ORIGINAL ARTICLE

SINONASAL AND ORBITAL MALIGNANT NEOPLASMS IN PEDIATRIC POPULATION: A STUDY FROM A TERTIARY CARE CENTRE IN INDIA

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ABSTRACT: INTRODUCTION: Paranasal and extra-ocular orbital malignant tumors are comparatively rare in pediatric patients and difficult to diagnose early. Malignant lesions in this region tend to be locally aggressive, often presenting at an advanced stage. Non osseous, extra ocular orbital tumors represent a different histologic spectrum in children than in adults. **AIMS:** To study the spectrum of malignant lesions of paranasal sinuses and orbital area in patients under 18 years of age. **MATERIALS AND METHODS:** A retrospective and prospective study was done from July 2004 to June 2014. Malignant paranasal and orbital neoplasms were recorded including clinico-radiological and cytological data. Review of histopathological slides along with immunohistochemistry (IHC) of selected cases were done. **RESULTS:** Total 69 cases were recorded over the ten year period as per our inclusion criteria. Out of these, 46 (67%) patients presented with malignant paranasal neoplasm and 23 (33%) with orbital mass. Most cases were found in the age group of 7-12 years, where females were preponderant. Rhabdomyosarcoma (RMS) was the commonest tumor arising in paranasal as well as in orbital area (33%). IHC aided the confirmation of our diagnoses. **CONCLUSION:** Paranasal malignancy in the pediatric population often presents with non-specific symptoms, and high index of suspicion along with better diagnostic tools like computed tomography (CT) scan is necessary for a timely diagnosis. IHC should be done in all malignant neoplasms of pediatric population to arrive at a proper diagnosis, to facilitate proper management to these patients.
KEYWORDS: Paranasal tumors, orbital tumors, children, immunohistochemistry.

INTRODUCTION: Paranasal and extra-ocular orbital malignancies are rare in young patients and difficult to diagnose early. The symptoms overlap with benign lesions; non-specific symptoms may persist for years before a neoplasm is suspected. Although CT scanning in the evaluation of presumed sinusitis is facilitating diagnosis of these lesions, it is often not affordable by many in developing countries.[1] Extra-ocular orbital lesions range from inflammatory lesions to neoplasms.[2-5] They tend to be locally aggressive and may affect vision. Additional dilemma in this age group is the morbidity associated with adjuvant treatment, including increased risk of a second primary cancer.[6] We present here a study of pediatric malignant lesions of paranasal sinuses and orbit of our institute in the last ten years.

MATERIALS AND METHODS: A retrospective and prospective study was done at the department of Pathology in collaboration with Otolaryngology (ENT) at our hospital. Patients from

birth to 18 years with the diagnosis of a malignant neoplasm of the paranasal sinuses and orbital area were included, benign tumors being excluded. Secondary orbital involvement of ocular malignancies was also excluded. The period of study was from July 2004 to June 2014. The clinical features, radiological and endoscopic findings were recorded from archival data and corroborated with the biopsy features. Data was also collected from follow up of recent patients. Resectioning of the formalin fixed, paraffin embedded archival blocks and restaining of Hematoxylin and Eosin (H & E) stains were done as required. Fine needle aspiration cytology (FNAC) slides were also studied. Special stains including immunohistochemistry (IHC) were performed when necessary to aid diagnosis. All procedures followed were in accordance with the institutional ethical standards.

RESULTS: In our study, total 69 cases were recorded over ten year period as per our inclusion criteria. Out of these, 46 (67%) patients presented with malignant neoplasm of nose/ paranasal sinuses and 23 patients (33%) in the orbital region. Maximum cases were found in the age group of 7-12 years where females were predominant. Epistaxis was the commonest mode of presentation of nasal/ paranasal malignant neoplasms seen in 14 (30%) patients followed by cheek swelling (22%). Orbital swelling was seen in 12 (52%) patients with orbital tumors. Maxillary sinus was the most common location of malignant tumors of paranasal sinuses. No case was reported in the sphenoid sinus. Archival sinonasal and orbital masses encountered in different age groups are mentioned in [Table 1]. Embryonal rhabdomyosarcoma (RMS) was found to be the commonest tumor arising in sinonasal as well as in periorbital area (33% of all tumors). The second most common tumor in the sinonasal area was Primitive neuroectodermal tumor (PNET) (12%) where maximum cases were in the age group of 7-12 years and all were reported in the maxillary antrum. Another three cases were encountered in the orbital region. In all it accounted for 13% of our tumors. [Table 1]

In our study five cases (11%) of Non-Hodgkin lymphoma (NHL) of nasal/ paranasal sinuses and six cases (26%) of orbital region were encountered. Leiomyosarcoma (LMS), fibrosarcoma (FS), germ cell tumour (GCT), synovial sarcoma (SS), osteosarcoma (OS) were also found in our study as 5%, 7%, 2%, 8% and 4% respectively. Six cases (26%) of alveolar soft part sarcoma (ASPS) were encountered in orbital region where most were between 13-18 yrs.[Table 1] In our study out of 69 cases of paranasal sinuses and orbital region 48, 12, 4 & 5 cases were true positive, true negative, false negative & false positive respectively. So, sensitivity was 92% and specificity was 72% whereas positive predictive value was 91% in our study. [Table 2]

DISCUSSION: The sinonasal cavity extends from the nostrils to the posterior nasal septum ending posteriorly in the nasopharynx. The nasal cavity floor is the hard palate, also the roof of the mouth. Three turbinate bones project medially from the lateral walls. Four aerated paranasal sinuses namely maxillary, ethmoid, frontal and sphenoid sinus surround the nasal cavity. The commonest tumor arising in paranasal as well as in orbital area is embryonal RMS (50%) followed by NHL (25%).[7] In our study also RMS was found to be the commonest tumor. The second most common tumor in our study was NHL along with PNET. [Fig. 1]. Primary rhabdomyosarcomas

(RMS) of the nose and the paranasal sinuses occur rarely. Soft-tissue sarcomas account for about 4%-8% of all malignant disorders in the age group younger than 15 years. About 50% of these belong to the RMS category. Incidence is 4.4 per 1 million children in the white population. About 70% of new cases appear in children below the age of 10 years, with a peak between the age of 2 and 5 years.[7] The orbit is the primary site in approximately 10% of these tumors.[8] In our study 8 cases (35%) of RMS were found in the orbit. All cases were confirmed by IHC. Descriptive reviews, single-case reports, and single-institutional series have been published suggesting that rhabdomyosarcoma is the most common paranasal sinus malignancy in children, followed by lymphoma, sarcoma, and olfactory neuroblastoma.[9,10] When Ewing sarcoma (ES)/PNET occurs in the maxillary sinus, the primary symptom is facial swelling, which is sometimes accompanied by facial pain due to inflammation of the maxillary sinuses and orbital involvement.[11] Our study also corroborates these features. NHL is the second most common tumor of all pediatric head and neck tumors. [12] The disease commonly involves the nasal cavity, paranasal sinuses, or multiple regions within the sinonasal tract, comprising about 25% of all pediatric head and neck NHL.[13] Fibrosarcomas arising in the sinonasal region are uncommon. Less than 50 cases of fibrosarcomas arising in the maxillary sinuses have been reported.[14,15] Fibrosarcoma of the maxillary antrum is one of the rarest locations and only few cases have been reported in the literature.[16] Synovial sarcoma (SS) has previously been described in the frontal, maxillary, ethmoid, and sphenoid sinuses.[17] SS causes the greatest diagnostic difficulties with other sinonasal tumors when it is poorly differentiated and with small cell morphology. In this setting, cytokeratin, EMA/CEA and BCl2 immuno-reactivity facilitate a correct diagnosis. In our study we also confirm our results with immunohistochemistry and it was strongly positive for EMA. Osteosarcomas of the head and neck have a reported incidence of 1.7-5% of all head and neck primary tumors, whereas maxillofacial osteosarcomas account for 4-9% of all osteosarcomas.[18] Potera et al observed that in young patients the head and neck region is a more common site of occurrence of Alveolar soft part sarcoma (ASPS) which frequently involves the orbit.[19] Appropriate management of these diseases need detailed history taking, proper clinical examination, special radiological investigations including CT scan and nasal endoscopic examination where necessary. Finally, for confirmation of diagnosis, histopathological study and IHC has to be done. IHC is essential in diagnostic confirmation of most of these lesions due to similar histological features.[20] In our study it was found that some original diagnoses had to be changed based on the IHC results, as IHC was not done initially in those lesions: In the paranasal and orbital tumors, following discrepancies were sorted by using IHC. IHC may have some inherent problems and may give false positive or false negative results. Causes of false positive staining may be due to insufficient peroxidase blocking, necrotic cells, dried preparation, cross reactivity of antibodies. False negative results may be due to low antibody concentration, denaturation of aspirated material etc.

CONCLUSION: Malignancies arising in the paranasal sinuses are heterogeneous. Accurate classification of sinonasal small round blue cell tumors may be challenging due to overlapping clinical, radiographic and/or histopathologic features. Diagnosis may be further complicated if the biopsy material is limited in size or of suboptimal quality. Prolonged constitutional symptoms

should not be ignored in children as they may indicate an underlying neoplasm. Better diagnostic tools like CT scan should be utilized when necessary. Immunohistochemistry should be done in all malignant neoplasms of paediatric population for proper management and reduce morbidity and mortality of these patients. So, IHC can thus be established as a routine technique in the diagnosis of undifferentiated tumors.

Age	RMS		NB	PNET		NHL		LMS	FS	GCT	SS	OS	ASPS
	paranasal n= 46	Orbit n = 23	paranasal n= 46	Paranasal n= 46	Orbit n = 23	Paranasal n= 46	Orbit n = 23	Paranasal n= 46	Paranasal n= 46	Paranasal n= 46	Paranasal n= 46	Paranasal n= 46	(orbit) n = 23
0-6 yrs	7	4	1	1	1	0	1	0	0	1	0	1	0
7-12 yrs	7	4	4	3	2	1	1	1	1	0	2	1	1
13-18 yrs	1	0	3	2	0	4	4	1	2	0	2	0	5
Total	(15) 33%	(8) 35%	(8) 18%	(6) 12%	(3) 13%	(5) 11%	(6) 26%	(2) 5%	(3) 7%	(1) 2%	(4) 8%	(2) 4%	(6) 26%

Table 1: Archival Paranasal and orbital tumors in different age groups

[RMS– Rhabdomyosarcoma, NB- Neuroblastoma, PNET- Primitive Neuro Ectodermal Tumor, NHL- Non Hodgkin lymphoma, LMS- Leiomyosarcoma, FS- Fibrosarcoma, GCT- Germ Cell Tumor, SS- Synovial sarcoma, OS- Osteosarcoma, ASPS- Alveolar soft part sarcoma].

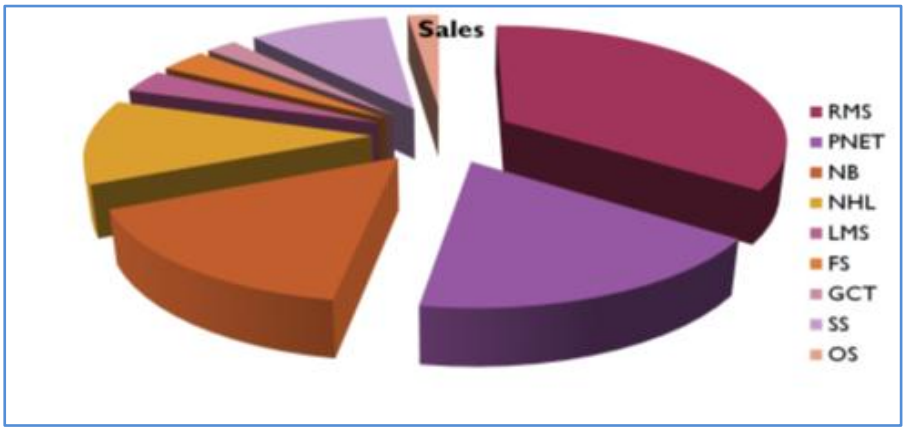

Fig. 1: Distribution of various lesions in paranasal and orbital region of children

ARCHIVAL HISTOLOGY	SITES	TOTAL NO. OF CASES (n=69)	IHC & HISTOLOGY CORRELATION	REMARKS
RMS	PNS	15	RMS- 09, Undifferentiated- 06,	TP- 09, TN- 4, FN- 2
	ORBIT	08	RMS-0 6, Undifferentiated- 02,	TP-6, FP- 1, FN-1

NB	PNS	08	NB- 05, Undifferentiated - 03	TP- 5, TN-3
PNET	PNS	06	PNET- 05, Undifferentiated - 01	TP-5, TN- 1,.
	ORBIT	03	PNET –0 2, Undifferentiated- 01	TP- 2, TN- 1
NHL	PNS	05	NHL-0 3, Undifferentiated- 02	TP- 3, TN-2
	ORBIT	06	NHL- 04, Undifferentiated - 02	TP- 4, FP-1, FN- 1
LMS	PNS	02	LMS-01, Undifferentiated- 01	TP-1, TN-1
FS	PNS	03	FS- 02, Undifferentiated-01	TP- 2, FP-1
GCT	PNS	01	GCT-01	TP-1
SS	PNS	04	SS- 03, Undifferentiated- 01	TP-3, FP-1
OS	PNS	02	OS-02	TP-2
ASPS	ORBIT	06	ASPS- 05, Undifferentiated- 01	TP- 5, FP-1,

Table 2: Comparison of original diagnoses and diagnosis after IHC (paranasal and orbital tumors)

TP= TRUE POSITIVE, TN= TRUE NEGATIVE, FP= FALSE POSITIVE, FN= FALSE NEGATIVE.

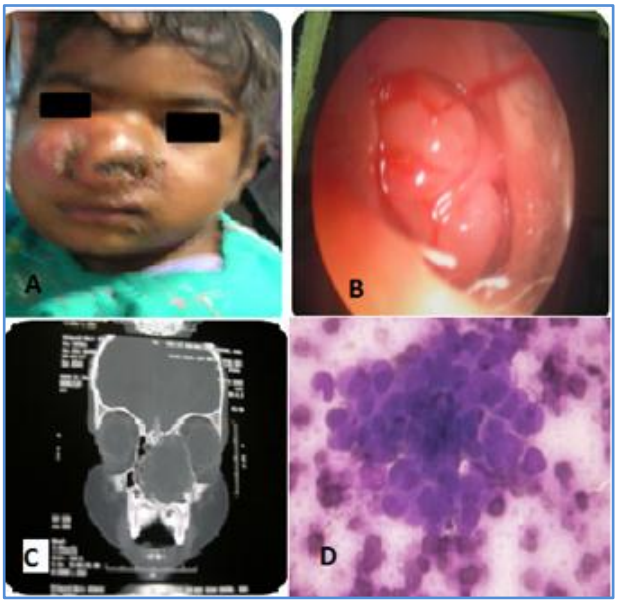

Fig. 2

Fig. 2:
A) A 6 yr child with 6x4 cm nasal mass,
B) endoscopy showing the paranasal mass,
C) CECT scan showing mass arising from maxillary antrum,
D) Paranasal mass- RMS, LG, X400.

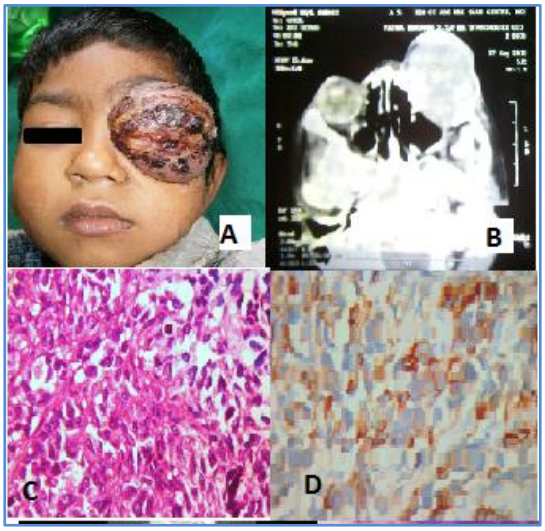

Fig. 3

Fig. 3:
A) 5 yr boy with a 7x 5 cm orbital mass,
B) CECT Scan showing homogenous left orbital mass with bone erosion,
C) RMS, H&E, x 400,
D) RMS, IHC, Desmin, x 400.

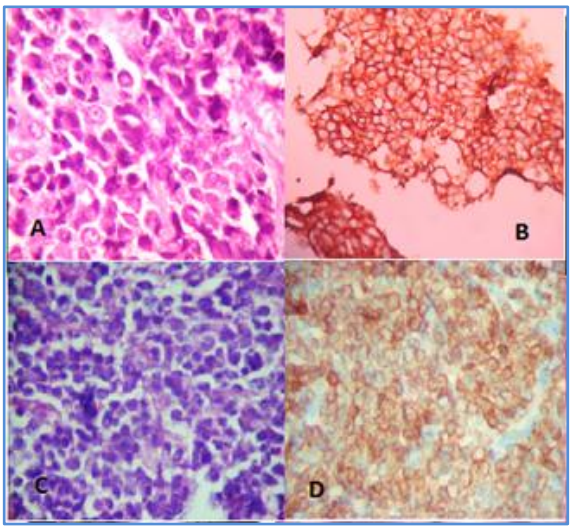

Fig. 4

Fig. 4:

A) PNET - malignant round cells with hyperchromatic nuclei and scanty cytoplasm, H&E x400,
B) PNET, IHC, CD99, x 400,
C) NHL, H&E x 400,
D) NHL, CD3, x 400.

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