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A GRANT-IN-AID INSTITUTE OF DEPARTMENT OF ATOMIC ENERGY, GOVT. OF INDIA
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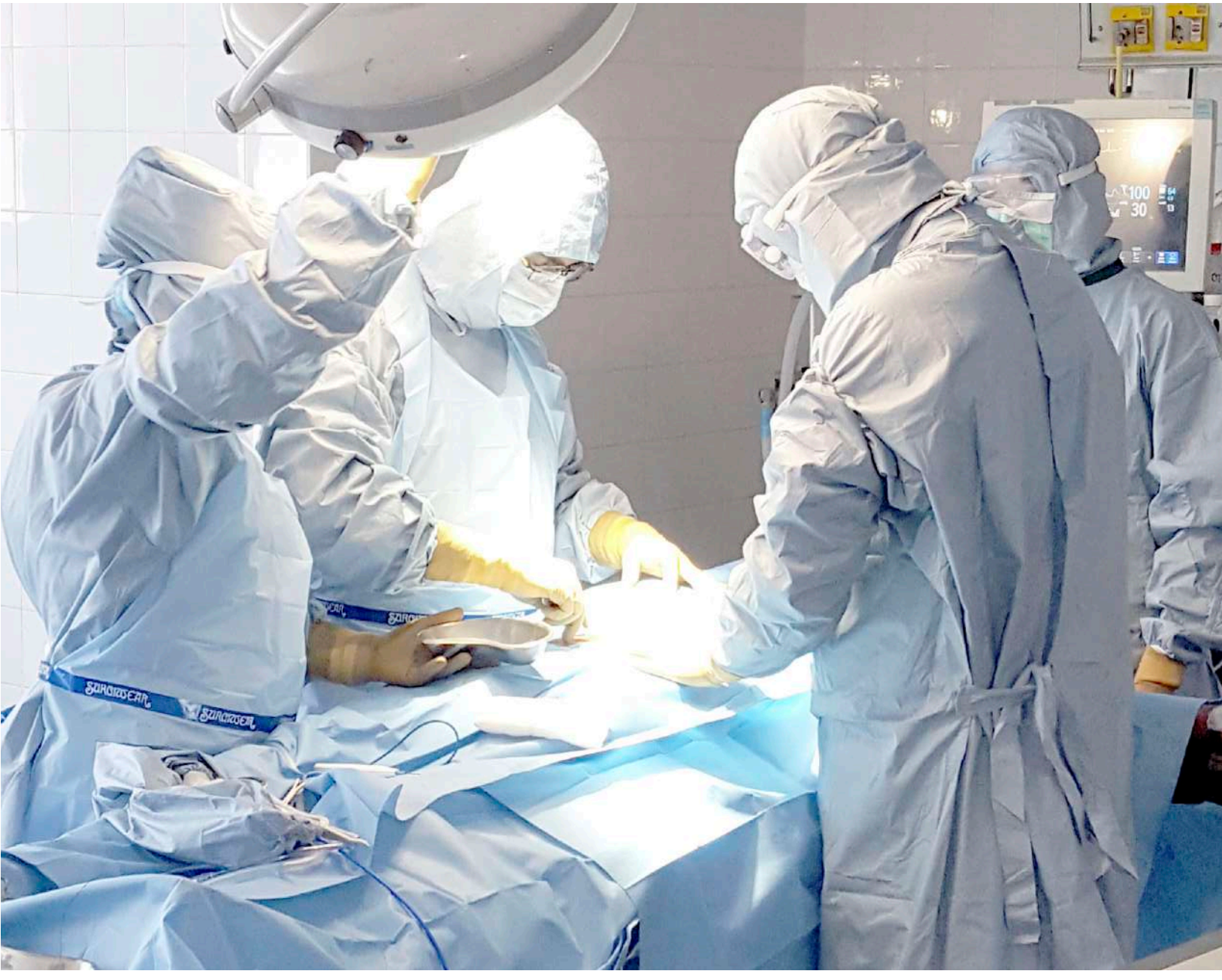
BBCI EDGE

A Science Magazine



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Director's Note

Dr A C Kataki
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I am delighted to release the first issue of **"BBCI EDGE - *A Science Magazine*"** in June 2020. The authors and the Editor with his team deserve all the appreciation for their efforts. I have read the content and do believe that the esteemed readers will find good material for scientific deliberation, which is indeed the goal of the magazine. With the growth of BBCI over the years into a flourishing teaching oncology Institute, and being one of the select few centres in India providing super-speciality courses in five recognized branches of oncology (MCh Surgical Oncology, MCh Head and Neck Oncology, MCh Gynaecological Oncology, DM Medical Oncology, DM Oncopathology) besides several other speciality oncology courses including PG Fellowship programmes, we have at our disposal a sizeable number of young and vibrant students from various parts of the country, who need an outlet for their academic fervour. We have always tried our level best to provide the proper growth environment and they have availed the access to the abundant and diverse oncologic patient community at BBCI to clinically hone their skills and become a resource for the country. Indeed, it gives me immense pride at having been able to supervise this transformation over the several years that I have been the Director of BBCI. Several important developments have occurred in the Institute in the last few months and find mention in this issue. Of particular significance is the spurt in the number of minimally invasive surgeries at BBCI, which helps us stay in relevance with the oncologic progress happening across the country. We have also had definitive strides towards skull base surgery. Our dedicated plastic surgery team has achieved persistently good results with microvascular repairs. Our medical and radiation oncology teams have projected their work at both national and international forums. The palliative medicine set up of BBCI has achieved several laurels and continues to make a strong impact among those who need us the most! Overall, the satisfaction of being at the helm of affairs is an unmitigated one. Let BBCI prosper and **BBCI EDGE** deliver the goods! ■

Message

BBCI: Marching Ahead Towards Academic Excellence

Dr. Debabrata Barmon
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Dr B Borooah Cancer Institute has seen a lot of academic achievement during the last one year. On 26th December 2018, I was entrusted with the responsibility of Principal academic coordinator of BBCI, Academia. I was a novice at that time as far as the administration of the Academia was concerned and even though I was a bit skeptical, our Director encouraged me for the job! The first few weeks were spent in understanding the working of the Academia. I got a lot of support from our Director and Dr M. Bhattacharyya, former Principal Coordinator of the Academia; also Dr Shiraj Ahmed and Dr Manigreeva Krishnatriya. Mention must be made of Mrs. Krishna Baruah (Sr. Librarian), Mr. Nisangka (Librarian) and Arundhuti, who form the backbone of BBCI Academia.

Once I understood the working pattern, my next big job was facing the MCh Surgical Oncology Recognition Inspection. We took the initiative to fill the necessary documentation and completed the formalities. The inspection coincided with the final MCh examination which was also something new for all of us and with the active cooperation of Dr Joydeep Purkayastha, HOD, and all the Surgical Oncology departmental colleagues we could initiate the first MCh examination process of BBCI. Dr. Niju Pegu was our first MCh student who passed out successfully. It was a very important day as we had Dr SVS Deo, HOD Surgical Oncology, AIIMS, New Delhi and Dr Quereshi from TMH Mumbai as our external examiners and Dr Ashish Singhal as MCI assessor. They were very much satisfied with the performance of our candidate and history was made when the first MCh Surgical Oncology student passed. Currently, BBCI has three seats in MCh Surgical oncology.

In the month of February 2019, FHNO announced the invitation of application for eligibility of hospitals for conducting FHNO fellowship program by various hospitals of the country. Dr Tashnin Rahman HOD, H&N Surgery along with her departmental colleagues took the opportunity and after discussion with our Director, who needless to say is always open to these ideas, we applied for the same and accordingly inspection

was carried out by Dr. P Arun from TMC, Kolkata. Eventually, we became one of the first centres in the whole of North-east to be a recognised centre for conducting fellowship programme under FHNO. Dr Saujanya Saikar from Maharashtra was our first FHNO candidate. We are hopeful that this association will go a long way.

In the month of March 2019 MCI notification of seat enhancement in post graduate courses was out and our Director wanted that we should avail this opportunity and he convened a meeting with Dr Apurba Kr Kalita, HOD, Radiation oncology along with his departmental colleagues. We decided to apply for four additional seats in MD, Radiation Oncology. Generally, this MCI related work is time bound and doesn't give the luxury of working in leisure. I am thankful to Dr A.K. Kalita and Dr M. Bhattacharyya along with all the faculties of the department for helping us in fulfilling all the necessary documentation within the prescribed time frame. I must thank Dr. Shiraj Ahmed for defying time shortage by flying to Delhi and submitting the form! An exhaustive Standard assessment form was filled up by the faculties from the departmentand mention must be made of Dr. Shashank Bansal , SR, Radiation Oncology who helped us a lot! Finally, the MCI inspection happened and to our joy we received three additional seats from the academic year 2020-21. Another milestone achieved!

Our Director envisioned super specialty courses in MCh Head and Neck Surgery, MCh Gynaecological Oncology and DM Oncopathology and it was exciting because only a few centres in the country had super specialty courses in all the five disciplines of Oncology. We were all mentally geared up to roll the ball and all the necessary documentation was systematically arranged. Our Director played a massive role in getting all the necessary papers in order. Here, mention must be made of the proactive role played by the Vice Chancellor of Srimanta Sankardeva University of Health Sciences Prof. (Dr) Deepika Deka madam along with all the office bearers of SSUHS for helping us in every aspects and finally we could apply for all the three courses on time. It must be mentioned that a lot of money is in stake as per subject we had to pay two lakhs as deposit which is forfeited if the application is not in order. Then came the stage of filling up of the SAF forms and all the Faculties / Residents declaration forms which was done very systematically by all the departmental HODs along with their faculties and we were ready for the Inspection. During this waiting period nobody in the concerned departments were allowed to go on leave as we were waiting for the MCI inspection, it was really a very difficult and anxious moment for all of us as according to the MCI calendar the inspection should be over by 31st December 2019, but it never happened by then and a few of our faculties had to forego or cancel their vacation plans in view of the uncertainties. Finally one after the another all three inspections happened, in the month of February and everything went on smoothly as by now we were expert in facing inspection having faced quite a few within a very short span. We got permission for all the three courses with two seats in each courses. That was one of the most important landmarks in our academic history which I am sure all of us will cherish throughout our life and our joy knew no bounds. Our Director was the happiest person during this time and he instantly wanted a grand celebration to mark this occasion, which we all did.

Last but not the least we are thankful to Dr R Badwe, Director, TMC, Mumbai and Prof. K. S. Sharma, Dean Academics Projects TMC for their never ending guidance and advice during this whole process and making our dream into reality. We will remain ever grateful to you Sir.

As I look back I feel really satisfied with the achievements which we all could achieve during the last one and a half year which I am sure will be cherished by all of us. Now if I ask myself where I go from here, I would definitely like to see the starting of MD Anaesthesiology at BBCI in the near future. ■

Editorial

Dr. Gaurav Das, MS, MCh
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Editor, BBCI EDGE

The **"BBCI EDGE - *A Science Magazine*"** is planned as a semi-annual publication intended to provide a platform to project scientific work. In these testing times of COVID19 pandemic, a relentless pursuit of scientific temper is in itself a harbinger of positivity. I am enthused by the generous input of articles from faculty and students of BBCI, which is a celebration of the aforementioned virtue. A few guest articles have also arrived on time to embellish this publication and I am very much thankful to all the authors.

The current issue focuses on orthopaedic oncology with several articles from the Institute and a guest article from Dr. Anand Raja, the Head of the Division of Musculoskeletal Oncology of Cancer Institute (WIA) to provide insights into primary bone tumours. As for an example, in the current scenario, about 2/3rds of patients with non-metastatic extremity osteosarcoma are long term survivors and about half of those who present with limited lung metastases may be cured of the disease. This encourages us to do the best for the functional outcomes, which depends on the extent of bone and muscle resection, the quality of the reconstruction and the complications. Limb salvage surgery is feasible in the vast majority of patients with extremity bone tumours. Proper patient selection and a planned resection are paramount. The adherence to multi-disciplinary management protocols is sine qua non. Proper work up with appropriate and comprehensive imaging before a properly done biopsy following all the known rules, and a complete staging work up is to be followed in all patients. The trend of inappropriate biopsies and unplanned surgeries has to be halted with dissemination of information across the medical fraternity. The histological response to chemotherapy and surgical margin status are vital prognostic information. All the aspects about delivery of appropriate systemic therapy are key factors in the treatment. This underscores the need to treat such patients in a dedicated unit of a cancer care centre. Our team at BBCI is gaining good experience in management of bone tumours.

This issue features a variety of rare presentations of malignant melanoma, which may be taken as another highlight. BBCI, being the premier teaching cancer Institute of the NE region, aims to achieve academic excellence and the **BBCI EDGE** is a key component of this endeavour. Hopefully, it will engage its readership and grow in the times to come. The contributors to this issue have done a commendable job towards that end. I regret that several articles could not be accommodated in this issue due to constraint of space and they will be incorporated in future ones. I would like to convey my special gratitude to the Director of BBCI for all the support and motivation. Mr. Ph. Surachandra Singha deserves much appreciation for the final look and presentation.▪

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Review Article | Special Guest Article

An overview of Primary Bone Tumours

Anand Raja

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Primary bone tumours are relatively uncommon and thus data regarding their true incidence and risk factors are limited. Benign bone tumours and bone metastasis far outnumber the primary bone tumours.

Surveillance, Epidemiology and End Results (SEER) Cancer Statistics Review of the National Cancer Institute reveal that bone sarcomas account for 0.2% of all malignancies diagnosed in the United States, and the age adjusted incidence rate for all bone and joint malignancies is 0.9 per 100,000 persons per year [1].

There is a bimodal age specific incidence distribution, with the first and second peak occurring in the second decade, and in patients older than sixty years of age respectively. This is related to the differential age distribution of the main histological subtypes, (Ewing's sarcoma and osteosarcoma are commonest in the first two decades, while chondrosarcoma, malignant fibrous histiocytoma, chordoma and secondary osteosarcoma show increased incidence after the fourth decade. There is no particular gender predilection for bone cancers. The vast majority of bone cancers arisesde novo with a rare minority arising in the context of inherited syndromes with no difference in histologic features or outcomes [2].

Bone tumours are classified based on line of differentiation of neoplastic cells and their resemblance to normal counterparts. These can be easily applied to cartilage-forming or bone-forming tumours, while other tumours lack a recognizable differentiation that can link them to a normal tissue, like for example Ewing's sarcoma. It is largely believed that sarcoma-genesis occursde-novo without precursor lesions (unlike epithelial tumours, which has multistep carcinogenesis) through molecular alterations affecting mesenchymal stem cells leading toneoplastic differentiation program. Thus, the current WHO classification of primary bone tumours has abandoned the concepts of histogenesis and cell of origin of the tumor, to focus on a combination of parameters that include morphology, phenotype and genotype.

Molecular phenotype of tumor cells has determined relevant changes in the classification schemes. Publication of the 5th Edition of WHO classification of soft tissue and bone tumours will bring many of these aspects to light. This is an exciting time for the reclassification and diagnosis of bone cancers as evidenced by an array of new Immunohistochemical and molecular markers, like antibody directed against mutant H3G34W in giant cell tumor of bone [3].

Diagnosis of bone cancers is by needle biopsy. The local staging needs an MRI of the entire bone including the adjacent joint. CT scan of the chest is used for metastatic evaluation. PET-CT scan is being performed as single stage investigation for metastatic workup of Ewing's sarcoma [4]. A breath-hold CT should always be performed in conjunction with a PET-CT scan. Biopsy is preferably done at the centre where definitive management is to be offered. Biopsy-related complications have been shown to lead to an amputation being required in cases where the limb might otherwise have been salvaged [5].

Management of bone sarcomas is multimodal with appropriate neo-adjuvant / adjuvant

chemotherapy/radiation.

The cornerstone of surgery for extremity sarcomas is excision with adequate margins, which can be defined as intralesional, marginal, wide, and radical.Concept, quality and adequacy of "quantitative" margins underwent a sea change from the after publication by Kawaguchi et al [6] of their concepts of qualitative margins based on tissue barriers.

Currently, every patient with a malignant tumor of the extremity should be considered for limb salvage if the tumor can be removed with an adequate margin and the resulting limb is worth saving. An adequate margin is one that results in an acceptably low rate of local recurrence of the tumor. A limb worth saving needs an acceptable degree of function and cosmetic appearance with a minimal amount of pain, and needs to be durable enough to withstand the demands of normal daily activities. Balancing these conflicting requirements is what makes limb salvage surgery a complex and difficult, but a rewarding process.

With increasing experience, indications of limb salvage have expanded with adverse factors like poorly placed biopsy incisions, major vascular involvement, encasement of a major motor nerve and pathological fracture of the involved bone no longer considered absolute contraindications [7]. The so-called "three strikes rule" is a simple but helpful method of assessing the feasibility of limb salvage. Each "strike" represents involvement of one of the four key components needed for a viable limb: the bone, the nerves, the vessels, and the soft tissue envelope. If just one or two of these key components must be resected in order to obtain an adequate margin around the tumor, then the limb may be salvageable. If three of these key components are involved, limb salvage is probably not worth considering.

The principles of reconstruction are to replace "like with like", eliminate potential dead space and transfer tissues to facilitate cover of bone grafts/prosthesis and allow adequate closure.

Bone sarcomas commonly arise near the metaphyseal regions of bone, so resections involve the epiphysis, metaphysis and adjacent diaphysis. If the joint is not contaminated by tumor a trans-articular resection are performed, else an extra—articular resection is required, taking the entire joint and joint capsule, and cutting through the uninvolved bone on the other side of the joint to achieve a wide margin. Intercalary resection and reconstruction can be performed for tumours that involve the diaphysis of bone.

Factors influencing choice of reconstruction include age, cause of the defect, need for pre- or postoperative adjuvant treatments, size/anatomical location of the defect, general health and lifestyle of the patient, functional expectations, social-cultural issues, cost of the procedure, the availability of a donor site, and whether there will be an auto/allograft or metal prosthesis. Soft tissue coverage and reconstruction with skin grafts, local flaps (fasciocutaneousand muscle flaps) or free microvascularised soft tissue flaps are major factors when considering the reconstructive options for all types of bone defects from any cause.

Metal prosthesis offer the convenience of immediate weight mobility and weight bearing but degrade over time needing replacement. Auto-allografts need long time for incorporation, but it essentially replaces "normal bone" with ability to remodel over time.

Pedicled frozen autografts as described by Tsuchiya et al [8] involving only one osteotomy is a simple, effective surgical technique and is being increasing used to reconstruct diaphyseal defects. The author performed this procedure for the first time in India in 2017.

Reconstruction of skeletal defects in growing children is a huge challenge. Non-invasive expandable prosthesis reduces the complication rates achieving adequate limb length.

Carbon ion radiation offers an alternative treatment option for unresectable bone and soft tissue tumours and chordomas [9].

CONCLUSION:

Bone cancers are rare tumours with diverse presentation. Multimodal treatment is the key. Adequate resection is the cornerstone of treatment. Choice of reconstruction is dictated by age, patients expectations, availability of resources and surgeons expertise.

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Original Article

Limb salvage surgery for bone tumors: Our experience in a Cancer Institute of North-East India.

Vinay Mamidala [1], Bibhuti B Borthakur [2], Gaurav Das [3], Sumanjit Boro [4], Srinivas Bannoth [5]

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INTRODUCTION:

Primary bone tumors are uncommon. Overall, bone sarcomas account for 0.2% of all malignancies, and the adjusted incidence rate for all bone and joint malignancies is 0.9 per 100,000 persons per year [1]. Limb salvage surgery (LSS) is the standard of care in extremity bone tumors [2]. This study evaluates the clinical and functional results of patients who underwent a limb salvage surgery at Dr. B.Borooah Cancer Institute.

MATERIALS AND METHODS:

Patients with bone tumors who were treated with limb salvage procedure from January 2018 to December 2019 were included. All patients were assessed for surgery by clinical examination, scanograms, MRI, bone scan, CT thorax. Additionally PET CT was done in Ewing's sarcoma patients. Endoprosthesis, vascularized free fibula graft, curettage with bone grafting, extracorporeal radiation therapy (ECRT), cryotherapy, excision were the methods employed for LSS. Systemic therapy was given as per institution protocol. Post-treatment monthly evaluation was done by clinical examination and Musculoskeletal Tumour Society (MSTS) scoring. Results were evaluated using basic statistical tools.

Fig 1 : Histology

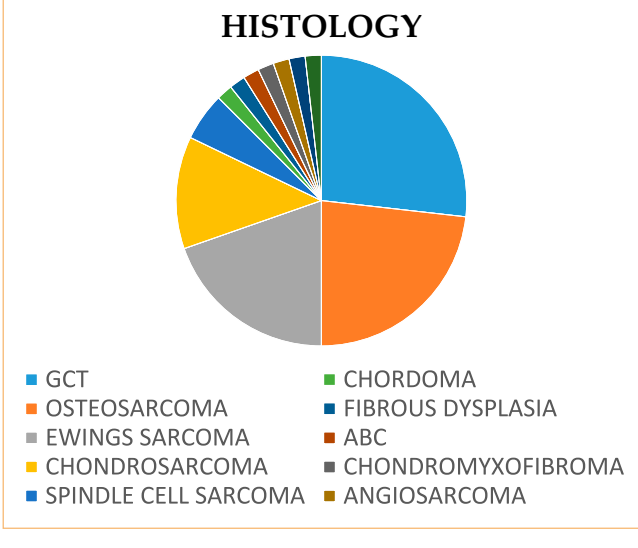

Table 1 : Location of various tumours.

LOCATION	
Proximal Tibia	17
Distal Femur	13
Humerus	9
Scapula	4
Pelvis	4
Fibula	3
Proximal Femur	1
Radius	1
Metatarsal	1

Table 2 : Procedure done.

PROCEDURE	
Endoprosthesis	23
Extended Curretage	16
Vascular graft	7
Metal Plate	3
Muscular Technique	2
Cryotherapy	1
ECRT	1

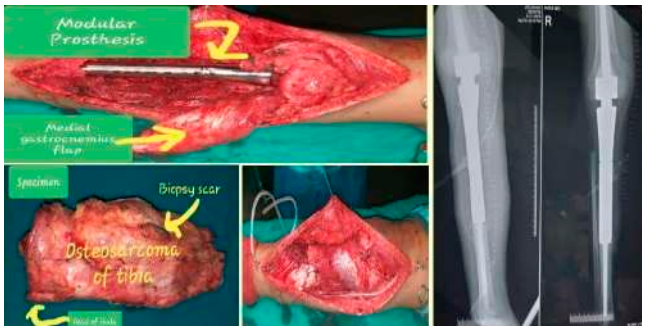

Fig 2 : Proximal Tibia.

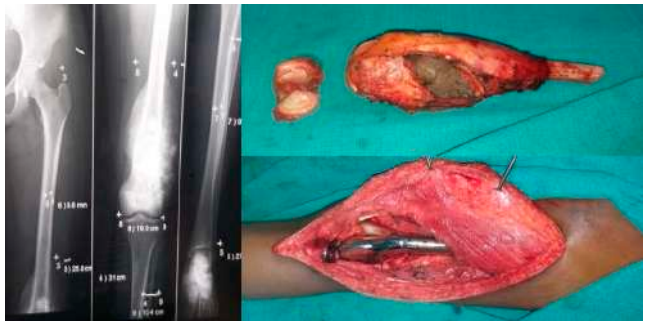

Fig 3 : Distal Femur

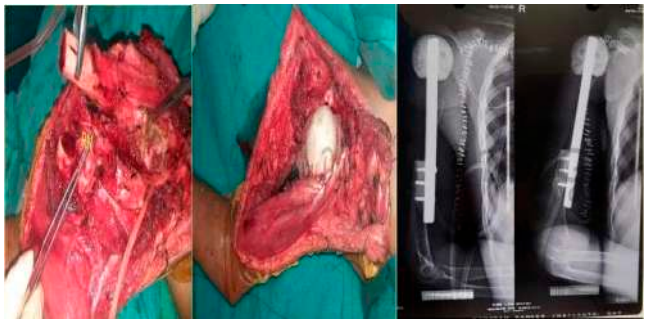

Fig 4 : Proximal Humerus

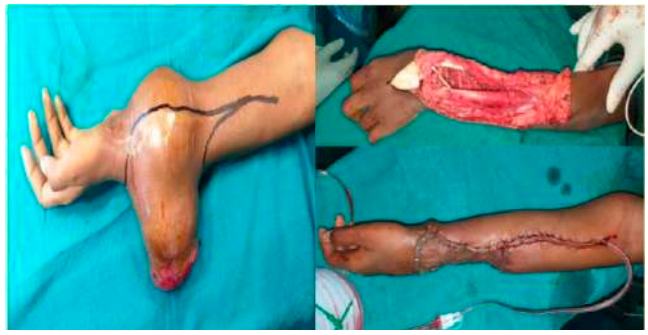

Fig 5 : Distal Radius

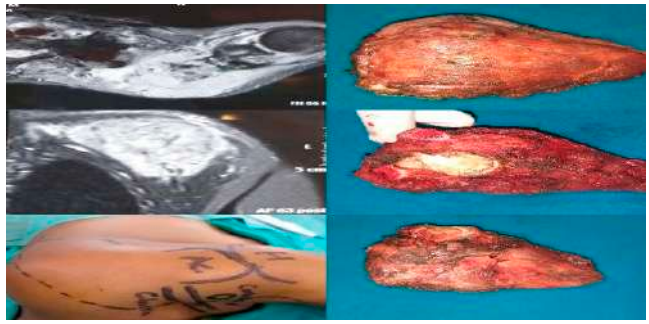

Fig 6 : Scapula

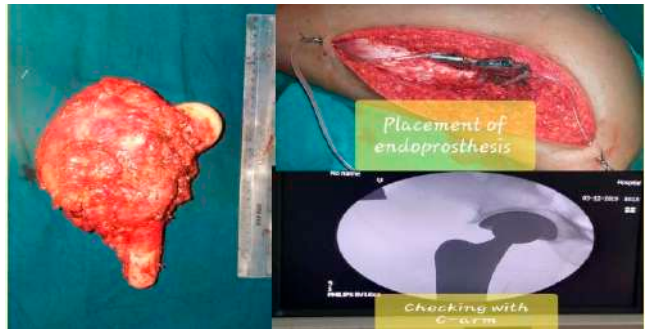

Fig 7 : Proximal Femur

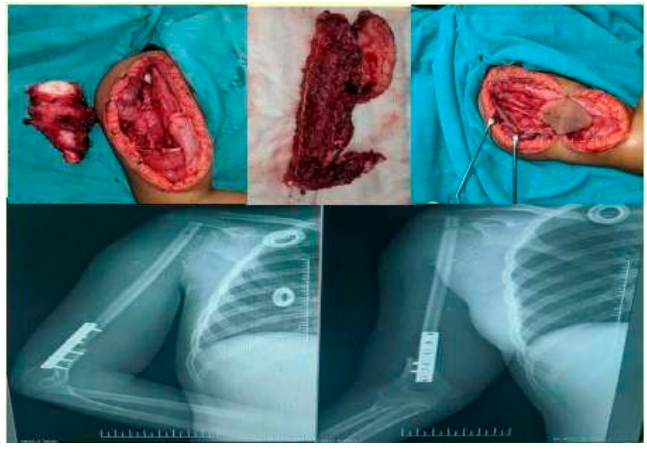

Fig 8 : Free Fibula Re-construction

RESULTS:

Fifty three patients were treated with LSS. Mean age was 13.5 yrs. (range of 6-59 yrs.). Most common histology were Giant cell tumor (32.6%) and Osteosarcoma (30.7%). Most common sites were proximal tibia (36.6%) and distal femur (34.6%). Median duration of follow up was 12 months (range 1-24 months). Average MSTS score at one month was 27 and at 3 months was 29. Among 22 endoprosthesis patients, 3 developed prosthesis infection leading eventually to amputation. 4 patients of Osteosarcoma and 1 Ewing's sarcoma patients developed systemic metastasis on a median follow up of 12 months. Three patients developed common peroneal nerve palsy. Two patients expired in post-operative period. There was no local recurrence.

DISCUSSION:

Until 1970 amputation was treatment of choice for primary high grade bone malignancies [3]. With advent of modern imaging, surgical techniques, newer chemotherapy drugs and radiotherapy techniques the treatment of primary bone tumors has been evolved from amputation to limb salvage surgery [4]. Limb salvage surgery (LSS) is current standard of care, but reconstruction of defects is challenging. However, there are problems with the long-term durability of the reconstruction, and some patients may require secondary amputation due to locally recurrent disease or surgical site infection (SSI). SSI requires irrigation surgery, the use of antibiotics for a long period, and delays in the treatment course, leading to increased mortality [5]. In our study, infection rate was around 6%, lower than the previous studies that have reported 9–28% after endoprosthetic reconstruction [6].

Many studies showed that LSS and amputation have similar survival rates and disease free periods [7,8]. However, quality of life has been found to be better with LSS [9,10]. The MSTS score provides standardized evaluation and comparison of the functional outcomes of patients. Use of standardized rehabilitation protocol results in improved patient functional outcome [11]. Recent meta-analysis in 2016 in 1330 patients has shown that LSS results in higher 5-year survival rates and better functional outcomes as indicated by post-operative MSTS functional scores of patients [12].

CONCLUSION:

With adequate training limb salvage surgery is a feasible option in any cancer center and should be the standard of care. Appropriate patient selection gives good and consistent results.

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Original Article

Initial experience with use of polypropylene mesh for stabilization of skeletal reconstructions after resection of bone tumours.

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INTRODUCTION:

Limb salvage surgery for bone tumors includes various surgeries designed to accomplish removal of a malignant tumor and reconstruction of the limb with an acceptable oncologic, functional, and cosmetic outcome.

Most of the bone tumors arise around joints and involves surrounding tissues, often requiring an extensive resection to obtain margins. As adequate resection takes precedence over function, proper reconstruction to get a satisfactory outcome is paramount. Endoprosthetic reconstruction following resection of a juxta-articular bony tumour often leads to subluxation or dislocation [1,2] Soft tissue reconstruction is a major part of such procedures and adherence of muscle to the prosthesis or allograft is key to achieve optimal function. Various methods of stabilization have been described, for example, tubes, Dacron sleeves, Merselene tapes, polypropelene mesh and muscle transfers [3,4,5]

MATERIALS AND METHODS :

This is retrospective study conducted in the bone oncology unit at our institute from January 2018 to December 2019. Patients undergoing limb salvage surgery (LSS) in which mesh was used as a part of reconstruction and had a follow up for a minimum of 6 months were included.

Surgical Technique: 15 x 15 cm polypropylene mesh was used for the reinforcement, fixed with Ethibond No. 5 suture.

(A) After shoulder girdle resections: after oncological resection of the tumor various techniques like endoprostheses or vascularized free fibular graft or metal plate and bone cement were used for humeral reconstruction. In intra-articular resections, upper part of the mesh was sutured to glenoid labrum forming a pseudocapsule and surrounding muscles and tendons were sutured to the mesh. This overlaid the graft in cases where vascularized free fibula was used (Fig 1). Similar technique was adapted for endoprosthesis and metal plate reconstruction methods (Fig 2) with mesh as an interface between prosthesis and muscles. For extra-articular resections, the mesh was fixed to holes drilled in the clavicle and the reconstruction material to enclose it as a pseudocapsule.

(B) After pelvic girdle resections: after an internal hemipelvectomy to remove the bony tumour, mesh sutured to the inter-trochanteric line on the femur and the whole unit was suspended from the remnant pelvic bony structure and the surrounding group of muscles were woven on to the mesh (Fig 3).

For shoulder girdle resections, hand movements were

allowed from the immediate postoperative period. The shoulder structure was supported with an arm sling for 4 weeks for endoprosthesis and metal plate reconstructions and for 8 weeks for free fibula reconstruction to allow healing and fibrosis because a stable shoulder joint with a fully functional elbow and hand movements is the eventual goal. Thereafter, gradual range of movements at the shoulder joint were started under the supervision of a trained physiotherapist. For patients who underwent a hemipelvectomy and a mesh reconstruction, absolute bed rest for 2 weeks was followed. Mobilization was done sequentially from non weight bearing to partial weight bearing to full weight bearing within a span of 4-8 weeks. Musculoskeletal Tumour Society Scoring (MSTS) scores were calculated in the follow up every 3 months.

RESULTS:

Total no. of patients studied were 17, out of which 9 were proximal humerus tumors, 4 scapular tumours and 4 pelvic tumours as shown in Table 1a, 1b, 1c

CASE No.	AGE	SEX	DIAGNOSIS	SURGERY	COMPLICATION	MSTS SCORE
1	15	M	Ewings Sarcoma	Endoprosthesis Free Fibula Graft	None	27
2	10	M	Ewings Sarcoma	Vascularized Free Fibula Graft	Recurrence and death	24
3	10	M	Ewings Sarcoma	Vascularized Free Fibula Graft	None	28
4	15	M	Osteosarcoma	Plating and Bone Cement	None	25
5	14	M	Ewings Sarcoma	Vascularized Free Fibula Graft	None	27
6	26	F	Gaint Cell Tumor	Plating and Bone Cement	None	24
7	12	F	Ewings Sarcoma	Vascularized Free Fibula Graft	None	28
8	30	M	Angiosarcoma	Vascularized Free Fibula Graft	Recurrence on Systemic chemo	24
9	56	F	Chondrosarcoma	Vascularized Free Fibula Graft	Osteoporotic fracture of humerus at the l ower graft fixation point	26

Table 1(a) : Scapular Tumors.
M-Male, F- Female, MSTS : Musculo Skeletal Scoring System.

CASE NO.	AGE	SEX	DIAGNOSIS	SURGERY	COMPLICATION	MSTS SCORE
1	24	M	Chondrosarcoma	Resection	None	27
2	46	M	Spindle Cell Sarcome	Resection	None	28
3	48	M	Angiosarcoma	Resection	None	28
4	11	F	Ewings Sarcoma	Resection	None	27

Table 1 (b) : Scapular Tumors
M-Male, F- Female, MSTS : Musculo Skeletal Scoring System.

CASE No.	AGE	SEX	DIAGNOSIS	SURGERY	COMPLICATION	MSTS SCORE
1	20	F	Giant Cell Tumor	Internal hemipelvectomy Type I+II	None	25
2	28	F	Myxofibrosarcoma	Internal hemipelvectomy Type I	None	23
3	45	F	Giant Cell Tumor	Internal hemipelvectomy Type II + III	Died on POD 22 due to sepsis	-
4	37	F	Spindle Cell Sarcoma	Internal hemipelvectomy Type I+II	None	24

Table 1 (c) : Pelvic Tumors
M-Male, F- Female, MSTS : Musculo Skeletal Scoring System.

Average duration of follow up 16 months (range 12-20 months) , In upper limb patients the mean active abduction was 75 degrees , average MSTS scoring was 26 (Fig 4,5,6,7) . For lower limb patients mean active hip abduction was 30 degrees and flexion was 20 degrees ,average MSTS score 24 (fig 8). Two patients developed lung metastases and one patient had osteoporotic fracture of the humerus at the lower fixation point of fibular graft. No patient had surgical site infection. One patient developed acute renal failure and ARDS, eventually succumbing to septic complications. Her surgical wound site healed in the meantime.

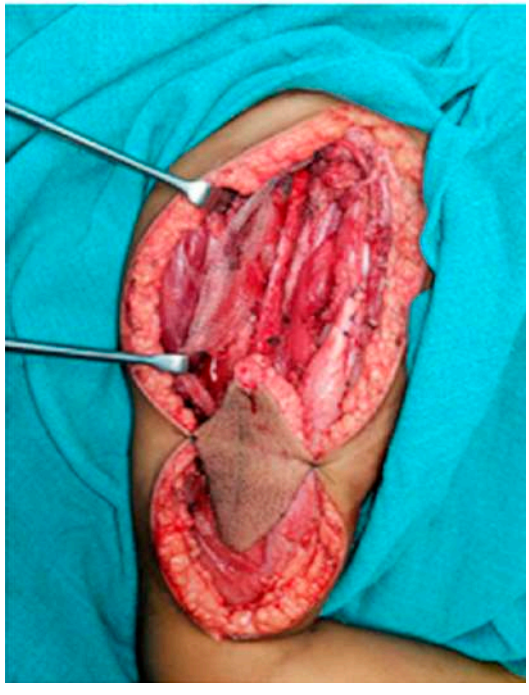

Fig 1 : Reconstruction using vascularized free fibula and polypropylene mesh after resection of a proximal humerus Ewing's sarcoma

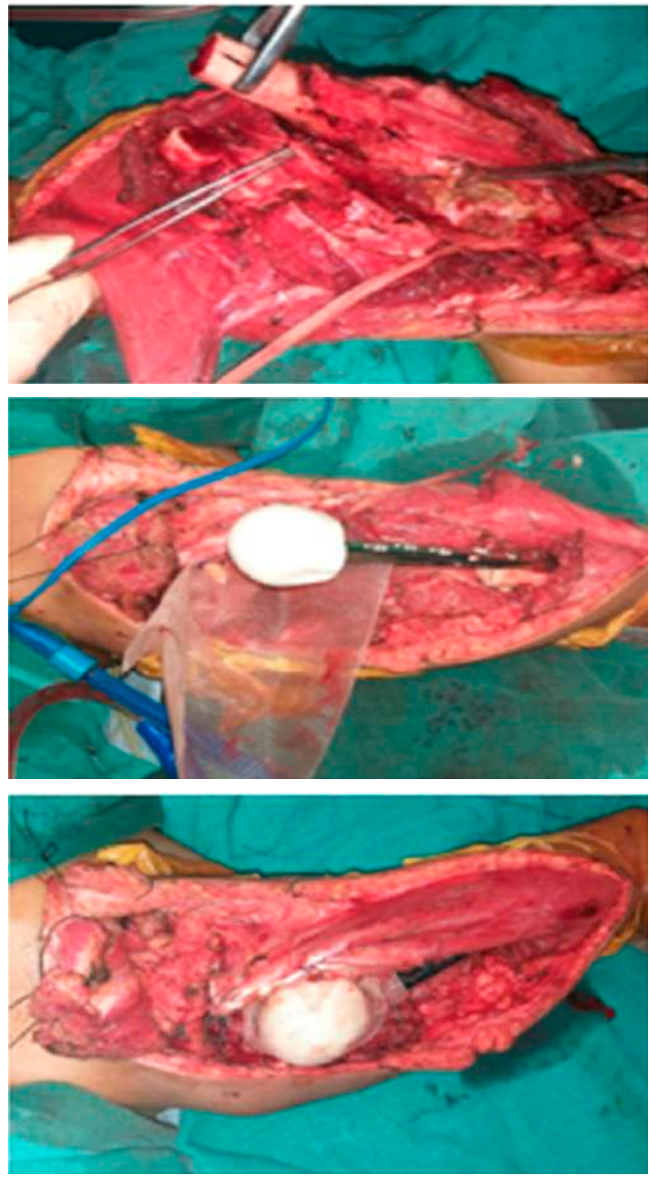

Fig 2 : Resection of a proximal humerus osteosarcoma and reconstruction using metal plate (DCP) and cement head with use of polypropylene mesh.

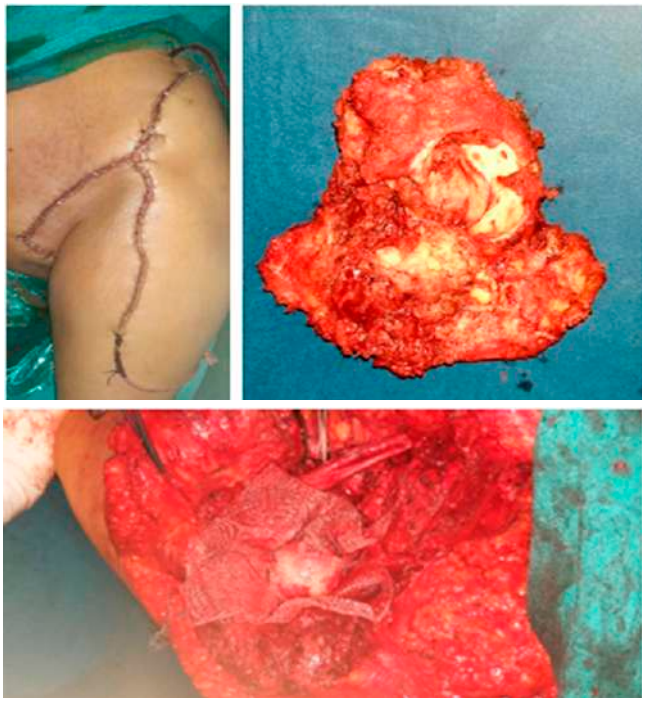

Fig 3: Mesh used in hemipelvectomy for pseudocapsule reconstruction after acetabular resection.

Fig 4: Showing the functional outcome and postoperative X-ray of the patient who underwent reconstruction of proximal humerus with metal plate and cement head withprolene mesh.

Fig 5: Free fibular graft with mesh .. post op limb movements in first two clinical photos (a, b) (c) bulk of the arm in 6 months follow up, (d) post op x-ray with graft positioned at scapula.

Fig 6: Limb movements and radiograph showing better cosmesis after using polypropylene mesh to stabilize the endoprosthetic reconstruction following tumor resection around the shoulder.

Fig 7: Clinical photograph and follow up x-ray of the patient where mesh and endoprosthesis has been used. Contour of the shoulder maintained with qualitative limb movements.

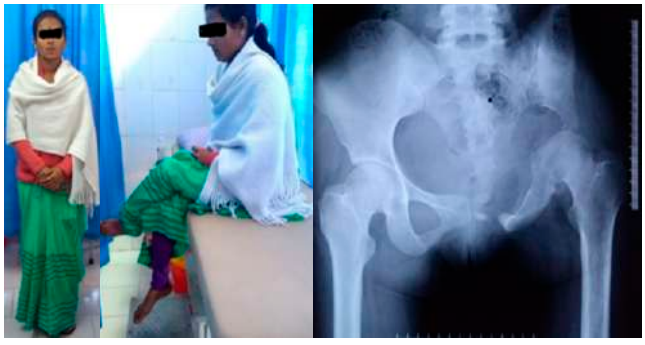

Fig 8: Hemipelvectomy patient in the follow-up with good lower limb movements and the post op x-ray where a part of ilium and acetabulum was resected and the head of femur was anchored to surrounding pelvic bone

DISCUSSION:

Limb salvage surgery for malignant bone tumors may result in extensive soft tissue loss. Reconstruction with good functional and a stable joint is challenging. Polypropylene mesh gives us an option for a stable reconstruction. It helps in:

1. Providing a platform for attachment of muscles to the graft/prosthesis, thus strengthening the joint.

2. Creating a pseudocapsule for stabilization of the fibular graft, humerus prosthesis, metal plate inside the glenoid labrum.

3. Anchoring the femur to pelvis and pseudocapsule formation for head of femur post internal hemipelvectomy, subsequent fibrosis to limit the eventual shortening and limb length discrepancy.

Mesh functions as a physical stabilizer during the early healing phase and serves as a scaffold into which fibroblastic tissue migrates. This fibrous connective tissue would gradually undergo a process of maturation forming a biological pseudocapsule [5].

Various orthopedic surgeons have described capsular replacement of the hip joint with synthetic mesh after wide resection of proximal femoral tumors and endoprosthetic reconstruction [6] and reconstruction of the joint capsule and abductors of the hip joint with artificial mesh after implantation of an endoprosthesis [7] As for the shoulder joint, the use of Trevira tube 3, Dacron tapes [8], and aortic graft mesh (Gore graft) [9] for reconstruction of soft tissue and joint capsules of the joints including the shoulder joint after implantation of an endoprosthesis have been described. All of them reported the effectiveness in stabilization of the reconstructed joint helping in prevention of dislocation. Indian experience regarding the use of mesh to augment various joint reconstruction techniques have also been very successful [5,10].

CONCLUSION:

Polypropylene mesh provides a good joint stability and scaffold for the surrounding tissue thus improving the overall clinical outcome. It is a simple but useful addition to the armamentarium of the orthopedic oncologist.

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Original Article

Fibular graft reconstruction for long bone defects after resection of tumour

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INTRODUCTION:

Bony defects can present a significant surgical challenge. Biomechanically fibula bears only 15% of axial load [1]. Can be utilized as vascularized or Non-vascularized fibular grafts. Reliable for reconstruction of bone defects more than 6-8cm [2]. Useful for reconstruction of large defects in young children and isolated diaphyseal defects.

MATERIALS:

Both prospective and retrospective observational study. Study period: 4 years. Young patients and patients with isolated diaphyseal defect reconstruction were taken for this procedure. Both vascularized (VFGs) and Non- vascularized fibular grafts were used. Post-operative bone scan performed for VFGs to assess perfusion.

RESULTS:

A total of nine patients. Seven males and two females. Mean age 22.5 years. Four cases of vascularized fibular grafts, five cases of non-vascularized fibular grafts. Average Functional score (MSTS score) was 23.

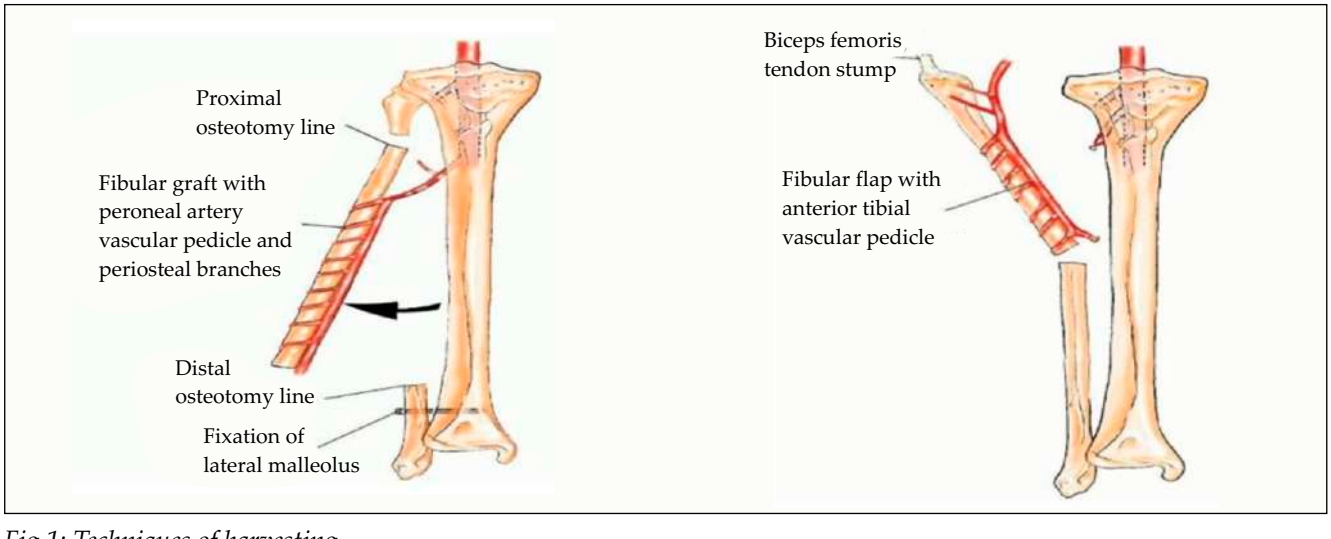


Fig 1: Techniques of harvesting

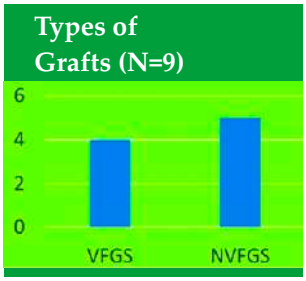


Fig 2 : Types of grafts harvested

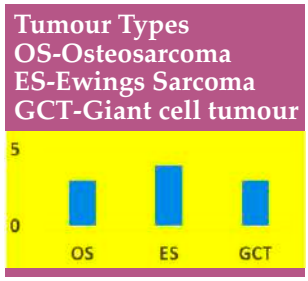


Fig 3 : Tumour histology

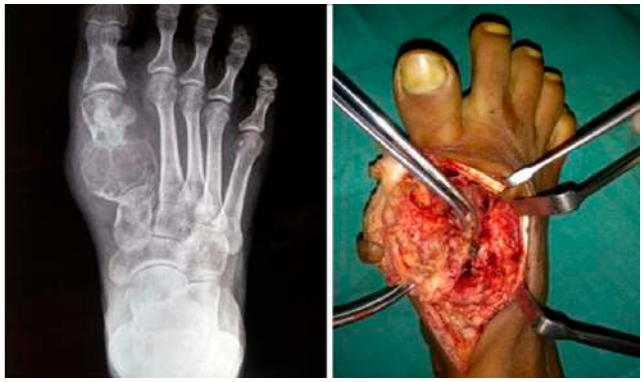


Fig 4 : Wide excision of metatarsal tumour with surrounding soft tissue done

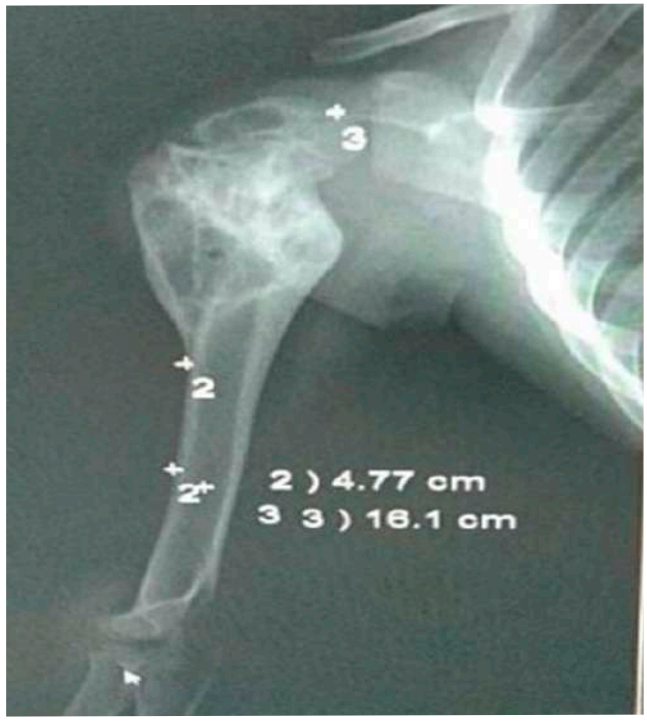


Fig 6 : Ewing's sarcoma of right humerus

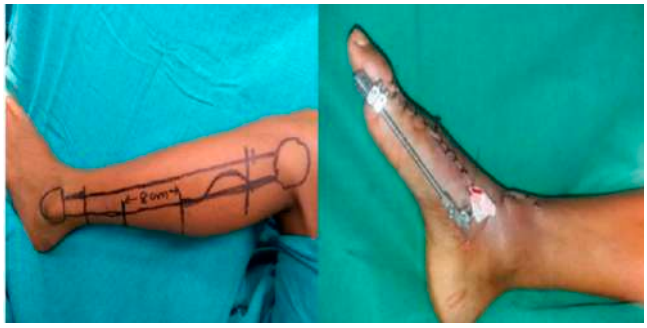


Fig 5 : Fibular graft interposed in this gap, fixed with external fixator with well-maintained arch.

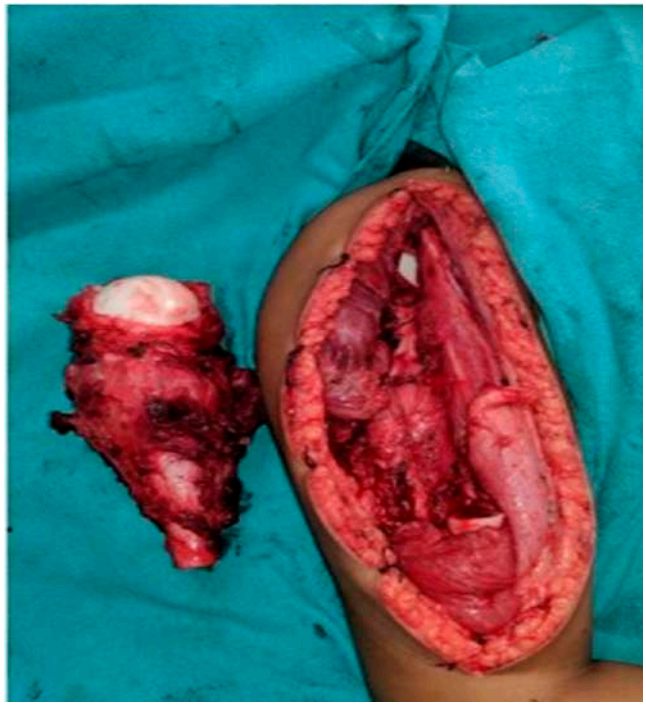
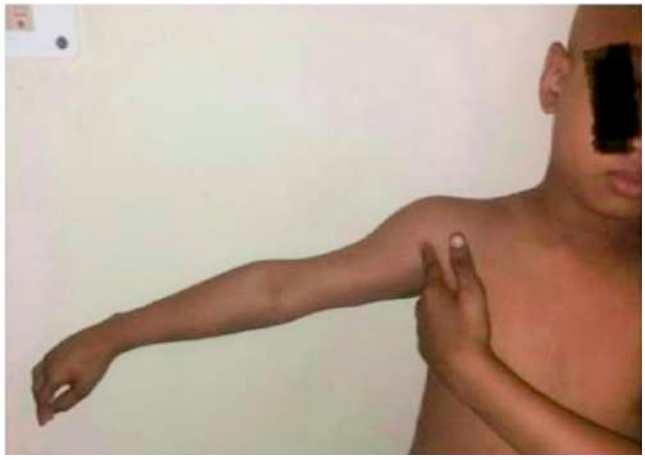


Fig 7 : Excision of tumour



Case 2

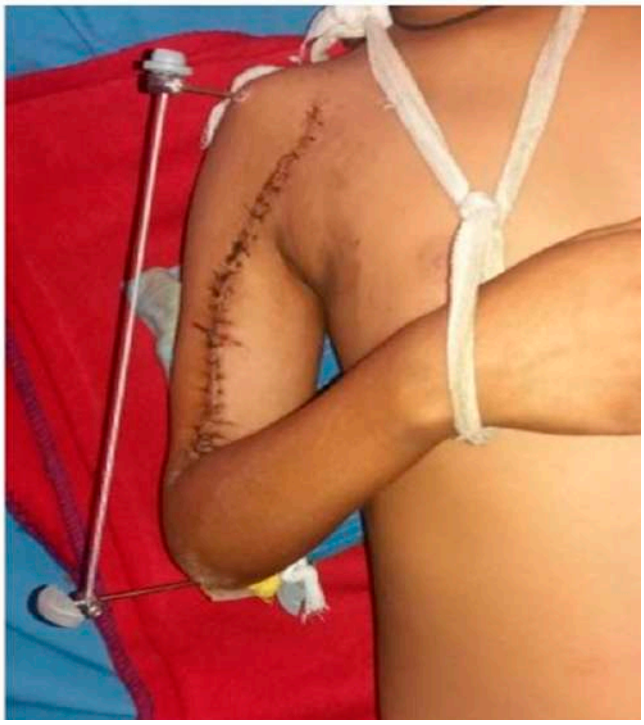


Fig 8 : Postop picture

COMPLICATIONS	NUMBER OF PATIENTS
Pin site infection	2
Muscle atrophy	1
Partial nonunion	1
Fixator loosening	2
R1 resection	1

Table 1 : Complications

DISCUSSION:

Vascularized bone graft, by definition, are placed with their vascularity intact, and thus are immediately viable. Bone graft and bone graft substitutes have a number of inherent properties which allow them to initiate, stimulate and facilitate bony healing [4, 5].

Biomechanically the fibula bears only 15 % of the axial load across the ankle, allowing for its use as an autogenous bone graft with minimal biomechanical consequences on the weight bearing status of lower limb [6].

The endosteal blood supply to fibula is provided by a nutrient artery which typically enters the posterior fibular cortex at the junction of proximal one third and distal two thirds. This nutrient artery is branch of peroneal artery. Fibula also receives additional vascularity from musculo-periosteal vessels which also emanate from peroneal artery [7].

Give the length of fibular diaphysis that may be harvested, free fibular grafts are well suited for the reconstruction of segmental defects of long bones, providing both mechanical strength and biological stimulus for healing. Based upon the fasciocutaneous arterial branches of peroneal artery, skin, fascia, and muscle may be harvested concomitantly with fibula to allow for more complex reconstruction. Apart from its advantages vascularized free fibular grafting is technically challenging. Donor site morbidity is seen in 10% of patients. Patients may also subsequently develop ankle pain, instability, and valgus deformity [8].

Preoperative planning should begin with exclusion of patients with peripheral vascular disease, deep venous thrombosis. Around 8% of population have hypoplasia or the absence of one or both of anterior and posterior tibial arteries, a condition called peronea arteria magna [9]. Absence of vessels at donor and recipient site is contraindication for this technique.

With current multidisciplinary approach for osteosarcoma limb salvage has become standard of care. Reconstruction with FVFGs are technically challenging but these have a very high bony union rates and can improve regional circulation, particularly when surrounding tissues have been damaged by chemotherapy and irradiation [10].

CONCLUSION:

Vascularized free fibular grafting though technically challenging that to its complex reconstruction in foot has shown better results and should be used whenever it's feasible. It provides immediate structural support and vascularity. Careful case selection and proper surgical technique results in better outcomes.

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Original Article

Microvascular Surgery in Limb Saving Procedures in BBCI

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INTRODUCTION:

Limb saving surgery is a set of surgical procedures designed to accomplish removal of a malignant tumour and reconstruction of the limb with an acceptable oncological, functional and cosmetic result. Every patient with tumour of extremity should be considered for limb salvage if the tumour can be removed with an adequate margin and resulting limb is worth saving. Vascular involvement is not an absolute contradiction for limb salvage surgery as vascular homograft can be used for reconstruction. There should be three goals for every case of limb salvage,

1. Painless limb,
2. Functional tumour free limb,
3. Good psychological outcome.

MATERIALS AND METHODS:

A retrospective observational study was done about the outcomes of the limb salvage surgery procedures done at BBCI during a 2 year period (2017-19).

Results and Discussion: In BBCI, till now, we performed nine limb saving procedures where microvascular expertise were required. Out of the nine patients, four were Ewing's sarcoma of humerus, one case each of osteosarcoma, chondrosarcoma and angiosarcoma of humerus, one case of aneurysmal bone cyst involving first metatarsal of foot and the latest one was recurrent leiomyosarcoma of arm. In all the bony sarcomas, we used free fibular osteocutaneous flap for reconstruction. We measured the expected bone loss from preoperative radiological investigations. Resection of the tumour and reconstruction of the defect started simultaneously. We harvested the free fibular osteocutaneous flap from left lower limb in all the cases. Using suitable plate and screws, harvested fibula was fixed with the native bone. Vascular anastomosis was performed with suitable adjacent artery and vein with the help of 8-0 round body ethilon under microscope/loupe magnification after solid fixation of the fibular graft. On the 2nd post operative week, Technetium 99 - methylene diphosphonate tri phase bone scan was performed to see the perfusion of the fibular graft, which was good in all cases. Post operative period was uneventful in all the eight cases. We were able to discharge all of them within two weeks post-surgery.

On follow up, we evaluated the recurrence, bony union and functional outcome. Sixth month post operative X-ray showed good bony union in all 8 cases. Functional score of each reconstructed limb was evaluated with Musculoskeletal Tumour Society Scoring System (MSTS). Six out of eight patients were able to perform their routine daily activities at follow up. One old lady developed fracture at graft site and plaster of Paris cast was used. Another patient died in the follow up period due to pulmonary metastases.

Noteworthily, the patient with recurrent

leiomyosarcoma of right arm was from a remote village of Assam. She was operated for the first time in a private setup in Guwahati. On radiological evaluation it was seen that the tumour was in close proximity to the brachial artery in lower third of right arm. On exploration we were able to excise the tumour totally but we had to sacrifice 14 cm of the brachial artery. Reconstruction was done with great saphenous vein graft taken from left leg and anastomosed with the remnant of brachial artery with 8-0 round body ethilon under loupe magnification in antegrade fashion. Post operative period was uneventful. Doppler USG after one year showed patency of the vein graft with good flow. She was having a good life post surgery for eighteen months and then she developed vertebral metastases, requiring chemotherapy [1].

CONCLUSION:

Microvascular surgery is a essential part of onco-reconstruction. During last two years in BBCI, we have used this expertise in the field of orthopaedic oncology and management of complicated extremity soft tissue sarcomas. Results are encouraging and hope in coming days it will be a big boost for the bone and soft tissue sarcoma patients of North East India.

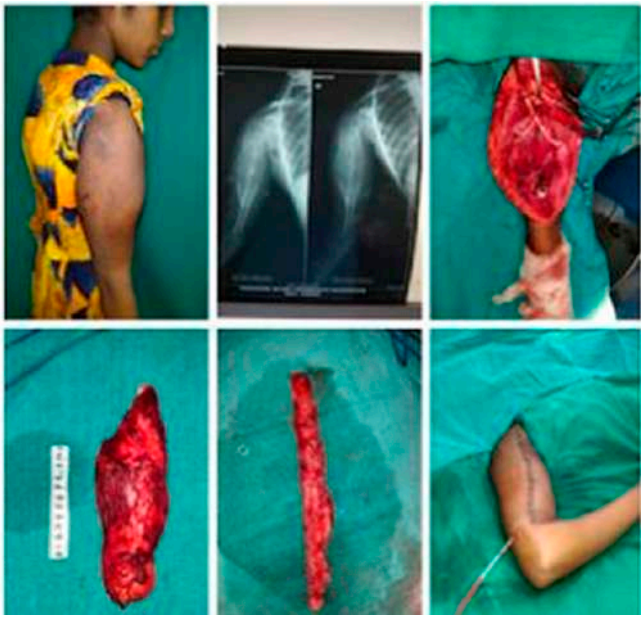

Fig 1 : Reconstruction of upper end of humerus with free fibular graft.

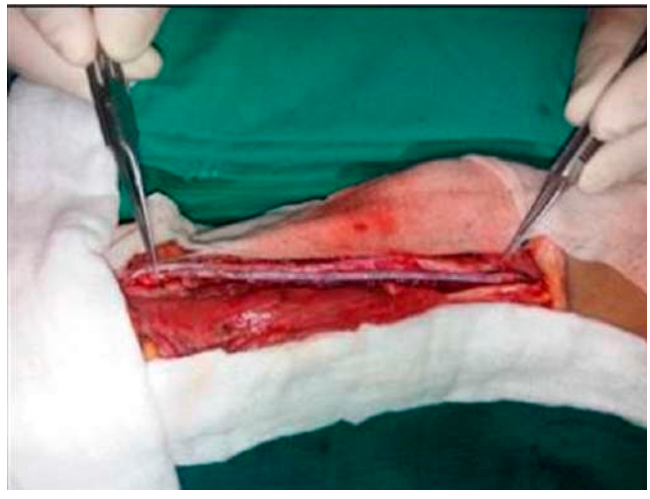

Fig 2 : Reconstruction of 14 cm of brachial artery with great saphenous vein graft taken from left leg.

REFERENCE:

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Original Article

Minimally invasive oncologic surgery at BBCI

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4. *Associate Professor, Dept. of Surgical Oncology*

INTRODUCTION:

The use of minimally invasive surgery (MIS) in oncology in certain cancers has been proven to be non-inferior to open procedures with superior short term outcomes in several randomized controlled trials [1]. For example, MIS has been associated with less incisional pain and reduced need for opioids, shorter length of stay, as well as lower overall morbidity and improved quality of life [2].

MATERIALS AND METHODS:

A retrospective study of MIS done for cancers of esophagus, lung, colorectal cancers and gastric cancers was done for the study period 1st Jan 2018 to 31st Dec 2019. Simple statistical tools were used for analysis.

RESULTS:

A total of 46 (54.7%) procedures were done with the use of MIS out of a total of 84 patients. Trans-thoracic esophagectomy (TTE) was done using VATS in 25 patients (62.5%) and the remaining were done using open right lateral thoracotomy 4 patients (10%) and trans-hiatal approach (THE) 11 patients (27.5%). Conversion to a thoracotomy was needed in 3 cases (12.5%). The indications were uncontrolled bleeding in two patients and a left bronchial injury in one patient. Anastomotic leak was noted in 3 patients (12.5%). A similar incidence (12.5%) of hoarseness of voice due to recurrent laryngeal nerve palsy was noted and it was transient in all instances. The median duration of ICU stay was 2 days (range was 1 to 4 days) and median duration of hospital stay was 12 days (range was 1 to 23 days). The median post-operative pain score was 2 (range was 1 to 4 days).

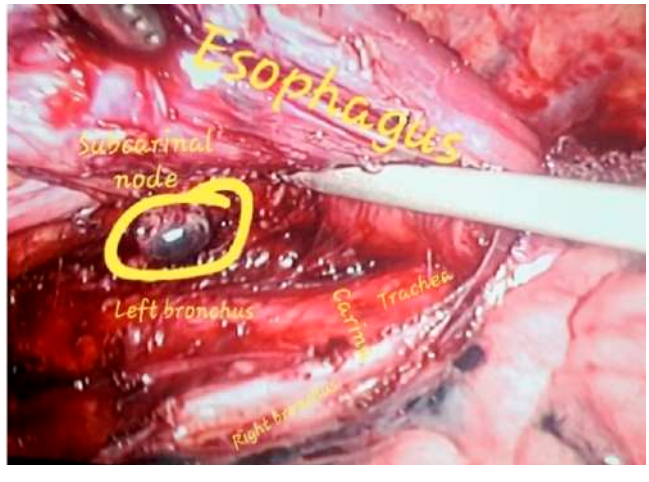

Fig. 1: Showing thoracoscopic mobilization of the esophagus (VATS TTE)

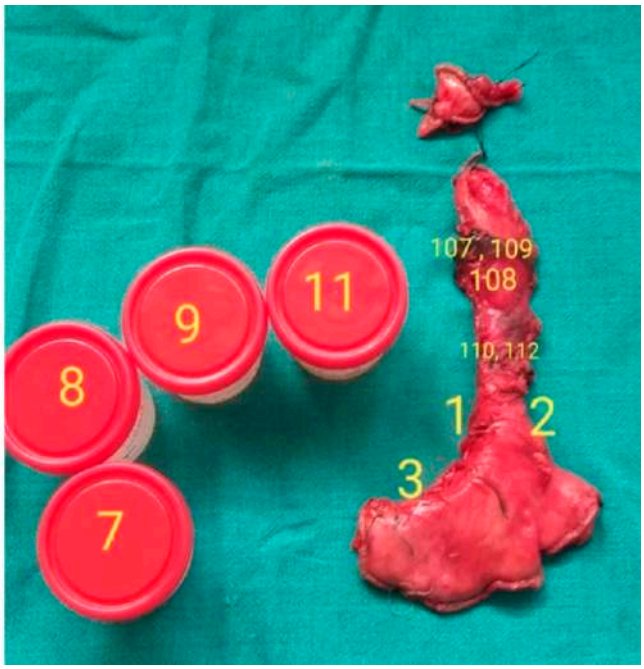

Fig. 2 : Specimen of esophagectomy

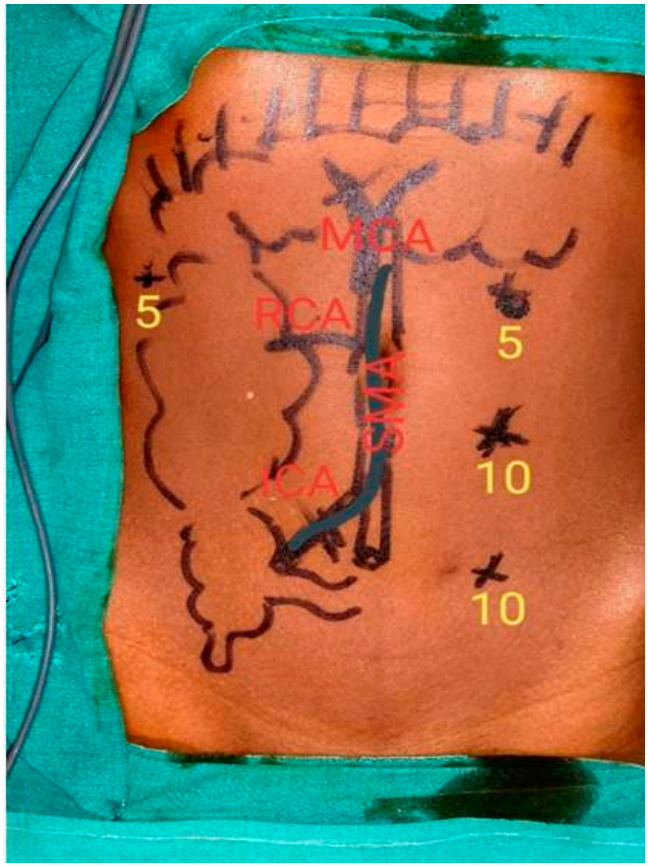

Fig.3: Surface marking of port placement for right hemicolectomy.

The number of surgeries done by MIS for colorectal cancers was 17 (44.7%) out of a total of 38 patients. This included 3 laparoscopic right hemicolectomies, 9 laparoscopic abdomino-perineal resections (APR), 5 laparoscopic low or ultra-low anterior resections (LAR/ULAR). The conversion rate to open procedure was 11.4%. The median ICU stay was 1 day (range was 1 to 3 days) and the median hospital stay was 11days (range was 7 to 26 days). These numbers compared favourably against the open surgery patients, where median values were 2 days (range 1 to 5 days) and 14 days (range 8th to 31 days) respectively. The incidences of surgical site infections (SSIs) were higher in the open surgery patients (3 vs 1). The median pain score was 3 in MIS patients and 6 in open surgery patients.

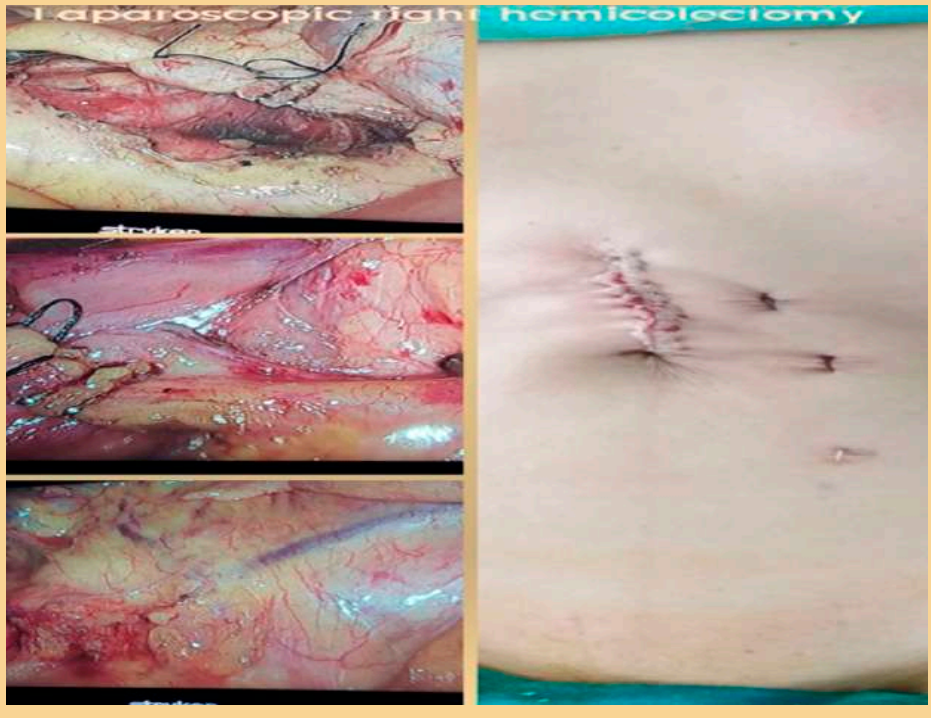

Fig. 4: Laparoscopic right hemicolectomy

There was one patient who underwent VATS left lung upper lobectomy, one patient of VATS right lung metastasectomy and 2 patients with laparoscopic-assisted distal gastrectomy with D2 lymphadenectomy.

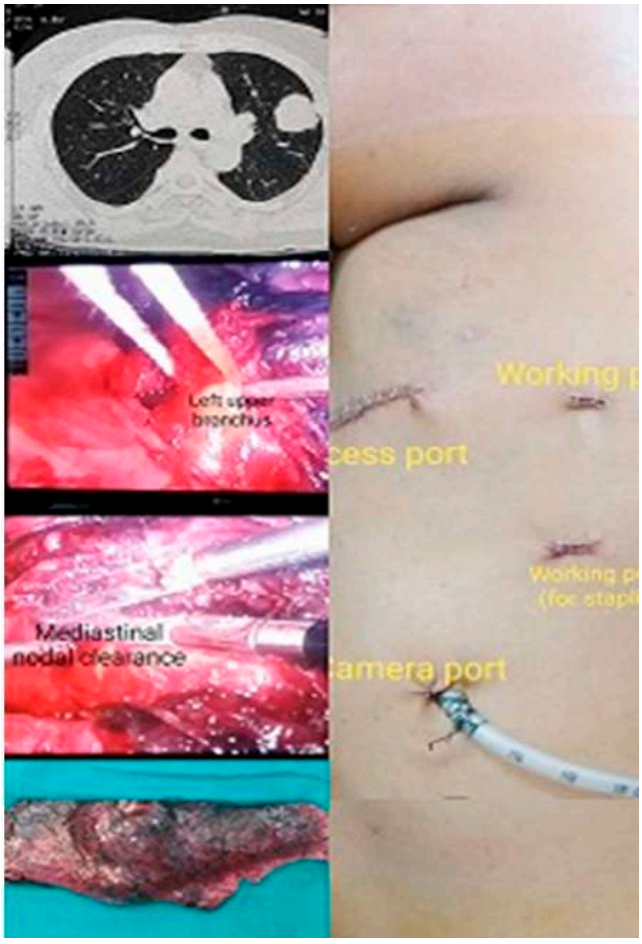

Fig. 5 : VATS left lung upper lobectomy.

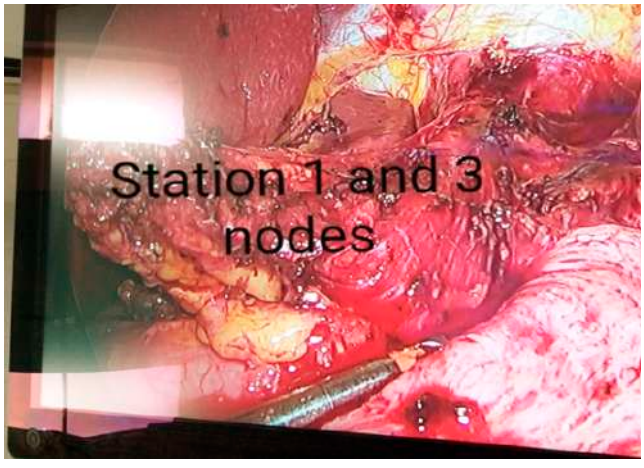

Fig. 6 : Nodal dissection in laparoscopic assisted distal gastrectomy

The numbers of MIS surgeries increased in the year 2019 compared to 2018 (Tables 1, 2, 3). There was an increase of 56% in MIS approach in esophageal cancer and 38% in colorectal cancer resections (Table 4).

Esophagectomy	2018	2019
Open TTE	14	04
THE	09	11
VATS TTE	02	25

Table 1 : Showing the number of surgeries for esophageal cancer

Colorectal Surgery	2018	2019
Open APR	09	07
Open LAR	09	12
LAP APR	02	09
LAP LAR / ULAR	01	07
LAP Hemicolectomy	00	03

Table 2 : Showing the number of surgeries for Colorectal cancer

Other Lap Cases	2018	2019
LAP Distal Radical Gastrectomy	00	02
VATS Metastasectomy	00	01
VATS Left Lung Upper Lobectomy	00	01

Table 3 : Showing the number of surgeries for other cancers

	2018	2019
Thoracoscopic Surgery	08%	64%
Laparoscopic Colorectal Surgery	14%	52%

Table 4 : Showing the percentages of surgeries done by MIS approach, year-wise.

DISCUSSION:

Minimally invasive surgery (MIS) refers to surgical procedures that limit the size of surgical incisions needed so that the blood loss, wound healing time, associated pain and scarring, hospitalization time, risk of infection, and postsurgical complications are usually less.

Surgery has long been thought of as a "stressor" with associated immunomodulation and possibly derivative effects on cancer progression. Many hypotheses exist regarding the immunologic response to surgery and whether a less "stressful" MIS might result in better oncologic outcomes [3].

Neoplasms such as early gastric cancer, colo-rectal cancer, and esophageal cancer are now preferentially approached with minimally invasive surgery with decreased pain, lower wound infection rates, better postoperative pulmonary function, and shorter recovery time compared with traditional laparotomy. Robust studies showed that minimally invasive techniques could provide equivalent outcomes compared with traditional open approaches in many cases [4,5,6,7,8]. At our institute, we have incorporated MIS techniques into our surgical practice, as per oncologic indications, in a very steadfast manner, for the last two years, as reflected in the data presented herein. Our experience is still very early and evolving, as we learn more and we hope to report a much bigger dataset in years to come.

We do not have a robot in our institute and our MIS experience is limited to laparoscopic approaches only.

CONCLUSION:

The use of MIS in our institute has produced favourable short term results which is very encouraging.

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Letter to the Editor

Pattern of invasion in Cancer : a brief review

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BACKGROUND:

Invasion and metastasis are the hallmarks of cancer, both being intimately related processes. They achieve clinical significance when they add to the prognostication of cancer. Many studies have been focussing on the pattern of tumour cell migration into the surrounding stroma and metastatic site. Lately, this concept has been put in focus when the term "epithelial-mesenchymal transition" was put forth by E.D Hay in 1995. This explains the mechanism whereby tumour cells detach from the main mass (epithelial layer) and gain motility. The process involves various molecular and cellular mechanisms broadly defining reduction or complete loss of intercellular adhesion molecules and gain of function of motility enabling structural proteins.

TUMOUR CELL MIGRATION:

Based on complex molecular and morphological studies, two types of tumour cell migration have been found: collective/group migration, i.e. when the whole group of cells interconnected by adhesion molecules moves and the other is: single/individual cell migration, i.e. when individual cells migrate freely through the stroma. Migration type depends on tissue microenvironment and molecular changes in tumour cells. Single-cell migration occurs via two mechanisms: mesenchymal and amoeboid. There may be a transition between these two mechanisms. In the mesenchymal type, cells acquire the mesenchymal property of fibroblast-like cells, and cells transform to become like spindle cells. This mechanism may be the sequence of epithelial-mesenchymal transition (EMT). Amoeboid movement is the most primitive and efficient mode of tumour cell migration, and this is the last resort for tumour cells to migrate when the other methods of migration have been inhibited or blocked. This movement is seen mainly in circulating tumour cells and is not appreciated in histomorphology.

TUMOUR BUDDING:

Based on this molecular idea, researchers have been studying the infiltrative edge of the tumour, and specific patterns have been described in several tumours, in particular, those of the prostate, bladder, head and neck, breast, endometrium and colon. Terminology such as "tumour budding" are assigned to describe these collective migration patterns. Tumour cells in infiltrative edge can show distinct patterns like tubular or acinar, trabecular, strips, solid or in singles. Several scoring systems have been validated based on these patterns in different organ-specific cancers. Most studies have correlated the pattern of invasion with a risk of metastasis in regional lymph nodes, in the early stage of cancers.

INFILTRATING TUMOUR EDGE AND RESISTANCE TO THERAPY:

The tumour cells in the infiltrating edge are not dividing but transforming into mesenchymal cells by acquiring mesenchymal property and this collective type of tumour migration renders the tumour cells chemo insensitive and radioresistant. The underlying molecular changes lend credence to these observations. The leading cells at the infiltrating edge express anti-apoptotic genes and also induce synthesis of ABC family protein responsible for efflux of

chemotherapeutic drugs out of the cells.

OUR EXPERIENCE:

A retrospective pilot study conducted at our institute on squamous cell carcinoma of the tongue showed that the worst pattern of invasion, that is the collective migration type of invasion is associated with the number of lymph nodes metastasis and perineural infiltration and is an independent prognostic factor.

Further tumour specific studies are needed to offer future insights into the nuances of the pattern of invasion in solid tumours and their clinical implications.

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Case Report

Axillary apocrine adenocarcinoma : a case report

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INTRODUCTION:

Apocrine adenocarcinoma is an uncommon cutaneous malignant neoplasm. It has male sex predilection and average age of presentation is 58years.[1] It is most commonly found in axilla, other sites include- the anogenital area, nipple, scalp, face, trunk, acral sites , wrist, fingertip and lip. [2] They can arise rarely from Moll's gland of eyelid. Clinically they start as a slow growing and painless swelling and then enlarge rapidly and become tender over time, red to voilaceous in colour [3]

CASE REPORT:

A 52 years male presented to our institute in September 2019 with painful left axillary ulcero-proliferative mass of size 8x7cm. There were no other significant findings on physical examination. Bilateral mammography showed left axillary mass (Fig 1). CT Thorax showed enlarged nodes in left axilla; no pleural effusion or lung parenchymal lesions. MRI left axilla showed left axillary infiltrating lesion abutting the axillary vessels (Fig 2). Biopsy of the lesion was done which came out poorly differentiated adenocarcinoma.

Fig. 1 : Mammography picture

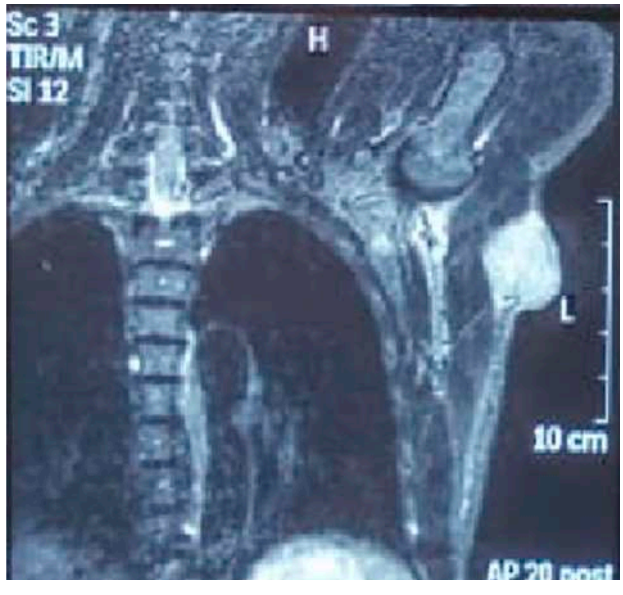

Fig. 2 : MRI Left Axilla

Immuno-histochemistry (IHC) panel which showed ER/PR negative, HMB-45 negative and CK positive; CK7 positive and CK20 negative; GCDFP15 focal positive. No lesion was detected on upper gastrointestinal endoscopy & colonoscopy. Tumor markers (AFP, PSA, CA19.9, CEA & Beta-HCG) were normal. After Tumour Board decision, patient underwent excision of the mass with axillary nodal clearance in November 2019. Reconstruction with latissimus dorsi (LD) flap was done.

Post-operative period was uneventful and patient was discharged on day 3. HPE confirmed primary cutaneous apocrine adenocarcinoma and 4/15 lymph nodes showed metastases. Patient was planned for adjuvant RT but refused and was lost to follow up.

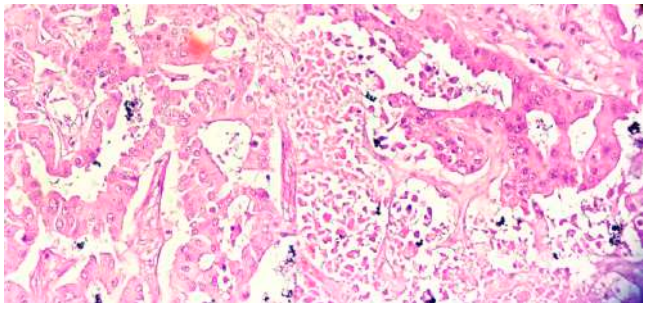

Fig. 3 : Histological Picture

DISCUSSION:

Differential diagnosis of cutaneous primary apocrine adenocarcinoma (CPAD) includes: mammary carcinoma , lymph node metastasis, extramamary Paget's, ceruminal carcinoma,

Classification of Cutaneous Apocrine Neoplasms: [6]

Benign:

1. Apocrine adenoma
2. Hidradenomapapilliferum
3. Apocrine hidrocystoma (cystadenoma)
4. Ceruminoma

Malignant:

1. Apocrine adenocarcinoma
2. Ceruminoma
3. Adenocarcinoma of Moll's glands

Extramammary Paget's disease was excluded from the above classification.[6]

Histologically, CPAD can occur in various forms- papillary, tubular, solid sheets, infiltrating pattern. The cells are large with abundant eosinophilic cytoplasm with luminal decapitate secretion. They show PAS positive diastase resistant intracytoplasmic granules. Features favoring primary apocrine adenocarcinoma over metastatic carcinoma includes- a transition zone between normal apocrine glands and neoplastic glands along with intracytoplasmic granules. [5,6] Our case microscopic findings were: epidermis was ulcerated with neoplastic cells infiltrating the deeper dermis and showing decapitation secretion. No in situ component seen.

IHC helps to differentiate CPAD from metastatic adenocarcinoma of other organs. CPAD are positive for EMA, GCDFP 15, CK. [3] In our case, CK7 was positive and GCDFP 15 focal positive while ER/ PR negative this diagnosis of PCAD was made and mammary carcinoma or metastatic adenocarcinoma was ruled out.

The treatment of choice is wide local excision with clear margins, with or without regional lymph node dissection depending on the node status. Postoperative radiotherapy and chemotherapy has shown little benefit on outcome in patients with moderately or poorly differentiated tumors [6]. The rarity of this type of carcinoma and the lack of clinical trials precludes set guidelines for the management of such cancers.

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Letter to the Editor | Guest Article

Unique challenges and research opportunities in cancer care of North East.

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Cancer incidence in North-East (NE) is rising and is higher compared to rest of India. Data from NE is reliable and of high quality due to broad coverage of National Cancer Registry Programme (NCRP) in all the eight states of North East. Predominant cancers in male are esophagus, lung, stomach, hypopharynx and mouth; whereas in female breast cancer is most common followed by cervix uteri, esophagus, lung and gallbladder. Population based cancer registry (PBCR) from Aizawl district, Papumpare district, East Khasi Hills district, Mizoram and Kamrup Urban have highest age adjusted incidence rate (AAR) in both sexes in the country. Mouth cancer, hypopharynx, esophagus, stomach, gall bladder, cervix uteri, and lung are higher in PBCR from NE. Major risk factors identified are tobacco, alcohol and indoor pollution across all the states of NE. [1]

Higher number of patients in NE present in locally advanced disease (58.5 % vs 42.1%) and metastatic disease (22.1% vs 12.5%) when compared to rest of India. This has resulted in poor 5 year cumulative survival in early stage head and neck cancer (40.5% vs 73.6%), locally advanced head and neck cancer (16.9 % vs 44.5%), early breast cancer (63.5% vs 88.6%) , stage III breast cancer (20.1 % vs 70.7%) and local advanced cervical cancer (33.9% vs 62.9 %) in comparison to rest of India. However, cancer diagnosis, cancer modalities and treatment at reporting institutions are similar to rest of India. [1]

North East is a cultural melting pot consisting of different ethnicities, cultural and food habits. As the number of patients are rising there is need of interventions at multiple level. First step will be identification of risk factors which are specifically related to North East for eg. betel nut, use of pesticides in tea garden, tobacco water etc. For identification of these risk factors there is need for surveys equipped with validated, reliable and feasible questionnaire to identify community specific risk factors.[2] Education and involvement at community level of health care workers to spread awareness about the risk factors is necessary for primary prevention.

Screening trials need to be designed for high risk population in selected communities for early detection and early referral. For eg.Papumpare PBCR has third highest AAR for stomach cancer and Kamrup PBCR has highest AAR for hypopharyngeal cancer on international comparison. These PBCR can be identified as target for screening trials and preventive interventions. We need to analyze patterns of care and outcomes in treatment of head and neck squamous cell carcinoma, breast cancer , stomach cancer, esophageal cancer and cervical cancer of North East and how do they differ from rest of India and where interventions will yield maximum outcome.

As majority of patients present in advanced stage, we need to develop interventions which are cost effective. Randomized control trial in carcinoma gall bladder is

feasible in North East which is rare in Western countries. Trials focused on neoadjuvant chemotherapy in squamous esophageal cancers versus neoadjuvant chemoradiotherapy can be considered where radiation facilities are limited can be considered. A molecular level study in patients from Meghalaya have identified novel genes in oral squamous cell cancer which have putative etiological role. [3] Similarly, germline mutation profile in breast and ovarian cancers in northeast should be done to identify founder mutations. Studies can be designed on oral microflora assessment in head and neck squamous cell cancers and their relationship with cancers. Molecular studies in unique ethnic groups of North East can give newer insights to disease mechanisms.

As large number of patients from NE specially from Sikkim (98.3%), Nagaland (21.3%), Manipur (62.4 %), and Mizoram (58.2%) opt for treatment outside NE, there is need for capacity building for treatment of cancer patients and awareness amongst patients that cancer care is available at NE. This will prevent patient's flow to other states which exacts heavy emotional, physical and financial price on the patient and patient's family.

To conclude, there is a need for comprehensive cancer plan encompassing prevention, early detection and management in order to stop North East becoming cancer hotspot in the country. Unique ethnicity and cultural habits give exciting cancer research opportunities in North East.

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Case Report

Recurrent metastatic malignant melanoma of orbit : a case report

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INTRODUCTION:

Orbital melanoma occurs as a primary disease, a secondary disease (local invasion from uveal, conjunctival or eyelid primary tumor), or a metastasis from distant origin, eg skin. Melanoma accounts for 5-20 % of metastatic and secondary orbital malignancy but a minute proportion of primary orbital neoplasia. Primary orbital melanoma has poor prognosis. Initial treatment for primary and loco-regional melanoma is surgery. Systemic therapy such as immuno-therapy has been the mainstay for adjuvant settings particularly metastatic setting.Melanomas are generally radio-resistant so apart from palliation radiation therapy has a limited role and can be used as an adjuvant therapy to control disease loco-regionally.

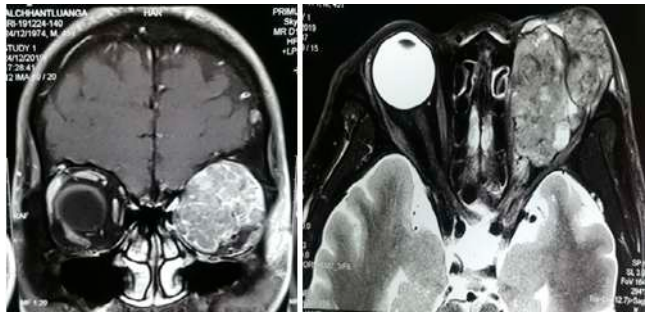
CLINICAL PRESENTATION:

A 45 Years old male came to OPD with chief complaint of swelling in left eye since 1 year. Biopsy at local place in 2018 which was suggestive of malignant melanoma Immunohistochemistry-HMB45 positive for which he underwent wide excision of mass and covering of bare area with artificial amniotic membrane at local place on 08/06/2018.Further he developed recurrence for which he underwent enucleation of lower eyelid on 24/1/2019. He received CTRT–20gy+3 cycles of chemotherapy.

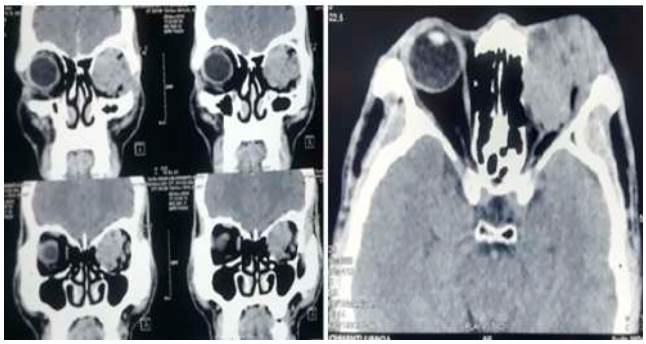
On examination, in our OPD, there is a mass in left orbit with enlarged non tender mobile left pre auricular lymph node measuring 4*3 cm; left level Ib node palpable measuring 4*5 cm, with complete loss of vision in left eye since 4 months.Biopsyfrom upper eyelid done which suggests malignant melanoma (CK, S100, HMB45 positive) and FNAC from left parotid region done suggestive of poorly differentiated malignant neoplasm.

MRI ORBIT:

81* 36 mm mass showing hyper and hypointense signal on both T1 and T2 wt images. Eye ball along with optic nerve complexes cannot be separately demonstrated. Extra-ocular muscles not visualized. Involvement of palpebral and orbital parts of lacrimal gland present. No extracranial extension or extension into ITF. 30*16 mm mass in left superficial parotid gland present.

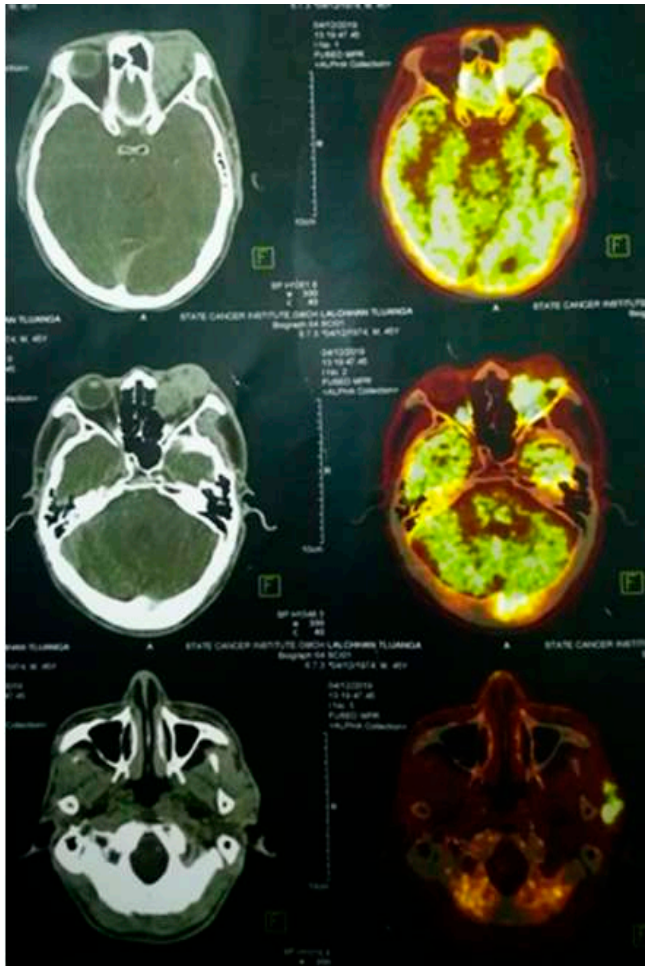


CECT: Mass in left orbit with loss of eyeball, obliteration of extraocular muscle and optic nerve. No intra cranial extension.



PET SCAN:

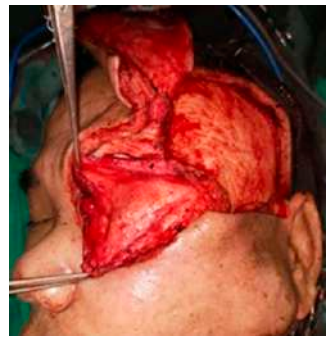
Metabolically active disease in left orbit suv max 8.1.Metabolically active few LN intraparotid, left level Ib,II suv max 6.7. No distant metastasis.



SURGICAL PROCEDURE:

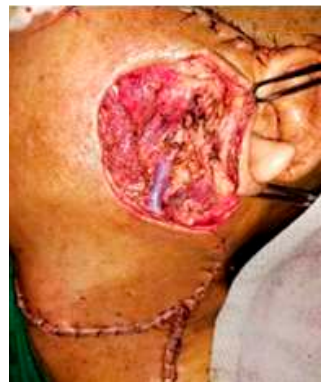
Wide excision +left orbital exenteration+ left radical parotidectomy+ left Radical Neck Dissection+ temporalis muscle flap reconstruction +STSG

Orbital exenteration

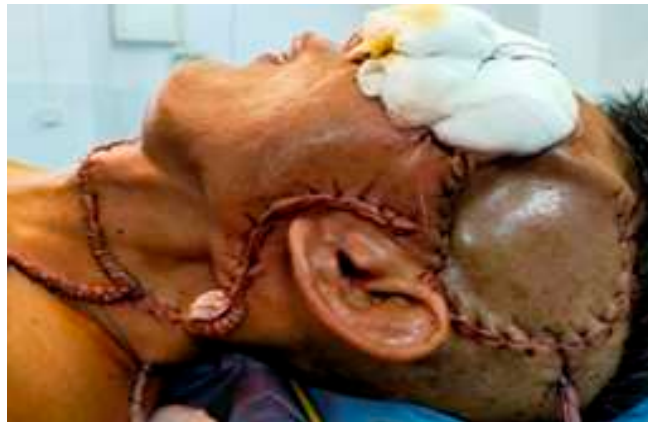


Temporalis muscle flap raised

Temporalis muscle sutured



Left radical parotidectomy +RND



Post-operative photo

POST OP HISTOPATHOLOGY REPORT:

Malignant Melanoma of left orbit infiltrating surrounding soft tissues and skeletal muscles. LVE and PNI present. All cut margins are free and away from tumor. Optic nerve cut margin free. Parotid tumor: metastatic malignant melanoma. Intra-parotid node shows metastatic deposits. 2/34 nodes with metastasis. Nasal mucosa, orbital apex, frontal bone, lateral orbit, infra-orbital bone, maxillary sinus mucosa, sphenoid mucosa free of tumor.

The patient is presently at two months of follow up and is disease free.

DISCUSSION:

Surgery is the main stay of treatment. Role of chemotherapy: melanoma usually does not respond to chemotherapy and is used only when tumor spreads. Radiation therapy has no definitive role but can be use as adjuvant in few settings apart from its role in palliation.

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Case Report

Primary malignant melanoma of vagina : a case report

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Melanoma is caused by the malignant transformation of pigment cells in skin and mucosal linings like gastrointestinal, respiratory, and urogenital tracts. Mucosal melanomas are rare and account for only 1.4% of all melanomas. In female genital tract, the predominant location of melanoma is the vulva whereas the vagina is rarely affected [1]. Malignant melanoma accounts for <10% of all female genital tract melanomas, for 2.4-2.8% of all vaginal malignancies, and for 0.3-0.8% of all malignant melanomas [2]. Primary malignant melanoma of the vagina usually occurs in women aged in their 60s or 70s, with the majority of patients being postmenopausal. Patients commonly complain of vaginal bleeding, vaginal discharge or a palpable mass.

CASE REPORT:

A 49 year old, P9L9, 3 years postmenopausal lady, known case of T2DM presented with complaint of whitish discharge per vagina for 2 years. Per speculum examination revealed a blackish lesion over anterior vaginal wall involving upto urethra and labia minora. Cervix was not involved clinically. On pelvic examination, uterus was of normal size, mobile without involvement of vaginal fornices. Histopathology (HPE) of anterior vaginal wall biopsy showed superficial spreading melanoma. Her physical examination was normal ruling out melanotic lesion elsewhere. Pap smear of cervix was negative for intraepithelial lesion or malignancy. MRI abdomen & pelvis revealed heterogeneously enhancing soft tissue involving the region of vagina and anterior perineum with adjacent fat stranding. Soft tissue thickening was seen towards region of urethra. Fat plane with urinary bladder base was compressed at places.

Fig. 1 : The clinical picture on per speculum examination

CECT thorax was normal. Final diagnosis was primary malignant melanoma of vagina FIGO stage II. She underwent Total vulvovaginectomy with total urethral resection, modified radical hysterectomy with bilateral salphingoophorectomy, bilateral pelvic lymph node dissection, permanent suprapubic cystostomy followed by bilateral inguinofemoral lymph node dissection after 2 weeks. Decision to perform the

inguinofemoral dissection at a later time was taken intraoperatively due to blood loss during vaginal dissection and pre-existing poor general condition of the patient. She was transfused 2 units of packed red blood cells postoperatively. Final HPE Report showed the size of the vaginal lesion was 2.5 x 1.5 cm2 showing features of malignant melanoma. Maximum depth of invasion was 0.2cm. Distance from the base was 0.5cm. Sections from other two blackish lesions showed features of malignant melanoma (suggestive of micro-satellites Metastasis). Distance from the vulvar resection margin is 2cm. Sections from left internal iliac lymph nodes showed one lymph node with metastatic tumour deposits. Inguinal lymphnodes were free of disease. Impression- Malignant melanoma of vagina p (T2N2cM0).

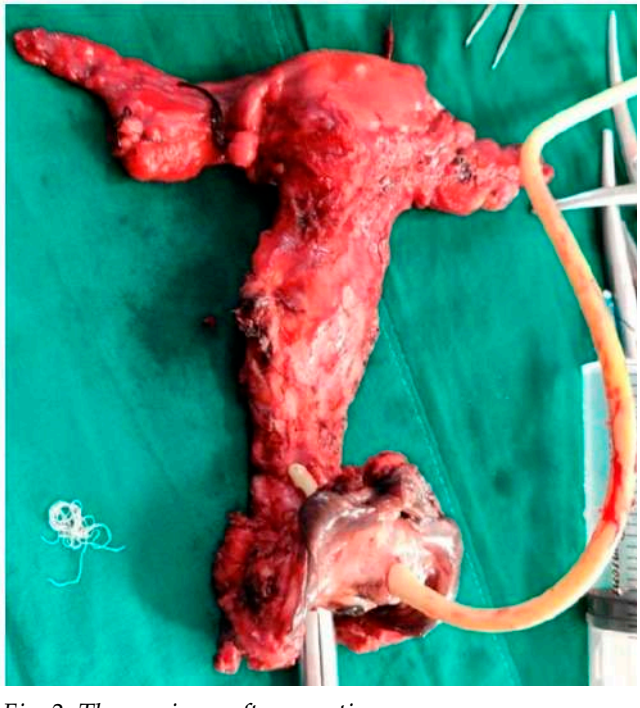

Fig. 2: The specimen after resection

DISCUSSION:

Primary Malignant melanoma of vagina is a rare gynaecological malignancy. It accounts for less than 1% of all malignant melanomas and less than 3% of all primary malignant tumours of the vagina. Although it was first reported in 1887, there have been no more than 500 primary vaginal melanoma cases reported worldwide [3]. The lesions most commonly arise in the distal part of the vagina, particularly on the anterior wall. Melanomas have a wide variety of size, colour and growth patterns. It may be single or multiple and pigmented or non-pigmented. Tumor size (<3cm) is the most important prognostic factor, whereas tumor thickness is only a weak predictor of survival [4]. Treatment options include local excision [5], radical excision with inguinofemoral and/or pelvic lymphadenectomy [6], radiotherapy [7], chemotherapy, and immunotherapy [8]. Surgical treatment is the preferred modality. Positive resection margins have higher local recurrence and are associated with a poorer prognosis. No difference has been demonstrated between radical and conservative surgery either in terms of overall survival or disease-free survival [9].

Radiotherapy can be applied as primary treatment for patients who are unable or unwilling to have surgery. It can be used preoperatively to reduce tumor size and enable a more conservative surge. Also it can be applied postoperatively as adjuvant treatment for patients with incomplete tumor resection or with pelvic metastases [10]. Overall prognosis is poor, with historic 5-year survival rates ranging from 5% to 30% regardless of treatment modality or extent of surgical resection [11]. Our patient is presently alive and disease-free for 4 months.

CONCLUSION:

Primary malignant melanoma of vagina is an extremely rare tumor with poor prognosis. Radical excision should be considered as the mainstay of treatment.

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Original Article

Early Experience with Oncoplastic Breast Surgery in a Tertiary Care Cancer Centre in North-East India

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INTRODUCTION:

The goal of oncoplastic procedures is to resect the breast tumour with negative histologic margins while preserving the contour of the breast, with good symmetry. Oncoplastic surgery merges the principles of oncologic and reconstructive surgery, utilizing a spectrum of techniques to fill defects and optimize cosmesis. The goals of treatment are to provide optimal local control while maintaining or reconstructing a cosmetically acceptable breast.

METHODS:

A prospective single centre study was conducted on patients with carcinoma breast for a period of one year, from 1st January to 31st December 2019. Patients opting for breast conservation surgery when amenable for the procedure with no contraindications for it were included for the study. All patient and tumour characteristics, surgical techniques, intraoperative and postoperative parameters and follow up details were noted in a prospectively maintained database.

SURGICAL TECHNIQUES:

Different techniques were used which included Breast tissue advancement flap, Grisotti flap, Benelli technique, LD flap. The choice of technique was dependent on achievement of safety margins, breast volume and its ptotic degree. Separate incision was used for axillary dissection.

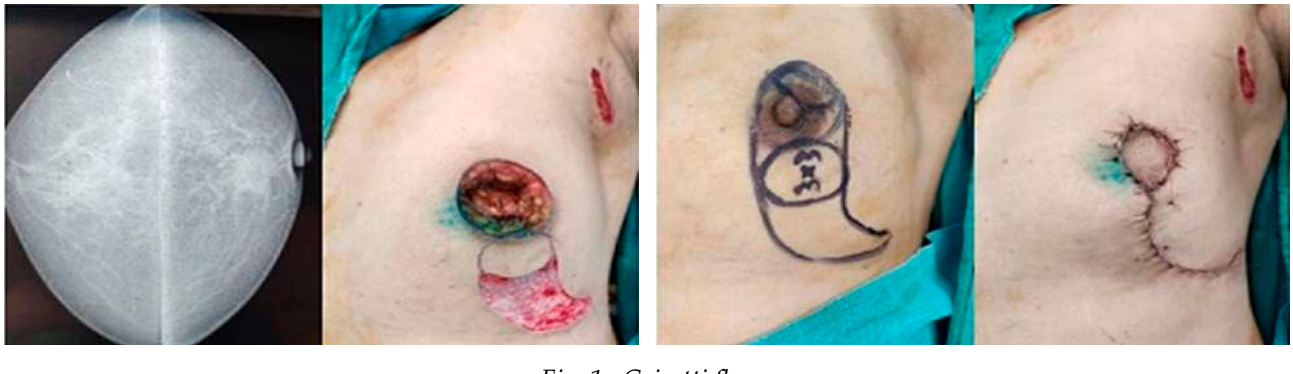

Fig. 1 : Grisotti flap

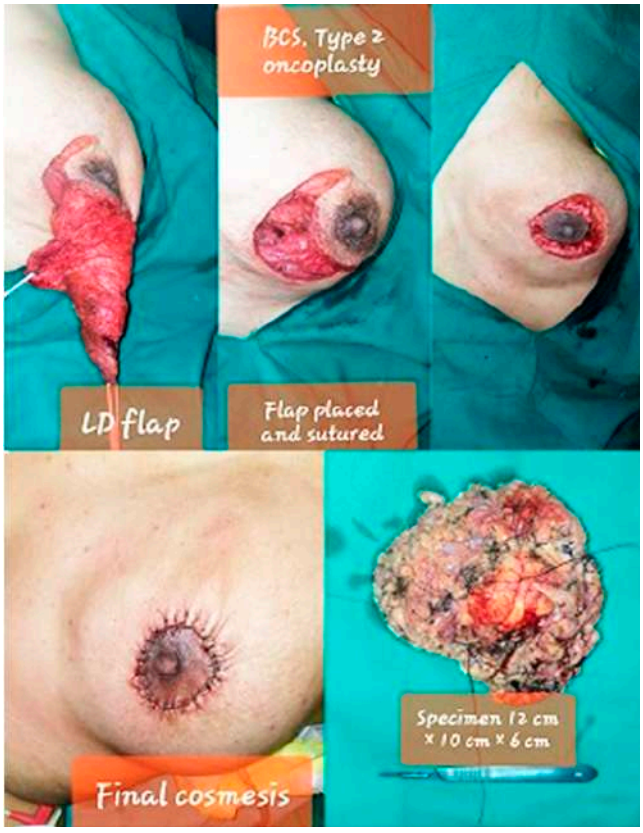

Fig. 2 : LD flap

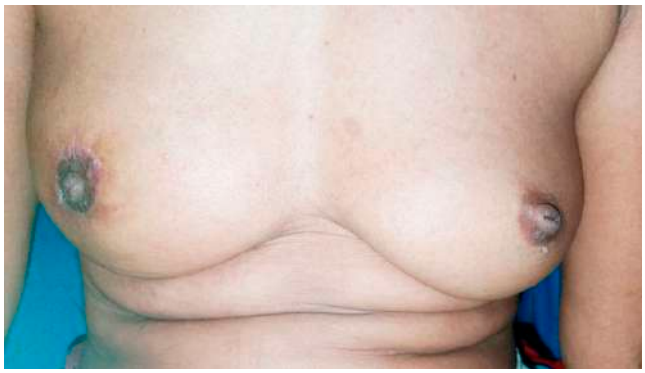

Fig. 3 : 2 weeks follow up

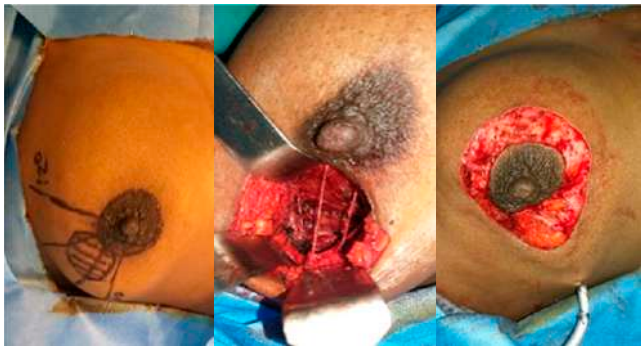

Fig. 4 : Benelli technique

RESULTS:

Of 248 patients who underwent surgery for carcinoma breast, 64 patients had breast conservation surgery (BCS). Median age was 46.5years (range 34 to 87 years). The median size of tumor was 3.5 cm. BCS with oncoplasty was done after downsizing of tumour with neoadjuvant chemotherapy in two cases. There were no major complications. All except one of the patients undergoing BCS had invasive ductal carcinoma. That one patient had ductal carcinoma in situ.

The oncoplastic techniques performed were breast tissue advancement flap (Type 1 Oncoplasty) in 49(76.56%), Grisotti flap 2(3%), Benelli technique 3(4.68%), LD flap 10 (15.62%).

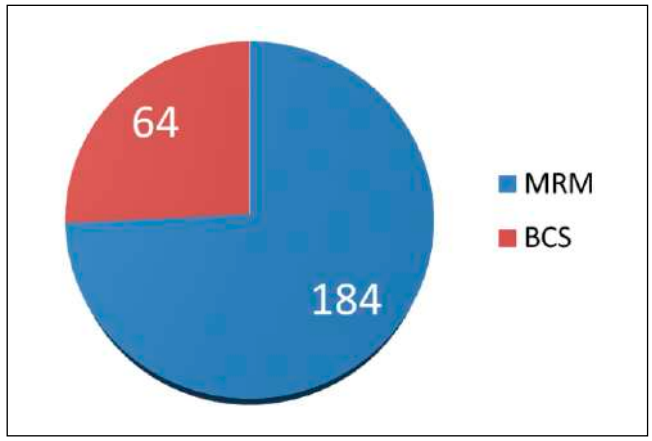

Fig. 5 : Type of Surgery

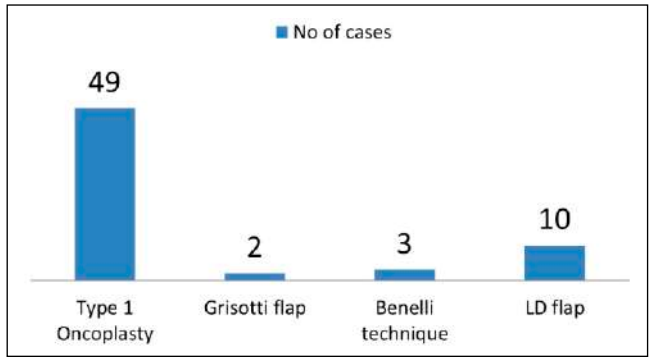

Fig. 6 : Type of BCS technique

At median follow up for 4.4 months, the patient satisfaction results were excellent based on subjective assessment. Based on objective assessment according to Harvard Scale, results were excellent in 37(58%), good 17(26.3%), fair 7(10.5%) and poor 3(5.2%).

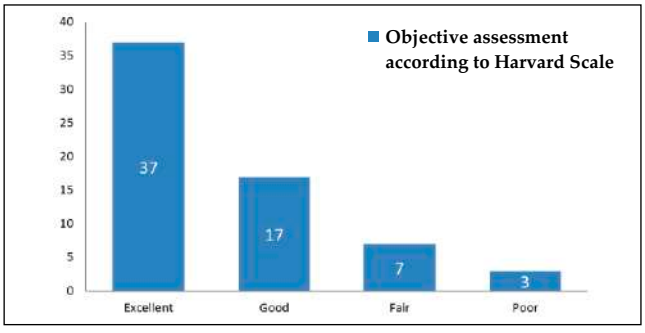

Fig. 7 : Objective assessment according to Harvard Scale

DISCUSSION:

Oncoplastic breast surgery aims to achieve good aesthetic outcomes for women with breast cancers who would have unacceptable outcomes with lumpectomy, and in addition, enable breast-conserving surgery for larger breast cancers. It also gives an option other than mastectomy in patients with larger tumours.

An oncoplastic procedure aims to minimise cosmetic impairment to the breast by obliterating surgical cavities that may create distortion. Thus, they utilize the principles of parenchymal redistribution or parenchymal replacement [1].

Poor cosmetic outcome after wide local excision is well predicted by the percentage of breast tissue being removed and the location (quadrant) of the breast cancer among many other factors. Prospective randomized clinical trials have shown that BCS followed by radiotherapy gives equivalent survival rates compared with mastectomy [2, 3]. So, with oncological safety being assured, the cosmetic outcome should be a priority.

A thoughtful incision planning is a first step, with an understanding of how breast deformity occurs in order to avoid it. Any resection cavity within the breast will collapse and pull both parenchyma and skin towards the cavity. And, any skin excision or even incision will contract and create some distortion. Also, central and medial cavities have relatively less laxity and volume and so they create more deformity.

In the current scenario, even large tumors are amenable to be treated with BCT, especially after tumour downsizing with neoadjuvant treatment. However, one of the major limitations is the ability to perform a large enough resection without compromising the cosmetic result. The larger the tumor, the greater the risk of lumpectomy margins being involved with tumor [4].

Oncoplastic surgery is a greatly useful tool in several such situations. Every time a lumpectomy was not suitable or where there was a need for a large resection, or where there was a high risk of deformity, oncoplastic surgery has been used liberally [5].

In the follow up period, clinical and radiologic examinations have not been affected by the remodeling procedure, and mammographic changes are not a hindrance for proper evaluation.

In the current study, no episodes of local recurrence or systemic metastasis were reported. This may be attributed to short term follow up, which is one of the acknowledged drawbacks of our study. We understand that our study does not include many other complex oncoplastic procedures as described in literature and performed in dedicated high volume centres of the country. Our endeavour to learn and practise more such procedures with adequate training will continue and we will report such results as and when applicable.

CONCLUSION:

Oncoplastic surgery is a very useful tool in the armamentarium of a breast surgeon. This approach has allowed us to obtain favourable aesthetic outcomes and to perform wider resections with good oncologic control and favorable cosmesis.

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Review Article

Prognostic and Predictive Biomarkers in Breast cancer

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BACKGROUND:

Breast cancer is the most common cancer among urban women and ranks second among rural women of India.1 It is highly heterogeneous in nature; both clinical and histo-pathologic examination come as a challenge to pin down appropriate treatment regimen.[1] Advances in molecular genotyping have identified several molecular subtypes of breast cancer, which differ in response to chemotherapy and prognosis.[2,3]

Molecular mechanisms at play during breast cancer are becoming clearer, with the arrival of a more comprehensive analysis of genetic information and gene products.[4] Breast cancer has various distinct subtypes, which require unique prognostic markers for deciding the therapeutic options. Globally, majority of breast cancers are estrogen (ER) or progesterone receptor (PR) positive, followed by 15%–20% of the cases presented with overexpression or amplification of human epidermal growth factor receptor (HER2) protein1. However, Indian patients are found to have low overall receptor expression, in addition to relatively higher percentage of young patients with breast cancer.[5]

BIOMARKER DEFINITION, TYPES, AND CHARACTERISTICS:

With the identification of cancer-predictive and diagnostic biomarkers, cancer management has taken a new paradigm shift, as these agents provide a great scope for improving the management by enhancing the efficiency of detection and efficacy of the treatment regimen in the subtype of breast cancer.[2,7] Biomarker is defined as a measurable and reliable indicator used to assess the disease process, or an outcome to estimate whether a therapeutic agent used in the treatment was effective.[8,9,10]

Various international guidelines have made the testing of ER, PR, and HER2 biomarkers mandatory, as they have markedly improved the prognosis and treatment of breast cancer. [11,12,13]

The ER pathway plays a vital role in the pathophysiology of the malignancy and ERα provides the index of sensitivity to endocrine therapy. Furthermore, overexpression of PR serves as a functional assay, as it indicates an intact ER pathway, even if the tumor is reported as ER-negative. ER and PR are thus used as predictive biomarkers for the endocrine therapy in the neoadjuvant, adjuvant, and advanced stage of the malignancy.[1,2,15[Another established biomarker for selecting response to all forms of anti-HER2 agents, such as trastuzumab, lapatinib, pertuzumab, and so on, is HER2 and, during analysis, overexpression or amplification of the HER2 gene is carried out.[14,15,16]

Emerging Biomarkers and Recent Advances: Clinical studies have proved that mutation or alteration of

function of the genes DAPK1, BRCA1, CDKN2A, MSH2, PGR, PRKCDBP, and RANKL is associated with the progression of breast cancer. These genes have varied roles, ranging from tumor suppression, regulation of transcription, pro-apoptotic activity, and kinase inhibition to cell survival regulation. [3,6] The triple-negative breast cancer is found to arise primarily from BRCA1 mutation carriers, followed by BRCA2 carriers. Hence, these can be a promising biomarker for young women with a high-grade TNBC and with negative family history of cancer.[1] Carbohydrate 15-3 (CA 15-3) and carcinoembryonic antigen (CEA) are used by physicians to follow up care of breast cancer and provide insight about the disease progression in metastatic and recurrent breast cancer cases. When used together, they facilitate early diagnosis of metastasis in >60% of breast cancer cases.[1] High level of another biomarker, i.e., Ki67, is associated with poor outcome in breast cancer patients. Various trials have supported the use of Ki67 as a surrogate biomarker to individualize adjuvant treatment. However, it is routinely not recommended because of concerns with assay threshold variability and poor reproducibility. With further clinical evidence, the routine use of this biomarker may be a value addition to the management of breast cancer. [4,15,16]

Urokinase-type plasminogen activator (uPA) and plasminogen activator type 1 inhibitor (PAI-1) are predictive indicators of tumor invasion and metastasis. Evidence reveals high levels of uPA/PAI-1 to be significantly correlated to lower disease-free survival among breast cancer patients who did not receive adjuvant treatment. They serve as an independent predictor of adverse prognosis of newly diagnosed invasive breast cancer cases, and are among the best validated prognostic biomarkers for breast cancer. However, further clinical evidence with different combinations of neoadjuvant therapies are underway for the same. [4,15,16] A few other potential and promising biomarkers are summarized in Table 1.

Table 1 : Emerging Biomarkers [4,6]

Biomarker	Characteristics/Comment	Type
PAK1	Amplification is associated with Tamoxifen resistance	Prognostic, Predictive and therapy-monitoring
Retinoic acid receptor α(RARA)	A potential biomarker for tamoxifen resistance; high RARA protein expression associated with high relapse-free survival	Predictive and therapy-monitoring
Osteopontin-C	High expression levels correlated with tumor recurrence, metastasis, and triple- negative subtypes	Predictive
Nanog	Altered expression contributes to metastasis of breast cancer, associated with poor prognosis	Prognostic and therapy-monitoring
Oct-4 and Nanog	Overexpression contributes to metastasis of breast cancer	Prognostic and therapy-monitoring
CXCL12 and CXCR4	Patients with altered CXCL12 methylation and unmethylated CXR4 have shorter overall and disease-free survival	Prognostic and Therapy-monitoring
CXCL12 and ADAM23	Hypermethylation associated with advanced stage and lymph node metastases	Prognostic and Therapy-monitoring
PFN1	Downregulated in metastatic breast cancer	Prognostic and Therapy-monitoring
Annexin A6	Increased expression in breast cancer	Prognostic and Therapy-monitoring
Vimentin	Upregulated in triple negative breast cancer	Prognostic and Therapy-monitoring
MMP-9	Overexpressed in breast cancer	Prognostic and Therapy-monitoring
10-Protein Signature expression panel	Stratify aggressive phenotype in familial breast cancer	Breast cancer predisposition, prognostic, and therapy-monitoring

Biomarker	Characteristics/Comment	Type
PLS3	High expression in circulatory tumor cell undergoing epithelial mesenchymal transition	Prognostic, Predictive and therapy-monitoring

Although the recent advancements in genetic and diagnostic sciences have offered us a plethora of promising biomarkers, further robust clinical trials, standardization of assay techniques, and validation of the disease-specific biomarkers are the need of the hour. This will not only pave our way to optimizing the treatment regimen but will also help in categorizing specific patient "molecular/genetic portrait" as a part of the diagnostic strategy in the early management of the malignancy.

SUMMARY:

A comprehensive understanding of the importance of biomarker is not only helpful for reliable diagnosis, but also in the selection of therapeutic agents currently available. Their use is imperative in the management of breast cancer. Substantial efforts need to be put into development of new specific and sensitive breast cancer biomarkers to keep patients away from under- as well as overtreatment.

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Case Report

Renal Cell Carcinoma metastasizing to Head and Neck Region : a case report.

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INTRODUCTION:

Renal cell carcinoma (RCC) which comprises 90 – 95 % of all renal neoplasm arising from the kidney, accounts nearly 3 % of all the adult malignancies. [1] RCC has a varied clinical presentation without specific early warning symptomsand is generally resistant to chemo radiation. Approximately one third of the patients with RCC have metastatic disease at initial presentation. Fifteen percent of metastasis from RCC is found in head and neck region, most commonly in the thyroid gland. Metastasis to other unusual sites i.e. nasal cavity, paranasal sinuses, skin, skeletal muscles, has also been reported in the literature.

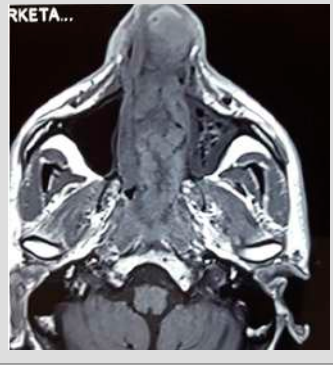
CASE REPORT:

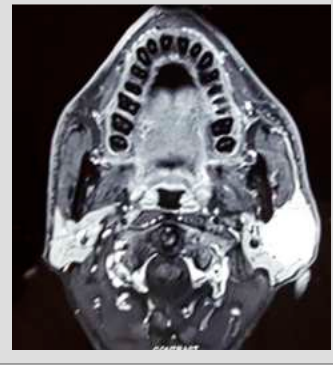
A 44-year-old man presented at an outside hospital with complaint of left sided nasal obstruction for last 3 years. He also had a swelling below the left ear for past 1 year. On examination he was found to have a mass filling up his left nasal cavity. Left parotid mass was nearly 2x2 cm [2] in size, hard and non-tender with restricted mobility (fig-a). Patient had a history of undergoing left-partial nephrectomy for 'Clear cell renal carcinoma' (pT1a N0 M0) five years back. No history of any adjuvant treatment following surgery was present.

CE-MRI revealed a sino-angiomatous polyp with expansion and bony remodeling and left parotid mass with image-features suggestive of a pleomorphic adenoma (fig-b &c).Histopathological examination of punch biopsy specimen taken from the nasal mass was suggestive of a hemangiomatous polyp, and fine needle aspiration cytology (FNAC) of left side parotid mass gave a diagnosis of a pleomorphic adenoma.

Fig. 1 :

[a] 

[b] 

[c] 

[a] Clinical finding of a left sided parotid swelling.

[b] Showing anenhancing polypoidal mass lesion with multiple vascular flow voids with its epicentre in the left nasal cavity involving ipsilateral ethmoid sinus causing expansion and bony remodelling of the left nasal cavity with retro-obstructive paranasal sinus collections - suggestive of sino-angiomatous polyp.

[c] Well-defined circumscribed enhancing mass lesion in the superficial lobe of the parotid with T2 hypointense rim – suggestive of pleomorphic adenoma.)

He subsequently underwent excision of the nasal mass with a lateral rhinotomy approachunder general anaesthesia 2 months back.Post-operative histopathology suggested a diagnosis ofsinonasal-paraganglioma. Tumour was rendered for Immuno-histochemical analysis and was found reactive for CD-10, Vimentin and Pax 8. It also showed focally positivity for 'epithelial membrane antigen' and 'pancytokeratin'. Tumour was nonreactive for synaptophysin, chromaganin and S100. A final diagnosis of 'metastatic deposits from clear cell carcinoma of renal origin' was made and patient was referred to BBCI for further management.

On evaluation in our outpatient department he was foundwell oriented to time, place and person. He had a good performance-status(ECOG=0) without pallor, icterus, cyanosis, clubbing or pedal edema. His vitals were within the normal limits. On local examination he was found to have a 4 x 3 cm firm to hard, non-tender swelling in the left parotid region with restricted mobility. Skin overlying the swelling was found normal. There were no signs of facial weakness or asymmetry.A scar from previous surgerywas noted in left side of face. Nasal endoscopy revealed no residual mass in nasal cavity. Rest of the head & neck was unremarkable. There were no palpable neck nodes.Systemic examination was within normal limits.CECT Scan of thorax, abdomen and pelvis showednodular lesions with variable exophytic components in left kidney suggestive of a recurrence.

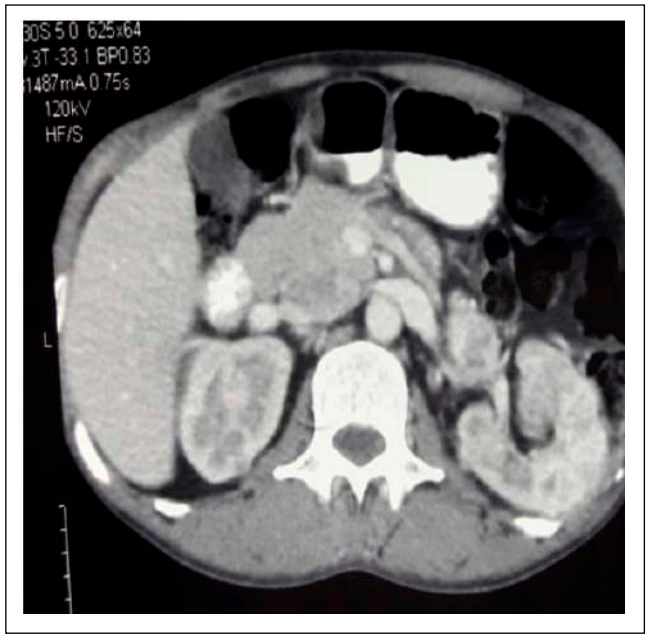


Fig 2 : Multiple heterogenous nodular lesions in the regions of both adrenals (R>L). Kidneys show nodular lesions with variable exophytic components.)

Review of slides from nasal mass showed features of 'Clear cell carcinoma' (Grade II). IHC on tissue from paraffin block confirmed a metastatic Renal cell Carcinoma.Slides from FNAC of parotid mass were suggestive of 'low grade Acinic cell Carcinoma'. With a final diagnosis of recurrent RCC with distant metastasis along with a 2nd primary in left parotid (Acinic cell carcinoma, cT2 N0 M0) was made. The case was subsequently discussed in 'Joint departmental tumour board'. A decisionto operate the patient for the 2nd primary in left parotid followed by targeted-therapy for RCC-with systemic metastasis (M1) was taken. Patient underwenta superficial parotidectomy. A neck dissection was avoided as intra-operative frozen section of ipsilateral level II node turn out negative for malignant cell.

In contrast to pre-operative FNAC final-histopathology confirmed 'metastatic deposits of renal cell origin' in excised parotid lobe with negative margins. Patient was reviewed after 3 weeks of surgery and put on targeted-therapy with Pazopanib – 800 mg daily as planned earlier. Patient is asymptomatic on regular follow-up.

DISCUSSION:

Renal cell carcinoma is the third most common infraclavicular tumour metastatizing to head and neck region . In most cases they will spread to neclk lymphnodes, but manifestation in the paranasal sinuses, skull,oralcavity, skin, larynx and thyroid gland has also been reported.[2] Although metastatic renal cell carcinoma is often resistant to chemotherapy and radiotherapy, Vascular Endothelial Growth Factor (VEGF) and non Vascular Endothelial Growth Factor receptor (non VEGFR) pathways should be taken into account for treatment of advanced renal cell carcinoma. Multi targeted VEGF tyrosine kinase inhibitors like sorafinib, sunitinib,pazopanib, axitinib and bevacizumab, mTOR inhibitors include temsirolimus and evarolimus can be used. [3]

CONCLUSION:

Our case report showed a late metastasis of renal cell carcinoma. Since most of the renal cell carcinoma have a clear cell morphology it is usually difficult to differentiate a primary clear cell tumour of the salivary gland or thyroid gland and metastatic renal cell carcinoma, which may lead to a diagnostic dilemma.

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Case Report

Modified long Tracheostomy Tube for airway management in lower tracheal obstruction

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INTRODUCTION:

Acute airway obstruction produces symptoms of dyspnoea, cough, stridor and may be life-threatening [1]. A patient may have lower trachea bronchial obstruction due to primary tracheobronchial tumour, a tumour from adjacent structures compressing the airway or metastatic disease to the airway [1]. Obstruction in the airway caused by malignancies in upper airway including nasopharynx, oropharynx, larynx or hypopharynx usually requires surgical intervention such as tracheostomy or cricothyroidotomy [2]. However, an obstruction at the lower tracheal level, tracheostomy and insertion of a regular tracheostomy tube may not alleviate the obstructive symptoms because the limited length of the tube may not bypass the obstruction [3]. Rigid therapeutic bronchoscopic intervention is increasingly accepted to treat such patients for palliation of the airway obstruction1, but this procedure requires expertise physician and proper facilities which are not commonly available in the emergency department.

In such case, tracheostomy is an easy procedure to perform, but in the absence of a long tube, the obstruction cannot be relieved, as the commonly available tracheostomy tube is only around 6-8 cm long [4]. Even though long tracheostomy tubes are commercially available, they are usually expensive and are seldom readily found. A feasible way is to use an endotracheal tube in such cases. However, an endotracheal tube is very uncomfortable and cumbersome to manage, as a substantial length of the tube lays outside the stoma, and it cannot be stabilized to the skin. The neck movement and mobility of the patient is severely affected, and the tube can be easily displaced. A modified endotracheal tube refashioned with the parts of a regular tracheostomy tube can easily overcome these disadvantages. For discussion purpose, henceforth, we call this tube a "Long Tracheostomy tube" (LTT). In this article, the author describes the method of making a long tracheostomy. We demonstrate the utility of the LTT with the help of two case scenarios.

The technique of making Long Tracheostomy Tube:

We start with a standard PVC endotracheal tube of 7.5mm or any size as required. We then remove the connector. The desired length is marked on the tube. If the cuff is not needed, then the tube is cut at this level with a sharp blade, and the cuff is meticulously removed off the tube with an eleven number blade. To preserve the cuff, whenever required, a sliver of the plastic tube is cut along the cuff pilot line above the desired length. The integrity of the cuff is checked by air inflation (Figure 1).

Fig 1.

Next, we try to make the flange, with the help of a tracheostomy tube. We cut the tracheal part of the tube at its attachment to the flange. The outer protruding part of the tracheostomy tube is also cut at its attachment with the flange. Now only the flange with a central hole with a part of the PVC tube remains.

The part is meticulously removed with the help of a number eleven blade and some traction (Figure 2).

Fig 2.

Now, the shortened endotracheal tube is inserted through the flange. The endotracheal tube connecter is reinserted in the tube.

It is crucial that the connector and the endotracheal tube fits tightly. Otherwise, there can be an accidental dislocation of the endotracheal tube into the tracheobronchial tree. The modified Long tracheotomy tube of the desired length is ready for use, as shown in figure 3. If bleeding is expected during changing of the tube, cuffed long tracheostomy tube can be made as we described above or as described by A Hydri [5].

CASE 1:

A 52-year-old man presented to the emergency department with severe respiratory distress. The patient is a known case of chronic smoker since last 15-20 years. He was restless, diaphoretic and not able to lie down. Computed Tomography (CT) scan of the neck showed an obstructing growth in the lower part of the trachea. There was almost complete obstruction of the trachea, and the patient was on severe respiratory distress. We did an emergency tracheostomy and regular tracheostomy tube inserted. However, due to the inferior location of the tumour, respiratory distress was not alleviated. We then passed an Endotracheal tube size 7.5mm through the stoma into the trachea, which relieved the distress.

Later a modified long tracheostomy tube was used to maintain his airway. The patient was stabilized, and a biopsy was taken. He was diagnosed with Squamous cell carcinoma of the trachea and was able to complete his chemoradiation treatment. The long tracheostomy tube not only helped the patient during the emergency but also in completing seven long weeks of treatment.

CASE 2.

A 59-year-old patient, post Total laryngopharyngectomy with tubed pectoralis major myocutaneos flap repaired presented in the emergency with acute onset difficulty in swallowing and respiratory distress. He was a tracheostomy tube dependent due to stomal stenosis. A quick assessment of the trachea with a flexible bronchoscope through the tracheal stoma showed an obstructing growth in the lower part of the trachea with trachea-oesophageal fistula. An emergency bronchoscopy guided endotracheal tube insertion was possible, and the patient's respiratory distress was relieved. A biopsy was taken, and an oesophagal stent was inserted to facilitate oral feed and prevent aspiration. The long tracheostomy tube was used subsequently, and the patient was swallowing and breathing normally. Presently, the patient is on palliative chemotherapy and responding well.

DISCUSSION:

Tracheostomy is a relatively simple procedure. An endotracheal tube and a tracheostomy tube are commonly available in the emergency department. Endotracheal tube alone can be useful for maintaining

the airway patent in lower tracheal obstruction but due to its length, keeping it for longer duration is a concern. Unlike a tracheostomy tube, an endotracheal tube lacks flange to stabilize it to the neck. Hence the tube may accidentally get extruded outside, which may put the patient in catastrophic airway obstruction, or has a high chance of migrating more inferiorly in the tracheal lumen and injured the carina or tracheal wall. An unnecessarily significant length of the endotracheal tube also remains outside. Because of this, frequent suction clearance becomes difficult.

On the other hand, a standard Tracheostomy tube is not effective in relieving lower airway obstruction due to its limited length. Both the tubes can be combined to make a long tracheostomy tube, which effectively does away with their disadvantage. This long tube can be easily made and kept in the emergency department.

When LTT is used, one has to keep in mind that the connector and the endotracheal tube had to fit tightly to each other. This joint can also be reinforced with glue. Tracheal secretion may make the connection loose and accidental dislocation may cause tracheobronchial obstruction, injury by the dislodged tube, or may present as a foreign body in the airway [6,7].

Both our patients were successfully managed with the LTT. Till the last day of follow up, there was no complaint from the patient or attendant in using the tube, and they are comfortable with it.

CONCLUSION:

Long Tracheostomy Tube is a combination of the standard tracheostomy tube and endotracheal tube of the same size. This tube can be easily made and kept in the emergency department for any respiratory obstruction in the lower trachea, which is not possible by a standard tracheostomy tube. In hospitals which are not well equipped with emergency airway instrument, we suggest using the Long Tracheostomy Tube as this is simple to make and convenient to use.

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Review Article

Ultrasound guided interventions in cancer pain management : A new paradigm

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Cancer-related pain is one of the most devastating problems faced by the healthcare systems worldwide. Unrelieved pain interferes with the physical functioning, social interaction, leads to psychological distress and impairs the quality of life.

Cancer pain is found in more than 70% in the advanced stage. Causes are multifactorial and consists of nociceptive, neuropathic and mixed types of pain. Treatment of cancer can be effective in controlling cancer-related pain but can also be the cause of pain. Pain is experienced in 33% after curative treatment, 59% on anticancer treatment and 64% with metastatic, advanced or terminal disease . Pain has a high prevalence earlier in disease course in cancer types such as pancreatic (44%), head and neck cancer (40%) and hematology.

Despite the guidelines and the availability of opioids (the mainstay of moderate to severe cancer pain management), under-treatment is common and 5 -10 % of cancer patients still suffer intractable pain not responding to conventional treatments. Patients refractory to all conventional strategies and/or with dose-limiting, analgesic related side effects can achieve pain control with interventional techniques when used alone or, more frequently, in combination with systemic therapy preferably at an earlier step in the WHO ladder.

A multicenter, randomized control trial of 109 patients receiving sympathetic blocks for abdominal and pelvic cancer before step 2 of the WHO ladder versus after step 3 showed that the early treatment group had a greater number of block responders ($p < 0.001$), decreased opioid consumption in the first 12 months ($p < 0.001$), and improved quality of life ($p < 0.05$).

Interventional pain techniques consist of neuraxial analgesia, minimally invasive procedures for vertebral pain, sympathetic blocks for abdominal cancer pain, neurolysis, neuroablation, peripheral nerve blocks and percutaneous cordotomy. These blocks are performed blind or under CT fluoroscopy and ultrasound (USG) guidance..

USG enhances diagnosis, precision, safety, outcome and decreases the cost and radiation effects compared with CT and is useful in pregnant patients and is portable too.

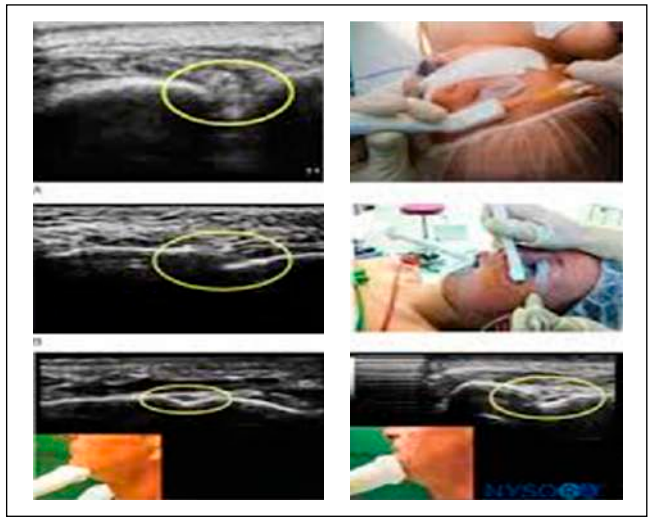

Fig 1 : Facial nerve blocks with us guidance

Dynamic and direct visualization of needles and surrounding images helps avoid complications. Spread of injectate can be observed and it avoids the need for use of contrast agents and its associated risks of allergic reactions, renal effects and cost.

Disadvantages are user-dependence, requiring experience and practice, sound understanding of anatomy and sono-anatomy. There is a lack of training, evidences and publications. Bone casts an acoustic shadow and produces artefact in USG image. It's difficult to visualize deep structures as resolution gets poorer. Whereas CT fluoroscopic guided interventions are effective for visualization of bony structures but not soft tissues and sometimes both are used together.

USG guided blocks have numerous uses in the field of cancer pain.The role of USG guided truncal blocks, including erector spinae, serratus anterior, pectoralis nerve I and II, transverse abdominis plane, rectus sheath and quadratus lumborum as well as intercostal ,paravertebral blocks are being evaluated and used with success recently. These are particularly useful in postmastectomy neuralgias, chest wall tumors, radiationburns, and extensive abdominal surgeries with residual neuropathic and somatic pain. USG guided brachial plexus blocks and suprascapular nerve block have been for shoulder and arm pain too. USG guided glossopharyngeal, mandibular, trigeminal and occipital nerve blocks are used to alleviate pain due to orofacial cancer. Ultrasound has shown accuracy and efficacy in ilioinguinal, iliohypogastric and genitofemoral blocks for inguinal and testicular pain. Lateral femoral cutaneous nerve injections are more accurate under ultrasound guidance, especially given the anatomic variation the nerve exhibits in cadaver dissections. USG guided stellate ganglion blocks has been used for orofacial pain, CRPS (complex regional pain syndrome) and shown to be effective in preventing soft tissue and vascular injury compared with the blind techniques. USG guided lumbar sympathetic block has been used in cases of rectal tenesmus and CRPS limbs in combination with CT fluoroscopy.

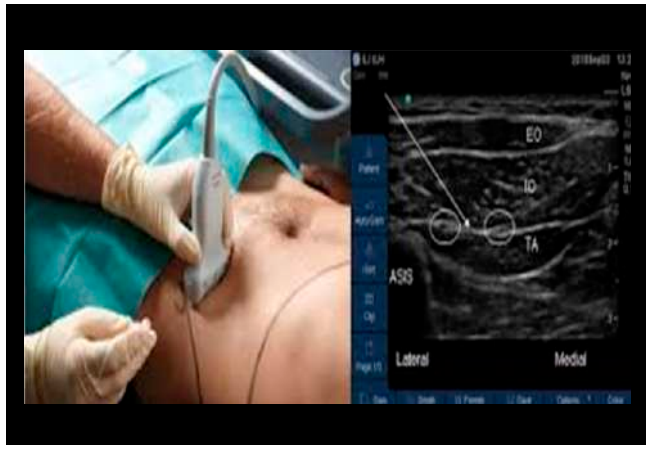

Fig. 2 : Abdominal plane block

USG guided coeliac plexus block is being used in pancreatic cancer where often it causes intractable pain that does not respond to pharmacological treatment. In a meta-analysis of seven randomized, controlled trials, Zhong and colleagues compared medical management to combined medical management with neurolytic coeliac plexus block. CPB was associated with significantly lower pain scores at 4 weeks. In all studies except for one, pain scores were lower at 2, 4, and 8 weeks. The combined group also had significantly lower drug use and incidence of nausea and vomiting. Interestingly, the meta-analysis found that the timing of the block may influence outcomes and patients undergoing the block prior to the development of severe pain had less long-term pain and delayed onset.
USG guided Superior hypogastric plexus blocks (SHPB) has been used to treat visceral pelvic pain coming from cancers of the uterus, cervix, ovaries, prostate, bladder, rectum .With the help of USG, Ganglion of Impar (GI) block is being givento treat perineal pain arising from cancer of the rectum, vulva, and anus, as well as metastases from other sites.

Injections into the knee, shoulder and hip joints are more successful when performed using ultrasound. Myofascial pain suffered by cancer patients are being treated effectively by trigger point injection by USG. Deep targets like facet joints or medial branches, caudal epidural, cervical epidural, sacroiliac joints can be accessed under USG guidance and these are used in patients with back pain of various etiologies including cancer . It may be difficult in degenerative spine and obese patients where a combination with fluoroscopy is recommended.

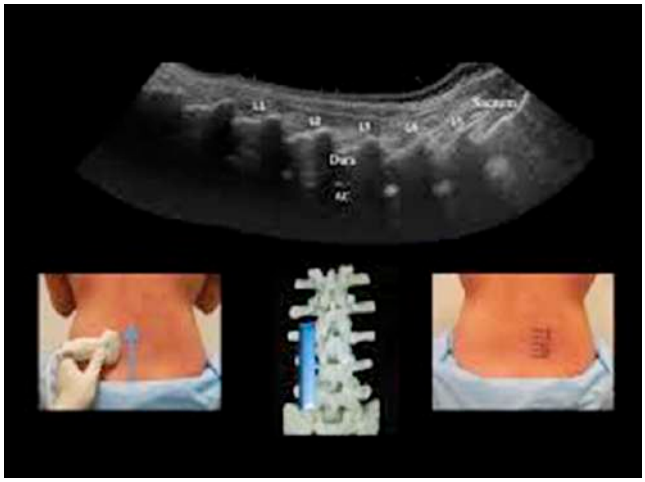

Fig. 3 : USG guided spinal intervention

For advanced interventions like spinal cord stimulator, intrathecal pumps, vertebroplasty, US may fall short in optimal use. New developments are in progress, such as needle navigation systems, optical recognition of different tissues, photonic needles, and ultra-high-definition USG. Given its benefits and limitations, USG is definitely a promising technique and has to be used by correct technique, correct person in correct patients.

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Case Report Guest Article

Synchronous cancers in Stomach and Colon : a case report

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INTRODUCTION:

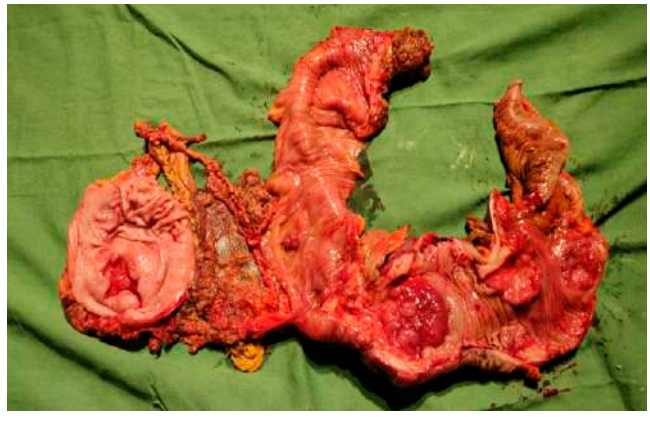
The development of synchronous gastric and colon cancers is a rare clinical entity. Here we report a case of gastric cancer with associated four synchronous lesions in colon.

CASE REPORT:

A 36 year old male presented at State Cancer Institute, GMC with complaints of abdominal pain for 10 months duration. There was no history of haemetemesis, melaena or vomiting. There were no significant examination findings. Upper GI Endoscopy showed a large ulcero-proliferative growth (UPG) extending from gastric body to antrum. Biopsy revealed mucin secreting adenocarcinoma. CEA was 60.2 ng/ml.

CECT abdomen showed mildly thickened wall of pylorus. It also showed heterogeneously enhancing diffuse circumferential wall thickening involving ascending colon, hepatic flexure and proximal transverse colon with peri-colonic fat stranding and prominent lymph nodes in peri-colonic and para-colic region of ascending colon. There was no evidence of metastasis. CECT Thorax was normal. Colonoscopy showed UPG in ascending colon with luminal narrowing. Scope couldn't be negotiated further. Single polyp was found in splenic flexure of colon. Patient was planned for surgery after tumour board approval. In between, patient started having haematochezia and significant pain abdomen. Hb was 6.6gm %. Patient was given 4 Units blood transfusion and planned for surgery. He underwent distal gastrectomy and D2 nodal dissection with extended right hemicolectomy on 9.1.19. Intra-operative findings: UPG found in distal body and pyloric antrum with no peri-gastric extension. A few enlarged nodes were found in peri-gastric area. Three ulcerated lesions were found in right colon: a) One in hepatic flexure b) Two in the Caecum. A solitary villous polyp was found in proximal transverse colon. Distal transverse colon and splenic flexure were normal. Descending colon, rectum and anal canal were normal. Multiple enlarged nodes were found in paracolic and principal node regions of right colon. No peritoneal dissemination was noted. The postoperative period was uneventful and patient was discharged on 7th post-operative day.

Histopathological examination showed Mucinous adenocarcinoma in stomach invading muscular propria with 6/15 nodes positive (pT2N2M0) and multifocal mucin secreting adenocarcinoma in caecum and right colon invading muscular propria and peri-colic soft tissues 3/41 nodes positive (pT3N1bM0). Patient received adjuvant chemotherapy (capecitabine and oxaliplatin doublet) and is now under regular follow-up and disease free for 18 months.



DISCUSSION:

The incidence of gastric cancer with asynchronous second primary cancer varies from 2.0% to 10.9% [1-8]. Although, any defect in DNA repair system might have a role in multiple cancer development, the reason for development of synchronous cancer still remains uncertain [9]. Gastric cancer is the most common extra-colonic cancer associated with hereditary non-polyposis colorectal cancer syndrome (HNPCC) [10]. Synchronous surgery is performed when possible. [3].A detailed pre-operation examination should be done to avoid missing synchronous cancers. Adjuvant treatment should be planned carefully to decrease the risk of relapse.

CONCLUSIONS:

1) Dual primary gastric and colon cancer is an uncommon entity.

2) High index of suspicion is required to rule out synchronous lesions.

3) Combined resection should be done whenever possible.

4) Doing genetic studies remains a challenge in our population due to financial constraints

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Original Article

Breaking Bad News (BBN) to Patients : Concerns of our patients' relatives

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INTRODUCTION:

Letting the patient know about the diagnosis and prognosis is necessary as per medical ethics. The relatives of most of our patients come to know it first and they decide whether they want to disclose it to patients or not. In a qualitative study in our hospital, we tried to know the views, beliefs and concerns of patients' relatives about disclosing the diagnosis to patients.

MATERIAL AND METHODS:

Grounded theory approach to study and understand the social world was used in the study. Information was collected by asking to answer a questionnaire in their comfort language. The broad topics of questionnaires included: how did you come to know about the diagnosis; does your relative patient know about the diagnosis, if yes what was his/her reaction; do you think your relative patient should be told about the diagnosis; what are your concerns about BBN to patient?

RESULTS:

Fifteen eligible and consenting participants of patients' relatives among age group of 18 to 60 years were recruited during their first visit to out-patient clinic. Patients were selected randomly from age group 18 to 60 years having cancer but without having any metabolic diseases. Although 93.3% of patients were eager to know the information, only 33.3% of relatives wanted to disclose all information to patients and 20% wanted to disclose the diagnosis only. Although some of the relatives wanted to disclose the diagnosis, but most of them did not! Most of the relatives were concerned about the psychological breakdown of patients leading to hopelessness and ultimately giving up after the news is heard. Some relatives were not in favour of disclosing the disease status fearing self harm by the patients. Relatives also opined that bad news should be conveyed in a warm and caring tone keeping in mind patient's mental ability to accept.

Relatives gave importance to wishes of the patient to live and think that not telling the diagnosis and disease status works as a tonic for them. If the patient is in pain and with other physical distressing symptoms then their relatives think that disclosing disease status will worsen the situation only. Some relatives think that giving false information about the disease is necessary to help the patient keep mentally strong. Psychological breakdown leading to depression, deny to undergo further treatment, lose hope, giving up, etc. are usually feared by the relatives. To some extent this is true also. It is up to the care giver how they handle the situation.

Apart from the above situations, some of the relatives are optimistic about telling the truth and also thinks that, letting know the disease status to the patient will set him free rather than a false hope of curability. In most of the cases the patient was eager to know about the diagnosis. But they knew very little or were given

very less information at the first by the relatives or by the care giver.

DISCUSSION:

According to medical ethics – Patient autonomy comes first and foremost of patient care. It means every patient has the right to know what is happening in his body and has the right to choose treatment. This principle should be followed with the background of respect for life. At the same time, patients are also not bound legally to accept the recommended treatment. The literature says that we should disclose everything to the patient if he wants to know. But some studies show that amount of information revealed may vary from country to country. A study in Spain and Canadian palliative care setting showed that Canadian patients and relatives preferred to be disclosed the information in full whereas Spanish counterparts 89% patients and relatives did not want full disclosure. Sometimes doctors are also in dilemma to how much information to be revealed. In a study in Portugal 71% of doctors revealed that they disclose the information in full to patients while others never disclose thinking it to be psychologically deleterious.

Moreover, truth telling should be central to communication between patients and their doctors and is related to the socio-cultural aspects of the patient. The relationship between patients and doctors was initially centered by what the doctors judged the best available medical treatment in their patients' interest.
The doctor and patient relationships based on trust. It would be unwise for the doctor to lie to his patients just to make the relatives happy. It would be unethical on doctor's part to give false reassurance. However, it is necessary to check level of awareness about the disease and whether he is ready to hear the news or not. If the patient says that he doesn't want to discuss further - we stop the process and observe. It would be wrong to start a fresh. The patient may be using denial as a 'coping mechanism'. Patient usually uses denial to avoid painful thoughts and feelings which are difficult to deal with. Usually we should not break this denial which is acting as a protection for the patient. This emotion to be respected and therefore the information should not be forced onto the patient until he co-operates with the treatment. However, it needs to be gently broken, if the patient is not co-operating with the treatment and is in distress.

If the patient wants to know more about his disease, it would be unwise not to tell the truth. It would be a breach of patient autonomy and the doctor-patient relationship will be at jeopardy if the patient later found out the truth. At the same time we would have to know the level of understanding of the patient and how much he already knows, what the previous doctor has informed him. It is necessary because some patient may also opt out of BBN after initial dialogue.

Most of the patients usually want to have all the information. A study conducted by Jenkins et al concluded that 87% of patients wanted all information. Our study shows that 93.3% of patients want to know the diagnosis, but only 53.3% have been informed about it. This may be due to doctors did not want to disclose the diagnosis as the patient did not ask specifically or the relatives asked the doctor not to disclose. Eagerness varies from patient to patient, depending on their knowledge and age. Information as of their health condition should be delivered tactfully and honestly step by step to make them comfortable to accept the report without any concern.

CONCLUSION:

BBN to patient and relatives is an art. The doctor or anyone revealing the diagnosis should take certain things in mind - whether the patient wants to know the diagnosis or disease status, how much he knows about it and how much he wants to know. Relatives also want the doctor to reveal the diagnosis in a slow and affectionate way.

Letter to the Editor

Chronic Myeloid Leukemia: a broken enigma

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Textbooks in our MBBS days taught us that Chronic Myeloid Leukemia (CML) is a slowing progressive blood cancer that culminates in as Acute Leukemia after a median interval of 1 year. Death was inevitable and the treatments that were available consist of Busulfan, Hydroxyurea, and Allogeneic Stem cell transplant. When I was an intern in 2009, I recall mugging Imatinib mesylate as the new drug of choice for CML. Little did I know about the transformation that the drug has caused in the field of cancer medicine, in the natural course of CML, and to the physicians treating such diseases.

CML was indeed a deadly disease in the 20th century. During 1990s, a group of clinical scientists led by Dr. Brian Druker of Oregon Health University carried out clinical trials confirming its efficacy in CML patients. The first clinical trial of Gleevec (Novartis) took place in 1998. It received accelerated FDA approval in 2001, only 2.5yrs after the new drug application was submitted. Druker along with Charles Sawyers of MSKCC, New York were recognised for their commendable role in "converting a fatal disease into a manageable chronic condition"

Gleevec was soon introduced into the CML treatment guidelines of all major cancer recommendation bodies. The median survival changed from 1 year to more than 10 years. Since the drug was very costly, Novartis as a part of their CSR introduced GiPaP program in India whereby patients got free treatment and subsidised molecular diagnostics and monitoring tests. It helped in two ways: created a good patient database with a robust clinical data, and improved diagnostic rates and drug acceptance. After 2011, generic Imatinib began to be manufactured and the cost of the drug depreciated significantly. In India, around 30 generic formulations of Imatinib mesylate are available, out of which 7-8 leading companies manufacture these drugs of same efficacy as that of the innovator. Hence more patients took to treatment and get promising results. However the concept of continuous treatment looked discouraging. In around 2014, the first trials of Imatinib withdrawal took place. Since now, we have started understanding the kinetics of BCR-Abl response to Imatinib, depth of response, relapse rates following withdrawal, and remission after re-introduction of the drug; hence the choice of patients and duration of treatment for subsequent drug withdrawal is possible.

In a vast country like India, scientific developments in laboratories and clinical trials take time to benefit the masses. It is important that people are made aware about the symptoms of the disease, understand the need of early diagnosis, long and often continuous treatment and frequent monitoring. It is on this ground that organisations around the world have initiated events and projects on "CML Awareness Day" on 22nd September to raise awareness of the needs of the patients living with CML. 9/22 represents the genetic change of chromosome 9 and 22 that is the hallmark of CML. September 22 (9/22) has been chosen as the date for global and local CML awareness activities – this adds symbolic significance to the campaigns.

Letter to the Editor COVID 19 Special

Radiotherapy as a Cure for COVID-19 Pneumonia: Is this a possibility?

Partha P Medhi [1], Shashank Bansal [2], Faridha J Momin [3], Ghritashee Bora [4]

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The present article is an attempt to kindle scientific interest towards an unconventional treatment modality for the current overwhelming health problem of the world which is COVID19.

Radiation induces cell death by destruction of DNA either directly or indirectly by production of free radicals (ions) inside the body. X-rays have been used as curative treatment of cancer since Emil Herman Grubbe treated the first patient in 1896. Benign intracranial tumors (e.g. Schwannoma, Craniopharyngioma etc), Glomus tumors, Juvenile Nasopharyngeal Angiofibroma and many other benign tumors are also treated by radiotherapy. Interestingly, there are reports of use of low dose radiation treatment in many acute inflammatory processes and infectious diseases such as gas gangrene, carbuncles, sinusitis, arthritis and mastitis in the pre-antibiotic era with significant cure rates. Even today, low dose radiation is prescribed for benign painful chronic inflammatory degenerative disorders such as periarthritis in Germany. Experiments over past three decades have revealed a multilevel interrelationship between low-dose ionizing radiation and inflammatory cascades which include: modulation of the inflammatory properties of leukocytes, macrophages, fibroblasts, and endothelial cells, as well as of the secretion of cytokines/chemokines and growth factors [1].

In the early 20th century, pneumonia was one of the dreaded diseases with mortality upto 40% even in treated cases. Before the advent of widespread use of antibiotics, Serum therapy was the only effective treatment for pneumonia, but it was expensive and carried a high risk of anaphylactic reactions. This led to the exploration of radiotherapy as an alternative curative option for pneumonia in the 1930s. The hypothesis was that X-ray treatment would increase the metabolic digestion of the exudative material, leading to a resolution of the pneumonia. Calabrese and Dhawan [2] have compiled a review of all the reported studies on this topic from the United States. In the time period 1905-1946, fifteen studies showed that over 800 patients of bacterial, viral and atypical pneumonia were effectively treated by low dose kilovoltage X-rays. All these studies reported significant improvement in clinical symptoms within hours of initiation of therapy and decrease in mortality incidence to less than 10% in their patients which was comparable to serum therapy and sulphonamide treatment during the same time period. Irrespective of the age, health status, etiology and other diverse clinical settings, these researchers consistently reported the benefit of a single low dose X-ray exposure to effectively reverse the course of pneumonia. Benefits were uniformly better when radiotherapy was instituted in the initial stages of the disease. The target

volume comprised of bilateral whole lungs and doses in the range of 20 to few hundred Roentgen were used, which given the attenuation through chest wall would likely have resulted in mean lung doses of less than 100 cGy range. The treatment became so popular that at one point of time some hospitals in US routinely treated pneumonia patients with therapeutic X-rays before admitting them for further treatment. However, with the emergence of the wonder drug Penicillin, the interest in this form of treatment for pneumonia gradually faded and there has not been a single published report in this aspect for over 70 years now.

The global pandemic of novel coronavirus disease has once again challenged medical knowledge and utility of existing therapies in preventing death from this form of community acquired pneumonia. In the absence of definitive treatment against SARS-CoV-2, clinicians have now turned to therapies with anecdotal evidence like the widespread use of hydroxychloroquine. This scenario has once again aroused the interest of some radiation oncologists of the present era to revisit the century old hypothesis of low dose X-ray therapy in pneumonia as a potential treatment of COVID-19. In an article published in Radiotherapy and Oncology journal in April, 2020, Kirkby and McKenzie [3] have called for a clinical trial to investigate the efficacy of whole lung low dose radiotherapy as potential treatment of COVID-19 pneumonia. They opine that a single fraction 30 to 100 cGy X-ray treatment could be easily delivered on a conventional megavoltage radiation therapy unit and at such low doses, common radiotherapy toxicities would not be of much concern. They believe it would present a very low risk to COVID-19 pneumonia patients, have the potential to reduce mortality and mitigate COVID-19 related burden on healthcare systems.

However, the astounding results of the studies of early twentieth century must be taken with a pinch of salt before we jump to conclusions. All the 15 reported studies by Calabrese [2] are case series of patients, without randomization of subjects and blinding of investigators and with no definite control groups for comparison, making their findings largely redundant in modern day practices of evidence based medicine. Only 2 out of the 15 studies dealt with viral pneumonia and SARS-CoV-2 being a positive-sense single-stranded RNA virus which still remains a mystery, whether the radiobiology of DNA damage applies for it, is also debatable. Add to that the complicated nature of planning and delivering bilateral whole lung radiation which comes with an inherent risk of cardiac toxicities and secondary malignancies. In today's era of precision and conformal radiotherapy, we are afraid that such an idea may find no supporters. Lastly, for a country like India where radiotherapy resources are already overburdened with existing cancer patients, incorporating COVID-19 patients into radiotherapy treatment facilities will be a herculean challenge.

Although the idea seems far-fetched, we believe it is not entirely devoid of merit. The COVID-19 pandemic worldwide has cost millions of lives, totally destroying the healthcare facilities of most developed of nations. If ever there was a time to explore radiation as treatment for pneumonia on a clinically useful setting, we believe it is now.

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Letter to the Editor COVID 19 Special

Will consumption of Vitamin D rich food help us in our battle against Covid-19 or it is just another dubious claim?

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Without antibody-mediated adaptive immunity, innate immunity may still be powerful enough tool to eliminate SARS-CoV-2 [1]. Vitamin D has been conclusively proven to strengthen innate immunity [2-4] for previous respiratory viruses [5]. Adequate levels of Vitamin D also help in moderating (to more appropriate levels) any excessive response of the adaptive immunity system, to prevent cytokine storm which is the main reason for Acute Respiratory Distress Syndrome followed by death in Covid-19. There is also strong evidence that Covid-19 infections and deaths have been higher in those with Vitamin D deficiency [6], such as those cooped up in Care Homes for elderly or in dense cities where they did not get sufficient exposure to sunlight. Italy and Spain have both experienced high COVID-19 mortality rates, and both countries population have lower average vitamin D levels than most northern European countries [6].

However, with all good things there is also some bad elements. Excessive Vitamin D can produce mild to severe toxicity in humans. The main consequence of vitamin D toxicity is a buildup of calcium in the blood (hypercalcemia), which can cause nausea and vomiting, weakness, and frequent urination. Vitamin D toxicity might progress to bone pain and kidney problems, such as the formation of calcium stones. For adequate quantity of Vitamin D in our food should include fish, mushroom, fortified milk and dairy products, fortified cereals, meat chops, soya bean, and eggs, which when coupled with good exposure to sunlight should help us in our individual battle against Covid-19. One should avoid prescription pills of Vitamin D to avoid its toxicity.

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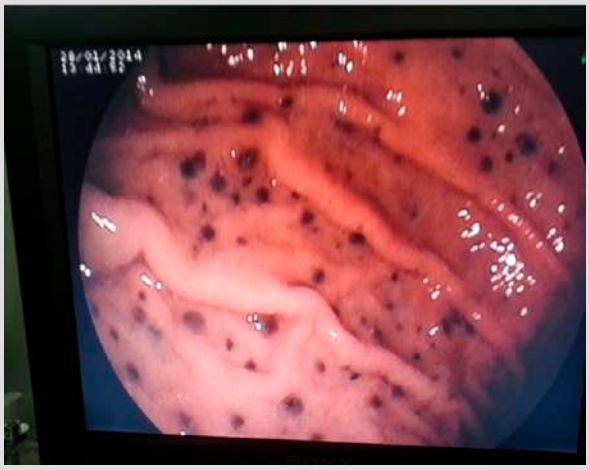
Images of the Issue



I have this archived endoscopic image from my days of Senior Residency at BBCI in 2013-14.

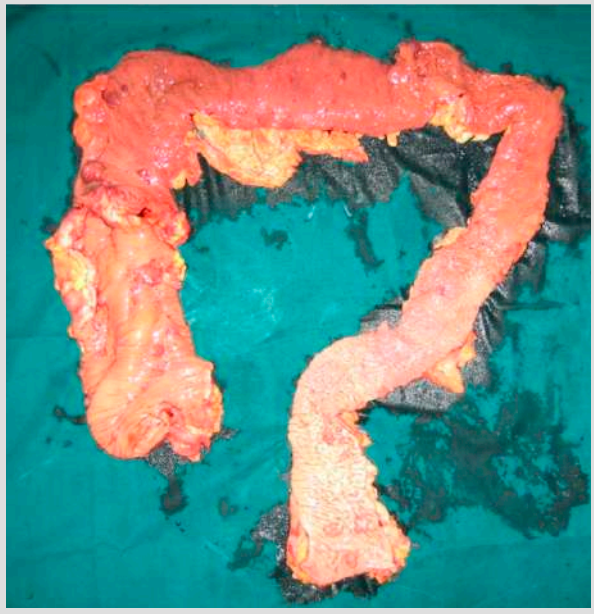
What could be the diagnosis?

a] Multiple malignant melanoma of stomach

b] Metastatic deposits in the stomach from a primary cutaneous malignant melanoma

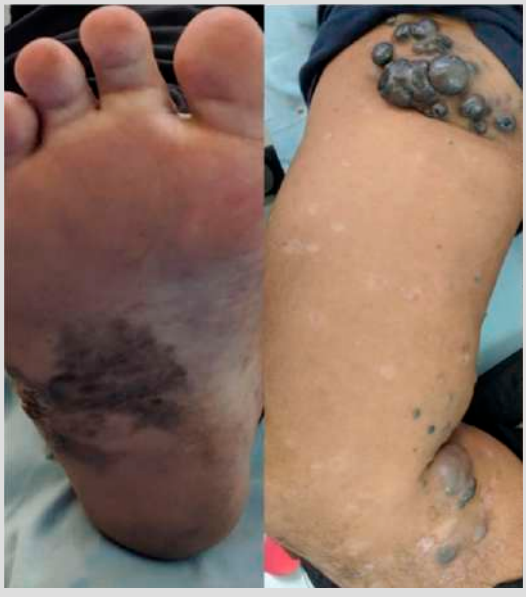
c] Pseudomelanosis

Contributor : Gaurav Das



60 year old lady presented with a history of passage of blood in stools. Colonoscopy showed presence of multiple polyps. The photo shows the specimen of sub-total proctocolectomy. The presence of polyps less than 100 in number suggest attenuated Familial Adenomatous Polyposis (aFAP).

Contributor : Joydeep Purkayastha



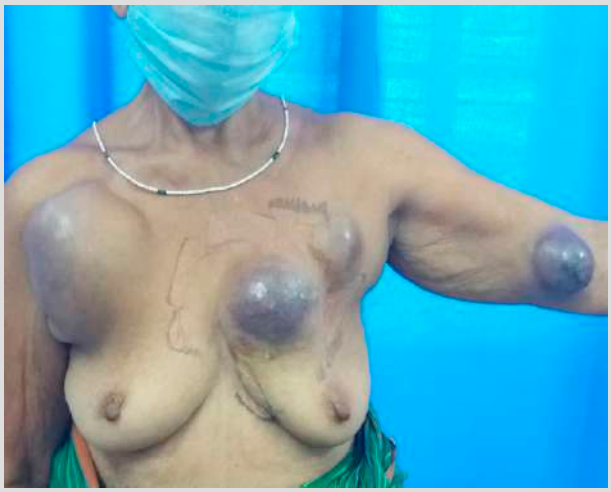
40 year old gentleman with a malignant melanoma of the right foot plantar aspect along with:

a] Skin and subcutaneous metastases including:
   1. Satellite lesions (those that occur within 2 cm of the primary),
   2. In-transit metastases (those that occur beyond 2 cm of the primary, within the drainage area of the primary drainage lymphatic basin)

b] Lymph nodal metastases in the popliteal and inguinal basins .

Contributor : Revanth K. Kodali

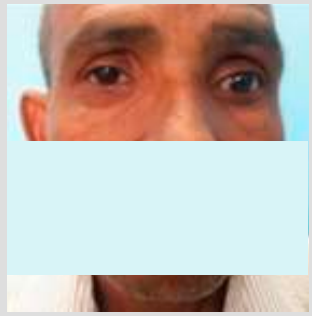
Images of the Issue



Widespread cutaneous metastases in a treated case of malignant melanoma of the left foot, after a DFI of 1 year.

Contributor : Gaurav Das

Pre NACT

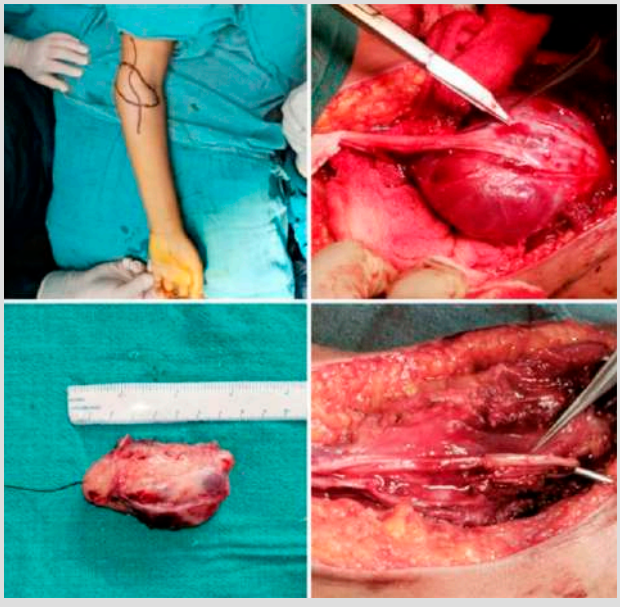


Post NACT

Post Op (Post NACT)

A patient with Esthesioneuroblastoma, showing excellent response to neo-adjuvant chemotherapy. Patient had a successful resection.

Contributor : Kaberi Kakati



Schwannoma of Median Nerve. Intra-operative pictures. Patient had excellent post-operative function.

Contributor : Sumanjit Boro

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