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ESTHESIONEUROBLASTOMA –A CASE SERIES

Pathology

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ABSTRACT

Small round blue cell tumor is a very common diagnostic finding after intraoperative diagnostic procedures such as squash cytology or frozen section. After proper biopsy techniques, histopathological diagnosis and immunohistochemistry confirmation,a diagnosis of Esthesioneuroblastoma is established. Due to its aggressiveness and high recurrence rate, it is mandatory to diagnose this tumor as soon as possible. In our three year study period, only 3 cases of Esthesioneuroblastoma were reported in which extensive Immunohistochemistry panel played an important role to differentiate it from others and come to a conclusive diagnosis. These cases were first diagnosed through squash cytology as a small round blue cell tumor. Later it was confirmed as Esthesioneuroblastoma by histopathology and immunohistochemistry using synaptophysin, chromogranin, CD 56 & CD 99. MIB-1 played an important role in grading of the tumor according to Hyam's histological grading.

KEYWORDS

olfactory, neuroblastoma, squash cytology, biopsy, immunohistochemistry

INTRODUCTION

Esthesioneuroblastoma is an extremely rare neoplasm with an incidence of 0.4 per 1,000,000 people.1 It is a locally aggressive idiopathic neoplasm of sinonasal area arising from olfactory neuroepithelium and its clinical course is characterised by indolent growth, persistent local recurrence and occasional distant metastasis. It has a wide range of age presentation (3 – 79yrs), mostly showing bimodal age distribution which peaks around first and fifth decade2, 3. Its probable site of origin is neuroectodermal. Being more precise, it is believed to originate from sustentacular cells of olfactory neuroepithelium in upper third of nasal septum, cribriform plate and superior turbinate. It has been given various terminologies such as Olfactory placode tumor, Esthesioneurocytoma, Esthesioneuroe pithelioma, and Esthesioneuroma. It is classified into 4 grades on the basis of Hyam's histological grading. Extent and survival rate is classified by Kaddish clinical staging system as discussed later.

CASE HISTORY

As found in various studies, Esthesioneuroblastoma typically presents with unilateral nasal obstruction or epistaxis.4-6 But in the 3 cases studied in our department, following clinical features were predominantly noticed.

1. 20 yrs male presented with complaints of left sided nasal obstruction, epistaxis, headache, anosmia, dimness of vision and abnormal facies.
2. 35 yrs male presented with complaints of large tumor in frontal region (extradural lesion involving orbit and maxilla eroding bone) restricting field of vision, proptosis.
3. 4 yrs female child presented with nasal mass with difficulty in breathing

These cases were first diagnosed by intraoperative squash cytology and later confirmed by histopathology and immunohistochemistry with synaptophysin, chromogranin, CD 56, CD99, MIB1.

TABLE 1 CLINICAL FINDINGS IN THREE CASES OF ESTHESIONEUROBLASTOMA

Case	Sex	*Age(years)*	Location and size	Symptoms	Treatment	Complications	Follow-up (from diagnosis)
1	M	20	Arising from nasal cavity 7cm x 7cm x 5cm	Headache, anosmia,	Complete surgical excision of tumor cranio-facial approach	On table death due to aggressiveness	Patient died due to operative complications
2	M	35	Arising from medial orbital wall eroding maxilla and frontal bone extending to nasal cavity 8.8cm x 8.4cm x 11cm	Visual disturbances, lachrymation	Complete surgical excision of tumor followed by chemotherapy	Residual tumor left	Patient reported with recurrence.
3	F	4	Nasal mass	Nasal obstruction, difficulty in breathing	Complete endoscopic surgical excision of tumor followed by chemotherapy and radiotherapy		Patient has not reported yet with recurrence

RADIOLOGICAL FINDINGS:

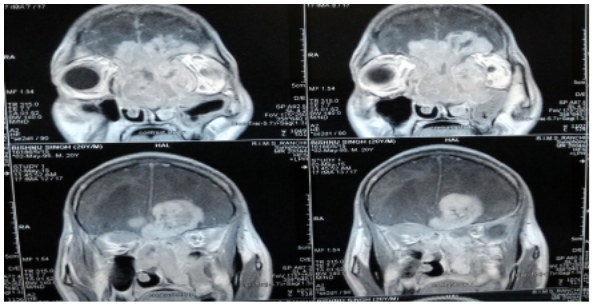


Figure1 showing large lesion of size 7cm x 7cm x 5cm heterodense mass arising from nasal cavity with extension into anterior cranial fossa and bilateral orbit, frontal ethmoidal sinus and maxillary sinus causing adjacent bony destruction.

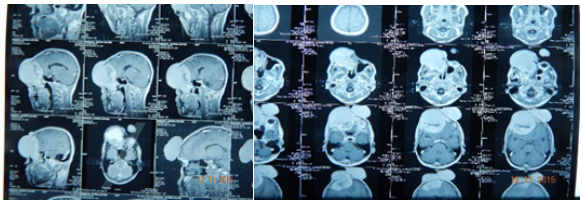


Figure 2 showing a large heterodense soft tissue lesion arising from medial wall of orbit involving orbital floor, maxillary & ethmoid nasal sinuses and nasal cavity.no midline shift .brain and optic nerve intact

TREATMENT PROVIDED:

First case: Craniofacial resection en bloc
Third case: Endoscopic craniofacial resection
Second case: Bone resection and graft placement, dacryocystorhinostomy, frontal sinusotomy.

During operative procedures, first case was described as Kadish stage D due to the tumor metastasis to distant cervical lymph nodes.

Second case was established as Kadish stage C due to extension beyond paranasal sinuses. The tumor was so aggressive that it eroded the frontal, maxillary bone and orbital wall.

Third case which affected a young child was observed as Kadish stage B due to its limitation to paranasal sinuses.

MACROSCOPIC FEATURES :

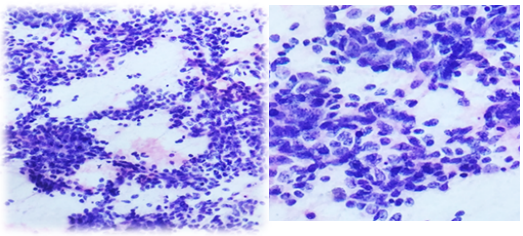
First case: It was a lobulated mass measuring 10cm x 3cm x 3 cm, greyish white in colour, firm in consistency. Cut open section showed few necrosed and calcified areas.

Second case: A 20cm x 6cm x 5cm irregular polypoidal mass was dissected. Cut open Section showed large areas of haemorrhage and necrosis.

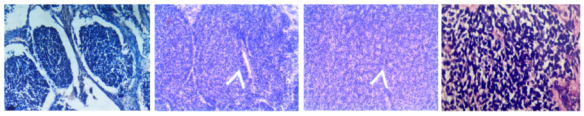
Third case: A 4cm x 3cm x 2 cm globular mass was endoscopically resected which showed no evidence of haemorrhage or necrosis.

MICROSCOPIC FEATURES -

SQUASH CYTOLOGY: Rosette like structures composed of small round cells around a fibrillary centre and cells with fragile cytoplasm and small round nuclei with speckled chromatin.



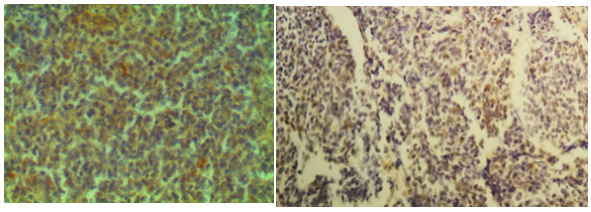
HISTOPATHOLOGICAL EXAMINATION: showed lobular architecture with uniform appearing round cells surrounded by a neurofibrillary material



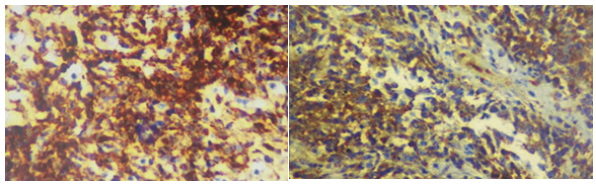
High power view shows Homer Wright pseudo-rossettes characterized by arrangement of cells in a circumferential fashion around neurofibrillary matrix but without a defining basement membrane.

High-grade neoplasm lacks neurofibrillary matrix and includes a pleomorphic cellular infiltrate with increased mitotic activity.

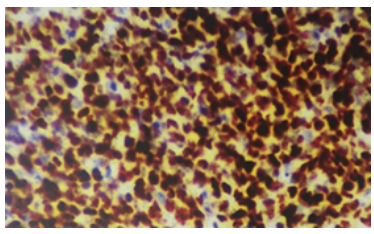
IMMUNOHISTOCHEMISTRY



SYNAPTOPHYSIN **CHROMOGRANIN**



CD 56 +ve **CD 99 +ve**



MIB-1 : 90% +ve
MIB – 1 is done to evaluate the proliferative index so that Hyam's histological grading can be done properly.

RESULTS

CASE	KADISH CLINICAL STAGING	DIAGNOSIS ON INTRAOPERATIVE SQUASH CYTOLOGY	DIAGNOSIS ON BIOPSY	HYAM'S HISTOLOGICAL GRADING
CASE 1	Stage D	Small Round Blue Cell tumor	Esthesioneuroblastoma	Grade 4
CASE 2	Stage C	Small Round Blue Cell tumor	Esthesioneuroblastoma	Grade 2
CASE 3	Stage B	Small Round Blue Cell tumor	Esthesioneuroblastoma	Grade 3

DISCUSSION

Esthesioneuroblastoma is mostly classified under two broader diagnostic terms 1) sinonasal neuroendocrine malignancies or 2) small

round blue cell tumors. The differential diagnosis which should be considered are Malignant lymphoma(NHL), primary melanoma, Plasmacytoma, Embryonal/alveolar rhabdomyosarcoma, Ewing sarcoma/ primitive neuroectodermal tumour, Sinonasal Undiffrentiated carcinoma, Sinonasal neuroendocrine carcinoma and Small cell carcinoma.

Though the patient presents with the symptoms quite late, early diagnosis is very important due to complex anatomical site and aggressiveness of the tumor. The pathologic grading system for esthesioneuroblastoma developed by Hyam's is as follows:-

Hyams' Histologic Grading System for Olfactory Neuroblastoma[341]

Microscopic Features	Grade 1	Grade 2	Grade 3	Grade 4
Architecture	Lobular	Lobular	± Lobular	± Lobular
Pleomorphism	Absent to slight	Present	Prominent	Marked
NF matrix	Prominent	Present	May be present	Absent
Rosettes	Present*	Present*	May be present†	May be present†
Mitoses	Absent	Present	Prominent	Marked
Necrosis	Absent	Absent	Present	Prominent
Glands	May be present	May be present	May be present	May be present
Calcification	Variable	Variable	Absent	Absent

Reproduced From Hyams V J 1982 Olfactory neuroblastoma (case 6). In: Batsakis J G, Hyams V J, Morales A R (eds) Special tumors of the head and neck. ASCP Press, Chicago, p 24-29

NF, Neurofibrillary.
*Homer Wright rosettes (pseudo rosettes).
†Flexner-Wintersteiner rosettes (true neural rosettes).
Grade I tumors have excellent prognosis and grade IV have worst prognosis with uniformly fatal outcome. For staging purposes, the best known and widely used system is that devised by Kadish[7] and modified by Morita.[8]

KADISH STAGING WITH MORITA'S MODIFICATION

A – limited to nasal cavity 75-90%
B – involving nasal cavity & sinuses 67-71%
C – extension beyond nasal & paranasal sinuses cavities 41-47%
D – tumor with metastasis to cervical nodes or distant sites <40%

Thus, it is important to clinically stage the tumor and histologically followed by prompt resection. It is important to follow-up the patient post-operatively due its high recurrence rate. The reported loco-regional recurrence rate in Esthesioneuroblastoma ranges from27 to 62% with most recurrences within first two years of diagnosis[9,10]

Few paraneoplastic syndromes have also been reported, most common being Syndrome of inappropriate Antidiuretic hormone secretion (SIADH).[11] Henceforth, it is important to diagnose the patient of Esthesioneuroblastoma as soon as possible and resect the tumor along with tumor margins followed by radiotherapy and chemotherapy.

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