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Genomic Testing Simplified

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Summary

One or more genetic abnormalities, either acquired or inborn, combine to cause cancers. Almost all cancers have a distinct set of molecular alterations. Technologies have been created to investigate tumors and identify genomic traits that will eventually affect therapeutic treatment.In fact, the discovery of important genetic abnormalities (molecular drivers) may eventually result in the creation of highly focused treatments that significantly improve patient outcomes. Cancers will soon be routinely characterized due to the increasing availability of newer, more potent, and more affordable technologies like next-generation sequencing, multiplex mutational screening, array-based methods that can determine gene copy numbers, methylation, expression, and others, as well as more advanced interpretation of high-throughput molecular data using bioinformatics tools like signatures and predictive algorithms. Over the past ten years, next-generation sequencing (NGS) has been used more frequently in cancer genomics research due to advancements in modern sequencing technologies. In order to improve individualized cancer treatment, NGS has recently been used in clinical oncology. The molecular justification for suitable targeted therapy is provided by NGS, which is also used to identify novel and uncommon cancer mutations and identify carriers of familial cancer mutations. Clinician has to choose wisely as the testing is available to more number of patients.

Reading, interpretation, and therapeutic application of test results is complex and needs expertise.

Introduction

Cancer treatment journey of a sufferer trails through twists and turns as it goes by systemic anti-cancer treatment by medical oncologist. This happens mainly because of rapid advancement in the field of diagnostics and treatment. The ancient era of broad spectrum chemotherapy is replaced by individualised treatment driven by the tumor's genetic makeup.

With the launch of genetic testing under AB PM JAY, our desire to test for genomics is fulfilled. But, we are yet to understand worth of that. We have started doing NGS on FFPE blocks for selected malignancies.

What and why genomic testing? Is it useful in our patient population?

Molecular methods are classified into two types: chromosomal structural alterations anomalies and other alterations

Cytogenetic methods detect abnormalities in chromosome structure:

I. Karyotyping

- It is a basic test to know about congenital anomalies.
- Used to identify gain and loss of chromosomes in several malignancies
- Example
- In colorectal cancers, gain of chromosomes 7, 8q, 13, 20 and loss of 8p, 17p, 18 is seen
- In breast cancers, gain of chromosomes1q, 8q, 17q, 20 and loss of 8p, 16q, 17p is seen

II. Fluorescence in situ hybridization (FISH)

- Mainly evaluates patients with known /pathogenic translocations and fusions
- Example is commonly found translocation t (9;22) or BCR-ABL fusion gene for patients with Chronic Myeloid Leukaemia (CML)

III. Chromosomal microarrays analysis (CMA)

- Can detect much smaller chromosomal abnormalities than karyotyping and FISH
- Provides First line analysis for developmental delay, intellectual disability, congenital defects.
- Limitation: will not pick up balanced translocations
- Examples - losses of 1p in mantle cell lymphomas and diffused large B cell lymphomas, Gain of 1q or loss of chromosome 13 in multiple myeloma.

IV. Quantitative fluorescence PCR (QF-PCR)

- It Is useful to find the pathogenic variant which is already known like it is present in parents/siblings or children
- Provides Information on quantitative data and not just qualitative aspect
- It does not report structural alteration in chromosomes which is a limiting aspect of the test

Molecular methods

Molecular methods detect abnormalities in DNA sequence.

Molecular testing is basically classified into 3 categories

I. Polymerase chain reaction (PCR)
II. Ligation mediated PCR e.g. MLPA
III. Next Generation Sequencing (NGS)

I. Polymerase chain reaction (PCR)

- Here amplification or multiple copies of known sequence/part of DNA is made.
- That sequence DNA is denatured to form single strands.
- Forward (PF) and reverse (PR) primers anneal.
- Further processing step results into amplified/copies of the original target of interest.
- Examples - Microsatellite instability testing in HNPCC-related genes; BRCA1/2 mutations testing by PCR
- Examples of PCR sequence based tests are: A) Targeted and single gene testing and B) Sequence Chromatogram

II. Multiplex Ligation-dependent probe Amplification (MLPA)

- Can detect small rearrangements
- Limitation - Cannot detect copy neutral loss of heterozygosity
- Example - Used for detecting exon deletions in BRCA1, MSH2, MLH1 in hereditary breast and colon cancer

III. Gene Sequencing Technologies

Types are

a) Sanger sequencing and b) Next-generation sequencing (NGS)

IV. Sanger sequencing

- Gold standard along with MLPA
- High accuracy but labour intensive
- Detects only small DNA changes (point mutations and/or indels)
- Limitations - Longer turnaround time and Limited throughput
- Examples –
- BRAF exon 15 containing the p.V600 hotspot mutation in varieties of CNS tumours like gliomas and glioblastoma multiformes
- TERT promoter region containing the c.-124C and c.-146C hotspots that are frequently mutated in IDH-wildtype glioblastoma in adults, IDH-mutant and 1p/19-codeleted oligodendroglioma, anaplastic (malignant) meningioma

V. Next-Generation Sequencing (NGS)

- Vast improvement with accuracy
- Shorter turnaround time
- High throughput
- Requires complex bioinformatics algorithms
- Has potential to detect LGRs
- Examples –
- NGS can help identify ROS-1 mutations in adenocarcinoma of lung which in turn can be treated by giving drugs like crizotinib.
- AKT3 amplificatons can also be detected by NGS in cases of lung cancer wherein drugs like everolimus can help

How to read Next Generation Sequencing (NGS)

NGS can accurately detect all the 4 types of genetic alterations which drive oncogenesis, namely:

1- Base substitution
2- Insertions and deletions
3- Copy Number Alterations
4- Re-arrangements (gene fusions)

NGS testing broads can be broadly divided into two types:

1- Hot spot panels
2- Comprehensive Genomic Profiling (CGP)

Hot spot approach- sequences only selected regions of a gene CGP- sequences coding regions of selected genes in their entirety.

Components of a CGP report

1- Patient Demographics: patient's name, DOB, Sex, ID number
2- Date of specimen collected, date of receiving, date of reporting results
3- Ordering physician's name
4- Specimen details – type (FFPE, Liquid biopsy), tissue information with diagnosis and tumor cell content.
5- Results:biomarker findings (MSI and TMB) and genomic findings (results along with variant allele frequency (VAF))
6- Range of the genes tested and coverage of testing
7- Sequencing depth
8- Methods and the steps of process involves the presence of target and its details, specimen enrichment method, limitation of detection of particular genetic alteration and other pitfalls of testing
9- Analytic interpretative comment
10- Clinical interpretative comment including approved therapies, level of evidence and clinical trial options based on genomic finding.
11- Pathologist / designee signature.

The classifications and scale used for interpretation of genetic variant detected:
ESCAT grading system for cancer treatment decision-making:

	Readiness for use in clinical practice	**Current examples of genomic alterations**
Tier (-A, -B, -C)	Targets ready for implementation in routine clinical decisions	HER2 in breast cancer BRCA1/2 in ovarian and breast cancer EGFR, ROS/ALK in NSCLC TRK, PD1 in multiple cancers BRAF in metastatic melanoma
Tier (-A, -B)	Investigational targets likely to define patients who benefit from a targeted drug, but additional data needed	PTEN pathway (PIK3CA, AKT1)
Tier (-A, -B)	Clinical benefit previously demonstrated in other tumour type or of similar molecular targets	BRAF in non-melanoma cancers PALB2 and other non-BRCA DNA repair mutations
Tier (A, B)	Preclinical evidence of actionability	Hypothetical targets for future clinical testing
Tier	Evidence supporting co-targeting approaches	P1K3CA in ER+, HER- breast cancer
Tier	Lack of evidence for actionability	

NSCLC = non-small cell lung cancer

ACMP/AMP tier system (American College of Medical Genetics and Genomics / Association for Molecular Pathology):
5- Pathogenic
4- Likely Pathogenic
3- Variant of Uncertain Significance (VUS)
2- Likely Benign
1- Benign

AMP 4 tiered system:
Tier 1- Variants with strong clinical significance
Tier 2- Variants with potential clinical significance
Tier 3- Variants of unknown clinical significance
Tier 4- Variants deemed benign or likely benign

Benign and likely benign variants:
1- population frequency > disease prevalence
2- No impact on amino acid sequence
3- Changes amino acid at poorly conserved position
4- Inheritance not supportive of a disease causing role

VUS: Not enough information available

Likely Pathogenic and pathogenic:
1- Rare
2- Severe protein impact
3- Reported in other individuals with consistent phenotype
4- Segregates with disease in families
5- De novo occurrence
6- Functional studies supportive of an impact

Basics of the NGS testing which needs to be checked before attempting to interpret genomic alterations

1- Sample: tumor cell content of the samples – the results may be falsely interpreted as range of detection for variety of genetic alteration varies with various assays. So, it is true that low tumor content results in false negativity for the genetic alteration in concern.
2- Assay Validation: before interpretation of particular genetic assay, assess for accurateness, preciseness, biological reference range and any restrictions of reportingetc One should also look how sensitive and specific is the analysis.Clinician ordering the test should know the validation of the requested array is done by the performing laboratory or not. The laboratory should also be doing regular and mandatory quality check and Q/A programmes.
3- Sequencing Depth versus Sequencing Coverage: Read depth indicates how many reads detected a specific nucleotide. Low depth means poor representation. Coverage is the percentage of bases covered by sequencing reads eg. 95% coverage means that 95% of the bases in sample have been sequenced (at depth 'n'). Good coverage is required for accurate variant calling.

Optimum depth is not defined but on an average it is taken as > x30.

NGS sequencing data is only reliable when supported by a sufficient number of reads.

As amount of DNA being sequenced increases, coverage will be sacrificed (decreased) .

Molecular insights of NGS/CGP reports
An assessment on following 4 levels is desired:
1- gene
2- specific variant

Databases with genomic data and where to check for relevance of alterations	
Database	**Comments**
Cancer Genome Atlas (TCGA)	Large databases including cancer-associated genomic alterations of >20000 cancer patients
International Cancer Genome Consortium (ICGC)	Global initiative to build a large database of genomic alterations in the most common tumor types
OncoKB	Memorial Sloan Kettering Cancer Centre precision oncology database including link to FDA levels of evidence
MyCancerGenome	Large database including cancer-associated genomic alterations of almost 100000 tumor samples
CIViC	Clinical interpretation of variants in cancer, open access open source, community driven
COSMIC	Large catalogue of somatic cancer mutations including data from >37000 genomes
ClinVar	Freely accessible, public archive of reports of the relationships among human variations and phenotypes, with supporting evidence
Online Mendelian Inheritance in Man (OMIM)	Comprehensive, authoritative compendium of human genes and genetic phenotypes
VarSome	Variant knowledge community, data aggregator and variant data discovery tool
Breast CncerInformatiomn Core (BIC) Database	Large BRCA1 and BRCA2 gene mutation database
ARUP BRCA1 AND BRCA2 mutation databases	Provides information on BRCA1 and BRCA2 gene mutations and their impact on risk of developing breast cancer, ovarian cancer and certain other cancers. Two types of databases are provided. One is a list of mutations curated from critical review of literature and family studies. The other provides in silico prediction of risk to help understand variants of unknown significance

3- sensitivity or resistance to a drug or group of drugs
4- tumor specific context

Detailed description of each genetic variant identified in tumor: type of alteration, exon position, transcript ID and Variant Allele Frequency (VAF)%.

VAF%:

- Gives the % of DNA that has the variant in the tissue. It identifies driver mutations and gives insights into various clones in the tumor.
- A report containing various mutations and amplifications with different VAF% represents multi-clonality of tumor.
- VAF% closer to 50% points towards the variant to be potential germline variant.
- VAF% also gives an idea regarding driver mutation (more VAF- likely to be the driver).
- Cut-off value of VAF% - when is it too high to be pathogenic? It depends on a number of factors : how common is the disease (prevalence), inheritance pattern, penetrance, how many genes or variants cause the disease.

Report also provides us description of studies and clinical trials giving insights to targeted therapy for the specific variant.

It also provides details on prognosis and frequency of the variant in cancer.

Mutations that are not targetable are also important as they can be helpful in finding which therapy might not be useful. (example- CTNNB1 (B-catenin) gene mutation – resistance to immune checkpoint inhibitor).

Important area to consider-

1- prioritization of targeted treatment options in case more than one actionable genomic alteration exists.
2- identification of the most promising targeted anticancer treatment when considering standard of care systemic treatment options as an alternative

Conclusion

Though genetic testing is now available to the patients, physician should consider it for the patients who are eligible for targeted treatment or when useful for diagnosis.

The test reports open up the Pandora's box with plethora of information and interpreting and applying in the right way is very important.

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Dr. Shilin N. Shukla Medical Oncology Oration Award - 2023

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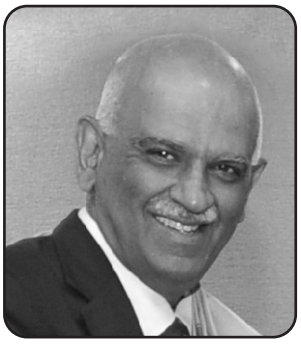
"GCRI - Transforming Students into Professionals"

GCRI is a Regional Cancer Centre and Speciality Medical Education Centre running DM, MCh, MD, PhD, MSc, Diploma courses admitting and training so many students every year. How GCRI is different from other such Institutes in the country? Why GCRIans are unique and have excelled in the country and internationally? GCRI is not only an Institute; it is a Family. There is an induction of a student in the GCRI Family with welcome meet, homing and care by the faculty, seniors and staff helping to overcome initial language barriers and homesickness. Well planned teaching programs, duties with opportunities to get training and experience of all aspects of oncology and faculties. Treating the patients and their caregivers with dignity, helping them procure right treatment from different resources was an art to learn. Morning presentations of various topics in the department in presence of colleagues, teachers and invited experts gave them confidence to analyze, organize, present and debate. They were always encouraged and supported to participate, present, publish at institutional, national, international level. Teachers utilized their contacts and institutional relations to arrange visiting programs. Research projects, clinical trials gave them extra skills in documentations and human relationships. Ongoing public awareness programs and cancer camps were the great experiences for them. Mock remedial examinations removed fears and weak points improving preparations for their final exams. Teachers were guardians taking care of their aspirations, needs, entertainment, celebrations of achievements and life events. GCRIans wherever they are, remain in close contact with each other as a proud GCRI family! We feel proud and satisfied when we see their presence at prestigious conferences and publications as experts and subject authorities.

It is an honour for me to be awarded with Dr. Shilin N Shukla, Medical Oncology Oration. I dedicate my talk to my beloved teachers - Padmashri Dr. Pankaj M. Shah, Dr. Kirti M. Patel and Late Dr. Shilin N. Shukla. During my journey at GCRI from 1980 to 1982 as a MD Student and 1983 to 2013 as faculty, I received training, love, bonding, motivation, guidance, assignments, support and faith from all of them.

गुरुर्ब्रह्मा गुरुर्विष्णुः गुरुर्देवो महेश्वरः /
गुरुः साक्षात् परब्रह्म तस्मै श्री गुरवे नमः //

Dr. T. B. Patel Oration Award - 2023



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Online Teaching Program for Post Graduates of Pathology

The online teaching program for post graduates of pathology (OTPPGP), a free curriculum based program was initiated at our centre on July 7, 2020. It went on for almost 20 months and ended on March 28, 2022. It included 161 talks and 82 slide seminars and a few workshops and debates. Three classes were arranged every week, Monday slide seminar and Tuesday/Thursday talks (all at 7pm IST). It is followed by OTPPGP2 which started on April 5, 2022 and completed on October 10, 2023. OTPPGP3 plan is ready and starts from October 17, 2023. OTPPGP2 and OTPPGP3 have two classes per week (Tuesday talk and a Thursday slide seminar at 7PM IST).

Curriculum include topics from biology, general and systemic pathology, clinical pathology, blood bank, haematology, cytopathology, various techniques from staining to routine tests, to advanced techniques like IHC, flow cytometry, cytogenetics and molecular diagnostics. Most of the talks give practical teaching to students, important in understanding of the subject and in day to day practice. We have been lucky to have best teachers in this program. Chairperson is selected from a clinical field. These theme based slide seminars have been extremely popular among students as well as teachers, where we select five to seven post graduate students/residents from different parts of country and outside. These students discuss cases live with the teacher/s, while remaining majority of students are attendees. The topic/theme is informed at least a month in advance, and slides (digitized or a ppt) are shared on the telegram app group (OTPPGP) two weeks in advance. Students are selected primarily based on recommendations by their teachers, Head of the Departments and few are volunteers. The replay link for all talks is kept till Sunday evening for those who missed the live session for some reason. The program has been very popular among Indians as well as other Asian and African countries. This OTPPGP is just a small supplement to the regular teaching within the department of Pathology.

Students and other pathologists can download the telegram app and join the OTPPGP group using the link https://t.me/+T-K7qS4eOAD6mAoQ. This way they will get all links and notifications. We have also created WhatsApp group with various Medical colleges across India, Asia and Africa. It helps us involve students from all across the Asia and Africa.

Clinicopathological Profile of Mediastinal Masses: Data from a Tertiary Cancer Centre in Western India

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Summary

The mediastinum is located in the middle of the thoracic cavity and it is home for many vital structures. Mediastinal masses are very rare and require a combined approach for diagnosis and management. In the present study, we aimed to evaluate the clinicopathological characteristics of mediastinal masses along with the utility of immunohistochemistry in diagnosis. This was a retrospective study performed over a period of 6 years (2016-2021). The data of mediastinal masses were collected from the hospital database. A total of 165 cases were enrolled in the study. The majority of cases were located in the prevascular mediastinum (82.2%). The mean age was 37.68 (±19.54) years with male preponderance (68.5%). The most common histology was lymphoma (30.3%) followed by metastatic (22.4%) and thymic (19.4%) lesions. T-Lymphoblastic lymphoma was most common lymphoid lesion while thymoma type B2 was most common thymic lesion encountered. The mediastinum is a pandora's box which contains many vital structures. Detailed Clinicoradiological evaluation along with histomorphology and immunohistochemistry is pivotal for the diagnosis and management of mediastinal masses.

Keywords: Mediastinal mass, Mediastinal lymphoma, Thymoma

Introduction

Primary mediastinal tumors are uncommon and account for only 3% of tumors of the thorax.[1,2] The mediastinum is the visceral compartment located in the middle of the thoracic cavity. It accommodates many vital structures except the lung.[1-3] The mediastinum is divided into three compartments by ITMIG[4] classification, prevascular (anterior), visceral (middle) and paravertebral (posterior) compartments. The majority of tumor involves prevascular mediastinum and the larger part arise from the thymus. Visceral mediastinal lesions include congenital cyst, (pericardial and bronchogenic cyst) while neurogenic tumors form majority of paravertebral mediastinal masses.[1,5,6] Combined approach of radiology, pathological and clinical information is necessary to narrow down the various differentials and for further management.[7,8] Existing literature shows different data regarding the incidence of various lesions arising from the mediastinum. Therefore, the present study aimed to evaluate the clinicopathological characteristics of mediastinal masses in our institution along with the usefulness of various immunohistochemical markers to reach the definite diagnosis.

Material and methods

The present study was retrospective and descriptive, conducted in the department of Oncopathology at The Gujarat Cancer & Research Institute in Western India from the year 2016 to 2021. A total of 165 cases primarily located in the mediastinum were included in the study. Tumors arising from the pleura, pericardium and chest wall structure were excluded. All the relevant clinicopathological parameters were collected from the database. All the specimens were fixed using 10% formalin and then embedded in paraffin. H and E staining and immunohistochemical (IHC) staining were done. Various antibody panels according to clinical and pathological differentials were used. All the obtained data was arranged in a tabulated form and analysed using SPSS software.

Results

A total of 165 cases were included in the study. Detailed clinicopathological characteristics are discussed in Table 1. The mean age was 37.68 (±19.54) years with a range of 1-78 years. Male preponderance with M: F ratio 2.2: 1. Lymphoma was the most common lesion followed by metastatic and thymic lesions. Out of 165 cases, 49 were resection specimen. Of these 49 cases, preresection biopsy was done in 30 cases. There is no major discordance occur between biopsy and resection specimen as prior immunohistochemistry confirmation was done in all difficult cases.

Lymphoid lesion

Of a total of 50 cases, 48 were located in prevascular compartment. The mean age was 23.28 (±13.72) years with a range of 2 to 62 years. The large population was under 20 years of age (65.31%). Slight male preponderance with M:F ratio 1.4:3.

Table 1: Clinicopathological characteristics of mediastinal tumors

Parameter	Number (n=165)	Percentage (%)
Age (Mean±SD)	**37.68 ± 19.54**	**-**
Sex		
Female	52	31.50
Male	113	68.50
Location (n=165)		
Prevascular	136	5.00
Visceral	24	82.20
Paravertebral	3.1	14.70
Histodiagnosis (n=165)		
GCT	17	10.30
Lymphoid lesion	50	30.30
Neurogenic tumors	13	7.88
Mesenchymal lesion	8 37	4.84 22.40
Metastatic lesion	32	19.40
Thymic lesion	8	4.84
GCT (n=17)		
Mature teratoma	6	35.29
Seminoma	4	23.53
Choriocarcinoma	4	23.53
Mixed GCT	3	17.65
Lymphoid lesion (n=50)		
CHL	8	16
T-LBL	27	54
Peripheral T- cell lymphoma	1	2
DLBCL	8	16
PMBCL	3	6
SLL	2	4
BCL-Unclassified	1	2
Thymic lesion (n=32)		
Thymoma Type A	2	6.25
Thymoma Type B1	5	15.63
Thymoma Type B2	8	25.00
Thymoma Type B3	2	6.25
Thymoma Type AB	7	21.89
Thymoma mixed type	6 1	18.74 3.12
Thymic carcinoma Micronodular	1	3.12

(GCT- germ cell tumor, CHL- classic Hodgkin's lymphoma, T-LBL- T-lymphoblastic lymphoma, DLBCL-diffuse large B cell lymphoma, PMBCL- Primary mediastinal B cell lymphoma, SLL- small cell lymphocytic lymphoma, BCL- B cell lymphoma)

Histomorphologically, 16% of cases were of CHL and 84% were of Non-Hodgkin's Lymphoma (NHL).

Thymic lesion

Thirty-two cases were of thymic origin and all were located in the prevascular compartment. The mean age was 53.5± (14.49) years with a range of 24 to 79 years. It shows male preponderance with M: F ratio 2.2:1. Maximum population (78.13%) was >40 years of age. Masaoka- Kaga staging was used. Total 40.63% cases were in stage I followed by stage IIa (37.5%). Stage IIb, IVa and IVb had two cases each while stage III had a single case.

Germ cell tumor

A total of 17 cases were of GCT, all were male and located in prevascular mediastinum. The mean age was 26 (±14.97) years with range of 1 to 65 years. A total of 52.94% of cases were between 20-30 years of age group. Mixed GCT includes immature teratoma with yolk sac tumor and seminoma with teratoma two cases each.

Neurogenic tumor

Out of 13, 7 were male and 6 females. All were located in paravertebral mediastinum. The majority cases (53.85%) were below 35 years of age. Out of 5 Ganglioneuroblastoma/neuroblastoma (GNB/NB) cases, 4 were < 20 years of age. Histomorpholigically, GNB/NB (5/13) was most common followed by malignant peripheral nerve sheath tumor (MPNST) (3/13) cases. Neurofibroma and schwannoma had 2 cases each and one case had ganglioneuroma.

Mesenchymal lesions

Of the total 8 cases, 6 were male and 2 females. Total 62.5% of cases were more than 30 years of age. Most cases (87.5%) were located in paravertebral locations while 12.5% were in prevascular compartment. Histomorphological monophasic synovial sarcoma (SS) (3/8) and Ewing's sarcoma/PNET (3/8) were the most common followed by epithelioid sarcoma (1/8) and Solitary fibrous tumor (SFT) (1/8).

Metastatic lesion

Metastatic tumor was the second most (22.42%) frequently seen lesion in mediastinum. It affects the most commonly prevascular compartment (91.89%) followed by visceral (5.41%) and paravertebral (2.70%). The mean age was 54.46 (±55) years with range of 17-75 years, of these, 91.89% of cases had ≥40 years of age. Adenocarcinoma (19/37) was the most common morphology followed by small cell carcinoma (SMCC) (12/37). Other include two cases of squamous cell carcinoma (SCC) and single case of choriocarcinoma, non-small cell lung carcinoma, NOS and poorly differentiated tumor. Lung (26/37) was the most common site of origin followed by breast (4/37). Another site includes colon, esophagous, gastrointestinal tract, ovary, pancreas, prostate, and testis. IHC panel used were AE1/AE3, CK7, CK20, p63 (SCC), Napsin A and TTF1 (lung), PAX8 and WT1 (Ovary), CDX2 (colon), GATA3 (Breast), PSA (prostate), B-hCG (choriocarcinoma).

Table 2: Detailed immunohistochemical profile and differentials

Tumor	Immunohistochemistry	Differential Diagnosis
Lymphoma		
CHL	PAX 5 Weak+*, CD45-*, CD3+/-, CD20-, CD15+*, CD30+*, MUM1+	Thymoma, PMBL
B-NHL	PAX 5+, CD3- , CD20+, CD15-, CD30-, CD2-, CD79A+, AE1/AE3-	CHL, Thymoma type B1, seminoma, T-LBL
T-NHL	PAX 5+, CD3+, CD20-, CD15, CD30-, CD99+, CD2+, TDT+, desmin-, AE1/AE3-, SYN-	Thymoma type B1, large B cell lymphoma, NB, RMS, PNET, NEC
Thymic lesion		
Thymoma type A	AE1/AE3+, CK19+/-, p63+, CD20-, CD5-	Thymoma type B3, SFT, Thymic spindle cell carcinoma
Thymoma type B1	AE1/AE3-, EMA-, CD99+#, CD3+#, CD5+#, TdT+#	Thymoma type B2, T-LBL
Thymoma type B2	AE1/AE3+, EMA-, CD20-, CD99+#, TdT+#, CD3+#	Thymoma type B1, Thymoma type AB
Thymoma type B3	AE1/AE3+, EMA+/-, CD20-, CD5-, CD3+#, TdT+#, TTF1-	Thymoma type A, Metastatic carcinoma
Thymic carcinoma	Cd5+, CD117+, p63+, PLAP-, EMA-/+	Metastatic carcinoma, GCT,
GCT		
Seminoma	PLAP+, CD117+, OCT3/4+, AFP+/-, LCA-, HMB45-	Metastatic GCT, Metastatic melanoma, DLBCL, CHL
Choriocarcinoma	PLAP+, EMA-/+, AE1/AE3+, B-hCG+	Metastatic carcinoma
Neurogenic lesion		
Ganglioneuroblastoma/ NB	NSE+, SYN+, CgA+, S100+, EMA-, vimentin-, WT-1-, CD99-, CD45-, Desmin-	Lymphoma, SMCC RMS, PNET
Ganglioneuroma	S100+, SYN+, desmin-, CK-, EMA-, WT1-	Neurofibroma, Schwannoma, DSRCT
Schwannoma	S100+, CD34 scattered, SMA-	Leiomyoma, GN
Neurofibroma	S100 weak+, CD34 strong, SOX10+, SMA-	Schwannoma, GN, leiomyoma
MPNST	S100+, EMA-, CD34-, SX10+, SMA-, Desmin-, SMA-	Leiomyosarcoma, RMS, SFT, Schwannoma
PNET	CD99+, SYN-, desmin-, WT1-	RMS, NB, DSRCT
Mesenchymal		
Synovial sarcoma	CK+, TLE1+, FL1-, CK5/6-, myogenin-, Desmin-, S100-SOX10-	Thymoma type A, Spindle cell thymic carcinoma, Cellular schwannoma, SFT, LMS, spindle cell RMS
Solitary fibrous tumor	CD34+, STAT6+, TLE1+/-, S100-, AE1/AE3-, desmin-	Thymoma type A, Spindle cell thymic carcinoma, monophasic SS, Schwannoma

(* in RS cells, # in lymphoid cells, RMS- rhabdomyosarcoma, DSRCT- desmoplastic small round cell tumor, + positive, - negative)

Other rare tumors include paraganglioma, neuroendocrine tumor and benign thyroid lesion two cases each followed by papillary thyroid carcinoma and neuroendocrine carcinoma single case each.

Various differential diagnosis was arising from the clinical and histological approaches. IHC plays the decisive role in confirmation of diagnosis. Detailed IHC and differentials were discussed in table 2.

Discussion

Mediastinal tumors are very rare and an integrated approach is needed to establish the accurate diagnosis. In our study, we found primary mediastinal tumors more frequent than metastatic, which was concordant with other studies.[2,4,9-13] We found 82.2% of cases were arises from prevascular compartment which was similar to the study of Sundaram and Vidhyalakshmi. There was a male predominance in the present study which was comparable with previous studies.[10-13]

In the current study lymphoma was the most common neoplasm with 54% T-LBL which was concordant with other studies.[15-17] PMBCL accounts for 2-3% of all NHL and is the second most common NHL after T cell[18], in our study 6% cases were of PMBL.

All thymic lesion originated from prevascular compartment[3,5,14] which was comparable with our study. Thymic carcinomas are rare malignancies

affecting 30 to 60 years age group with slight male preponderance.[19] In our study single 53 year old case of male thymic carcinoma was noted.

Primary mediastinal GCTs are very rare and account for 10-15% of mediastinal tumors in adults and 19-25% in children.[20,21] GCT most commonly affects the prevascular compartment most common.[22,5] Teratoma was the most common morphology encountered followed by seminoma[20] which was similar to our study.

Primary mediastinal MPNST is rare and the majority arises in the posterior mediastinum[23] all three cases in our study were located in posterior compartment. PNET is uncommon. It most frequently affects children and young adults.[24] we also found similar findings

Primary soft tissue tumor is unusual in mediastinum and comprising of <10% of mediastinal tumor,[25] which support our study. The histopathological spectrum of sarcoma is broad and includes pleomorphic tumors (liposarcoma, leiomyosarcoma and RMS) and monophasic spindle cell pattern (monophasic SS, sarcomatoid/spindle cell carcinoma, sarcomatoid malignant mesothelioma, solitary fibrous tumor, MPNST and fibrosarcoma).[26,27] Broad spectrum of tumors arises from the mediastinum. Definite histological diagnosis on biopsy material has several challenges. IHC overcome this limitation and plays a pivotal role in supplementing histology for clinching the diagnosis.

Conclusion

Large number of tumors arise from the mediastinum and knowledge of it is utmost necessary for diagnosis and management. The present study enumerates the histomorphological spectrum of mediastinal tumors. Definitive diagnosis requires collaborated approach of clinicoradiology, histopathology and immunohistochemistry(IHC) findings.

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The Neurological Rehabilitation - The Untouched Territory in India

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Rehabilitation is an educational process for disabled person with the final aim of assisting that individual to cope with family, friends, work, and leisure as independently as possible and to involve the disabled person in making plans and setting goals that are important and relevant to their own circumstances. Rehabilitation includes various interventions that aim to reduce disability, activity limitation, and participation restriction among individuals with health conditions in interaction with their environment. The need for rehabilitation services becomes greater in neurological disorders, some of which are incurable and/or may lead to permanent sequelae.

India is the most populous country in the world overtaking China. According to a recent study, 2.41 billion individuals globally suffer from health conditions that would benefit from access to rehabilitation services as of 2019. Thus, every 3rd individual would require rehabilitation at some point in time. Furthermore, there were more than 7 million cases of traumatic brain and spinal cord injury, 1 million incident cases of stroke, 7 lakh cases of Parkinson's disease, 1 lakh cases of multiple sclerosis, 49,300 cases of brain and CNS cancer and 25,000 cases of motor neuron disease in India in 2019. Hence, the burden of neurological disorders requiring rehabilitation services in India is huge and neuro rehabilitation services are still in an infancy phase.

The barriers to accessing neuro rehabilitation services in the health care system in India may be due to lack of enough rehabilitation professionals including the physicians and supporting staff, limited health care workforce dedicated towards rehabilitation; and<1 rehabilitation professional /100,000 population), logistical factors (including the distance to service, lack or cost of transport), poverty and non affordability, lack of knowledge regarding the existence of services, lack of funding, and lack of political will. As a result, neuro rehabilitation services become limited to large private super specialty centres in urban areas and still remain untouched territory in tier 2 & 3 cities and rural part of India & has immense potential to grow.

Basic approaches in neurological rehabilitation

This process can be conveniently broken down into three key areas:

- Approaches that reduce disability
- Approaches designed to acquire new skills and strategies, which will maximise activity
- Approaches that help to alter the environment, both physical and social, so that a given disability carries with it minimal consequent handicap.

The Rehabilitation Process

The last point encompasses another fundamental principle of neurological rehabilitation. The process of rehabilitation is set around the establishment of goals. The first goal to be set is the long-term strategic aim. Once a realistic and achievable long-term goal has been established then the smaller steps needed to achieve that goal are determined. The goals must be precise. There is no point in setting vague and subjective goals as neither the rehabilitation team nor the disabled person will be able to monitor where they are in the process. A useful mnemonic to remember what the goals should be is SMART:

- Specific
- Measurable
- Achievable
- Relevant
- Time limited

The Rehabilitation Team

It is important to emphasise that a key principle of neurological rehabilitation is the close

working together of all relevant health professionals. The majority stakeholders are rehabilitation professionals, audiology/speech language pathology specialists, neurologists, neurosurgeons, and palliative care physicians. Other specialists and supporting staff can be added according to the requirement. So government can work in way to increase the number of these professionals to improve overall care.

WHO, in February 2017, launched Rehabilitation 2030, "A call for Action" rallying stakeholder towards concerted and coordinated global action to scale up rehabilitation. In order to achieve this, 10 priority areas for action were identified:

1. Creating strong leadership and political support for rehabilitation at sub-national, national and global levels.
2. Strengthening rehabilitation planning and implementation at national and sub-national levels, including within emergency preparedness and response.
3. Improving integration of rehabilitation into the health sector and strengthening intersectoral links to effectively and efficiently meet population needs.
4. Incorporating rehabilitation in Universal Health Coverage.
5. Building comprehensive rehabilitation service delivery models to progressively achieve equitable access to quality services, including assistive products for all the population, including those in rural and remote areas.
6. Developing a strong multi disciplinary rehabilitation workforce that is suitable for country context, and promoting rehabilitation concepts across all health work for CE education.
7. Expanding financing for rehabilitation through appropriate mechanisms.
8. Collecting information relevant to rehabilitation to enhance health information systems including system level rehabilitation data and information on functioning and utilizing the International Classification of Functioning, Disability and Health (ICF).
9. Building research capacity and expanding the availability of robust evidence for rehabilitation.
10. Establishing and strengthening networks and partnerships in rehabilitation, particularly between low-, middle- and high-income countries.

Many studies had identified the lacunae in reporting service needs, provision and outcome monitoring. So, identifying real need for neurological rehabilitation, removing the barriers and lacunae & amp; accelerating and expanding delivery of neuro rehabilitation services is of utmost important. An effective way for equitable delivery of services in India could be via community based rehabilitation (CBR) services. CBR can be especially useful in India where healthcare workforce is limited, and active community participation by various stakeholders (example community based health workers, family physicians, care givers, neurologists, community-based nurses, psychologists, and trained physiotherapists/occupational therapists) in terms of identifying disabled individuals, education and counselling, spreading exceptional knowledge regarding rehabilitation services, physiotherapy, and vocational training and provision of various assistance devices could be of utmost importance in integrating neuro rehabilitation services at the primary and district level. Thus multi disciplinary services at tertiary care centres can be reserved for severely disabled patients who require more resources.

To prepare the communities of similar disease individuals will help the patients to understand the disease process and improve understanding regarding the disease and treatment options with rehabilitation process like for Parkinson's disease, Indian and International Parkinson's and movement disorder society and brain tumor patients had National brain tumor society.

Strengthening the tele neuro rehabilitation services in India can also improve its delivery with faster pace in resource poor environment in a cost-effective way. Video conferencing can connect stake holders like nurse and physician or neurologist with one another and also tele neuro rehabilitation can be helpful in a neuro degenerative disease like Parkinson's disease in a covid -19 pandemic or other natural calamities.

To conclude, strengthening the neuro rehabilitation services in India at primary and district level would help greater uptake of these services across the society and lead to better functional outcome and quality of life of patients with neurological disorders. To improve the services, careful attention needs to be given to the training and skills of neuro rehabilitation workforce and monitoring them at regular basis. Establishment of rehabilitation centres separately for patients who don't require any acute hospital care and can work with community-based rehabilitation.

A Rare Case : Spindle Cell Rhabdomyosarcoma of Mandible

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Summary

Rhabdomyosarcoma is the commonest soft tissue sarcoma in 15-45 years.[1] We report a case of aggressive rhabdomyosarcoma of mandible (spindle cell variant) in a 27 year female patient, describing the clinicopathological findings and radiological findings of the patient and its management in our centre.

Keywords: Oral spindle cell variant rhabdomyosarcoma, mesenchymal tumour

Introduction

Rhabdomyosarcoma is aggressive malignancy and commonest malignant soft tissue sarcoma of children and young adults.[1] RMS primarily involves the head and neck. It is soft tissue malignancy which arises from mesenchymal tissue. Its incidence is more in within 20 years of age.[1] The present incidence of RMS in oral cavity is 0.041 cases per 100,000 people.[2] This is a case of a 27-year female with spindle cell rhabdomyosarcoma wherein clinico-pathological and clinicoradiological correlation led to the diagnosis.

Case Report

A 27-year-old female with the chief complaints of progressive swelling and growth over the mandibular region presented to us with a rapid increase in size over the previous four weeks. She also had a history of significant loss of weight. Inspection showed protrusion of lower lip with exophytic mass resting over it. It measured 6x5x3cm. on palpation localized tenderness was present. Skin overlying the chin was involved (Figure 1). On intraoral inspection, the ulceroproliferative mass was noted in anterior part of oral cavity, involving the anterior part of mandible, gingivobuccal sulcus and buccal mucosa.

Contrast Enhanced Computerized Tomography-Paranasal sinuses, Neck, Thorax revealed a 7.7x7x7.3 cm lesion arising from the central arch along with its erosion. Lesion involved bilateral body of mandible, mandibular canal, lower buccal space and gingivobuccal space. Lesion involved angle of mouth and overlying skin and shows exophytic growth with soft tissue defect. It involved bilateral gingivolabial and bilateral gingivolingual. The lesion extended into floor of mouth and involved mylohyoid muscle, ventral surface of tongue, and intrinsic component of tongue. There is reduced distensibility of adjacent buccal space, with bilateral level IB and II necrotic nodes (Figure 2).

A biopsy was performed and showed a malignant spindle cell tumour with moderate pleomorphism with >20 mitosis /hpf.

Figure 1: Preoperative picture of case

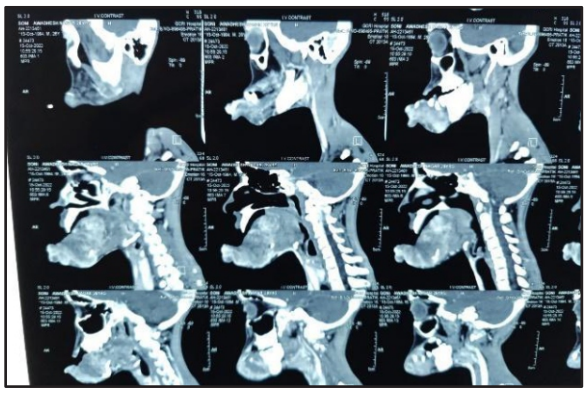


Figure 2: Preoperative CECT of the case

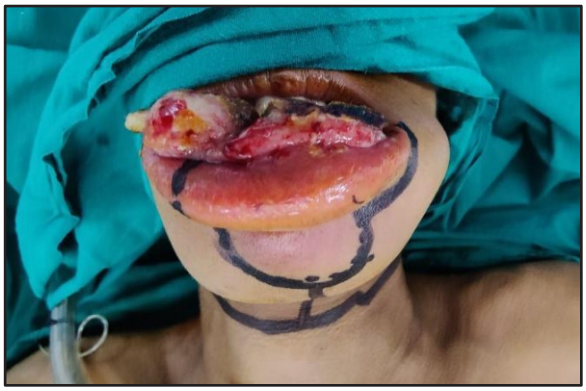


Figure 3: Intra operative picture of the case

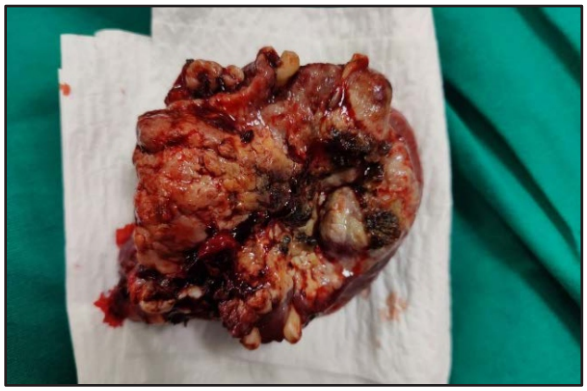
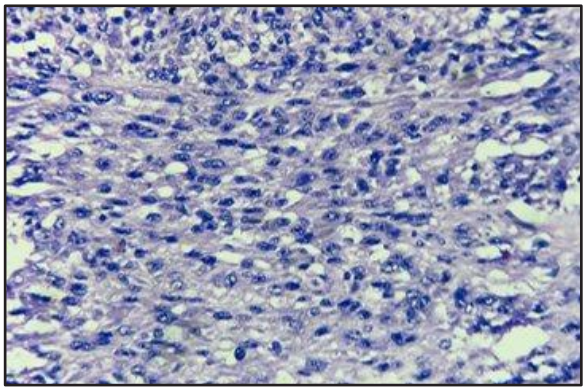


Figure 4: Wide local excision of the lesion



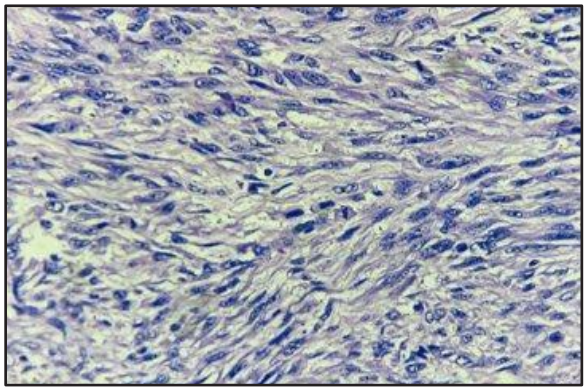


Figure 5 a, b: The haematoxylin and eosin sections show proliferation of predominantly spindle cells with moderately pleomorphic nuclei, distinct nucleoli and eosinophilic cytoplasm. 40x objective

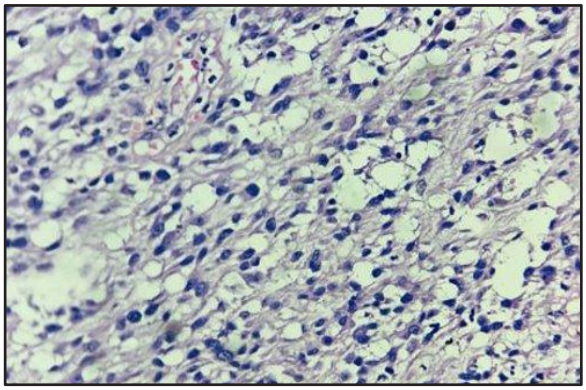


Figure 5c: Scattered rhabdoid cells are seen with eccentrically pushed hyperchromatic nuclei having amphophilic cytoplasm. 40x

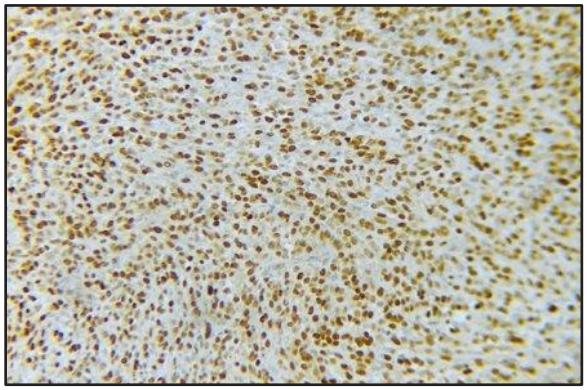


Figure 5d: MyoD1 immunostain shows diffuse nuclear positivity in all the tumour cells, 40x

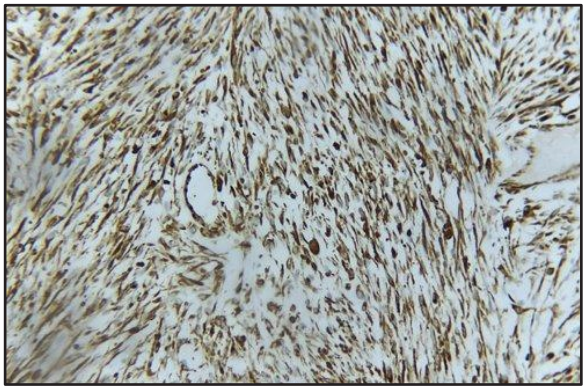


Figure 5e: Vimentin immunostain shows diffuse cytoplasmic positivity in all the tumour cells, 40x

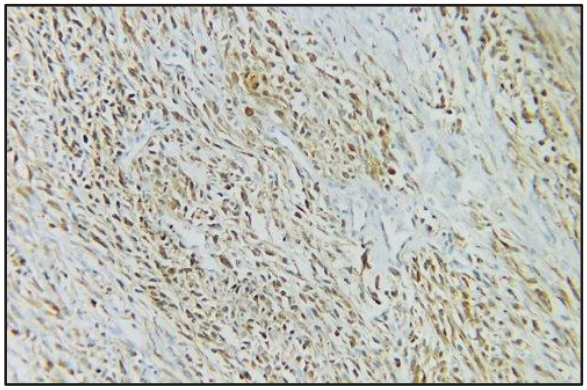


Figure 5f: EMA (epithelial membrane antigen) immunostain shows diffuse cytoplasmic positivity in all the tumor cells, 40x

Immunohistochemistry was performed and it was positive.

Patient was planned for neoadjuvant chemotherapy, and was started on VACM regimen. After taking one cycle, she developed severe vomiting, generalized weakness and diarrhoea. Since she was unable to tolerate neoadjuvant chemotherapy, she was planned for salvage surgery. Wide local excision of central arch with segmental mandibulectomy and bilateral modified neck dissection type II was done. Reconstruction with a bilobed pectoralis major myocutaneous flap was performed (Figure 3). Later, patient developed skin necrosis, hence debridement followed by deltopectoral flap cover was done (Figure 4). Final histopathology showed high grade spindle cell sarcoma – spindle cell Rhabdomyosarcoma of size 8x6x4 cm histologic grade 3, mitotic rate 4-5/10 hpf, 20% necrosis due to effect of chemotherapy, multifocal tumour, no lymphovascular invasion and perineural invasion and anterior cutaneous margin was 0.3cm away from tumour rest margins greater than 0.5cm and free of tumour. pT4aN0. Patient was subsequently referred for completion of chemotherapy after removal of sutures. However, before chemotherapy could be started, she developed a nodule over right cheek. Core biopsy from the same showed recurrent spindle cell rhabdomyosarcoma. Disease free survival was 2 months. Patient was subsequently sent for palliative systemic therapy. Final IHC suggestive of spindle cell rhabdomyosarcoma with AE1 weak positive and MyoD1 positive, EMA focal positive and occasional positive (Figure 5).

Discussion

Spindle cell rhabdomyosarcoma (RMS) is a rare type of RMS. It can affect any age group, more common children and in male with a ratio of 6:1. Histological types of RMS are: alveolar,embryonal, and pleomorphic.[3] It's the commonest soft-tissue sarcomas of childhoodand embryonalhas the highest incidence.[4] It accounts only 5-10% of all solid tumours cases and 4-8% of all malignancies.

Spindle cell, rare type of RMS, was initially grouped under embryonal RMS which was more common in head-and-neck region. Some of the embryonal tumours showed hyaline sclerosis and pseudovascular growth pattern, as found in sclerosing RMS. Both embryonal and spindle cell tumours demonstrate recurrent mutations of the MYOD1 gene and are therefore classified as a single type in WHO classification.[5] The Spindle cell variant of embryonal RMS was first recognized as a rare one in 1992 by German-Italian Cooperative STS Study.[6] Patients comes with painless firm swelling most commonly.[7] The size of tumor may range from as small as 1.5 cm to around 35 cms.[8] Histologically, RMS shows small, round-to-spindle-shaped cells having moderate nuclear pleomorphism. Large rhabdomyoblasts having an eccentric nucleus and eosinophilic cytoplasm.[9]

Previously classification was based on collagen density in between the tumor cells and was collagen rich or collagen poor type.[10] Cellular type spindle-cell tumours may be similar to leiomyosarcomas, MPNSTs and fibrosarcomas. Similarly, desmoplastic melanoma and spindle cell carcinoma are the first differentials in adults, inflammatory myofibroblastic tumour and synovial sarcoma are other differential diagnoses.

Immunohistochemistry helps to confirm the diagnosis. Morphology and immunoprofile of leiomyosarcomas and RMS are indistinguishable. Presence of rhabdomyoblasts confirms RMS, other than this IHC markers such as desmin, myogenin and MyoD1, indicative of skeletal muscle differentiation helps to conclude diagnosis.[11] Spindle cell variant of RMS is negative for S100 .[7]

These tumours have a more aggressive course in adults. Their prognosis relies on the size, resectability and staging of the tumour.[7] In our case also, complete resection was done with histologically free margins but the patient came with recurrence within two months of resection, showing the aggressiveness of the disease.

Conclusion

This case demonstrates that spindle cell rhabdomyosarcoma is a rare but aggressive malignancy and it requires upfront chemotherapy and completion surgery and additional nutrition therapy is essential in order to tolerate treatment.

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Retroperitoneal Recurrence of Sex Cord Stromal Tumour with Annular Tubules A Rare Case Report

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Summary

Sex cord tumour with annular tubules (SCTAT) are rare pure sex cord tumours with low malignant potential. Majority of cases are sporadic and around one-third are associated with PeutzJeghers Syndrome (PJS). Sporadic cases have tendency for late recurrences commonly in retroperitoneal region. Surgery remains the mainstay treatment. A 38-year-old lady presented to us with retroperitoneal recurrence of ovarian tumour which was encasing and thrombosing IVC. Lesion also partially encased infrarenal aorta and common iliac artery. She underwent cytoreductive surgery following neoadjuvant chemotherapy (NACT). Final histopathology revealed SCTAT. Stable disease was noted on NACT. Cytoreductive surgery was performed with multidisciplinary team and adjuvant chemotherapy given. Patient is disease free till last follow up.

Keywords: Sex cord tumor with annular tubules, Cytoreductive surgery, Neoadjuvant chemotherapy, Retroperitoneal recurrence

Introduction

Sex cord tumour with annular tubules (SCTAT) are rare, distinct tumours and account for less than 1% of sex cord stromal tumours (SCST). They have intermediate features between granulosa cell tumour and Sertoli cell tumour.[1] Majority cases are sporadic and around one-third are associated with PeutzJeghers Syndrome (PJS). Since very few cases are reported, no agreement upon standard treatment is available. Recurrences are reported in sporadic cases.[2] Here we report a case of retroperitoneal recurrence of SCTAT treated with cytoreductive surgery following neoadjuvant chemotherapy (NACT).

Case Report

A 38-year-old P4L4 was referred to our hospital with an abdominal mass present since 2 years. She had history of surgery 7 years ago in 2014 for adnexal mass, details were not available. Patient gives history of laparotomy again 2 years back in 2019 outside and declared inoperable with intra-operative findings noted as large retroperitoneal mass on right side adherent to right ureter, iliac vessels and mesenteric vessels. Biopsy from retroperitoneal mass was taken but report was not available. She had regular normal menstruation. Patient had no comorbidities or significant family history.

On examination, vitals stable, general examination including oral cavity normal. Per abdomen, 2 vertical scars midline, one supraumbilical and other subumbilical noted. A hard fixed mass was noted in right iliac fossa reaching midline of 15x10cm size. On per speculum, cervix was bulky. On per vaginal examination, uterus bulky and mobile. On per rectal examination, lower border of mass felt. Her CT Scan showed large retroperitoneal heterogeneously enhancing centrally necrotic soft tissue mass of 10x16x22cm size in infrarenalretrocaval region extending upto right iliac fossa markedly compressing and thrombosing IVC. Lesion partial encased infrarenal aorta and right common and external iliac artery without causing stenosis. Lesion markedly displaced right ureter and posteriorly lesion was in contact with psoas muscle without invasion.

Since mass was radiologically and clinically inoperable, biopsy was done from mass which was reported as low grade cells arranged in nested pattern with abundant hyaline sclerosis surrounding nests. The cells show abundant cyanophilic cytoplasm and central nucleus with occasional nuclear grooving. These features were suspicious for epithelial/ neuroendocrine tumour/ lymphoma. Immunohistochemical markers were put on this biopsy and was EMA, synaptophysin, LCA, PAX5, HMB45, Actin, Desmin, MYOD1, MUC4, S 100 Negative and positive for vimentin, Inhibin and calretinin. Based on these, sex cord stromal tumour of ovary was suggested. Her CA125 was 6.47 U/ml and HE4 92.4pmol/L and other germ cell markers were

normal. Her serum inhibin B level was measured as biopsy suggested SCST and was found to be >1050pg/ml. She was started on LMWH therapeutic dose for 1 week which was converted to Tab Apixaban 5mg BD on cardiology advice for IVC thrombosis. Patient was planned for neoadjuvant chemotherapy considering inoperability.

She received 3 cycles of paclitaxel and carboplatin as neoadjuvant chemotherapy, following which tumour marker and CT scan were repeated. Serum Inhibin B levels remained >1050pg/ml and CT Scan revealed 8x14x16cm lesion in right adnexal region displacing right ureter and encasing branches of superior mesenteric artery and loss of fat plane with IVC and right common iliac vessels (Figure 1). No other lesions were noted. Since patient had 27% reduction in length diameter, one more cycle of chemotherapy followed by debulking surgery was planned.

After detailed risk consent, cytoreductive surgery was planned with multidisciplinary team involving gynaecological oncologist, gastrointestinal oncologist, cardiothoracovascular surgeon and anaesthetists. Patient underwent right retroperitoneal mass excision with paraaortic node dissection with retrocaval node removal with omentectomy, total abdominal hysterectomy and left salphingo-oophorectomy (cc score-0). Intra operatively, uterus was bulky, a 20x18cm mass in right retroperitoneum with right ureter passing through its capsule with right infundibulopelvic ligament adherent to it and ovary not seen separately. Mass was densely adherent to infrarenal abdominal aorta and right common iliac artery. Infrarenal IVC was found to be flat with mass encircling it. Ureter was meticulously separated from mass and then mass was separated from vessels (IVC, Right common and external iliac vessels) by sharp dissection (Figure 2). Inferior mesenteric artery identified and preserved. No blood flow was noted in infrarenal IVC and common iliac vein but retroperitoneal collateral veins draining into IVC noted. Graft was not placed as collaterals were well established. Perioperative anticoagulation managed as per cardiology opinion. Patient recovered well in post operative period.

Her final histopathology suggested sex cord stromal tumour with annular tubules of 23X18X7cm size in retroperitoneal mass with capsule infiltration by tumour (Figure 3). On cutting, nodular, yellowish

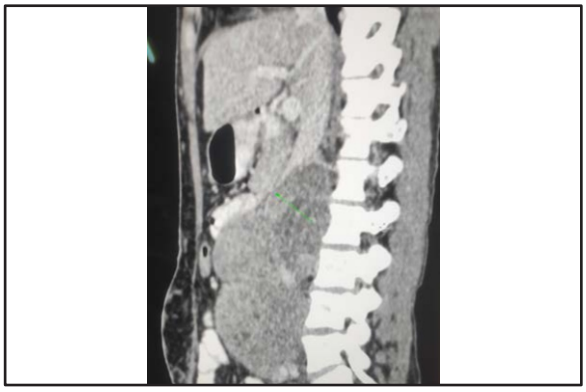

Figure 1: CT Scan showing mass adherent to IVC. Green arrow shows IVC.

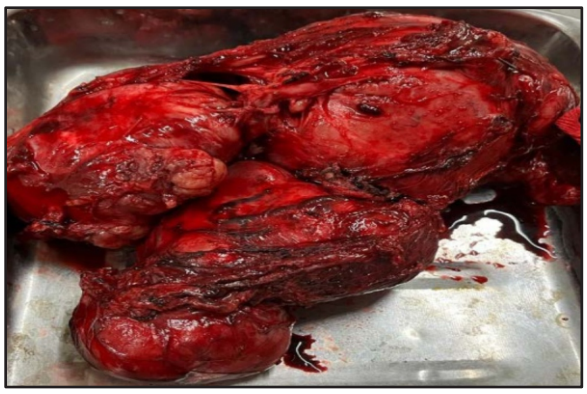

Figure 3: Retroperitoneal tumour after removal

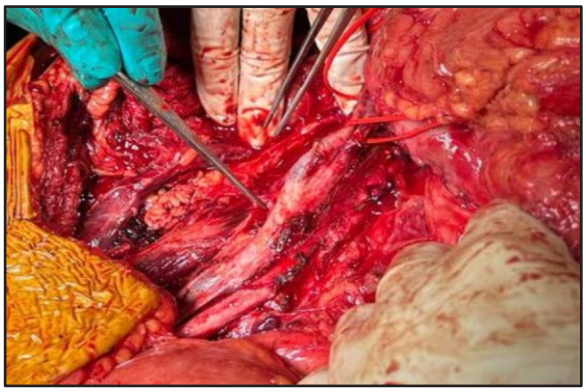

Figure 2: Retroperitoneum after tumor removal; Forceps point towards area where tumor was adherent to IVC.

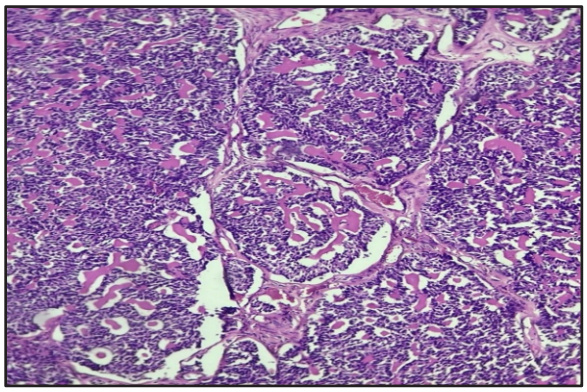

Figure 4: Microscopic picture of SCTAT

white and haemorrhagic areas were seen. Microscopy showed tumour arranged in lobules containing sharply circumscribed ring shaped tubules containing hyalinised basement membrane like material (Figure 4). Endometrium was proliferative and other ovary was normal. Two of five retrocaval nodes were positive and omentum was free of tumour. Her post operative inhibin B was 2pg/ml. Patient received 2cycles of adjuvant paclitaxel and carboplatin (total 6 cycles of chemotherapy with last dose in May 2022). Patient is doing well and disease free at present (last follow up in February 2023).

Discussion

SCTAT are very rare neoplasms comprising less than 1% of sex cord ovarian tumors.[1] Robert Scully described them for first time in 1970 and considered these tumours as a distinctive phenotype intermediate between granulosa cell and Sertoli cell tumours. He considered granulosa cells as probable origin with a growth pattern more characteristic of Sertoli cell tumors.[3]

Two varieties of SCTAT exists. First one associated with PeutzJeghers Syndrome (PJS) seen in one third of cases. These tumours are usually benign, multifocal, calcified, bilateral, very small (<3cm) or even microscopic and present at younger age (mean age 27 years). Second variety is sporadic tumours usually occur in older patients (mean age 36years), are unilateral, large, and have malignant potential in 22% cases.[1,4] Our patient even though did not undergo genetic testing for STK11, but her clinical picture fits into sporadic case i.e, unilateral, large tumour, recurrent with malignant potential.

Since the tumour secretes hormones, patients present with features of hyperestrogenism such as heavy menstrual bleeding, precocious puberty or irregular bleeding. Few reports of tumour secreting progesterone also exists with decidualised stroma in hysterectomy specimens.[4] Our patient had no menstrual complaints and histopathology was normal.

Various studies reported no elevation in CA 125 or CEA levels and Inhibin and Mullerian Inhibiting substance as potential markers.[2] As seen in our case also, CA125 was normal and Inhibin B was elevated which normalised post tumour removal. SCTAT diagnosis is usually based on pathological examination of the tumour and preoperative or intraoperative SCTAT diagnosis is rather difficult.[2] Similarly in our case, final histopathology diagnosed SCTAT.

Recurrences were reported as early as 3 months to as late as 20 years. Malignant behaviour in SCTAT has been noted only in sporadic cases. Lymphatics is main channel of spread with pelvic, para-aortic and supraclavicular lymph nodes reported as common sites of metastasis. Other sites of tumour recurrence and metastasis noted in literature include retroperitoneum, parietal and visceral peritoneum, liver and lung.[5] Even in our case lymphatic spread is noted to external iliac and aortocaval nodes.

Surgical treatment and staging are similar to other ovarian cancers. Since the tumour is very rare, no standard treatment protocol exists. For primary treatment, staging laparotomy followed by adjuvant chemotherapy for stage II to IV is commonly practised. Fertility preservation can be considered for non-syndromic SCTAT. As discussed earlier, recurrences are noted in retroperitoneum and nodes and lymphatic spread is common. Hence pelvic and para-aortic lymphadenectomy should be considered during surgery. Chemotherapy used is cisplatin, etoposide and bleomycin (BEP).[2,6]

For recurrence, treatments include Secondary cytoreductive surgery, chemotherapy with docetaxel, paclitaxel/ifosamide, and paclitaxel/carboplatin, radiotherapy or hormone therapy. Neoadjuvant chemotherapy in recurrent setting was used by Ping Zheng et al with 3 cycles paclitaxel liposome and nedaplatin.[6] Only 2 case reports with paclitaxel and carboplatin (TC) for recurrence in adjuvant setting are reported.[2,6] Our patient received TC as neoadjuvant chemotherapy in recurrent setting with 27% decrease in tumour size (stable disease as per RECIST 1.1 criteria). Considering indolent nature of tumour growth, poor chemoresponse was anticipated in our patient and surgery was planned. Even though surgery was very challenging, team work yielded excellent results and CC score 0 was achieved.

SCTAT is an ovarian tumour with low malignant potential and late recurrence. In study by Qiuhong Qian et al with cohort of 13 patients, recurrence rate was 46.2% and multiple recurrences in 38.5% of patients. Recurrences were located mainly in retroperitoneum, such as pelvic and para-aortic lymph nodes. Apart from retroperitoneum, three patients had supraclavicular lymph node metastasis and two patients had extensive metastasis in the abdominal and pelvic cavity. Most recurrences were controlled by surgery with or without adjuvant therapy. One year and 5-year PFS were respectively 92% and 67%. With increasing numbers of recurrences, PFS shortened. The 5-year Overall survival was 100%. This study observed that though the recurrence rate is high, the prognosis is relatively favourable. This study also suggested that effect of chemotherapy is not clear in these tumours and role of lymphadenectomy at primary surgery should be further studied as most recurrences were in retroperitoneum and despite chemotherapy.[2]

Conclusion

Considering its unusual behaviour with delayed recurrence, regular long-term follow up is essential in SCTAT. Surgery forms the mainstay of treatment for recurrence. Multidisciplinary team approach is needed to achieve optimal results.

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Primary Ependymoma of Ovary- A Rare Case Report

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Summary

Ependymoma is a glial tumor characterized by its differentiation towards ependymal cells, typically originating from the central nervous system. Primary ovarian ependymoma is an exceedingly uncommon entity with no established treatment protocol. Here we report a case of a young female who presented with ovarian mass. Initial imaging was suggestive of cystic mass arising from the right ovary. Tumor markers were negative. Patient underwent right salpingo-oopherectomy. The histopathological diagnosis of primary ovarian ependymoma was determined based on the strong expression of glial fibrillary acidic protein (GFAP), AE1, S100, and epithelial membrane antigen (EMA) observed in IHC. Patient was then treated with Etoposide based adjuvant chemotherapy. After 9 months of treatment patient is doing well with no evidence of disease. Although rare, this diagnosis should be kept in mind as a differential diagnosis of ovarian mass in a young female.

Keywords: Ependymoma, ovarian tumor, ovarian germ cell tumor

Introduction

Ependymoma is a glial tumor characterized by both neuro-ectodermal and ependymal differentiation, primarily found in the central nervous system. While extracranial and extraspinal ependymomas are exceedingly rare, they have been documented in various locations such as ovary, broad ligament, presacral and sacrococcygeal region, lung and mediastinum.[1] Compared to their CNS counterparts, extracranial ependymomas generally have a more favorable prognosis.[2,3] Primary ovarian ependymoma is an extremely rare form of ovarian cancer, with approximately 35 reported cases in medical literature to date. Due to the scarcity of these cases, there is currently no established treatment strategy for these tumors. In this report, we present a case of an 18-year-old female who presented with ovarian ependymoma. She underwent salpingo-oopherectomy followed by adjuvant chemotherapy.

Case Report

An 18-year old young unmarried female presented with abdominal pain and discomfort since 2 months. Her past medical history was unremarkable. Initially, USG was performed and it showed a 16x13x9 cm cystic hypo-echoic lesion arising from the pelvis with right ovary not seen separately from the lesion. Consequently, abdominal CT scan was done which showed 17x16x13 cm well defined multi-loculated cystic lesion with internal heterogeneously enhancing solid component, arising in the right adnexa. Right ovary is not seen separately from the lesion. (Figure 1)

All routine blood tests and serum tumor markers like CA125, HE4, βHCG, AFP, CEA, and LDH were within normal limits. She underwent exploratory laparotomy with right salpingo-oophorectomy with omental biopsy. Intra-op frozen report of right adnexal mass showed a solid cystic mass with multiple papillary projections and histo-morphologically two possibilities were suspected as 1) Cystic teratoma with area of ependymoma (Monodermal teratoma) and 2) Sex cord stromal tumor. On final HPE report, grossly 17x13x10 cm solid exophytic mass with adherent cyst wall was seen in right adnexa. External surface of the adnexal tumor was bosselated with nodular areas and outer surface was encapsulated. On cut surface it had solid cystic brownish tan with multiple papillary projections seen. On final histology, adnexal mass had sieve-like appearance and cystic spaces lined by pseudo-stratified columnar cells. Many areas showed bipolar fibrillary processes forming perivascular pseudo-rosettes and occasional true rosette formation (Figure 2). No other germ cell components were seen. Fallopian tube and omental biopsy were free of tumor. Peritoneal wash cytology was negative. Lymphovascular emboli was absent. After histo-pathological examination, a provisional diagnosis of primary monodermal teratoma-ovarian ependymoma was made. IHC showed positivity of AE1 (focal positive), EMA (dot like positive), GFAP (positive),

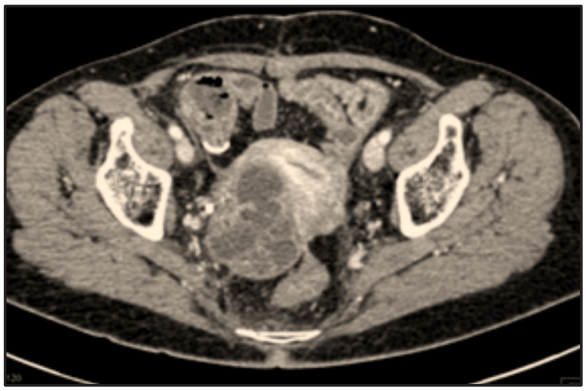

Figure 1: CT scan showing right adnexal mass.

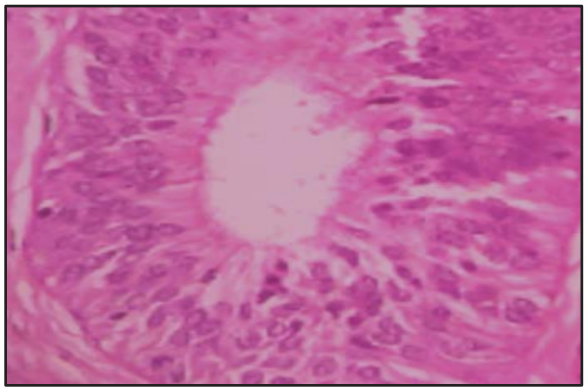

Figure 2: H&E stain showing ependymal rosette formation.

S100 (positive), Inhibin (occasional positive) and negative for synaptophysin, AFP, OCT3/4, CK7 with MIB index 8-10%. Post-op imaging showed no evidence of disease at operated site. MRI brain and spine showed no CNS lesions. Patient then received adjuvant chemotherapy with BEP regimen. Patient is now on regular follow up for last 9 months. She is now doing well with no complaint.

Discussion

Ependymoma is a glioma characterized by both neuro-ectodermal and ependymal differentiation, typically originating in the central nervous system. As per the WHO histological classification of Ovarian Tumors, ovarian ependymomas fall under the category of neuro-ectodermal tumors. Within the ovary, PNETs are divided into three classes: (1) differentiated tumors consisting of ependymoma, oligodendroglioma and astrocytoma; (2) primitive tumors encompassing neuroblastoma, ependymoblastoma, medulloblastoma, neuroectodermal tumors, and medullo-epithelioma; and (3) anaplastic type comprising glioblastoma multiforme.[3,4] While ependymomas primarily develop in the brain, extra-neural ependymomas often arise from remnant parts or displaced nests of the neural tube present in other organs. Ependymomas of the ovary, para-ovarian tissue, posterior mediastinum, omentum and lungs are very uncommon. Primary ovarian ependymomas typically affect individuals between the ages of 6 and 60years, with a higher incidence seen in young patients, presenting unilaterally and without extra-ovarian involvement.[5] Our patient, a young female, also presented with unilateral involvement. In the literature, though these tumors commonly manifest unilaterally.[5] Few bilateral cases have been documented with extension into other pelvic organs.[6,7]

The exact histo-pathogenesis of ovarian ependymomas remains unknown. Unlike other neuro-ectodermal tumors of the ovary, primary ovarian ependymomas rarely coexist with teratomas. Ovarian neuro-ectodermal tumors can resemble several primary and metastatic ovarian tumours.[8] Initially, the presentation often mimics more common ovarian malignancies such as epithelial carcinoma and germ cell tumors. In our case, due to the patient's young age, a germ cell tumor like yolk sac tumor was excluded based on histology and IHC, which demonstrated the lack of hyperchromasia, irregularly formed nuclei, limited presence of mitotic figures, and absence of AFP staining, with normal serum AFP level. Other potential differential diagnoses included ovarian serous carcinoma, endometrioid carcinoma, granulosa cell tumor, and Sertoli-Leydig cell tumor.[9] Definitive diagnoses were reached based on typical histological findings such as rosette formation, fibrillary cytoplasm, strong positivity for GFAP and S100 on IHC, and WT1, PAX 8, AFP and inhibin being negative, along with normal serum markers.

The standard treatment protocol for ovarian ependymoma is yet to be defined. Most cases described in the literature, underwent surgery and adjuvant therapy. In a recently published study, a stage III patient survived for 8 years following treatment with oral etoposide only.[10] Hence, the authors concluded that etoposide-based therapy could impede the growth of ependymomal tumors and is worth considering post-surgery. In several other cases, the BEP chemotherapy regimen was utilized. Our patient also received BEP-based chemotherapy. Ovarian ependymomas generally exhibit a more favorable prognosis in terms of recurrence-free survival and overall survival when compared to their CNS counterparts. In the present case, our patient remained asymptomatic and was doing well 9 months after completing treatment.

Conclusion

Primary ovarian ependymoma is an uncommon tumor and exhibits significantly improved prognosis compared to CNS ependymoma. Therefore, it is crucial to consider it in the differential diagnosis of ovarian neoplasms, particularly among younger females. While there is no established treatment protocol, surgical intervention followed by adjuvant chemotherapy appears to hold promise as an effective approach for managing advanced ovarian ependymoma.

Declaration of patient consent

The patient has provided consent for clinical data to be documented in the journal. The individual acknowledge that her name and personal details will not be disclosed. Reasonable measures will be taken to safeguard her privacy; however, complete anonymity cannot be ensured.

Conflicts of interest

Nil

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An Aggressive Angiomyxoma of Vulva - A Rare Entity

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Summary

Aggressive Angiomyxoma is a rare slow growing mesenchymal tumor preferentially arising in the pelvic and perineal regions of young adult females of reproductive age group and has a marked tendency for local recurrence. We report the case of a 36-year-old female who presented with swelling of the vulva arising from Labia majora.

Keywords: Aggressive angiomyxoma; Mesenchymal tumor; Vulval tumor.

Introduction

Aggressive Angiomyxoma (AA) is a benign mesenchymal tumor that is very rare and slow growing in nature. It is usually seen in females of reproductive age and typical site of presentation is pelvic and perineal region with infiltration into adipose tissue and skeletal muscles.[1] The most common presentation is a painless growing mass. It can also present as dull aching pain, dyspareunia or even with urinary symptoms like urinary retention or dysuria. The common differential diagnoses that can often be misleading are groin hernia, abscess, sarcoma, gynecological malignancy, Bartholin gland cyst or lipoma. Rosai and Steeper first described this entity in 1983.[2] It usually presents as a painless mass in the vulvoperineal region. Less than 350 cases have been reported till date with this tumour which emphasizes on it's rarity.[3] The term aggressive refers to the infiltrative nature of the disease and also to the multiple local recurrences seen with the disease.[4] Mostly local recurrences were noted between 2 months to 15 years after initial diagnosis of the disease and recurrence rate varies from 9% to 72%.[5] The tumour is associated with high rate of incomplete resection due to local extension to urethra, rectum, anal sphincter, vagina and pelvic diaphragm leading to high risk of local recurrence. These tumors grow more during pregnancy due to the high rate of estrogen and progesterone receptor positivity found in AA. Because of this hormone positivity, these patients usually respond to hormonal manipulation. Due to the locally aggressive nature of the tumor, early diagnosis and appropriate treatment is most important to prevent future recurrences. Appropriate follow up schedule is also important to prevent recurrence. Aggressive Angiomyxomas exhibits typical radiological features. These are related to the typical location of tumor which is almost always found in the perineal and/or pelvic region. The other typical feature is characteristic demonstration of "swirled" appearance of relatively low-intensity internal stranding on MRI in both T1- and T2-weighted images. Due to the rare nature of the tumor consensus is still lacking on the treatment plan and follow-up schedule of the tumor. So, we are submitting the present case of a patient who underwent local excision for an AA followed by radiotherapy due to margin positive disease followed by hormonal therapy.

Case Report

A 36-year-old female presented with complain of vulval swelling for past 1 year that has gradually increased in size. There was no history of any bleeding or discharge from genital area. There was no history of local pain except a sensation of hanging mass while standing. Patient had a past history of similar lesion at the same site for which she underwent surgery at some local hospital three years back for which no records were available with the patient. She had taken no adjuvant treatment after the surgery. She then presented to us with recurrence. On local examination a large well circumscribed polypoidal mass approximately 10 cm x 10 cm x 17 cm was observed. The lesion was soft, spongy in consistency and non-tender. There was no lymphadenopathy associated with the mass. On gynecological examination, no abnormality was seen on cervix and vagina and no mass was palpable per rectum. Multiple warts of size <1cm were seen on mons pubis. Her laboratory investigations were all

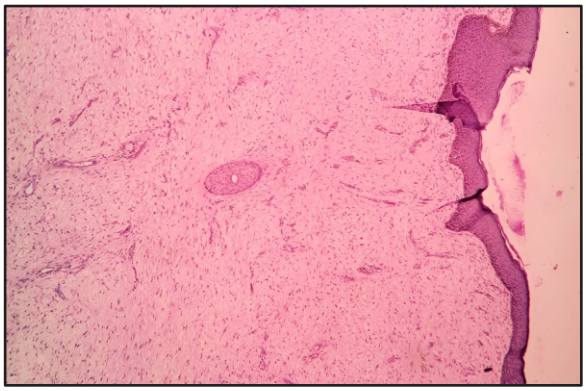

Figure 1: Histological section showing discrete stellate to spindle cells in myxoid stroma with multiple thin walled capillaries.

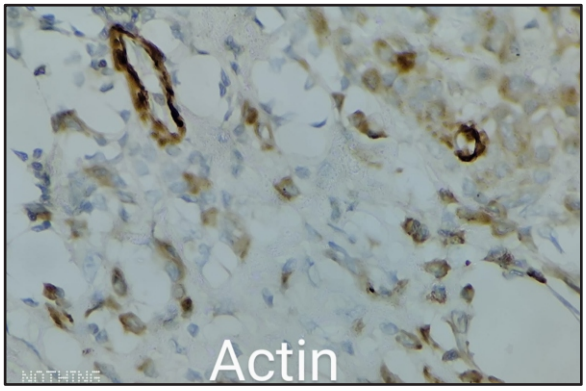

Figure 2: IHC staining - Actin.

within normal limits and ultrasonography of abdomen showed no abnormality. She was diagnosed to have hypothyroidism for which thyroxine 100 mg/day was started 1 month back. Magnetic Resonance Imaging (MRI) pelvis showed ill-defined mixed signal intensity mass involving skin and subcutaneous soft tissue of vulva in midline and both sides. Patient was planned for local excision and a simple vulvectomy was done. The specimen was then sent for histopathological examination. Gross examination of the specimen showed a large lesion of size 17 cm × 10 cm × 6 cm that was completely covered with skin. Overlying skin had nodular appearance and tumor was abutting it. On cut section, mass was pale white, smooth at places and infiltrating the surrounding fat. Microscopic examination showed epithelium with superficial ulceration and dense inflammatory cells. Stroma and deep tissue showed tumor composed of spindle cells. Blood vessels and rarely few mitotic figures were observed in between spindle cells. Right lateral mucocutaneous margin was positive. Diagnosis of spindle cell tumor possibly aggressive angiomyxoma was given on histopathology report (Figure1). On immune-histochemistry (IHC), tumor cells were positive for Calponin- 1, Actin, CD34, desmin, estrogen receptor (ER) and negative for beta

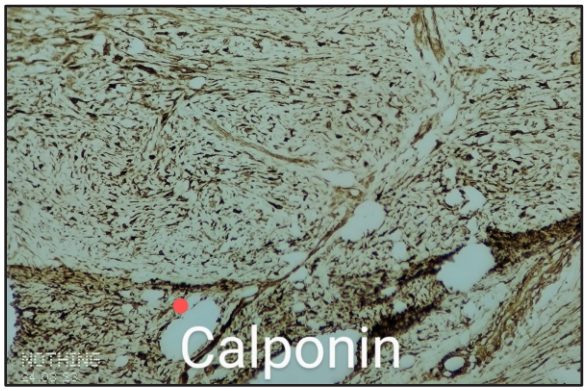

Figure 3:IHC staining - Calponin.

catenin and SOX- 10 (Figure 2 and 3). IHC confirmed it as a case of aggressive angiomyxoma of vulva. In view of positive margins on histopathology report radiotherapy opinion was taken and patient was planned for the same after adequate wound healing. Patient was given adjuvant radiotherapy (50.4 Gy/28#) followed by adjuvant hormonal therapy. Patient was started on GnRH agonist- Injection Leuprolide 3.75 gm deep intramuscular once a month and 3 injections were given following which patient was put on observation with regular follow up visits. Patient is on follow up on an outpatient basis and is doing well.

Discussion

Angiomyxoma is divided into superficial Angiomyxoma and aggressive Angiomyxoma. Superficial Angiomyxoma is also known as cutaneous myxoma and these can occur in setting of carney complex.[6] Superficial Angiomyxoma lesion is usually observed in males of middle age group and occur superficially mostly involving trunk, lower extremities and head and neck. Most lesions are usually asymptomatic and indolent polypoidal cutaneous lesions and can be confused with skin tags or cysts.

Aggressive Angiomyxoma is found in females of reproductive age group almost exclusively and very rarely in perimenopausal females and children. The usual presentation is an incidental finding or a painless indolent mass, which may go unrecognized for many years. The common differential diagnoses are groin hernia, abscess, sarcoma, gynecological malignancy, Bartholin gland cyst or lipoma. After collecting pertinent history and performing a detailed clinical examination, proper utilization of radiological imaging can help to narrow down the differential diagnoses. To document the exact extent of the tumor, MRI and contrast enhanced CT scan is recommended. These tumors show well defined margins on CT scan and also show attenuation

that is less than that of the muscle. On MRI, these tumors show extremely high signal intensity on T2 weighted images. Other feature is characteristic demonstration of "swirled" appearance of relatively low-intensity internal stranding on MRI in both T1- and T2-weighted images. The high signal intensity noted on MRI is due to high water content and loose myxoid matrix of AA.[7] The preferred imaging modality to detect recurrence is MRI.

The exact pathogenesis of AA is still unknown. However, due to positivity of tumor cells for desmin and smooth muscle actin on IHC the likely origin is either from specialized mesenchymal cells or from multipotent perivascular progenitor cells.[8] This is also supported by the immune-histochemical expression of actin along with desmin in the tumor cells in few cases.

The desired goal of the treatment is complete surgical resection of the mass with negative margins. Sometimes this can be difficult because of unencapsulated and infiltrative nature of the tumor. Superficial tumors are easily resected with wide local excision, while surgery in patients with large and deep seated tumors is very extensive and morbid. Sometimes to decrease the extensive surgical morbidity, resection with close or positive margin is accepted. This is mainly done to preserve fertility or to decrease morbidity. Adjuvant treatment with hormonal agents like tamoxifen, raloxifene or GnRH agonists like leuprolide acetate are usually beneficial when the patient is hormonal receptor positive. There was a case reported by Fine et al. in which patient with recurrent Aggressive Angiomyxoma of vulva was only treated with 3 months of GnRH agonist without any surgical resection or any other medical therapy.[9]

Our patient was most likely a case of recurrent AA as history of local surgery at similar site was likely due to the same etiology. Post surgery, radiotherapy was given to patient in view of positive lateral margin on histopathological examination to prevent recurrence of the tumor.[10] Usually chemotherapy and radiotherapy are not used in AA. Only hormonal therapy has a role but due to high recurrence rate and positive margin radiotherapy was used in our patient followed by adjuvant hormonal therapy.

Specific guidelines for post-operative follow up of vulvar AA is lacking but due to high recurrence rate and extensive morbidity associated with recurrences that might go unrecognized, several authors recommend a periodic evaluation with physical examination and MRI for up to 15 years after excision.[9]

Conclusion

Aggressive angiomyxoma is a locally aggressive and rare neoplasm. It should always be kept as a possibility whenever a patient present with growth in the vulvo-vaginal region, perineum or pelvis. As high local recurrence is well known with the tumor, early diagnosis and treatment with surgical excision and adjuvant treatment is beneficial for the patients.

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Pulmonary Large Cell Neuro-Endocrine Carcinoma with ALK-EML-4 Fusion with Good Response to ALK Inhibitors

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Summary

Large cell neuroendocrine carcinoma (LCNEC) is a rare but aggressive cancer with very poor outcome. Lung and gastrointestinal tract are the primary sites for majority of cases. Hereby, we are presenting a case report discussing the importance of understanding the molecular biology and use of targeted therapeutics to improve survival in such unusual entity.

Keywords: LCNEC, ALK fusion, ALK inhibitors, Alectinib, Lorlatinib.

Introduction

Lung cancer is the second most common cancer worldwide and is most common cause of cancer related deaths. There are various common types of lung cancer such as small cell carcinoma and non-small cell variants including squamous cell carcinoma, adenocarcinoma and other rare variants such as oat cell carcinoma, large cell carcinoma, carcinoid tumor and large cell neuro endocrine carcinoma.[1]

Large cell neuro-endocrine carcinoma [LCNEC] of lung is a rare entity and LCNEC with ALK-EML4 fusion is even rarer. ALK fusion is seen in adenocarcinoma of lung patients. ALK-EML-4 fusion is seen in about 2% to 5% of non-small cell lung cancer patients. In studies using SEER data, age adjusted incidence of pulmonary LCNEC is 0.3 per 100,000 with a rise by 0.011 people per 100,000 per year from 2004-2015. It is even rarer in other variants such as large cell neuro endocrine tumors with less than 10 cases reported in literature.[2-10]

Here, we present a case report of metastatic ALK-EML-4 fusion positive large cell neuro endocrine carcinoma of lung.

Case Report

A 44 year old male resident of Ahmedabad, non-smoker presented with dry cough, intermittent fever and significant weight loss for 3 months. On examination there was a right supra clavicular (SCF) node and on chest x-ray there was widening of mediastinum and mild pleural effusion. CT chest revealed a large conglomerated lymph nodal mass involving right lower para tracheal and pre-vascular region and multiple pleural based nodules. Excision biopsy from right supra clavicular node was done which showed possibility of medullary carcinoma of thyroid. Immunohistochemistry revealed possibility of medullary carcinoma or large cell neuro endocrine carcinoma. Serum calcitonin was normal and thyroid imaging showed no lesion involving thyroid and was diagnosed as large cell neuro endocrine carcinoma of lung with pleural and lymph nodal metastasis.

Whole body PET-CT showed right lung upper lobe mass lesion with multiple nodular pleural lesions involving right pleura, mediastinal and right supra clavicular nodal metastasis and liver metastasis. Patient received 3 cycles of chemotherapy (carboplatin plus etoposide) and was re-evaluated with whole body PET-CT which showed regression in size of pleural nodules and mediastinal nodules but new appearance of bone metastasis in skull and vertebrae and clinically patient was worsening with continued weight loss.

Patient presented to us (The Gujarat Cancer & Research Institute, Ahmedabad.) with ECOG-3 performance status and weight on presentation was 30 kgs. Patient had continuous projectile vomiting which was investigated with MRI brain which revealed multiple cerebral and cerebellar metastasis. Patient received whole brain radiotherapy of 30 GY in 10 fractions. Biopsy sample from right supra clavicular node was sent for Next Generation Sequencing (NGS) which revealed EML4-ALK fusion and other variants

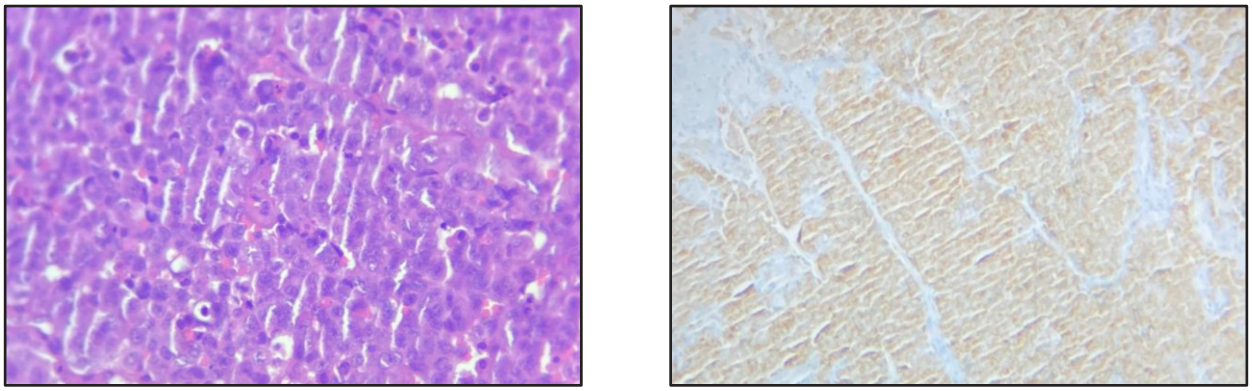

Figure 1: Showing SCF Node Histology on Microscopy and ALK Fusion by Immunohistochemistry

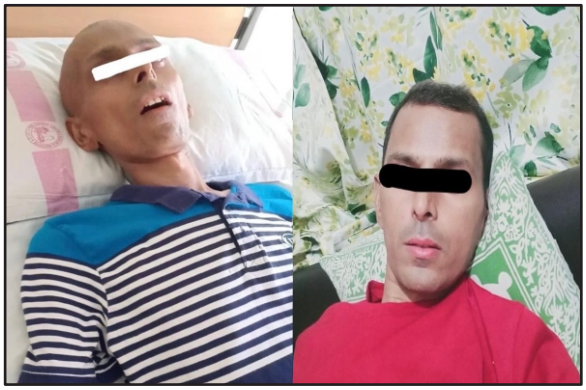

Figure 2: Comparision of Pre Treatment PET CT with Post 4 Months of ALK Inhibitor Therapy

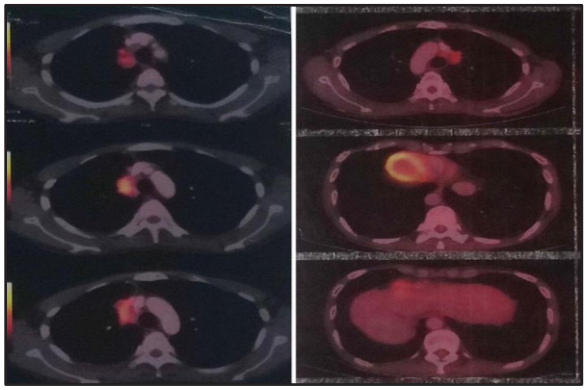

Figure 3: Showing Pre Treatment and Post Treatment General Condition of Patient after 4 Months of ALK 4 Inhibitor Therapy

of unknown significance such as ATR and PTEN mutation. ALK fusion was confirmed by IHC as shown in Figure 1, patient was started on second generation ALK inhibitor, alectinib 600mg BD plus denosumab for bone metastasis.

Results

Patient tolerated Alectinib well and was clinically responding with decrease in cough and increasing weight. After 4 months of therapy patient's weight increased to 35 kgs as shown in Figure 3 with complete resolution of symptoms like cough and fever, patient's performance status improved to ECOG 1 and he started attending his office. Whole body PET-CT revealed significant reduction in size and metabolic uptake of pleural and lymph nodal lesions as shown in Figure 2. Alectinib and Denosumab was continued for 5 more months. Patient's weight increased to 45 kgs with ECOG PS-1.

Re-evaluation PET CT revealed ametabolic sclerotic bone lesions, increase in size and uptake of mediastinal lymph nodal lesion with re appearance of mild pleural effusion suggestive of progression. MRI brain revealed new brain lesions for which patient received whole brain re-irradiation (20 Gray in 10 fractions).

Patient was started on 3rd generation ALK inhibitor, Lorlatinib 100 mg once daily. Patient received Lorlatinib for 3 months. Two months of Lorlatinib therapy improved patient's general condition but after 3rd month of therapy patient presented to emergency with poor performance status and severe weight loss and was managed symptomatically. Patient eventually expired after 15 days of inpatient care.

Discussion

LCNEC is a rare lung cancer which is treated with surgery and adjuvant chemotherapy if patient presents in early stage. For metastatic disease platinum based chemotherapy is the chemotherapy of choice. It is treated similar to the small cell carcinoma due its similarity with small cell carcinoma of lung.[11-12]

But large cell carcinoma of lung rarely harbour ALK fusion and other mutations which may be targeted using targeted therapies. This also shows the importance of molecular testing in such rare cases. Our patients NGS has also revealed other variant mutations of unknown significance such as ATR, PTEN (tumor suppressor genes).

Previously it has been reported that ALK positive LCNEC is not responsive to crizotinib[5] as

expected but our patient had responded well to alectinib similar to a case reported from Japan.[13] The good response to ALK inhibitor-alectinib is mostly due to the fact that the patient was a young, non-smoker and had better cancer biology unlike other patients.

Conclusion

Pulmonary LCNEC is a rare, aggressive entity with dismal prognosis. Patient must be evaluated thoroughly with all available investigations including next generation sequencing. Particularly in non-smoking patients ALK by IHC can also be done in patients with limited resources.

ALK-EML4 fusion positive pulmonary LCNEC do respond to alectinib/lorlatinib and should always be considered before starting chemotherapy due to better quality of life and ease of administration with targeted therapy.

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Isolated CNS Relapse in a Case of Pancreatic Plasmablastic Lymphoma

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Summary

Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL). With features overlapping with myeloma and lymphoma coupled with its relapsing, aggressive clinical course and lack of consensus regarding standard treatment in the upfront and relapsed setting, PBL poses a diagnostic and therapeutic challenge and has a dismal prognosis with multi-agent chemotherapy. An isolated central nervous system (CNS) relapse of plasmablastic lymphoma associated with HIV infection in a 28 year old patient is reported here. He presented with altered sensorium and quadriparesis. He was evaluated outside with fluorodeoxyglucose positron emission tomography (FDG-PET) and magnetic resonance imaging (MRI) of brain which showed multiple parenchymal metastases in left cerebral hemisphere. He underwent whole brain radiotherapy (WBRT) outside and was referred to our institute for further management. He was treated with salvage chemotherapy regimen comprising of dexamethasone, cytarabine and cisplatin (DHAP). Despite best efforts, the patient succumbed after receiving one cycle. Our objective is to report the unusual site of disease coupled with the unique nature of relapse and review the complexity in diagnosis and treatment.

Keywords: Plasmablastic lymphoma; relapse; unusual; HIV

Introduction

Plasmablastic lymphoma (PBL), first described in the oral cavity of a patient infected with human immunodeficiency virus (HIV) in 1997,[1] is a rare and aggressive lymphoma. It was recognized by World Health Organization (WHO) as a variant of diffuse large B-cell lymphoma eleven years later.[2] The B cell nature and clonal origin along with an immunophenotype of a plasma cell with cells showing an immunoblast morphology makes the diagnosis of PBL challenging.[3] Since the original report, PBL has been described in a variety of both sites and clinical settings. It occurs predominantly in HIV infected population but it can also affect immunocompetent individuals, post-transplant patients and patients with other immuno deficiencies.[3] There are no standard guidelines in the management of PBL due to the rarity of this disease. Due to its aggressive and relapsing natural history, along with lack of standard treatment guidelines and difficulty in diagnosis, PBL is a challenging disease to treat and has a dismal outcome.[3]

Case Report

A 28 year old male was diagnosed with HIV infection in December 2021 and was started on antiretroviral therapy. His CD4 count at diagnosis was 53/uL. He presented with abdominal pain and vomiting since 2 months. A contrast enhanced computed tomographic (CECT) scan of abdomen and pelvis revealed a 9.6 x 6.6 x 8.9 cm mass involving head and uncinate process of the pancreas along with liver and bony metastases as shown in figure (Figure 1).

A tru-cut biopsy of the pancreatic mass and subsequent histopathological examination showed medium to large round plasmacytoid cells. Immunohistochemistry (IHC) showed atypical cells positive for CD-138, CD79A, c-MYC, CD10, MUM-1 and negative for Bcl-2, Bcl-6, CD30, CD3, Tdt, kappa and lamba light chains with Ki-67 of 80-85%. A chromogenic in situ hybridization (CISH) showed Epstein Barr virus–encoded RNA(EBER) positive.

He received treatment at a tertiary care hospital and his treatment record revealed that he was started on pulse dose of prednisolone followed by 6 cycles of Dose-adjusted EPOCH (etoposide, prednisone, vincristine, doxorubicin and cyclophosphamide). A FDG PET/CT dated 17th august 2022 showed complete metabolic response. After a disease free interval (DFI) of 4 months, a FDG PET/CT done on 27th December 2022 showed multiple hypermetabolic lesions involving left cerebral cortex (Figure 1). He received WBRT (10#/30Gy) till 23rd January 2023 and was referred to

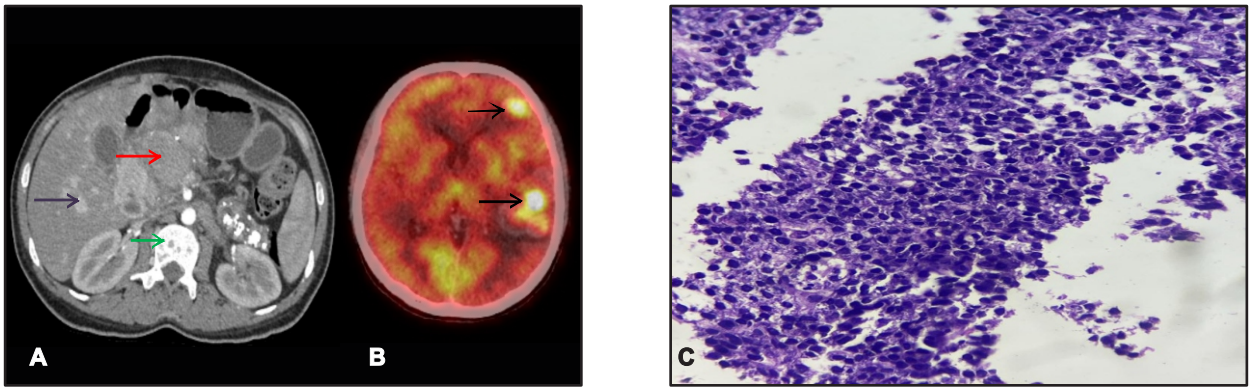
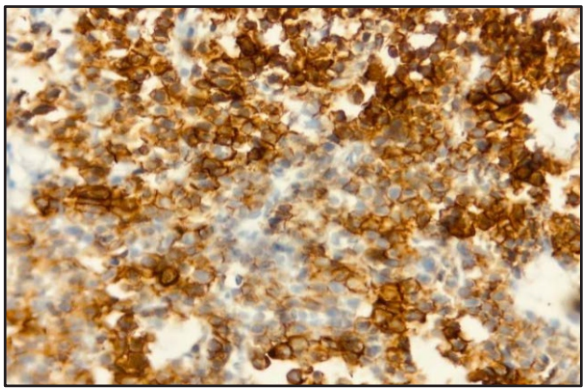
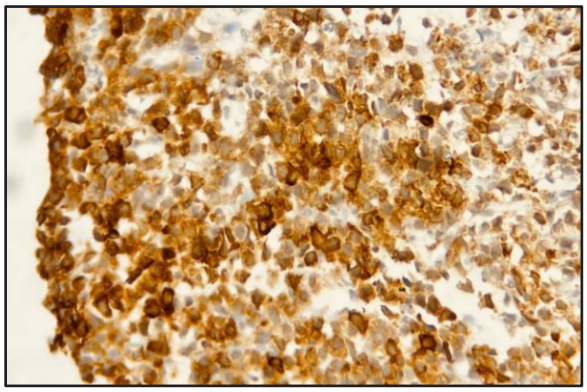


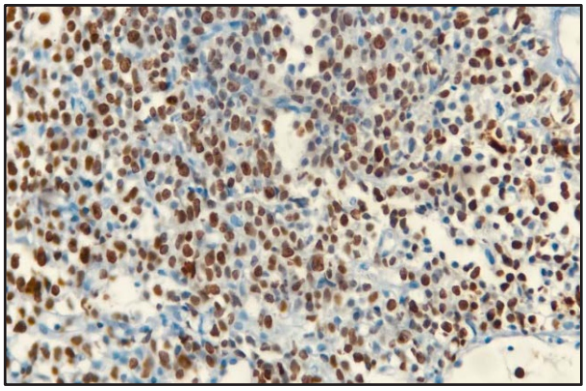
Figure 1: Clockwise from top left- **A)** CT imaging of the abdomen showing pancreatic mass (red arrow), hyperdense liver lesions (purple arrow) and lytic lesions in vertebral body (green arrow) **B)** FDG-PET showing hypermetabolic lesion in left cerebral hemisphere (black arrows) after DFI of 4 months **C)** Histopathology of pancreatic biopsy shows sheets of atypical medium sized to large cells with round nuclei displaying vesicular chromatin and distinct nucleoli with moderate amphophilic cytoplasm and brisk mitotic activity



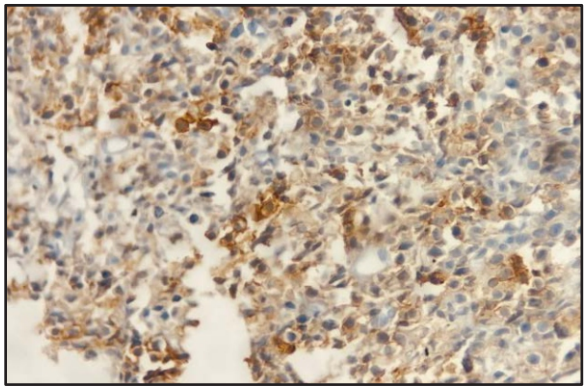
A) CD138 positve



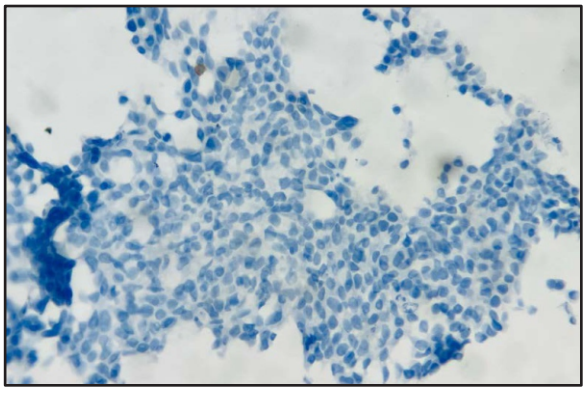
B) CD79a positive



C) MUM 1 positive (nuclear)



D) CD38 positive



E) CD20 negative

Figure 2:IHC showing cells positive for A)CD138, B) CD79a, C) MUM 1, D) Cd38 and negative for E) CD20

our institute for further management. Blood investigations including complete blood count, liver function tests, renal function tests and lactate dehydrogenase were within normal limits. The pancreatic biopsy and histopathology review was done at our institute (Figure 1). IHC showed cells that were positive for CD79a, CD38, CD138, MUM-1 and negative for CD20, CD3, PAX 5, AE1, synaptophysin (Figure 2). His cerebrospinal fluid examination was haemorrhagic. Bone marrow aspiration and trephine bone biopsy, serum protein electrophoresis, immunofixation and free light chain assay done to rule out plasmablastic myeloma were found to be normal.

He was started on DHAP as a salvage regimen but unfortunately the patient died of infectious complications secondary to neutropenia despite prophylaxis with pegylated granulocyte stimulating factor.

Discussion

PBL accounts for 2% of HIV-related lymphomas in incidence. The association of PBL with HIV and EBV coinfection occurs commonly, but its occurrence in patients with autoimmune disorders, lymphoproliferative disorders and in those who have undergone solid organ transplantation has also been described.[4] PBL has a tendency to involve extra medullary sites like oral cavity (most common), lung, bone, sinus, testicles and gastrointestinal tract.[5] At first presentation, our patient had a pancreatic mass and at relapse, he had involvement of left cerebral hemisphere.

PBL is thought to originate from plasmablast, an activated B cell that has undergone somatic hypermutation and class switching recombination.[4] The cells in PBL show an immunoblastic morphology with an immunophenotype suggestive of plasmacytic differentiation with CD38, CD138, IRF-4/MUM-1 and BLIMP-1and negative for B-cell markers CD19, CD20 and PAX-5.[4] EBER is expressed in 70% of the cases & it is the most sensitive method of detecting EBV infection within malignant cells and is more commonly seen in HIV-positive patients (75%). Plasmablastic or anaplastic multiple myeloma is the closest differential as they may be morphologically and immunophenotypically identical to PBL.[4] Features that are in favour of PBL include an association with HIV infection and EBER positivity in neoplastic cells while monoclonal paraproteinemia, hypercalcemia, renal dysfunction and lytic bone lesions favour myeloma.[4] Our patient's investigations showed EBER positivity but also had multiple lytic lesions. But further investigations such as protein electrophoresis, immunofixation, trephine bone biopsy showed absence of monoclonal protein and absence of bone marrow plasmacytosis.

Cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) is not considered adequate therapy[4,5] and current guidelines favour more aggressive regimens such as infusional EPOCH,[6] cyclophosphamide, vincristine, doxorubicin, methotrexate alternating with ifosfamide, etoposide, and cytarabine (CODOX-M/IVAC),[7] or hyper fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with methotrexate and cytarabine (hyper-CVAD).[8] There is a high risk of CNS progression at time of initial treatment or during relapse which makes intrathecal CNS prophylaxis essential.[4,9] Although our patient had complete remission post EPOCH, he did not receive intrathecal CNS prophylaxis while being treated elsewhere which could explain the isolated disease recurrence in the CNS within three months.

Conclusion

PBL is a rare disease, typically extranodal in nature, can have unusual presentations both at diagnosis and at relapse. Differentiating this entity from myeloma is important. Intrathecal CNS prophylaxis is an essential component in the management of PBL. The disease poses challenges in diagnosis, treatment and has a dismal outcome. Ideal management strategy has not been established in the relapsed setting.

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A Rare Case of Primary Neuroectodermal Tumor of the Ovary-Ependymoma

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Summary

Primary ependymoma of the ovary is a rare entity, very few cases of which have been described in the literature. There is still no uniform consensus on the management of these cases. Here we are presenting a case of an 18-year-old girl, who came with a history of abdominal distension for 2 months and loss of appetite. Imaging revealed the presence of a large adnexal mass. She underwent fertility sparing surgery with the removal of the adnexal mass with surgical staging. On gross examination, there was a well encapsulated cystic mass with papillary projections. On microscopic examination, perivascular pseudo rosettes were seen. On immunohistochemistry, GFAP was positive. Hence a final diagnosis of ependymoma was made. She received postoperative adjuvant chemotherapy withbleomycin,etoposide and cisplatin. The patient is alive and her menstrual cycles have resumed. Despite being a rare entity, ependymoma should always be included in the differential diagnosis of adnexal masses in young women.

Keywords: Primaryneuroectodermaltumor, primary ependymoma, ovarian ependymoma

Introduction

Ovarian ependymoma is an extremely rare gynaecological malignancy, classified under the category of neuroectodermal tumors of the ovary.Given its extreme rarity, it poses numerous diagnostic and treatment challenges. The clinical behaviour, molecular profile, and optimal therapy are incompletely characterised.[1]

Ependymomas, usually arise from the central nervous system and are classified under gliomas. It can easily be misdiagnosed as a case of mature cystic teratoma. Although histogenesis has not been fully elucidated, they are thought to represent monodermal teratomas of neural type.[2] Kleinman was the first person to describe a case of ovarian ependymoma in 1984.[2] Since then, 36 cases have been reported in the literature, two of which have been described during pregnancy.

Here we describe a case of an18-year-old girl with ovarian ependymoma diagnosed and managed at our institute, GCRI (Gujarat Cancer & Research Institute)

Case Report

An 18-year-old, unmarried girl was referred witha CT scan report showing a right adnexal mass of 10x16x17cm.

She complained of abdominal distension for 2 months and loss of appetite and indigestion for 15days.She had attained menarche at the age of 14 years and her menstrual cycles were regular since then with no history of excessive bleeding/scanty menses. She had no urinary or bowel disturbances. Her medical and family history was unremarkable. On clinical examination, there was a 26-28weeks size mobile cystic mass, that felt separate from the uterus.

An outside CT scan was reviewed at our centre, which revealed a well-defined multiloculated cystic lesion of 10x16.8x17.3cm arising from the right adnexa. The lesion showed heterogeneously enhancing solid components within. The right ovary was not seen separately from the lesion. Minimal free fluid present. The left kidney could not be visualised, which was an incidental finding (Figure 1). An ultrasound done at our institute showed the same findings and characteristics of the lesion.

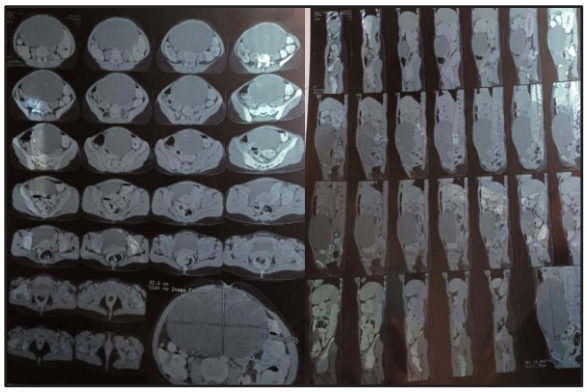

Figure 1: CT scan images showing a large predominantly cystic adnexal mass occupying the whole pelvis in axial and sagittal sections

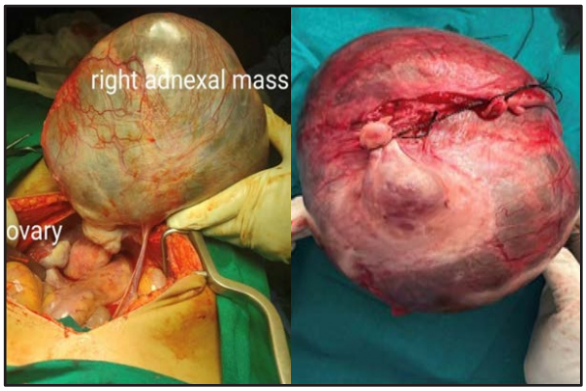

Figure 2: Intraoperative finding: Cystic adnexal mass of 17x14cm with few papillary projections

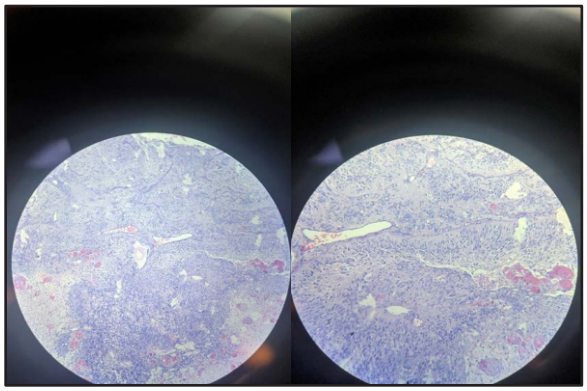

Figure 3: Microscopy findings: Perivascular pseudorosettes

Her tumor markers were as normal(CA-125=24 U/ml, HE-4= 52pmol/L, CEA- 1.8 ng/ml, alpha-fetoprotein= 1.68ng/ml, beta HCG<0.2 IU/ml, LDH=176 U/L).

She underwent a staging laparotomy in June 2022.Intraoperatively a large cystic mass of 10x12cm was noted in the right adnexa. Peritoneal washings were obtained. The mass was removed and sent for a frozen section. The opposite ovary and uterus were inspected for disease. On exploration, there was no evidence of disease in the abdomen and pelvic cavity, under surface of the diaphragm, omentum and mesentery. The frozen report turned out to be a benign ovarian lesion with a probable diagnosis of cystic teratoma. There was no evidence of disease apart from the right ovary. Fertility sparing surgery was planned for her. She was treated with unilateral salpingo-oophorectomy and a large omental biopsy and peritoneal washings were taken. The final histopathology report was ependymoma of the ovary

Gross Examination

There was a well-encapsulated right adnexal mass measuring 17x13.5x10cm. The external surface of the tumor showed nodularity and papillary projections. The largest papillary projection measured about 4x4x2cm. Ovarian surface involvement was present. The omentum was free of tumor (Figure 2). On the cut section, it was solid, friable, soft, and dull grey in colour, with areas of haemorrhage and necrosis. The peritoneal cytology was negative for malignant cells.

Microscopy

Perivascular pseudo rosettes, characteristically described for ependymomas were seen. These pseudorosettes were formed by tumor cells surrounding blood vessels like the"spokes of a wheel". Ependymal rosettes comprising tumor cells encircling a lumen were also seen. There was no evidence of lympho vascular space invasion (Figure 3).

Immunohistochemistry (IHC)

IHC staining by the immunoperoxidase method showed strong positive staining for glial fibrillary acidic protein(GFAP)
The detailed report was as follows:
AE1-Occasional focal positive
EMA- dot like positive
GFAP-positive
S100-positive
Inhibin- occasional cell positive
Synaptophysin-negative
AFP-equivocal
OCT ¾- negative
CK7-few cells focal positive
M1B1- 8-10%

The patient was diagnosed to have Stage 1c ovarian ependymoma. The patient received 3 cycles of adjuvant therapy with Bleomycin, Etoposide and Cisplatin, the last cycle concluded in November 2022. She has been advised regular follow up.

Discussion

Extra-cranial ependymomas have been described in the extraspinal, and sacrococcygeal regions, in pre-sacral tissues and the sacrum as well. Other locations include the ovary, Para ovarian tissues, broad ligament, omentum, mediastinum and the lung. The World Health Organization's (WHO) Histological Classification of Ovarian Tumor has classified ovarian ependymomasunder ''Neuroectodermal Tumors", which are monodermal teratomas. Monodermal teratomas are defined as germ cell tumors derived from a single germ layer. It may comprise neuroectodermal, vascular, sebaceous and mucinous tissues.[2]

Primary neuroectodermal tumors of the ovary are further classified under 3 groups: (1) Differentiated group: ependymoma, astrocytoma, and oligodendroglioma; (2) Primitive tumors: neuroectodermal tumors (PNETs), neuroblastoma, ependymoblastoma, medulloblastoma, and medulloepithelioma; (3) Anaplastic group: glioblastoma multiforme.[2]

The differentiated type– ependymoma of the ovary usually presents at a younger age but can occur in a wide age range (6–69 years). It usually presents with unilateral mass and without the extra-ovarian disease.Usually arising from the central nervous system, ependymoma is a glioma with differentiation toward ependymal cells. These cells are located in the spinal canal or the wall of the ventricles. In very rare cases, they arise from an ovarian teratoma.[2]

Ovarian ependymomas may often cause diagnostic dilemmas because of highly variable histology and hence mimicking other common conditions. The histological picture may harbour papillary areas with psammoma bodies, pseudo follicles, trabeculae, and microcysts, and may mimic other ovarian tumors such as struma ovarii, granulosa cell, Sertoli-Leydig cell, serous, and Wolffian tumors. Ependymomas can be falsely reported as mature teratomas as occasionally glial and ependymal elements have been observed in them.[3]

Many surface epithelial and stromal tumors, specifically serous and endometrioid borderline tumors and carcinomas, sex cord-stromal tumors, including Sertoli-Leydig cell tumors and granulosa cell tumors and certain tumors of Wolffian origin can resemble ependymomas and lead to diagnostic errors. The combination of long fibrillary cytoplasmic processes, the perivascular rosettes, and GFAP-immunopositivity helps the pathologist in clinching the diagnosis of ependymoma.[3]

IHC plays a very important role in the identification of ependymoma of the ovary. The classical marker is GFAP. In our case, GFAP and S100 were positive and EMA was dot positive which helped in the diagnosis. Hence the final histopathology in our case was reported as ependymoma.

The treatment of malignant germ cell tumors serves as a guide for the management of ovarian ependymomas as very few cases have been reported in literature. The treatment consists of surgical debulking followed by adjuvant chemotherapy. In cases of fertility preservation, surgical debulking includes removal of the adnexal mass, peritoneal washings, omentectomy, exploration and excision of all the disease while preserving the opposite ovary and the uterus. In those women who do not desire future fertility, surgical debulking involves total abdominal hysterectomy, bilateral salpingo-oophorectomy, comprehensive staging and removal of all the macroscopic disease.

In the cases reported so far in the literature, the traditional first-line chemotherapy regimen consisting of bleomycin, etoposide and cisplatin(BEP) for germ cell tumors has also been proven to be effective for ovarian ependymomas. Hinoe et al. have suggested an effective second-line therapy incorporating paclitaxel, ifosfamide, and cisplatin therapy in cases resistant to BEP therapy.[4] Our patient received BEP as adjuvant therapy.

A case reported by Takano et al illustrated that even in Stage 3c ovarian ependymoma, fertility sparing approach followed by adjuvant chemotherapy can be employed for the successful management of these tumors. After 16 months of follow up, the patient reported regular menstrual cycles and no evidence of recurrence during follow up in their study.[5]

Sevil Sayhan et al also reported a study in which a fertility sparing surgery was done on a 33-year-old woman diagnosed with ependymoma on a background of monodermal ovarian teratoma followed by adjuvant chemotherapy. The patient was alive with no signs of recurrence on 3 years follow up.[6] This case also illustrated the diagnosis and management of ependymoma in a young woman of reproductive age group utilising a fertility sparing approach in early-stage cases.

Other options such as hormone therapy including aromatase inhibitors and the use of GnRH analogues are also being explored as alternatives to chemotherapy in these tumors.

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Presentations at Clinical Meetings

(January 2023 to June 2023)

Sr No.	Date	Speaker/Department	Title
1	09.01.2023	Gandhi Jhanvi Oncopathology	Current Prognostic and Predictive Biomarkers for Endometrial Cancer in Clinical Practice. Recommendation / Proposal from the Italian Study Group
		V Priyanka Gynaecological Oncology	A Study on Correlation Between Preoperative Diagnostic Parameters and Clinicopathological Features in Borderline Ovarian Tumors
2	23.01.2023	Raiya Birva Immunohematology Lab	Leukemia Stem Cell Frequency at Diagnosis Correlates with Measurable / Minimal Residual Disease and Impacts Survival in Adult Acute Myeloid Leukemia
		Jain Khushboo Medical Oncology	Oligometastases: Emerging Evidence
3	21.02.2023	Pawar Ajinkya Surgical Oncology	Basic Principles of CRS and HIPEC with Intraoperative and Postoperative Management
		Shah Anand Community Oncology	Consideration of Single-Dose HPV Vaccination from the SAGE (Strategic Advisory of Experts) Perspective
4	28.02.2023	Raval Lekha Palliative Medicine	Safety and Efficacy of Povidine-Iodine Pleurodesis in Malignant Pleural Effusions
		Mistry Mittal Molecular Diagnostics & Research Lab-I	A Custom DNA Based NGS Panel for the Molecular Characterization of Patients with Diffuse Glioma: Diagnostic and Therapeutic Applications
5	15.03.2023	OzaVikramaditya Neuro Oncology	Dilemma Over Dorso Lumbar Junction Lesion
		Bhatt Harikrushna Radio Diagnosis	Bone Tumors: Imaging Features of Common and Rare Benign Entities
6	29.03.2023	Gajjar Kinjal Molecular Diagnostics & Research Lab-II	Next-Generation Sequencing Targeted Panel in Routine Care for Metastatic Colon Cancers
		Ratanchandani Krishna Radiation Oncology	Role of Extra Corporeal Radiotherapy in Bone Tumors
7	22.06.2023	Khoja Jasmin Physiotherapy	Clinical Benefits of Facial Nerve Monitoring During Cerebellopontine Angle Surgery
		Nasir Imran Surgical Oncology	Usage of 3D Model (RPT) in Head and Neck Malignancy

About the Journal and Instructions to Authors

About the Journal

Gujarat Cancer Society Research Journal is a biannually (April and October) peer-reviewed journal published by the Gujarat Cancer Society (formerly published as GCS Research Bulletin). The journal's full text is available online at http://www.cancerindia.org

Scope of the Journal

The Journal intents to cover basic, clinical, clinico-basic research and medical education carried out by the staff of the Gujarat Cancer Society and Gujarat Cancer and Research Institute related to human well being including ethical and social issues in the field of Oncology. The Journal gives preferences to original scientific papers, case reports, anecdotal reports and minireviews. It may comprise invited review articles, publish oration speeches and work presented in the clinical meetings and the journal clubs. Hence it will continue to serve as an academic-research bridge between the basic sciences and the applied sciences, viz. various disciplines of medicine within and outside GCS-GCRI.

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- Final approval of the version to be published. Each contributor should have participated sufficiently in the work to take public responsibility for appropriate portions of the content of the manuscript.

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2. Case report: It should have maximum limit up to 1000 words (excluding summary and references) and should have the following headings: summary (unstructured - max. 200 words), Keywords, Introduction, Case report, Discussion, Reference (max. up to 10), Table and Figure legends.

3. Review article: It should have summary (max. 200 words), Introduction/Historical Background, Discussion, Conclusion, References, Tables and Figure Legends.

4. Short communication: The length of it should not exceed 1000 words and References 10.

Note: Discussion and conclusion can be combined in one section. Please do not add numbers before subtitles. Write subtitles and headings in sentence case.

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Include in the title page the manuscript title, author's name(s), affiliations, and corresponding author's phone/fax number and/or email. The name of the department(s) and institution(s) to which the work should be attributed

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Language and grammar
- Uniformly American English
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- Originality (truly original or known to you through foreign or specialist publications or through the grapevine)
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- Methods adequately described?
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Nuclear Medicine Department

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Introduction

Nuclear medicine is a medical specialty that uses radioactive substances, called radiopharmaceuticals, to diagnose and treat disease. Radiopharmaceuticals are made up of two parts: a radioactive atom and a carrier molecule. The radioactive atom gives off radiation, which can be detected by special cameras. The carrier molecule helps the radiopharmaceutical travel to the specific organ or tissue that the doctor wants to study.

There are three main uses of nuclear medicine:

- **Diagnosis:** Nuclear medicine scans can be used to diagnose a variety of diseases, including cancer, heart disease, gastrointestinal disorders, and neurological disorders. The scan can show how the organ or tissue is functioning and whether there are any abnormalities.
- **Treatment:** Nuclear medicine can also be used to treat cancer. Radioactive substances are used to deliver a targeted dose of radiation to cancer cells. This can help to destroy the cancer cells while minimizing damage to healthy tissue.
- **Research:** Nuclear medicine is also used in research to study the body's functions and to develop new treatments for diseases.

Major Milestone of Nuclear Medicine Department of GCRI

- Started with rose bengal labelling of 131 Iodine in late 1980s
- Department and Gujarat received its 1st Single headed Gamma Camera with help of British High Commission in 1994
- Gujarat 1st radio-iodine ward was established in 2002 in GCRI, Ahmedabad
- Single headed Gamma Camera was replaced with Dual headed Camera in 2007
- Department and Gujarat received its 1st PET/CT machine in 2010
- Second PET/CT machine was established in 2018

Current Equipment and Services available at Department

- **PETCT** - Whole body FDG PETCT scan, Whole body PSMA PETCT, regional FDG PETCT scan, Cardiac FDG PETCTscan and Brain FDG PETCT scan.
- **SPECT** : Bone scan, DTPA, DMSA, HIDA, Sulphur colloid scan, Thyroid scan, GI bleed scan, Meckel scan, HYNIC TOC scan, para thyroid, Milk scan, Salivary scan, Sentinel scintigraphy and MUGA scan.
- **Therapeutic** - High dose radioiodine therapy and low dose radioiodine therapy.

Future Prosepects of Department

- Department is planning into make itself a completely self-reliant for its radiopharmaceutical needs.
- For this ambitious target honorable Chief Minister of Gujarat has approved 1st state aided Cyclotron Project in May 2023 and the project is expected to be completed in next 18-24 months.
- As all of us are aware of rising cases of cancers in parts of world and to meet demand of higher diagnostic facilities for these patients, Department is planning to setup a new advanced diagnostic facility which will includes all technologically advanced diagnostic machines such as Digital PET/CT machine, SPECT/CT machine and PET/MR machines
- "If cancer is curse than radiation is boon to society" this dictum very well explained the upcoming role of radiation in cancer treatment and for same department is planning to setup a 20 bedded ward specifically designed for various radiation based therapies
- Medicine is a continuous evolving branch and to fulfill the moto of research given by our institute, department is planning to setup an advanced animal research facility with animal PET/CT machine installation.

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Nuclear Medicine Department

Gamma Camera Spect - 1

PHILIPS - PET CT Machine

GE - PET CT Machine

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