'treats' the same lesions. While the concept of theranostics is widely used in various molecular probes in oncology, the most relevant application of theranostics is in nuclear medicine where it is called Radiotheranostics. Paired radionuclides attached to a common probe are used first for imaging the tumour with a specific PET scan and then treating the same using a therapeutic radionuclide attached to the same probe. This strategy is aligned to the concept of personalised precision medicine, which leads to enhanced therapy efficacy, manageable adverse events, improved patient outcome and lower overall costs.

The Department of Nuclear Medicine at the Fortis Memorial Research Institute (FMRI), Gurugram, has been one of the apex centres in the country practising Radio-theranostics since 2013. Prostate cancer, neuroendocrine tumours and thyroid

cancers are the most common tumours being treated by Radiotheranostics. The Ga68 PSMA scan, which is a highly specific PET scan for prostate cancer, is increasingly becoming the standard of care for the staging of prostate cancer. The radioactive tracer (68Ga-PSMA-11) attaches to PSMA proteins which are overexpressed in prostate cancer cells, both within the prostate gland and in the metastatic sites. The PSMA PET scan thus pinpoints the location of the tumour within the prostate gland and accurately stages the disease by identifying all the metastatic sites beyond the prostate gland where the cancer may reside. This allows the surgeon, the Radiation Oncologist and the Medical Oncologist to correctly strategise which patient gains by local therapy like surgery or definitive radiotherapy and which needs systemic therapy like chemotherapy. Lu177 PSMA, a therapeutic radio-theranostics agent, is then used to treat metastatic prostate cancers, especially those that are refractory to systemic hormonal therapy or chemotherapy. Treatment with these radio-theranostics agents not only improves survival in these patients of advanced prostate cancer but also significantly improves their quality of life. At the Nuclear Medicine Centre at FMRI, more than a thousand treatments have been carried out in prostate cancer patients over the last eight years.

Another tumour where radiotheranostics is often used is in well differentiated neuroendocrine tumours. Patients of neuroendocrine tumour often have advanced disease at presentation with the liver often being extensively involved in the metastatic process. Delivering cytotoxic levels of radiation without damaging the surrounding normal tissue is often the challenge in these patients. Ga68 DOTANOC, a diagnostic radio-theranostic agent, identifies the somatostatin receptors which are overexpressed in these tumours. Lu177 DOTANOC therapy, also called PRRT (Peptide radionuclide therapy) a therapeutic radiopharmaceutical, then seeks out these somatostatin receptors on the tumours, attaches to the receptors and delivers a high payload of radiation to the tumours. Since the penetration of the ionising radiation in tissue is only few micrometres, the surrounding normal tissue is spared. PRRT is also used in the treatment of meningiomas and paragangliomas, which also express the somatostatin receptors. Sometimes, PRRT is combined with highly targeted stereotactic external radiotherapy to deliver combined internal and external radiotherapy to deliver a double whammy of damaging radiation to the tumour cells (COMBIERT).

While traditionally, the therapeutic theranostic agents used beta radiation emitting tracers like lutetium, in the past few years, alpha emitting radionuclides like Ac225 (Actinium 225) and Bi213 (Bismuth 213) have opened up an entirely new era in nuclear theranostics. Alpha emitting radionuclides deliver up to 20 times higher cytotoxic radiation dose to the tumours. And since the penetration of these alpha rays in tissue is manifold less than the beta emitting radionuclides, the damage to surrounding tissue is far less. Often called the magic bullet therapy, targeted alpha therapy is changing the paradigm of radio-theranostics. The Nuclear Medicine Department at FMRI was the first centre in the entire South-east Asia to start performing targeted alpha radiation therapy.



Even today, the department receives patients not just from the Asian or Arab countries but even from Europe and USA for targeted alpha therapy.

The role of radio-theranostics in expanding rapidly with the development of multiple new molecules, peptides and small bodies, which are capable of binding to a specific target in the tumour and suitable for both imaging and therapy. Tracers, which will help in tumours such as breast cancers, brain tumours, neuroblastomas, AML and lymphomas, are already being used in clinical trial settings. The Department of Nuclear Medicine at FMRI is running three such clinical trials, one looking at tumour microenvironment imaging, the other using specific probes targeting $\alpha v\beta 6$ integrin and yet another using radiolabelled Zolendronate for bone pain palliation. Radio-theranostics is rapidly being incorporated in standard oncology diagnostic and treatment protocols and is becoming one of the mainstays of precision personalised oncology practice.





Intra-operative Radiotherapy – A Leap Towards Lesser, Faster, Better

Dr Sandeep Nayak Director - Surgical Oncology Fortis Cancer Institute, Bengaluru



Dr Nisha Vishnu Consultant- Radiation Oncology Fortis Cancer Institute, Bengaluru

A 61-year-old lady, from Bangladesh, came to India to get operated for an early-stage hormone receptor positive, node negative, Carcinoma of the left breast. She underwent a breast conservation surgery. What followed was a favourable (margin negative, sentinel lymph node negative) frozen section report with a single large fraction of radiotherapy on the OT table itself which would enable her to travel back to her native country in a week's time. Her family thanked us for not having to stay back in a foreign country for two extra months; for all the time, effort, money and sheer logistical issues that they could bypass without having to compromise on the treatment outcome. She was the first patient of intraoperative radiotherapy (IORT) done at Fortis, Bannerghatta Road, after the installation of the Carl Zeiss intrabeam IORT machine. Today, we have handled four successful cases and are looking forward to many more.

Cancer treatments are mostly

notorious for being cumbersome and frustrating. And in pursuit of overcoming this reputation, we oncologists are in constant quest of methodologies that could make it quicker, easier and of course better. Adoption of breast conservation surgery (BCS) over a modified radical mastectomy (which would potentially scar a woman's identity for life) in early breast cancers is an apt example of how sometimes 'less is more'. In a typical breast cancer case, if the patient chooses to undergo BCS followed by the mandatory radiotherapy, it could take anywhere from 4-10 weeks to complete the treatment (if systemic therapy is not taken into account). With IORT, we reduce 4-10 weeks to one day; while of course not compromising the outcome.

THE GOLDEN CIRCLE (LITERALLY) OF WHAT, WHY AND HOW

What is intraoperative radiotherapy?

In fact, let us start with the question -What is radiotherapy? Killing of cancer cells using ionising rays (usually X-rays) is radiotherapy. The X-rays are generated by giant machines called linear accelerators (Linac) which converts the energy of extremely fastmoving electrons into X-rays. The energy generated is usually mega-volt which ionises the track it passes through. The ionisation of DNA molecules directly or the ionisation of water molecules in the cells generating free radicals which could indirectly ionise the DNA, induces single and double stranded breaks, the accumulation of which finally lead to cell death. Generally, these X-rays are targeted and channelised into the body from the outside; what we call external beam radiotherapy (EBRT). And generally, the 8000 kg, 9-footer LINACs are placed in lead lined

bunkers away from other departments. In IORT, we have miniaturised the linear accelerator into a 6 ft, 275 kg transportable machine which can be placed inside the very operation theatre (OT) where in the breast conservation surgery is done. After the surgeon removes the tumour with a margin, and after confirming the sentinel node/margin status, we go ahead and treat the cavity with a spherical applicator attached to the LINAC. Where the usual dose delivered in conventional EBRT is 2 Gray (Gy) per fraction to the whole breast, the dose delivered in IORT is 20 Gy to the cavity and few millimetres beyond.

Why IORT at all? Were we not doing pretty well with conventional treatment?

Breast is one of the areas wherein we have attained tremendous treatment heights. Not only have we reduced the local recurrences to 2%, but the survival rate of an early-stage breast cancer is as high as 98%. The question is why a new technique?

While treatment time reduction comes as a huge advantage especially for patients who are older or for the ones residing in remote areas, it is not the only benefit IORT could boast of. With the best of the external beam techniques available, there is invariably some dose to the underlying heart and lung while there is almost none with IORT. This probably explains the increased survival rates observed in IORT group in comparison to the conventional arm in the TARGIT trial 10-year update, recently published. Also, the inaccuracy of the boost cavity marking (which otherwise is marked following ques from the clips placed by surgeons and as per pre-operative imaging) along with the extra



margins of breast irradiated in order to tide over the inaccuracy, is all a matter of the past with IORT, where in the applicator is placed into the cavity, live, on the table. The cutting down of extra margin can potentially lead to better cosmesis in the long run as well. Reduction of man hours and more efficient channelisation of hospital resources are certain other indirect benefits.

How does dose around cavity translate to benefits?

When I first heard of IORT, my question was, "But, isn't breast cancer multi-centric in nature?" A TATA Memorial study conducted in the 1990s, which chopped up the mastectomy samples into smaller units and observed under microscope revealed that the sampled breast indeed had multiple other microscopic neoplastic niduses. By this theory, treatment of the whole breast, rather than the cavity, should be the norm. Nonetheless, it was proven beyond doubt, and repeatedly, that almost all recurrences in un-irradiated breasts happens in and around the cavity and not from one of the (probably dormant) distant niduses. And that explains the conclusion of TARGIT - a trial done on 3,451 patients from over 33 centres in 11 countries, which put across that for selected early breast cancer patients, risk adapted immediate single dose TARGIT-IORT during lumpectomy is an effective alternative to EBRT, with comparable long-term efficacy for cancer control and lower non-breast cancer mortality. It is hypothesised that radiation induced cell death is maximal just after the surgery when the tumour bed is maximally oxygenated compared with weeks later. In Radiobiology, we use a term called alpha/beta ratio as an indicator of a tissue sensitivity to hypofractionation (larger doses per sitting). The lesser it is, the more is the

effect of hypo-fractionation. If, for other tumours it is 10, for breast cancers it is 4. And just like that, it makes sense to TARG'I'T it.

Beyond the circle – Is IORT a 'fit for all, bar none' therapy?

Definitely not. Since we, at Fortis, are the only ones in the country with an intrabeam facility, and since we are starting, our selection criteria are even more stringent than the existing recommendation. IORT as a sole radiation treatment is offered only to women with breast cancers who fulfil all the following criteria:

- > 50 years old
- Tumour measuring 2 cm or less, unifocal
- Hormone receptor positive
- No nodal involvement and negative margins (Determined on table after the frozen section)

The treatment is risk adapted, that is - If we find a node to be positive in frozen report or if there is a high-risk feature like lympho-vascular invasion, we go ahead and treat the cavity anyway, only to follow it up with external beam radiotherapy to the whole breast.

Looking forward

Fast, efficient and yet effective these are surely exciting times for Fortis family. Our team is enthusiastically working towards treating more while recording the side-effects very closely. Though the article entirely focuses on early-stage breast cancers, we do offer IORT as an adjunct to external beam radiotherapy for cavity boost in all BCS cases and would be making IORT useful in other established areas of indications like pancreatic cancers, recurrent rectal cancers, retroperitoneal soft tissue sarcomas, post salvage surgery in head neck tumours, brain tumours etc. We seek your active support and wishes as we thread through the exciting path of innovation and transformation.





HIPEC in Ovarian Cancer: A Promising Approach



Dr Rashmi Rekha Bora Consultant - Gynae Oncology Fortis Memorial Research Institute, Gurugram



Dr Rama Joshi Principal Director and Head -Gynae Oncology and Robotic Surgery Fortis Memorial Research Institute, Gurugram

Ovarian cancer affects women of all ages, but is most commonly diagnosed at 50 to 60 years of age. More than 75% of women are diagnosed at an advanced stage because early-stage disease is usually asymptomatic and symptoms of latestage disease are non-specific. Surgery and chemotherapy are the cornerstones in the management of advanced stage. The treatment modalities can be primary surgical cytoreduction where a maximum effort to reduce the tumour burden is done followed by six cycles of platinum/paclitaxel-based intravenous chemotherapy. Alternatively, interval surgical cytoreduction can be performed after three cycles of neo adjuvant chemotherapy. Advanced epithelial ovarian cancer (EOC) has a wellcharacterised pattern of spread within the peritoneal cavity. This pattern makes intraperitoneal chemotherapy an attractive treatment by enhancing drug delivery at the peritoneal surface which will improve outcomes by eliminating residual microscopic peritoneal disease more efficiently. GOG 172 a

randomised control trial comparing intravenous chemotherapy with intravenous and intraperitoneal chemotherapy had shown better overall survival in the latter but at the expense of increased toxicity and poor quality of life during treatment. ^[1] Hence to mitigate the concerns of patient tolerance and catheterrelated morbidity seen in normothermic intraperitoneal chemotherapy another method i.e. Hyperthermic Intraperitoneal Chemotherapy (HIPEC) which is performed after achieving optimal cytoreductive surgery was developed.

HIPEC in ovarian malignancies was first explored in the 1980s in conjunction with cytoreductive surgery (CRS). It has now become pivotal in the treatment of peritoneal disease and improving survival outcomes in selected patients with peritoneal surface malignancies. Peritoneal carcinomatosis was historically seen as a fatal stage in malignancy, and only in the past twenty years, HIPEC has evolved as an effective treatment for such stage. In addition to advanced-stage ovarian cancer, approximately 10–15% of patients with primary gastrointestinal malignancies (including appendiceal, colonic and gastric malignancies) present with peritoneal carcinomatosis. Application of HIPEC to the ovarian cancer population has renewed interest due to its advantages over standard adjuvant Intraperitoneal (IP) chemotherapy protocols. HIPEC is a single treatment delivered at the time of cytoreductive surgery, where fluid distribution is not impeded by post-operative adhesions and the surgeon can control delivery time and distribution using standardised techniques. The goal of HIPEC is to target remaining microscopic residual tumour at the time of cytoreductive surgery following an optimal resection. The rationale of HIPEC is multifold, as compared with standard systemic chemotherapy. By delivering chemotherapy directly within the peritoneal cavity there is an increased exposure of poorly vascularised tumour to the high concentration of chemotherapy. The blood-peritoneal barrier also limits the passage of this high concentration of chemotherapy thereby reducing systemic toxicity



while maximising local effects. Heat has direct cytotoxic effect and it improves the penetration of chemotherapeutic agents into tissues. The commonly used chemotherapeutic agents include cisplatin, paclitaxel, oxaliplatin, and mitomycin c. Hyperthermia has been shown to reduce the mechanisms of induced cellular resistance to cisplatin. The completeness of cytoreduction score (CC-) is the major prognostic indicator in both noninvasive and invasive peritoneal surface malignancies. Patients that receive the most benefit are those who undergo complete cytoreduction, although patients with small-volume residual disease will also benefit from the procedure.

A randomised phase III trial conducted in Netherlands ^[2] showed that amongst patients with stage IIIC epithelial ovarian cancer, women in the HIPEC arm (122 patients) had longer average relapse-free survival compared to the surgery group (123 patients), at 14.2 months and 10.7 months, respectively. Overall survival (OS) was also improved with HIPEC, with median OS being 45.7 months in the HIPEC arm versus 33.9 months in the surgery arm. Also addition of HIPEC did not result in higher rates of side effects.

Experience of Cytoreductive surgery followed by HIPEC in the Department of Gyne Oncology at FMRI

Twenty-seven patients of advanced ovarian cancer who underwent cytoreductive surgery followed by HIPEC were evaluated. Twenty-one patients were given HIPEC during interval surgical cytoreduction and six patients in the recurrent setting. HIPEC was administered with the use of the semi-open technique at the end of the cytoreductive surgical procedure. Complete cytoreduction i.e CC0 was achieved in 25 patients and CC1 in two patients. Heated saline was circulated intraabdominally maintaining a temperature of 42°C in all the four quadrants. Perfusion was done with cisplatin at a dose of 100 mg per square meter and at a flow rate of 1 litre per minute. The perfusion volume was adjusted such that the entire abdomen was exposed to the perfusate. The HIPEC procedure took an additional 120 minutes in total, including the 90-minute perfusion

period.

HIPEC was successfully performed in all the cases following a complete cytoreductive surgery in advanced and recurrent ovarian cancer with no intraoperative complications or mortality. Most of the perioperative complications were Grade II according to the Clavien Dindo Scale. Grade III and Grade IV complications were seen in four and three patients respectively. Out of the 27 patients only two patients required ICU management and they recovered completely. The median hospital stay was 10 days.

In our experience with proper selection of patients, HIPEC is feasible with good perioperative outcome.

References

- Armstrong DK, Bundy B, Wenzel L, Huang HQ, Baergen R, Lele S, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. N Engl J Med. 2006;354(1):34-43.
- van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer. N Engl J Med. 2018;378(3):230-40.



Figure 1: After achieving complete cytoreduction (CC0) including total peritonectomy



Figure 2: After achieving complete cytoreduction (CC0) including total peritonectomy



Figure 3: Placement of intraperitoneal Inlet and Outlet tubings for HIPEC



Figure 4: HIPEC in progress



Innovations in Surgical Oncology



Dr Hitesh R Singhavi Head and Neck Surgeon Fortis Hospital, Mulund



Dr Anil Heroor Head - Department of Surgical Oncology Fortis Hospital, Mumbai

"Innovation is the unrelenting drive to break the status quo and develop anew where few have dared to go," as Steven Jeffes, Marketing and Business expert has so aptly put, is what we do best. We adapt, we improve, we create to break the status quo to do better for our patients. Our surgical colleagues are constantly striving to improve the surgical environment and adapt surgical techniques for additional benefits. Some of the innovations we have made in the field of Surgical Oncology include:

TRACHEOSTOMY MULTI-UTILITY BOX DURING COVID TIMES

In the year 2021, we experienced waves of novel coronavirus with variety of variants including alpha, beta, gamma, delta, omicron and many other. As the virus evolved, we also evolved to make our surgery safe and providing healthy environment to both clinician, paramedics and patient amidst xenophobic virus. During the first wave of COVID-19, scientist and doctors were still evolving with their knowhow about prevention and treatment of SARS-Cov-2. Frontline healthcare workers were at utmost

risk of getting infected during airway associated procedure including endotracheal intubation, Tracheostomy, positive pressure ventilation, oral suction, extubation, decannulation of tracheostomy and change of tracheostomy tube. Studies had estimated that transmission rates in airway associated procedure increases by 420% ^[1]. Till May 2020, there were reports that underreported value of healthcare workers being infected was as high as 90,000. Thus, novel draping technique was proposed by the team led by Singhavi et al ^[2]to reduce the aerosol exposure to frontline healthcare workers

during tracheostomy procedure, which was modified into a tracheostomy box (Figure 1) later. We offered a novel draping technique within the infrastructural limits of general operation theatre with the use of simple equipment including:

- L shaped anaesthesia screen (steel rod)
- Clear Plastic transparent drape
- Marker pen
- Sterile surgical scissors
- Staplers/micropore tape as described in case report published in the year 2020.



Multi-utility Tracheostomy Box





There are many advantage to the technique. It can be an adjunct to standard risk reduction efforts including PPE. It reduces the aerosol exposure at source. Thus, it not only protects the operating surgeon but also other healthcare personnel (Anaesthesia Team, OT Technician, Nursing Team) present in the operation theatre. It is simple, easily available and cost effective technique. It is also ergonomically viable as height of the drape can be adjusted as per patient size. Also, since its single use consumable which can be used one after the other without delay. Limitations include visibility concerns due to creases of the drape. It should only be used as an adjunct.

NO-TOUCH TECHNIQUE FOR THE TRANSFER OF PEDICLE OF FREE FLAPS IN HEAD AND NECK CANCER RECONSTRUCTION

According to Globocan 2020, the annual incidence of lip, oral cavity and pharyngeal cancers was 6,93,733 and is predicted to rise by 59% by 2035. These tumours are responsible for approximately 340907 deaths, with 50% of it occurring in India ^[3]. Surgery is still the mainstay of the treatment in oral cavity cancer^[4,5]. Majority of all the advanced operable oral cavity cancers which undergo surgical excision require free flap reconstruction most commonly being radial free flap, anterolateral thigh flap, and free fibula ^[6].

Challenge

One of the challenges faced during such a procedure is injury to the pedicle. Transfer of the pedicle from the oral cavity to the neck in the presence of intact mandible or floor of the mouth is a blind procedure, which raises the chances of being injured during the process, especially due to sharp bony edges postablative procedures. Thus, team led by Prasad and Singhavi et al proposed

a novel atraumatic technique of transporting the vessel under the mandible without touching it ^[7].

Novel technique

This technique has its role in the transfer of pedicle to the recipient site after harvesting [Figure 2] and division of the flap pedicle. As the usual length of the pedicle (radial forearm free flap) is 15-18 cm in length and 3 mm in diameter, segment of the 12 mm diameter suction tube is cut measuring about 15 cm to accommodate both cephalic vein and radial artery. Next, the floor of the mouth is pierced with a large haemostat. The cut suction tube is passed into this space and positioned near the recipient vessels [Figure 3]. The flap pedicle is placed into the tube, and low powered suction is applied to the other end [Figure 4]. Care is taken to avoid direct contact of the pedicle with a suction tip. The gentle suction acts as a traction of the pedicle within the tube as the entire unit is pulled into the neck without

mechanically touching it, thus permitting an atraumatic passage of the pedicle [Figure 5]. The diameter (12 mm) of the tube ensures that the tunnel in the floor of the mouth is of adequate diameter. Once the pedicle is in the neck, light suction is turned off, and tube is removed [Figure 6]. Then, a microvascular clamp is applied to the pedicle tip to prevent displacement of the pedicle from the neck during the flap inset. Its advantage includes It being atraumatic, simple, cost-effective procedure of transferring the pedicle into the neck. This procedure creates enough space in the neck to prevent its compression preventing vascular insufficiency, it does not require exclusive expertise and instrumentation. Thus usage of a suction tube not only provides structural protection but also facilitates atraumatic transfer of pedicle due to light suction. Thus, the use of "No Touch" atraumatic transfer of pedicle using suction tube can be used safely in the selected cases.

No-touch Technique





Figure 5

Figure 4



Figure 6



RETRO AURICULAR APPROACH FOR SELECTIVE NECK DISSECTION

Elective neck dissection (END) is the standard of care for treatment naïve operable oral cavity cancers. Robotic assisted neck dissection is paving its way in its effort to improve aesthetic outcome without compromising R zero resection. Retro-auricular approach has been popularised in robotic assisted neck surgeries. However robotic surgeries require skilled manpower with advanced infrastructure which inflates the procedural cost. These cost constraints limit the accessibility of the centres to provide these services. Therefore, team led by Pawar et al developed an assembly of selfretaining retractors for skin flap retraction, with a provision for endoscope assisted visualisation for performing neck dissections by the retro-auricular incision^[9].

Surgical Technique

Patient is positioned in supine position as shown in Figure 7. Skin incision in the midpoint of the preauricular sulcus, just below the tragus, going around the ear lobule, turning backwards in a straight line towards the mastoid tip, so that the incision lies hidden behind the ear lobule. The incision is made and flap is raised just below the subcutaneous fat onto the sternocleidomastoid. Greater auricular nerve and external jugular vein are the important landmark in this approach. Platysma is seen just anterior to external jugular vein. Once identified, rest of the flap is raised as conventional neck dissection. Instruments required include customised (Figure 8) 1. Customised Self retaining retractors with illumination and suction ports (Kalelker surgicals, Mumbai), Self retaining retractors system (Thompsons retractors system)*, Endoscopes – 0 and 30 degrees, 4 mm endoscopes, Endoscope Holder

(Kalelker surgical, Mumbai), LED Light cables and light sources.

Better cosmetic outcome and higher patient satisfaction even in the postoperative period without bearing the overhead cost of the robot is the highlight of this technique. The scar remains hidden in the hairline behind the ear. Also since incision is made away from the field of great vessels, wound dehiscence would not expose the major vessels of the neck. However, limitation of this technique involves narrow field, learning curve and initial increased operating time.

Caution

Experienced head and neck surgeon with good exposure to conventional neck dissection is necessary before contemplating a retroauricular approach. Level 1 A should be carefully dissected to avoid skin breach and narrow surgical field.

The changing trend from conventional transcervical incision to the retroauricular incision in head and neck surgery is promising Our initial experience with the retroauricular approach to the neck surgery has shown that this approach is oncologically safe, highly cost effective, reproducible and can be used in early stage invasive OSCCs with a clear cosmetic benefit.

References:

1. Tran K, Cimon K, Severn M, Pessoa-Silva

CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers a systematic review. PLoS ONE. 2012; 7: e35797.

- Rajendra Singhavi H, Pawar P, Banerjee S, Khan S, Shetty V, Heroor A. Novel Draping Technique during Tracheostomy to Minimize Aerosolization in the Times of COVID19 Pandemic. Int J Innov Surg. 2020; 3(1): 1012.
- Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin.
 2 0 2 1 ; 7 1 (3) : 2 0 9 - 2 4 9 . doi:10.3322/caac.21660.
- Shah JP, Gil Z. Current concepts in management of oral cancer Surgery. Oral Oncol 2009;45:394-401.
- Almadori G, Rigante M, Bussu F, Parrilla C, Gallus R, Barone Adesi L, et al. Impact of microvascular free flap reconstruction in oral cavity cancer: Our experience in 130 cases. Acta Otorhinolaryngol Ital 2015;35:386-93.
- Cha YH, Nam W, Cha IH, Kim HJ. Revisiting radial forearm free flap for successful venous drainage. Maxillofac Plast Reconstr Surg 2017;39:14
- Prasad S, Heroor A, Bangera S, Jain K, Singhavi HR. "No touch" novel technique for positioning of free flap pedicle in head-and-neck oncoreconstructive surgeries. Turk J Plast Surg 2021;29:149-50.
- Pawar P, Vaishampayan S, Shah DH, Pai A. Retro-auricular endo assisted selective neck dissection (how I do it). Oral Oncol. 2020;110:104942. doi:10.1016/j.oraloncology.2020.104942



Figure 9

Figure 10

Figure 11



RABIT (Robotic-assisted Breast-Axillo Insufflation Thyroidectomy): Our Experience

Dr Sandeep Nayak Director - Surgical Oncology Fortis Cancer Institute, Bengaluru



Dr Abhilasha Sadhoo Consultant - Head & Neck Oncology Fortis Cancer Institute, Bengaluru

A young lady came to me recently to invite me for her wedding. I had operated on her about three years back for thyroid cancer that had spread to the lymph nodes in her neck. She was 24 then. Her biggest worry at that time was a scar in front of the neck. If it was done by open surgery, she would have had a large J shaped scar in front of her neck. When she came to meet me other day, it was impossible to tell that she was a patient who had undergone such a major surgery in her neck.

This is the story of many patients who undergo robotic thyroid surgery by RABIT technique.

Robotic thyroid surgery started with an intention of avoiding a scar in front of the neck. However, today, we believe that the advances are more than just superficial. We have learnt to utilise every bit of the technology to the advantage: the precision, 3D vision, magnification, etc.

RABIT provides a symmetrical view of both thyroid lobes for optimal

visualisation and dissection of vital structures, which closely resembles that of conventional open thyroidectomy. This technique helps in maintaining the specimen integrity. Also, it has the largest operative angles between the instruments that can distinctively prevent the instrument crowding or fighting. Most importantly, excellent cosmesis can easily be achieved because of the five separate and small incisions instead of a single long scar over the neck or other remote sites

Robotic thyroidectomy has till date been mainly used for cosmetic reasons. The incision has been placed away from anterior neck to make it cosmetically acceptable which makes it a remote access surgery more than an open surgical invasion. Moreover, the robotic systems enable better magnification of anatomical structures to identify and preserve them, an Endowrist function for high degree of motion, elimination of physiological tremor and a rapid learning curve add favour to the surgeon. Moreover, for patients, less bleeding and pain, shorter hospital stay and rapid recovery have made robotic thyroidectomy a preferred surgical option despite high cost and longer duration of surgery.

RABIT, a novel approach for thyroidectomy, has several advantages over other minimally invasive remote access techniques, including symmetrical view of both the lobes of thyroid, which is similar to conventional open thyroidectomy. This approach helps to maintain specimen integrity and enables total thyroidectomy in addition to a highdefinition three-dimensional vision with the help of robotic system technology. Additionally, the largest operative angles prevent collision between the operating instruments and use of an assistant port along with three robotic and camera part is helpful for better handling of the gland. However, limitations with the use of robotic instruments are high cost which could restrict its accessibility to fewer patients.

Based on our findings, RABIT is a safe and feasible technique and has a lesser potential to cause any postoperative complications. It is ontologically safe and ensures complete tumour removal, which is evident in the post-surgery radio iodine scan, which is done to detect remnants of cancer. In addition to being almost scarless, robotic surgery is precise. We feel it is better than open surgery in our hands. It is utilising the technology to the best.



Figure 1: Thyroid swelling



Figure 2: RABIT Technique



Figure 3: Open Technique



Sentinel Lymph Node Mapping in Endometrial Cancer Staging -Minimal Access Robot-Assisted Surgical Approach

Dr Rama Joshi Principal Director & Head -Gynaecologic Oncology Fortis Memorial Research Institute, Gurugram



Dr Tarini Sonwani DNB Trainee, Senior Registrar Department of Gynaecologic Oncology Fortis Memorial Research Institute, Gurugram

Endometrial cancer is one of the most common gynaecological malignancy in women with a worldwide incidence of approximately 3,20,000 cases diagnosed annually. Globocan 2020 India showed annual incidence of 16,413, annual death of 6,385 and a 5-year prevalence of 43,484 per 1,00,000. The incidence of both lowand high-grade endometrial cancer continues to increase secondary to the rising rates in obesity, hypertension, diabetes mellitus and life expectancy.

Treatment of endometrial cancer is based on the stage of disease. Surgery is the primary treatment for uterus confined endometrial c a r c i n o m a, w h e r e i n lymphadenectomy is the standard procedure for surgical staging of endometrial cancer. In node positive patients, chemotherapy plays an important role as adjuvant treatment. However, the incidence of metastases to the pelvic lymph nodes in patients with corpus-confined endometrial cancer varies between 5% and 18%. Complete pelvic and para-aortic lymphadenectomy is associated with major morbidities including lymphoedema, lymphocyst formation, genitofemoral nerve injury and is technically difficult to achieve in obese populations, which represent a substantial proportion of patients with endometrial cancer.

Recent evidence indicates that sentinel lymph node mapping has a low perioperative morbidity as compared to systemic lymphadenectomy and provides similar information regarding nodal status.

What is Sentinel lymph node?

The concept of SLN biopsy refers to the selective and directed sampling of the first-in-chain lymph nodes that drain from a malignant tumour. Theoretically, the SLN is the node most likely to harbour metastatic disease. By selectively removing this node, it can focus lymph node resection and allow more concentrated efforts by pathologists (such as ultra-staging) to detect metastases. Dyes or tracers are used to identify SLN.



Figure 1: SLN algorithm for surgical staging



Sentinel lymph node mapping

Single-agent ICG or the combination blue dye (isosulfan blue 1%, methylene blue 1%, patent blue 2.5% sodium) with Tc99 have the highest detection rates, greater than 90% overall detection and greater than 80% bilateral detection. Blue dyes used alone are associated with the lowest detection, approximately 70%, and particularly bilateral detection rates which rarely exceed 50%.

Challenges that are encountered with the use of these blue dyes and tracers include the discomfort of a separate pre-operative injection, co-ordination of care with nuclear medicine departments, and the costs associated with the equipment, dyes, and additional procedures. Indocyanine green (ICG) when injected interstitially, is carried by



Figure 2: Common cervical injection sites

lymphatic pathways to lymph nodes similar to blue dyes and Tc99 and emits a wavelength in the near infrared range that can be detected by specialised near-infrared imaging devices. Its ease of detection and quick uptake are virtues of this tracer.

Injection site

Cervix is the preferred site for dye injection as SLN detection rate has been reported to be the highest, ~97%.

Accuracy of SLN biopsy for endometrial cancer

In the FIRES multicentre, prospective, cohort study (2017), SLN biopsy yielded a sensitivity to detect nodepositive disease of 97.2% and a negative predictive value of 99.6% using ICG in robotic surgery in patients with uterus confined endometrial cancer. Thus, the study concluded that sentinel lymph nodes identified with indocyanine green have a high degree of diagnostic accuracy in detecting endometrial cancer metastases and can safely replace lymphadenectomy in the staging of endometrial cancer, exposing fewer patients to the morbidity of a complete lymphadenectomy.

An experience at Department of Gynaecologic Oncology, FMRI

An interim analysis of ongoing study at Department of Gynaecologic Oncology, Fortis Memorial Research Institute, Gurugram, on SLN biopsy has shown 98% detection rate of sentinel lymph node mapping, 97.9% NPV and 97.6% accuracy. All the patients had undergone SLN mapping as well as systematic lymphadenectomy by minimal access robot-assisted surgical approach. Thus, SLN biopsy through intraoperative cervical injection of ICG dye appears to be feasible with high detection rate and accuracy for defining the nodal status in clinically uterus confined carcinoma endometrium.



Figure 3: SLN mapping with ICG dye in robot-assisted surgery



MR-LINAC: A Cutting Edge Radiation Technology for Cancer Patients



Dr Anil Kumar Anand Senior Director & HOD, Department of Radiation Oncology, Fortis Memorial Research Institute, Gurugram

Radiation therapy is delivered to 60-70% of cancer patients during their treatment. Efficacy of radiation therapy depends upon the dose of radiation delivered to the tumor while minimizing dose to surrounding normal organs.

Currently, many radiation equipments called Linear Accelerators (LA) are available which can deliver radiation with high accuracy. However, tumors do not remain static during their whole course of radiation therapy. Tumors can shrink, or displace from their original position which can affect both the tumor dose and introduce uncertainties to the radiation dose received by normal tissues.

At present, various imaging devices like CBCT (cone beam CT scan) and Xrays are available on LA to track the position of tumors. However, these devices have poorer soft tissue contrast which affects our ability to clearly visualize the tumor and surrounding normal organs.

With the introduction of 'hybrid' machine - 'MR Linac' consisting of MRI and a Linear Accelerator has greatly enhanced our ability to

correctly visualize the tumor before the radiation is delivered. It would have best features of both the machines to provide high end cancer.

Another distinct advantage of "MR-Linac" is that it provides end to end "Adaptive Radiation Therapy". Due to clear visualization of tumor & tumor edges, tumor regression and tumor shift can be accurately visualized with superior technology of MRI. It has also helped in adapting the radiation dose to changing position of the tumor so that a higher radiation dose can be delivered to the tumor while better sparing the surrounding normal organs. Another advanced feature of this machine is that radiation dose can be re-planned on-line depending upon tumor

shrinkage and displacement of tumor which is currently not possible in any other machine available to deliver radiation therapy.

Thus, this technology would provide both improved tumor control and reduced side effects and would provide a significant improvement in the treatment of cancer.

Fortis cancer institute at Fortis Memorial Research Institute (FMRI) at Gurugram (Delhi NCR) is acquiring this technology which would provide quantum jump in how radiation therapy is delivered to our patients. 'MR – Linac' would be the first of its kind equipment in India and we would join the league of countries equipped with this latest technology to provide world class cancer care.



Figure 1: MR-LINAC





Figure 3: MR Linac can precisely treat critically located tumor near the spinal cord



Pain Management and Palliative Care



Dr Kailash Kothari Spine and Pain Management Consultant Fortis Hospital, Mulund

Cancer and interventional pain management

Pain in cancer patients can be caused by one or more factors. Patients may have combination of various types of pain (eg, somatic, neuropathic and visceral).¹

By following World Health Organization (WHO) ladder² (Figure 1) for pain management, we can achieve adequate analgesia in 75% to 95% of all patients with cancer pain. But a huge number of patients still suffer from severe intractable pain e.g. those with significant bone involvement, extensive metastatic disease or those with plexopathies or they suffer from opioid-related side effects. Role of interventional pain management is very significant in such group of patients.

Interventional pain management includes following

- Non-neurolytic nerve blocks Using local anaesthetics with or without steroid
- Neurolytic nerve blocks Using Radiofrequency ablative techniques, Chemical neurolysis (Alcohol, Phenol)

Nerve Blocks include – Sympathetic blocks (Stellate ganglion, T2-T3 Sympathetic chain, Splanchnic and Coeliac plexus, Hypogastric plexus, Ganglion Impar), Neuraxial (Epidural/intrathecal) nerve blocks, peripheral (e.g. Maxillary, Madibular, Intercostal, Ilioinguinal, pudendal, Lumbar plexus etc)

- 3. Intrathecal drug delivery system implantation (most commonly used drug is Morphine sulphate)
- Spinal Cord Stimulator Implantation – for neuropathic pain syndromes (for painful chemotherapy-induced peripheral neuropathies, neuralgias, and complex regional pain syndrome)
- Percutaneous Vertebroplasty and Kyphoplasty – for osteoclastic compression fracture of vertebra

Inadequate pain management in cancer can dramatically affect the patient's quality of life, physical activity, psychological state of mind and social life. Indeed, intractable pain can be the underlying reason for poor or low performance status.3, 4 Therefore dynamic and positive interaction between oncologists and various healthcare specialists managing cancer with interventional pain specialist is very useful to manage cancer pain adequately and aggressively.

National Comprehensive Cancer Network (NCCN) guidelines major recommendations in relation to interventional pain management include the following 1:

Inadequate pain relief despite
 pharmacologic therapy



Figure 1. Modified "analgesic ladder" for cancer pain, including interventional management. Adapted from World Health Organization. World Health Organ Tech Rep Ser. 1990;804:1-73; Miguel R. Cancer Control. 2000;7:149-156 and Krames E. Med Clin North Am. 1999;83:787-808

- Patient not tolerating opioids
- Some patients may prefer interventions instead of chronic medication regimen
- Patients on very high doses of medications may benefit by interventions and doses can be brought down, thereby reducing side effects and improving quality of life
- Interventions are not appropriate if patients are unwilling or in patients with infections, coagulopathy, or with very short life expectancies.
- Interventions are not appropriate if technical expertise is not available

Palliative care and Cancer

The World Health Organization (WHO) describes palliative care as services designed to prevent and relieve suffering for patients and families facing life-threatening illness, through early management of pain and other physical, psychosocial, and spiritual problems.2 There is growing awareness about palliative care in cancer and terminal illnesses. The advantages are to:

- Improve quality of life
- Prevent unnecessary hospital admissions
- Reduce burden by reducing the use of health services
- Patients who received early palliative care had less aggressive care at the end of life and had longer survival than patients who received standard oncologic care alone⁴

The American Society for Clinical Oncology (ASCO) recommends⁵:

- Start palliative care as soon as a patient's cancer becomes advanced
- For newly diagnosed advanced stage cancer involve palliative care

within 8weeks after diagnosis

 Both in-patients and outpatients with advanced cancer should receive dedicated palliative care services early in the disease course concurrent with active treatment.

Essential components of palliative care according to ASCO⁵:

- Building rapport and relationships with patients and family caregivers
- Managing symptoms, distress, and functional status (eg, pain, dyspnea, fatigue, sleep disturbance, mood, nausea, constipation)
- Exploration of understanding and education about illness and prognosis
- Clarification of treatment goals
- Assessment and support of coping needs (eg, provision of dignity therapy)
- Assistance with medical decision making
- Coordination with other care providers
- Provision of referrals to other care providers as indicated

Conclusion

The need for Interventional pain management and palliative care is

increasing with advancement in these fields. Patient satisfaction is much better, less distress and psychological issues, improved and cordial social interaction and relations, overall better quality of life is achieved. Interaction between various healthcare workers with Interventional pain management and palliative care specialists is key in achieving good quality of life and dignified end of life care.

References

- 3 Portenoy RK, Lesage P. Management of cancer pain. Lancet. 1999;353:1695-1700.
- 2. 4 De Leon-Casasola OA. Critical evaluation of chemical neurolysis of the sympathetic axis for cancer pain. Cancer Control. 2000;7:142-148
- 2 World Health Organization. Palliative Care. Available at https://www.who.int/ en/news-room/fact-sheets/detail/ palliative-care
- 4. 1 Adult cancer pain, Version 3.2019,NCCN, Clinical practice guidelines in oncology (https://jnccn.org/view/ journals/jnccn/17/8/article-p977.xml? ArticleBodyColorStyles=full%20html)
- Jacox AK, Carr DB, Payne R, et al. Management of Cancer Pain: Clinical Practice Guideline No. 9. Rockville, Md: Agency for Healthcare Policy and Research, US Department of Health and Human Services, Public Health Service; 1994: AHCPR Publication No. 94-0592.



Adapted from Prager J, et al. Clin J Pain. 2001;17:206-214





Psycho-oncology



Dr Samir Parikh Director - Mental Health and Behavioural Sciences Fortis National Mental Health Programme

Cancer is an illness that doesn't just affect the body. It has a significant impact on the emotional health and well-being of patients, as well as caregivers. Besides the physical distress associated with the treatment of cancer itself, patients may experience fear, anxiety and low moods, difficulty with adjusting to the new lifestyle changes, changes in body-image and feelings of dependence or a loss of dignity. The experience is similar for the loved ones of those suffering from cancer, where the burden of caregiving can take a toll on their well-being.

A comprehensive cancer care programme must therefore consider the psychosocial needs of patients with cancer, and this is where psycho-oncology, the interface between psychology and cancer care plays a role. The role of psychological support begins with the diagnosis of the illness and continues throughout the patient's journey with the disease. Psycho-Oncologists work with patients to cope with the shock of the diagnosis, building acceptance, managing pain and discomfort, encouraging compliance to lifestyle changes, as well as the challenges associated with survivorship. They also provide a crucial support system to family members, to encourage open and honest communication, helping them cope with the distress, and supporting them in times of grief.

As part of the psycho-oncology programme at Fortis, our team ensures that the emotional needs of patients and families are addressed as an integral part of treatment. We run a dedicated psycho-oncology helpline - 8586091051 to support people throughout their journey.

With an understanding of the role of psychological risk factors, we also work towards the prevention of cancer, conducting community based programmes such as smoking cessation and life style management.





CLINICAL CONVERSATIONS

Interesting Cases

- Innovative Reconstruction for a Complex Resection: Offbeat Case -Dr Shubham Garg
 - Retroperitoneal 10 kg Recurrent Lipo Sarcoma Dr Madhu YC
 - Intraoperative Radiation Therapy (IORT) Winning Combination of Technology and Teamwork *Dr Vineeta Goel, Dr Kapil Kumar*
 - Colonic Cancer with Lynch Syndrome Dr Hemanth Kumar
 - Neuroendocrine Carcinoma of Cervix A Case Report -Dr Mamta Mishra, Dr Neema Sharma '& Team
 - Unsuspected Low Grade Endometrial Stromal Sarcoma -Clues to Improve Preoperative Diagnosis - Dr Mamta Mishra, Dr Neema Sharma & Team
 - Simultaneous Surgical Management of Malignancy and Coronary Heart Disease: Our Meritorious Experience - Dr Sandeep Nayak, Dr Bharath C, Dr V Sreekanth Reddy, Dr Sudarshan, Dr Nischal RP



Innovative Reconstruction for a Complex Resection: Offbeat Case

Dr Shubham Garg

Senior Consultant - Surgical Oncology Fortis Hospital, Noida

Chest wall resections are always tricky as the reconstruction has to match the contour of the resected chest wall and be compatible with the remaining chest wall musculature so that functionality is not compromised. Traditionally, a bone cement mesh is used for reconstruction, but we got an opportunity to innovate in a complex resection.

A 73-year-lady, who had undergone radical nephrectomy in February 2020, presented with isolated bony metastasis in manubrium and sternal body after a DFI of 18 months. Biopsy confirmed it to be a metastatic lesion from clear cell carcinoma. Crosssectional imaging had shown a lesion involving both the sternoclavicular junction and posteriorly abutting the right brachiocephalic vein bifurcating into subclavian and IJV. It was discussed in the Tumour Board and the patient was given two treatment options. First was surgical wide local excision with reconstruction, pending surgical fitness for surgery in view of age and the second being definitive radiation to this bony site. The patient was ready for the surgery and was found to be fit for same.

The patient was taken up for surgery and made to lie in supine position with neck extended and both hands by the side of the body. A large bore cannula was taken in the lower limb. Midline incision was taken with little extension on the right side along the SCM. Skin flaps were raised and the soft tissue widely excised followed by bony cuts taken on the clavicles at the junction of medial 1/3 and lateral 2/3 and 1st and 2nd ribs with adequate soft tissue. Right IJV/subclavian and brachiocephalic trunks were preserved.

For reconstruction, we used the titanium mesh of size 15 x 10 cm, which is used in neurosurgery for rigid reconstruction. The mesh was superiorly cut in a curved fashion to mimic the sternal notch. The mesh was placed on the defect (Onlay Fashion) and stitched to the clavicle and ribs after drilling a hole in the bones. It was important that the clavicular ends were fixed at the same distance as the excised specimen to avoid splaying of the shoulder girdle. The mesh was further fixed to the chest wall muscles intermittently. As almost all the soft tissue was lost from the skin, left sided pectorals major muscle was harvested and used as a cover over the mesh. To preserved the IJV from the sharp edges of the mesh, sternocleidomastoid muscle and strap muscles were also sutured into the mesh. Bilateral ICDs were inserted and a negative pressure drain was inserted above the mesh.

The patient was extubated on table and discharged on POD6.

The ideal reconstruction for any bony defect would be to replace it with a similar rigid structure. 3D printed customised prosthesis are the newest

modality available and may be the gold standard but it has several problems. One, it is expensive and, two, it takes almost two-three weeks to be available. Also there is almost no chance of any extension in resection else the prosthesis will not fit. A low cost prosthesis was use of bone cement mesh where the proline mesh was sandwiched between Polymeth methacrylate (PMMA). The problem with this is that once it hardens (within 10 minutes), its shape cannot be re-moulded. Second, it is heavy and requires good muscle cover so that it does not impinge the skin.

Titanium mesh provides the middle path by being not exorbitantly expensive (ours costed Rs 25,000) and gives the ability to cut the mesh and mould it repeatedly in the shape and curvature that is required desire. As with all metallic implants, it requires good muscle cover and we also need to address the issue of sharp edges which develop if you have to cut the mesh.

Our experience with titanium mesh has been good and we will continue to use it till 3D printed prosthesis are not made locally available and within the budget of the patient.





Retroperitoneal 10kg Recurrent Lipo Sarcoma



Dr Madhu YC Surgical Oncology Fortis CG Road, Bengaluru

A 45-year-old male patient presented with complaints of abdominal pain, abdominal distention and breathing difficulty. The patient had undergone surgery for retroperitoneal liposarcoma twice in the last two years.

He was thin built and moderately nourished. Abdominal examination revealed significant abdominal distention with a large hard mass occupying the entire left abdomen with no mobility. Patient was haemodynamically stable and systemic examinations were normal.

Investigations revealed Haemoglobin of 6.8 gm% and Se. Albumin of 1.5 gms.

CT scan of abdomen and pelvis reported a large heterogeneously enhancing lobulated mass in the left retroperitoneum measuring 21 x 20 cms in size with multiple adjacent satellite mass lesions. The mass was seen to displace the left kidney and tail of pancreas anteriorly and cause deviation of the abdominal aorta to the right. The mass was occupying the left retro peritoneum extending from left hemi diaphragm to the pelvis. Multiple large nodular mass lesions were noted in the mesentery, splenic hilum, peri splenic region and close to the region of hepatic flexure of colon. The largest single lesion in the region of hepatic flexure of the colon measuring 8.9 x 6.7 cms. Left sided fatty inguinal hernia was seen. Small bowel loops were displaced to the right.

Intense mesenteric fat stranding with

calcific density/ post-operative changes in the left anterior para renal region were observed.

In view of low haemoglobin and low albumin levels, the patient was transfused with packed red cells and albumin infusion was given in preparation for the surgery.

The surgery lasted for eight hours and all tumours were removed successfully including the spleen as there were multiple tumours over the spleen. The largest tumour weighed 5 kgs and rest of the abdominal tumours weighed 5 kgs, making it a total of 10 kgs.

The patient tolerated the surgery very well. Post operatively, the patient was monitored in the ICU. The low haemoglobin was corrected with packed cell volume transfusions and albumin infusions. The patient was started orally from the first postoperative day with liquids and gradually switched over to semi-solids and soft diet. The patient was discharged on the fifth post-operative day in good general condition.



Figure 1: CT Scan showing the tumour



Figure 2: Operative picture showing large tumour



Figure 3: Resected large single large tumour with multiple tumours of varying sizes and spleen



Intraoperative Radiation Therapy (IORT) -Winning Combination of Technology and Teamwork



Dr Vineeta Goel Director & HOD, Radiation Oncology Fortis Hospital, Shalimar Bagh, New Delhi



Dr Kapil Kumar Director & HOD, Surgical Oncology Fortis Hospital, Shalimar Bagh, New Delhi

Intraoperative radiation therapy (IORT) refers to a single shot of high dose radiation therapy given to the tumour bed (area of cancer) during cancer surgery. IORT is a form of precise and impactful radiation therapy. IORT improves the chances of local control of cancer many times with least side effects.

Many people confuse IORT with perioperative brachytherapy. In perioperative radiation, brachytherapy catheters are placed in tumour bed during surgery and radiation therapy is delivered or started four-five days after surgery and continues for the next three or four days while IORT involves the delivery of a single, high dose of radiation at the time of surgery.

IORT is especially useful in previously radiated recurrent head neck cancers, rectal cancers and abdomino pelvic nodal recurrences.

There are very few centres across the world where IORT is practised routinely. We are fortunate that at Fortis Hospitals, we practise this technique judiciously. At Fortis Hospital, we practice HDR Brachytherapy based IORT. One can practise IORT only if there is strong culture of Tumour Board and collaboration within the Oncology Team.

We recently treated a patient with IORT for a recurrent lymph nodal lesion from a primary tongue cancer. Our patient was a 70-year-old lady who had squamous cell cancer in right lateral border tongue with right sided neck lymph nodes. She underwent near total glossectomy with bilateral neck dissection and reconstruction of tongue. Her histopathology report showed a cancer in tongue and bilateral positive lymph nodes without extracapasular extension. After surgery, she was treated with postoperative radiation therapy to oral cavity and bilateral neck. On first follow up, her PET CT scan showed a solitary contralateral single neck lymph node within previous operated and radiated field. She was taken up for salvage neck dissection and IORT catheters were placed after nodal clearance. The patient was then moved to brachytherapy room while she was still on anaesthesia machine.

The patient was given HDR Brachytherapy 10 Gy in a single shot. She was then wheeled back to the operation theatre. IORT catheters were removed and she underwent completion of surgery.

Take Home Message

Intraoperative RT is an effective form of radiation therapy, especially in challenging circumstances.



Figure 1: Intraoperative Radiation Therapy



Colonic Cancer with Lynch Syndrome in a 14-year-old Adolescent -A Rare and Interesting Case Presentation



Dr Hemanth Kumar Kasaragod Senior Consultant and Unit Head Department of MAS, GI and Bariatric Surgery Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Case History

A 14 year old boy presented with vague abdominal pain, loss of appetite, progressive constipation and loss of weight (12kgs) since 2 months. He was initially evaluated by a gastroenterologist, who did an ultrasound abdomen and upper GI endoscopy. Both were normal. He was then put on symptomatic treatment. However the complaint persisted. On follow up, CT abdomen was done which showed a obstructive growth in the descending colon with proximal dilated colon and dilated terminal ileum. Colonoscopy was done which showed a non-passable stricture growth in the descending colon. Biopsy was taken from the growth which showed a moderately differentiated adenocarcinoma. The PET CT done showed FDG avid enhancing circumferential mural involving the descending colon causing intestinal obstruction, with few mildly FDG avid abdominal and retroperitoneal lymph nodes suspicious of mitotic pathology.

A multi-disciplinary approach was adopted involving a surgeon,

anesthesiologist, oncologist, paediatrician, child counsellor, pathologist and the ICU team. The difficulty we had initially managing the case was the emotional turmoil faced by the child and his parents in accepting the condition, especially with the child having malignancy. The young age at presentation with features of obstruction were not helping either. Counselling was done in depth including the psychological aspect involving the entire multidisciplinary team. Nutrition in the child was another issue as the complaints extended over a period of two months, loss of appetite, weight loss of over 12 kgs and an obstructive growth with proximal dilatation of the bowel. There was electrolyte imbalance, hypo-albuminaemia and elevated leukocyte count. The

obstruction precluded bowel preparation.

The anaesthesia concerns included higher chances of aspiration in view of the obstruction, management of pain both during the intra-operative and post-operative period (epidural anesthesia was considered), measures to ensure on table extubation, maintaining adequate volume during the surgery and minimizing the use of blood and blood products.

The patient was taken up for surgery as a semi urgency- a laparoscopic left extended hemi-colectomy under general anesthesia. He was prepared prior to the surgery with continuous Ryle's tube aspiration, hydrated well with fluids, electrolyte imbalance correction, albumin was given and



Figure 1: CT Showing Obstructed Growth with Proximal Dilatation of Large and Small Bowel



antibiotics were started. Risk of the procedure and anesthesia was explained to the family. Informed consents were taken.

Patient underwent laparoscopic extended left hemi-colectomy with proximal ileostomy under general anesthesia and epidural on 20/12/2021. What made this surgery unique and difficult was the presence of obstructive tumor growth with grossly dilated and oedematous proximal bowel loops. Proximal diverting ileostomy was done in view of this finding.

The question of laparoscopy is debatable in these cases. However, with the desired expertise and advanced equipment, we could perform the surgery without compromising the oncological principles. Minimally invasive surgery has the benefits of decreased length of stay, smaller incisions, less narcotic use, less blood loss, and improved pulmonary function after surgery.

There was minimal intra-operative blood loss and no blood or blood products were transfused. Patient was extubated and shifted to the surgical ICU for monitoring.

Subsequently, he was shifted to the room and discharged on the 5th postoperative day on oral high protein diet and a functional stoma.

His final histopathological diagnosis was adenocarcinoma colon (PT3, PN2a, PMX) - stage iii b. Immunohistochemistry testing for mismatch repair showed tumor is MMR proficient (PMMR) and likely microsatellite stable with a high probability of Lynch Syndrome.

On follow up, the patient is doing well and will be started on chemotherapy shortly.

Colonic malignancy in adolescent- A Review of Literature

Colorectal cancer, one of the most common malignancies among adults,

is rare in adolescence. Colorectal cancer (CRC) is a formidable health problem worldwide. It is the third most common cancer in men (10.0% of all cancer cases) and the second most common in women (9.4% of all cancer cases). The number of CRCrelated deaths accounts for 8% of allcancer deaths and making CRC the fourth most common cause of death due to cancer. In India, the annual incidence rates (AARs) for colon cancer and rectal cancer in men are 4.4 and 4.1 per 100000, respectively. The AAR for colon cancer in women is 3.9 per 100000. Colon cancer ranks 8th among men. For women, colon cancer ranks 9th. Of those reported cases, less than1% are found in children. This low incidence coupled with non-specific symptoms and aggressive natural history leads to a poorer prognosis than in reported adult series.

Although CRC still remains a disease of older adults, incidence has been increasing in recent years amongst adolescents and young adults (AYAs) . The presenting symptoms and signs are similar to the more common conditions found in childhood but, because of its rarity, often leads to a delayed diagnosis and hence presents at an advanced and incurable stage. The prognosis is therefore likely to be far worse than in adults. The outcome in adolescents with this disease is markedly worse than in adults with several possible explanations ranging from late diagnosis to aggressive biology.

The age-adjusted annual incidence rate is 0.31 per million per year in the age range 0-19 years .There does not appear to be any geographical or racial difference in the studies published, but there is a 2:1 male to female ratio in most studies. Some have suggested a possible increased risk among lower socioeconomic groups especially in the third world, related to poor nutrition or chronic gastrointestinal infections, such asamoebiasis and schistosomiasis, which are associated with an increased incidence of malignancy.

Numerous risk factors have been proposed to explain the rising incidence of CRC in younger patients, but uncertainty remains. Possible



Figure 2: Upper G.I Endoscopy Showing Obstructive Tumor

Clinical Connect Eastering a culture of innovation and excellence

acquired risk factors include diet (eg, high consumption of red meat and fast food), obesity, diabetes, changes in gut microbiome, and infectious agents.

Acquired risk factors for young onset CRC include prior abdominal radiation for the treatment of childhood malignancies and inflammatory bowel disease, especially ulcerative colitis.

Several inherited polyposis syndromes predispose to CRC, including familial adenomatous polyposis (FAP), MUTYH-associated polyposis, juvenile polyposis syndrome, Cowden syndrome, and Peutz-Jeghers syndrome.

CRC in AYAs may be associated with a familial cancer syndrome, although without universal screening for germline mutations in this group it is difficult to quantify the rate of heritable cancers. While inherited cancer syndromes are more likely to affect a younger population, most CRC cases in AYAs are sporadic in nature. In addition, only 22% of AYAs with CRC have a family history of the disease. Identifying an inherited cancer syndrome has important implications for both the patient and his or her family with respect to cancer surveillance and other means of managing inherited cancer risk.

The most common hereditary cancer syndrome associated with CRC is Lynch syndrome (LS).Lynch syndrome, is an autosomal dominant genetic condition.LS was previously termed hereditary non-polyposis colon cancer. Because patients with Lynch syndrome can have polyps, the term HNPCC has fallen out of favour. In some series, LS is associated with a lifetime risk of CRC as high as 70%. While the median age of onset is in the fifth decade, 40% of CRC cases in LS are diagnosed before age 40. Often, colonic tumors in LS are mucinous, high grade, and right sided. Synchronous or metachronous

lesions are also common .Lynch syndrome-causing mutations are found in approximately 3% of all diagnosed colorectal cancers.

People with Lynch syndrome are more likely to get colorectal cancer and other cancers, and at a younger age (before 50), including

- Uterine (endometrial),
- Stomach,
- Liver,
- Kidney,
- Brain, and
- Certain types of skin cancers

Lynch syndrome is due to inherited changes (mutations) in genes that affect DNA mismatch repair, a process that fixes mistakes made when DNA is copied. These genes (MLHL, MSH2, MSH6, PMS2, and EPCAM) normally protect one from getting certain cancers, but some mutations in these genes prevent them from working properly

Genetic counseling and genetic testing are recommended for families, preferably before the onset of colon cancer. Colonoscopies are recommended as a preventative method of surveillance for individuals who have Lynch syndrome, or LSassociated genes. Specifically, it is recommended that colonoscopies begin at ages 20–25 for MLH1 and MSH2 mutation carriers and 35 years for MSH6 and PMS2 mutation carriers. Colonoscopic surveillance should be performed at a 1-2 year interval for Lynch Syndrome patients.

Presentation

The symptoms of CRC in AYAs are often nonspecific, including vague abdominal pain and weight loss. Less common presenting symptoms include diarrheoa, constipation, nausea, vomiting, anorexia, rectal bleeding, abdominal distension, and intestinal obstruction.

Left-sided tumors, most common

among AYAs, may cause change in stool caliber and bowel habits, whereas right-sided tumors are more likely to cause symptoms of anaemia. Rectal tumors may lead to blood per rectum and tenesmus.

Delay from symptom onset to diagnosis often exceeds 6 months among AYAs due to low suspicion for malignancy in this age group. Advanced stage at presentation is more likely in AYAs compared to older adults with CRC, perhaps due to diagnostic delay and lack of screening.

Regarding symptom burden from cancer and cancer-related treatment, younger patients (less than 40 years) more commonly report moderate to severe pain, nausea, fatigue, dyspnea, drowsiness, and distress. Greater impairment of activity, mood, relationships, employment, and enjoyment of life has also been reported in this age group.

Prognosis

Long-term survival rates for CRC are improving for both AYAs and older adults. Whether prognosis is different for young patients is a matter of controversy. Some studies indicate worse survival among AYAs with CRC compared to older adults, perhaps related to higher stage at presentation in younger cohorts. Other studies do not support worse outcomes among AYAs Stagematched analyses suggest similar or better outcomes for young patients, particularly with advanced-stage disease. For example, 5-year



Figure 3



survival rates for patients with stage 4 CRC in one study were 18.1% versus 6.2% for AYAs and older adults, respectively. These findings are likely influenced by administration of cancer treatments. Younger patients are more likely to receive systemic therapies at any stage of disease and more likely to receive radiation for rectal cancer. Younger patients with advanced disease are likely to have sufficient functional reserve and limited comorbidity, allowing for multimodality therapies including surgical metastasectomy and systemic drug therapy with combination chemotherapy and biologic agents.

Lynch-syndrome related cancers, which are associated with a favorable prognosis, occur more frequently in AYAs; however, sporadic cases with MSI are more frequent in older adults. How intrinsic differences in biology influence CRC-related prognosis by age category remains uncertain.

Management of CRC

Since CRC in AYAs remains relatively uncommon, this age group is underrepresented in clinical trials. Treatment guidelines are based largely on evidence from older adults. Multidisciplinary care is crucial for management of CRC and prompt referral to centers experienced in the care of AYAs should be considered for young patients.

Early-stage disease: For the purpose of this review, early-stage disease refers to stages 1-3 CRC (ie, nonmetastatic). In this setting, radical surgery is the pillar of curative treatment.

Oncologic resection involves removal of the tumor and draining nodal basins with clear margins. This is achieved by removing the major vascular pedicle and lymphatics supplying the tumor, and en bloc resection of organs infiltrated by the tumor. A margin of 5 cm of bowel both proximal and distal to the tumor should be removed (although this distal margin may not be feasible with a low-lying rectal tumor). Right hemicolectomy is carried out for tumors proximal to the splenic flexure, whereas left hemicolectomy is carried out for tumors of the descending colon.

Adjunctive treatments may be considered for localized tumors. Evidence for adjuvant chemotherapy is largely based on older adults as AYAs are markedly underrepresented in clinical trials. Some studies suggest differences in toxicity among younger patients (eg, more nausea and less neutropenia), but survival benefit associated with adjuvant chemotherapy does not differ between AYAs and older adult populations

Adjuvant chemotherapy may be considered for reduction of cancer recurrence risk for resected stage 3 or high-risk stage 2 CRC. Features of a stage 2 tumor that confer higher risk of recurrence include tumor penetration of the peritoneum (T4), high grade, perforation or obstruction at presentation, lymphovascular or perineural invasion, and inadequate lymph node sampling.

After surgery and adjuvant therapy, surveillance including periodic clinical assessment, computerized tomography scan, colonoscopy, and carcinoembryonic antigen levels are pursued to monitor for recurrence.

Metastatic disease: Combination chemotherapy plays a role in prolonging survival and reducing cancer- related symptoms in the context of extensive metastatic disease. Biologic agents including anti-angiogenics (eg, bevacizumab) and antibodies against the epidermal growth factor receptor (eg, cetuximab and panitumumab) for RAS wild type tumors can also prolong survival with metastatic disease. With sequential lines of therapy, median survival now exceeds 2.5 years.Much like adjuvant therapy, the evidence for treatment of metastatic CRC is based largely on an older adult population, but age less than 50 years is not predictive of different survival outcomes with the use of palliative chemotherapy

In the case of a limited burden of cancer spread, surgical resection of metastatic deposits may result in a disease-free interval, or cure in a minority of cases.

Metastasis limited to the liver, lung, or peritoneum may be operable. Resection of peritoneal disease is often offered in conjunction with h e a t e d in tra - periton e al chemotherapy, although there is uncertainty regarding the added value of this therapy compared to surgery alone. Multidisciplinary review and expert surgical consultation are imperative.

Conclusion

Unlike in older adults, CRC in AYAs is on the rise. Younger patients are often afflicted with advanced-stage disease, in part from delayed diagnosis. Most cases are not associated with a familial syndrome and a full understanding of the biology of CRC in this age group is lacking. Since AYAs are underrepresented in clinical trials, the treatment parallels that for older adults. Optimal management hinges on multidisciplinary collaboration, with special attention to the unique needs of patients in this age group with respect to pregnancy, fertility preservation, parenting responsibilities, and threat to livelihood from treatment toxicity. Given the rising incidence of this disease, research is needed to define the role of earlier screening and to tailor treatment paradigms for young patients.
Neuroendocrine Carcinoma of Cervix - A Case Report



Dr Mamta Mishra Director, Obstetrics & Gynaecology Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj



Dr Neema Sharma Director, Obstetrics & Gynaecology Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Dr Shoma, Dr Nitin Dumeer and Dr Gopendro Singh Naorem Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Abstract

Neuroendocrine carcinoma of cervix is a very rare cancer of the cervix. Till date, treatment modalities are not clear and the prognosis is said to be poor. We report a case where a woman presented with irregular bleeding and on examination there was a mass which looked like a cervical polyp arising from posterior lip of the cervix. However, left lateral vaginal fornix looked eaten up, which was unusual finding with the polyp. Cervical biopsy was done and neuroendocrine tumour of cervix was diagnosed. Currently, the patient is on chemotherapy and is stable.

Introduction

Neuroendocrine tumour can occur at rare site such as the female genital tract. The incidence is 0.9% to 1.5% of the tumours of cervix. The lung and the pancreas are among the more common sites of neuroendocrine tumours. Staging is done as for other cancers of the cervix. Treatment options are usually extrapolated from small-cell lung cancer. For early stages radical hysterectomy followed by chemotherapy or concurrent chemoradiation is suggested. For advance stage, it is mainly chemotherapy. Awareness among gynaecologists is essential for timely referral of these aggressive malignancies.

Case Report

A 46-year-old P2L2 presented with irregular bleeding since last two years in OPD, in September 2021. She had a PAP smear done a year ago, which was normal. General and abdominal examination was normal. On per vaginal examination, there was a mass 4 cm x 2 cm, which was arising from the posterior lip of cervix and extending towards left fornix and involving one fourth of the anterior lip. Three-fourth of the anterior lip was normal. Ultrasound was done. It suggested normal sized uterus with thin endometrium. The cervix was bulky and a heterogenous, large hypoechoic irregular lobulated measuring 21 x 19 mm posteriorly and a similar 18 x 13 mm lesion was seen in the cervical canal. Both ovaries were normal. She was admitted for

examination under anaesthesia and cervical biopsy. Clinical findings were confirmed during examination under anaesthesia, parametrium and rectal mucosa appeared free. Histopathology revealed poorly differentiated large cell neuroendocrine tumour of cervix. In immunohistochemistry PANCK, P63, synaptophysin, chromogranin was positive in tumour cells. Ki 67 was very high. MRI was done, which suggested that the parametrium was free and one internal iliac node was enlarged measuring 10 x 14 mm. A multidisciplinary meeting was conducted and she was advised chemotherapy. The patient went for a second opinion. A PETCT was done. It was suggestive of an FDG avid ill-defined thickening in uterine wall extending in to the upper vagina likely representing a primary mitotic pathology with right paracervical extension with right external and common iliac lymph nodes and no evidence of distant metastasis. She was started on chemotherapy Cisplatin and Etoposide at FMRI Gurgaon. She is stable as of now.

Discussion

Squamous cell carcinoma of cervix is the most common cancer of cervix. Neuroendocrine tumours account for only 1-2% of all cervical cancers. These are rare and aggressive cancer of cervix derived from neuroendocrine cells. It is classified as well differentiated and poorly differentiated. (Refer to Table 1). Our case was a poorly differentiated large cell carcinoma.

Aetiology

Due to rarity of these tumours, the aetiology is poorly understood. It is more common in Asian women with mean age at diagnosis of 49 years. However, several studies have demonstrated its association with Human Papilloma Virus (HPV). But so far, no pre-invasive lesion has been identified with neuroendocrine tumour. So, whether PAP smear test which is used worldwide for cervical cancer screening, can be used as a screening test for this cancer, is not known. In our case, PAP smear done a year ago was normal.

Symptoms

Presentation is same as in case of other cervical cancers, which is mainly abnormal bleeding, vaginal discharge, post-coital bleeding, etc. As these are very aggressive cancers, they usually present when the disease is at an advanced stage.

Sometimes, it can present with paraneoplastic syndrome such as hypercalcemia, Cushing syndrome, SIADH or neurologic disorders.

Diagnosis and Role of PAP Smear

Sometimes it may be detected by routine screening PAP smear. However, the efficacy of PAP smear as a screening modality is not clear as of now. Some women with this cancer of cervix have had normal annual PAP smears till the time they were diagnosed with cancer. It is to

| Classification | | Mitotic Index | Ki 67 Index |
|--|-------------------------|---------------|-------------|
| Well- Differentiated | | | |
| NETGI | | <2/10 | ≤ 2 |
| NETG2 | | 2-20 | 3-20 |
| NETG3 | | >20 | >20 |
| Poorly
Differentiated Nen | | | >20 |
| | Small Cell
Carcinoma | | |
| | Large Cell
Carcinoma | | |
| Table 1: Grading of neuroendocrine neoplasia of the cervix | | | |

be noted that our patient also had normal PAP smear a year ago.

Definite diagnosis is by biopsy of any cervical mass. Immunohistochemical stains is done to confirm it.

As these tumours are very aggressive MRI, PET/CT are usually recommended for proper staging and treatment.

Treatment

Multimodal approach to treatment is usually recommended. Knowledge gained from treatment of NEC affecting other sites of origin has been extrapolated to the treatment of cervical NEC.

For early-stage disease that is confined to the cervix and no lymph nodes or distant metastasis, the initial treatment depends on tumour size and involvement of local tissue.

For tumours < 4 cm in size, initial treatment frequently includes surgery in the form of radical hysterectomy and removal of appropriatelymph nodes. Ideally, this should be performed by a Gynaecologic Oncologist. After that chemotherapy with a combination of cisplatin and etoposide (EP) is recommended. Frequently, this is given at the same time as a radiation therapy and additional chemotherapy is given following completion of chemoradiation. An acceptable alternative approach for initial treatment of women in this category may be with chemoradiotherapy followed by chemotherapy alone, without surgery.

For early-stage disease with tumours (> 4 cm), chemoradiation is recommended. There is limited data about the use of neoadjuvant chemotherapy then proceeding with surgery, followed by more chemotherapy with consideration for radiotherapy as well.

For locally advanced disease including those with lymph node metastasis, the recommended approach includes a combination of chemotherapy and radiation.

Prognosis

When looking at patients diagnosed at all stages, five-year survival for NEC of the cervix is worse than that for other more common types of cervical cancer (36 vs 60-70%).



Unsuspected Low Grade Endometrial Stromal Sarcoma -Clues to Improve Preoperative Diagnosis

Dr Mamta Mishra

Director, Obstetrics & Gynaecology Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Dr Neema Sharma

Director, Obstetrics & Gynaecology Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Dr Shoma, Dr Nitin Dumeer and Dr Gopendro Singh Naorem Fortis Flt Lt Rajan Dhall Hospital, Vasant Kunj

Abstract

Endometrial stromal tumours are extremely rare, having an incidence of one or two among a million women. Pre-operative diagnosis is difficult and most often, the diagnosis is only established after surgery. We report a case where low-grade endometrial sarcoma was diagnosed after hysterectomy in a young woman. Retrospectively, we analysed to look for clues which could help to improve pre-operative diagnosis.

Introduction

Low grade endometrial stromal sarcoma (LG-ESS) is a rare malignant neoplasm of the uterus (affecting the body of the uterus more than the cervix) and extra-uterine sites. It commonly presents as abnormal uterine bleeding and pelvic pain. However, it can present as uterine mass and metastases to the adnexa, lymph nodes and lungs. It is a slow growing tumour and recurrences, either local or distant, can occur even after 20 years. Pre-operative diagnosis is extremely difficult. Ultrasound can easily misdiagnose it as fibroid, adenomyosis or polyp.

Case

A 32-year-old P2 woman presented with secondary dysmenorrhea since

last six months. She also had recently developed prolonged and intermenstrual bleeding. Due to COVID, she delayed medical consultation initially. However, her pain gradually worsened with each cycle. She used to take injectable diclofenac sodium for pain relief for 6-7 days in each cycle. On examination, her vitals were stable. However, she looked pale. Abdominal examination revealed a 14-week-pregnancy-sized, non-tender, firm mass with regular margins and arising from the pelvis. Per vaginum examination confirmed that uterus was enlarged, of 14 weeks' size and mobile.

USG done revealed 5 x 3.5 x 4.8 cm submucosal fibroid. MRI was done, which also confirmed submucosal fibroid. Her hemoglobin was 10.0gm/dl. CA 125 and LDH were 45IU/dl and 250 respectively. Pain was disproportionate to the clinical and ultrasound finding. Strategies to conserve the uterus were discussed. However, as the pain was severe and there was a small chance of recurrence of fibroid, it was decided to do hysterectomy. Total Laparoscopic Hysterectomy with conservation of tubes and ovaries was done on 16.12.20 at Fortis Hospital, Vasant Kunj, New Delhi.

Histopathology showed a tumour with infiltrating margins into the myometrium characterised by tongue-like extensions. Mitotic activity was low (<5/10hpf). No necrosis was seen. It was suggestive of low-grade endometrial sarcoma. Immunohistochemistry was done. Vimentin was diffuse and strong positive in tumour cells. CD10 and proliferative marker KI67 was also positive whereas desmin and H Cal Desmon were negative.

A multidisciplinary meeting was held

and it was decided to do bilateral s a l p i n g o - o o p h o r e c t o m y . Laparoscopic bilateral salpingooophorectomy was done on 05.01.2021. Histopathology of tubes and ovaries were unremarkable.

One year after surgery, the patient is absolutely fine.

Discussion

The prevalence of unsuspected sarcoma is one in 352 women and the risk of leiomyosarcoma is one in 498 in women with presumed fibroids.

It is not uncommon to misdiagnose low grade stromal tumour as leiomyoma preoperatively. This can lead to a conservative approach such as delaying treatment, opting for medical management or myomectomy and morcellation rather than hysterectomy.

So, is there a possibility to improve diagnosis preoperatively.

Clinical Findings

Abnormal vaginal bleeding and pelvic pain are nonspecific symptoms which are commonly present in both fibroids and uterine cancer. In our case, the pain was very severe, of short duration and was worsening with each cycle. In fact, the decision to do hysterectomy was taken mainly because of severe pain.

Serum Markers

Only a small number of studies are currently available that evaluate the use of serum markers in predicting uterine cancer, and none have been reliable. Mostly, studies are done to correlate CA125 and LDH with leiomyosarcomas and not endometrial stromal sarcoma.

In our case, CA125 and LDH were mildly raised. Although, nonspecific



but does appear significant when analyzed retrospectively.

Imaging

Ultrasound is not a good modality to distinguish between leiomyoma and endometrial stromal sarcoma. MRI findings were evaluated again so as to improve the pre-operative diagnosis.

Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) can be useful for a pre-operative diagnosis. It can alert us to leiomyoma variants and possibly endometrial stromal sarcoma. In our case it revealed polypoidal circumscribed mass arising from anterior myometrium projecting into the endometrial cavity, it has well defined margin appears isointense on T1 sequence, hyperintense on T2 weighted images with restricted diffusion. Contrast images show moderate homogenous enhancement within the mass and the presence of a thin enhancing capsule. The important feature in MRI is the presence of bands of low-signal intensity within the area of myometrial invasion. This is due to the worm-like permeation of tumour cells into the myometrium.

Leiomyoma on the other hand shows low T2 signal similar to myometrium often with inner whorled and nodular structure. However, leiomyoma can have variable appearance on MRI depending on cellularity and presence of degeneration, necrosis and calcification.

Decision to do hysterectomy was difficult and was taken in view of severe pain. Later on it turned out to be a wiser move.

Conclusion

Low grade endometrial stromal sarcoma is a rare pathology, more so in young women. However, awareness about the diseases is essential for clinicians for proper counselling and management. High degree of suspicion along with subtle signs may help to diagnose it pre-operatively.

Learning Points

- Endometrial stromal sarcoma is rare malignant tumour of the uterus
- Cases are reported in young women
- It is often misdiagnosed as fibroid uterus
- Awareness about this condition is important for the clinician
- A high degree of suspicion is required to diagnose it preoperatively



Figure 1: H&E 10x; Tumour showing cells with ovoid nuclei and minimal mitotic activity; entrapped spiral arterioles seen



Figure 2: H&E 20x



Figure 3: IHC CD-10; diffuse uniform strong positive in tumour cells



Figure 4: Saggital T2 image showing hyperintense mass



Simultaneous Surgical Management of Malignancy and Coronary Heart Disease: Our Meritorious Experience

Dr Sandeep Nayak Director - Surgical Oncology Fortis Cancer Institute, Bengaluru

Dr Bharath C, Dr V Sreekanth Reddy Dr Sudarshan, Dr Nischal RP

Introduction

Coronary heart disease and cancer are the most common causes of mortality due to disease across the globe ^[1]. It has been a dilemma for surgical team to decide which surgical procedure should be done first. Performing Coronary artery bypass graft (CABG) first leads to mandatory initiation of anti-platelets which may delay the oncological procedure leading to cancer progression^[2]. And performing cancer surgery first puts the patient at risk in view of the existing cardiac issues. It has been shown that simultaneous surgical intervention for cardiac and non-cardiac purposes is feasible ^[3]. We are herewith describing our case series of combined surgeries

Combined Surgical Procedure

All patients underwent combined CABG and oncological resection under same general anesthesia. CABG was performed first ensure cardiac revascularisation first followed by oncological resection. Coronary anastomosis was performed on beating heart using off pump CABG surgery in supine position with a median sternotomy approach.

Then, patient was handed over to surgical oncology team for the oncological resection. Wherever possible minimal access approach was followed for the ablative procedure to reduce the surgical stress. One patient underwent right upper and middle bilobectomy through the same open sternotomy approach. Another person underwent wide local excision of

breast lesion after closure of the sternotomy incision. Maintenance of sterility was a challenge in this case but post operative period was uneventful. One patient underwent laparoscopic distal gastrectomy with D2 lymphadenectomy after closure of the sternotomy wound. Complete D2 lymphadenectomy along hepatoduodenal ligament, common hepatic region, celiac, left gastric and proximal splenic group region were carried out without compromising oncological clearance. One patient underwent similar D3 lymphadenectomy for growth in hepatic flexure without any compromise. Both these laparoscopic resections had uneventful post-surgery period. Two head and neck surgeries were performed involving neck dissection. One was wide local excision of tongue lesion and another was of buccal mucosa along with reconstruction with naso-labial local flap.

Follow up

Median follow up of present study was 31.5 months (6-38). One patient of carcinoma lung developed recurrence after 6 months after which targeted therapy was initiated and patient is in remission after a follow up of 32 months. Rest of the patients are disease free.

Discussion

Performing both the procedure under same anaesthesia requires expertise from both surgical teams and anaesthesia team. Role of anaesthetist is extremely crucial. It is important to maintain oxygen demand and supply for all patients with CHD under surgery. Various factors can aggravate the burden and influence oxygen supply and demand like sympathetic system stimulation, use of anaesthetic drugs, endotracheal intubation and blood loss^[4].

In our study no compromise was made in terms of achieving oncological

clearance. It is well known and proven in multiple studies that minimal access surgery reduces the surgical stress and has significantly improved short term outcome and recovery compared to open surgery.

Simultaneous procedures are feasible and safe but there are certain prerequisites that should be kept in mind

- a) Oncological resection must be curative. Disease must be nonmetastatic.
- b)Cardiac function should be adequate to tolerate dual procedure, that is ejection fraction must be atleast 40% and patient should not be in failure.
- c) The combined procedure should not be performed on emergency basis.
- d) Patients with history of chest or cardiac surgery or with pleural adhesion should also avoid undergoing combined procedure.

References

- Dagenais GR, Leong DP, Rangarajan S, Lanas F, Lopez-Jaramillo P, Gupta R, Diaz R, Avezum A, Oliveira GB, Wielgosz A, diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. The Lancet. 2020 Mar 7;395(10226):785-94.
- Chassot PG, Delabays A, Spahn DR. Preoperative evaluation of patients with, or at risk of, coronary artery disease undergoing non-cardiac surgery. British journal of anaesthesia. 2002 Nov 1;89(5):747-59.
- Yang Y, Xiao F, Wang J, Song B, Li XH, Li J, He ZS, Zhang H, Yin L. Simultaneous surgery in patients with both cardiac and noncardiac diseases. Patient preference and adherence. 2016;10:1251.
- 4. Zhao X, Li Y, Kong HY, Zhang L, Wen XH. Anesthetic management of off-pump simultaneous coronary artery bypass grafting and lobectomy: Case report and literature review. Medicine. 2017 Dec;96(50).Parambath SR. Variations in common

TRIVIA

Crossword



DOWN

- 1. _____vaccination is highly effective against development of anal and cervical dysplasia.(3)
- 2. A ____ Scan uses a radioactive drug(tracer) to show both normal & abnormal metabolic activity.(3)
- 3. _____ is the removal of a small section of the tumor for analysis by the histopathologist for a precise diagnosis.(6)
- 4. Around 400 B.C., ______ is said to have named masses of cancerous cells karkinos Greek for crab.(11)
- 5. _____ Markers are substances in the body that may indicate the presence of cancer.(5)

ACROSS

- 6. Most likely site of an asymptomatic recurrence of head and neck cancer is _____.(8)
- 7. The amino acid depleted in carcinoid tumors is _____.(10)
- 8. The British surgeon Percival Pott, in 1775 identified the first cause of cancer; the cancer of the _____ was a common disease among chimney sweeps.(7)
- 9. _____ Care is designed to relieve symptoms and improve the quality of life of one suffering from cancer.(10)
- 10. On October 2, 1996, Lance Armstrong was diagnosed with _____ cancer.(10)
- 11. _____ died on October 5, 2011 after a battle with pancreatic cancer.(5,4)



CLINICAL RESEARCH

Ongoing Innovative Oncology Projects at Fortis

- Study on Autologous Dendritic Cell Immunotherapy for use in Refractory Prostate, Ovarian, Colorectal and Lung Cancer Dr Rajeev Bedi
 - Phase IV Study on Regorafenib in patient with Metastatic Colorectal Cancer (mCRC) - Dr Boman Dhabur
 - A Phase III Comparison Study between SB12 (proposed Eculizumab biosimilar) and Soliris[®] in Subjects with Paroxysmal Nocturnal Hemoglobinuria -Dr Rahul Bhargava



Study on Autologous Dendritic Cell Immunotherapy for use in Refractory Prostate, Ovarian, Colorectal and Lung Cancer



Dr Rajeev Bedi Principal Investigator, Department of Oncology Fortis Hospital, Mohali

Introduction to the Study Product

Phase IV/ PMS study on APCEDEN[®] is the first autologous cellular immunotherapy designed to elicit a T cell response to cancer and was approved for use in refractory prostate, ovarian, colorectal and lung cancer by APAC Biotech Pvt. Ltd.

This is the first of its kind product, and is manufactured from the patient's own peripheral blood mononuclear cells (PBMCs). The product is designed to induce an immune response targeted against antigens expressed in cancer tissue.

It is a completely Made in India product, with Indian approval and Indian Patent.

Pl's opinion about the Investigational Product

Current Status - "Patient Prospects"

APCEDEN[®] is approved for use in refractory cancers where the patient has multiple chemo-failures and has exhausted all possible conventional treatment options. Moreover, being

completely autologous in nature, it is completely safe and associated with near-zero to negligible side effects.

It has shown improvements in quality of life, survival benefit as well and can also be used adjuvantly with other treatment options.

The clinical trial was conducted on refractory patients. They had exhausted all possible treatments. In such a challenging patient pool APCEDEN had shown considerable improvement in quality of life as well as survival benefit advantage. After multiple chemo failures, most patients are highly weak and improvements in their QOL are noticeable. The immense potential of dendritic cells is utilised to boost and enhance the patient's immune system to start fighting cancer better.

Phase IV Study on Regorafenib in patient with Metastatic Colorectal Cancer (mCRC)



Dr Boman Dhabur Principal Investigator, Department of Oncology Fortis Hospital, Mulund

Introduction to the Study Product – Regorafenib

Regorafenib is a multi-kinase inhibitor that potently blocks multiple protein kinases, including kinases involved in tumour angiogenesis (VEGFR1, VEGFR-2, VEGFR-3, TIE-2), oncogenesis (KIT, RET, RAF-1, BRAF, BRAFV600E), and the tumour microenvironment (PDGFR, FGFR).

In particular, Regorafenib prevent cancers from developing and spreading for a period of time. The product was first approved by FDA IN 2013 and by EMA in 2014. In July 2014, it was approved by DCGI.

The drug is used in patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan based chemotherapy, an anti-VEGF and anti-EGFR therapy.

The drug helps in reducing the risk of death up to 21% and 51% reduction in disease progression. The common side effects observed is anaemia, fatigue and decreased appetite.

Pl's opinion about the Investigational Product

Tablet Regorafenib is an acceptable drug modality. The benefits of the study to our patients would be, free of charge availability of the drug (Cost of drug INR 30000 for 1 bottle of 30T) and the associated tests/procedures which include haematological and radiological investigations will be paid by the study sponsor.

A Phase III Comparison Study between SB12 (proposed Eculizumab biosimilar) and Soliris[®] in Subjects with Paroxysmal Nocturnal Hemoglobinuria



Dr Rahul Bhargava Principal Investigator, Principal Director & HOD Haematology FMRI, Gurugram

Introduction to the Study Product

TThe Samsung Bioepis Co., Ltd had developed SB12, a similar biological medicinal product to Soliris[®]. SB12 and Soliris[®] have identical primary structure and the active substance for both products is Eculizumab, a humanised monoclonal antibody (IgG2/4 kappa immunoglobulin).

SB12 is produced by recombinant deoxyribonucleic acid (DNA) technology in a Chinese hamster ovary (CHO) mammalian cell expression system and purified by various affinity and ion exchange chromatography steps that include specific viral inactivation and removal procedures.

Aims and Benefits

The benefits of the study to our patients is the free availability of the drug and other associated laboratory tests or procedures.

The study aims to compare the safety, efficacy, pharmacokinetics and immunogenicity between SB12 (proposed Eculizumab biosimilar) and Soliris[®].

Pl's opinion about the Study:

Conducting clinical trials are very essential to mankind when done ethically. This drug is life saving for the patients. These patients could have been dead if the medication was not given to them.





ONCO CONNECT

Pan-Fortis Tumour Board Cases

- Case 1 Dr Sandeep Nayak, Dr Bharath G, Dr V. Sreekanth Reddy, Dr Kunal Nandi, Dr Ameenudin Khan
 - Case 2 Dr Sandeep Nayak, Dr Bharath G, Dr V. Sreekanth Reddy, Dr Deepak Ramraj, Dr Deva Prasad



Pan-Fortis Tumour Board Discussions

CASE 1:

Dr Sandeep Nayak Director - Surgical Oncology Fortis Cancer Institute, Bengaluru

&

Dr Bharath G, Dr V. Sreekanth Reddy Dr Kunal Nandi, Dr Ameenudin Khan

59-year-old female presented at our centre with history of bleeding per vagina and rectum since 1 month. There was associated abdominal pain on and off with no bowel bladder abnormalities. Per abdominal examination revealed a large uterus extending to umbilicus. Per vaginal examination was suggestive of bulky cervix and rectal examination was suggestive of a small polyp in posterior wall of rectum at 4 cm from anal verge. A contrast enhanced computed tomography (CECT) of abdomen and pelvis was performed which revealed multiple fibroids in uterus. A colonoscopy was performed which showed a 1x1cm polyp in the posterior wall of rectum at 3 cm from anal verge. Biopsy findings were tubular adenoma with high grade dysplasia.

A laparoscopic hysterectomy and bilateral salpingooophorectomy and transanal excision of the polyp was

performed and sent for frozen section. The uterus did not have any signs of malignancy on frozen section and rectal polyp revealed adenocarcinoma grade 2 infiltrating submucosa (SM2). Depth of submucosal invasion is less than 1mm. LVI/PNI negative. Base of resection was 0.1cm from tumor. Margins were revised after frozen section report. Tumor bud score was low. Histopathology report was discussed with the patient and relative and 9% chance of local nodal spread was explained. The patient was then planned for robotic intersphincteric resection in view of oncological clearance. Post-surgery was uneventful and patient was discharged in 3 days on full diet.

Early colorectal carcinoma are those which have invaded only the submucosal layer [1]. These are usually managed by colonoscopic polypectomy or transanal microsurgery [1]. Colonoscopic polypectomy is usually not an adequate treatment for a sessile T1 carcinoma. However, many of these patients can be adequately locally excised in the low rectum, provided there are no adverse risk factors for local recurrence and metastasis. Despite favourable selection, the results of local excision of T1 adenocarcinoma of the low rectum vary widely. There are several studies that report a high incidence of recurrence and lymph node metastasis after a full-thickness local excision. Depending on degree of submucosal invasion there are three groups, upper third (sm1), middle third (sm2), and lower third (sm3) [Figure 1]. In a study by Nascimbeni et al they found 8% in sm2 group had lymph node metastasis [4]. Based on these data in the present patient, surgery was planned.

References

- Morson BC, Bussey HJ. Predisposing causes of intestinal cancer. Current problems in surgery. 1970 Feb 1;7(2):1-50.
- Garcia-Aguilar J, Mellgren A, Sirivongs P, Buie D, Madoff RD, Rothenberger DA. Local excision of rectal cancer without adjuvant therapy: a word of caution. Annals of surgery. 2000 Mar;231(3):345.
- Lamont JP, McCarty TM, Digan RD, Jacobson R, Tulanon P, Lichliter WE. Should locally excised T1 rectal cancer receive adjuvant chemoradiation?. The American journal of surgery. 2000 Dec 1;180(6):402-6.
- Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Diseases of the colon & rectum. 2002 Feb;45(2):200-6.



Figure 1: Classification on the basis of one third invasion in the submucosa



CASE 2:

Dr Sandeep Nayak Director - Surgical Oncology Fortis Cancer Institute, Bengaluru

Dr Bharath G, Dr V. Sreekanth Reddy, Dr Deepak Ramraj, Dr Deva Prasad

Patient is a 68-year-old gentleman with Diabetes and Hypertension on treatment. He did not give any significant family history of malignancies and gave no history of previous surgeries. He was evaluated for dysphagia for solids gradually progressing to liquids for three months.

On examination, his performance status was good. The general and abdominal examination were unremarkable. Initial work-up of Upper GI endoscopy showed an ulceroproliferataive growth, which

was circumferential extending from 35 cms to 40 cms (GE junction). The mid esophagus showed erythematous patches and dilated veins in upper esophagus. The scope negotiated beyond the growth; rest of the Upper GI was normal. Biopsy from the lesion showed moderately differentiated adenocarcinoma. PET CET showed a circumferential FDG avid mass in the distal esophagus extending across the GEJ unto the lesser curvature (SUV- 6.5). There were prominent lower paraesophageal, left gastric, GH nodes (SUV - 1.9). There were no visceral or skeletal lesions. The diagnosis was carcinoma of the gastroesophegeal junction. The patient underwent diagnostic staging laparoscopy, it was non metastatic. Right subclavian chemoport insertion was done. The patient received neoadjuvant chemotherapy - four cycles of FLOT (LD- 30.11.21). Post chemotherapy, PET scan showed significant interval decrease extent and FDG avidity at the primary site. Significant interval decrease in the nodes in lower paraesophageal, left gastric and GH region. Appearance of FDG avid nodes in the right upper paratracheal and highest mediastinal region, largest node is 8x 7 mm (SUV – 5.7); the right Supraclavicular nodes, 8x 9 mm (SUV – 4.5).

The case was discussed in the Tumour Board. Sampling of the new onset nodes either by image guidance or EBUS was not feasible because of the small size and location. Even on PET the sizes of the nodes were less than 1 cm.

Considering these factors, it was decided to consider these nodes as not significant and give the benefit to the patient and to consider surgery with curative intent.





LEARNINGS FROM COVID-19

- The Second-vs First-wave of COVID-19: More of the Same or a Lot Worse? A Comparison of Mortality between the Two Waves in Patients Admitted to Intensive Care Units in Nine Hospitals in Western Maharashtra - Dr Rahul Pandit
 - Hydroxychloroquine Pre-exposure Prophylaxis Provides No Protection Against COVID-19 Among Health Care Workers: A Cross-sectional Study in a Tertiary Care Hospital in North India -Dr Parvinder Chawla, Dr Shivani Juneja



The Second-vs First-wave of COVID-19: More of the Same or a Lot Worse? A Comparison of Mortality between the Two Waves in Patients Admitted to Intensive Care Units in Nine Hospitals in Western Maharashtra



Dr Rahul Pandit Director – Critical Care Medicine & ICU Fortis Hospitals, Mumbai

Kapil G Zirpe¹, Subhal Dixit², Atul P Kulkarni³, **Rahul A Pandit**⁴, Priya Ranganathan⁵, Sayi Prasad⁶, Zafer Khan Amanulla⁷, Vatsal Kothari⁸, Sourabh Ambapkar⁹, Sushma K Gurav¹⁰, Shrikant Shastrabuddhe¹¹, Vinod Gosavi¹², Mukund Joshi¹³, Bindu Mulakavalupil¹⁴, Charlotte Saldhanah¹⁵, Saanvi Ambapkar¹⁶, Madhura Bapte¹⁷, Sweta Singh¹⁸, Abhijit Deshmukh¹⁹, Khalid Khatib²⁰, Anmol Zirpe²¹, Gowri Sayiprasad²², Ameya Joshi²³

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-24042

ABSTRACT

Background:

India, along with the rest of the world, faced the challenging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. The second wave in India lagged behind that in the Western world, due to different timing of seasons. There is scarce data about the differences between the two waves, for intensive care unit (ICU) patients. We present the data of 3,498 patients from 9 ICUs of western Maharashtra.

Materials and methods:

We collected prospective data of hospitalised, RT-PCR confirmed, coronavirus-2019 (COVID-19) patients, from nine tertiary centers, after institutional ethics committee (IEC) approval. Then, we segregated and analysed the data of patients a d mitted to the ICU, for comorbidities, high-resolution computed tomography (HRCT) score, ventilatory support, etc. The primary outcomes were ICU and hospital mortality. We also performed multivariable analysis for predictors of ICU mortality.

Results:

Overall, there were 3,498 ICU patients. In the first wave, 1,921 patients needed ICU admission, while in the second wave, 1,577 patients. Patients in the second wave had significantly higher ICU (26.1 vs 13.4%, p <0.001) and hospital mortality (29.9 vs 18.2%, p <0.001) and need for ventilatory support of any type. More patients received steroids during the second wave. On multivariable regression, male gender, ICU admission during the second wave, increasing HRCT score, and need for intubation and mechanical ventilation were significant predictors of ICU mortality.

Conclusion:

ICU patients admitted during the two waves were of the similar age, but there were more females, and more patients had comorbidities during the second wave. The ICU and hospital mortality were significantly higher during the second wave.

Keywords:

Comorbidities, COVID-19, First wave, ICU mortality, Second wave, Ventilatory support.



Hydroxychloroquine Pre-exposure Prophylaxis Provides No Protection Against COVID-19 Among Health Care Workers: A Cross-sectional Study in a Tertiary Care Hospital in North India



Dr Parvinder Chawla Senior Consultant - Internal Medicine Fortis Hospital, Mohali



Dr Shivani Juneja Associate Consultant - Clinical Pharmacology Fortis Hospital, Mohali

Shivani Juneja, Proteesh Rana, Parvinder Chawala, Rekha Katoch, Kulvir Singh, Shobha Rana, Tamanna Mittal, Bhavnish Kaur and Simaranjot Kaur

https://doi.org/10.1515/jbcpp-2021-0221

Received August 15, 2021; accepted December 20, 2021; published online January 7, 2022

ABSTRACT

Objectives:

The use of Hydroxychloroquine (HCQ) prophylaxis has been recommended by the National task force constituted by the Indian Council of Medical Research (ICMR) for the prevention of corona virus disease 2019 (COVID-19) among healthcare workers (HCWs). However, this recommendation was based essentially on the preclinical data and limited clinical experience. The aim of this study was to evaluate the efficacy and safety of HCQ as a pre-exposure prophylaxis for COVID-19 infection among Indian HCWs.

Methods:

A cross-sectional study was conducted among HCWs of a tertiary care hospital in north India. The HCQ prophylaxis was initiated among 996 HCWs and they were followed up to 8 weeks for conversion to COVID-19 positive status and any adverse drug reaction (ADR).

Results:

About 10.3% of the study participants were tested positive for COVID-19 which was comparable to the positivity rate among HCWs not taking HCQ prophylaxis (9.7%).

Conclusions: HCQ was well tolerated at a weekly dose of 400 mg for 8 weeks but provided no additional benefit in prevention of COVID-19 among HCWs.

Keywords:

COVID-19; Hydroxycholoroquine; prophylaxis.



Answers To The Crossword



DOWN

- 1. HPV vaccination is highly effective against development of anal and cervical dysplasia.(3)
- 2. A PET Scan uses a radioactive drug(tracer) to show both normal & abnormal metabolic activity.(3)
- 3. Biopsy is the removal of a small section of the tumor for analysis by the histopathologist for a precise diagnosis.(6)
- 4. Around 400 B.C., Hippocrates is said to have named masses of cancerous cells karkinos Greek for crab.(11)
- 5. Tumor Markers are substances in the body that may indicate the presence of cancer.(5)

ACROSS

- 6. Most likely site of an asymptomatic recurrence of head and neck cancer is thoracic.(8)
- 7. The amino acid depleted in carcinoid tumors is Tryptophan.(10)
- 8. The British surgeon Percival Pott, in 1775 identified the first cause of cancer; the cancer of the Scrotum was a common disease among chimney sweeps.(7)
- 9. Palliative Care is designed to relieve symptoms and improve the quality of life of one suffering from cancer.(10)
- 10. On October 2, 1996, Lance Armstrong was diagnosed with testicular cancer.(10)
- 11. Steve Jobs died on October 5, 2011 after a battle with pancreatic cancer.(5,4)

The Fortis Network



Please send your comments, feedback and suggestions to <u>clinical.connect@fortishealthcare.com</u>