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Original Article

Esthesioneuroblastoma – A Clinicopathological Study

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ABSTRACT

Background: *Esthesioneuroblastoma is a rare tumour accounting for only 3% of all intranasal tumors. Its proximity with important structures and aggressive behavior presents a diagnostic and therapeutic challenge. CT, MRI and histopathology forms the basic pillars of management.* ***Methods:*** *A prospective study was conducted between Feb 1998 to Feb 2004 in the Department of ENT, JNMC, AMU Aligarh. All the five patients taken up for study proved histopathologically to be cases of esthesioneuroblastoma.* ***Results:*** *Of the five patients, three presented with unilateral nasal obstruction (60%) and two with epistaxis (40%). Proptosis was present in one patient. Anosmia, headache and pain were other associated symptoms.* ***Conclusions:*** *hepatic and renal involvement occurs in patients suffering from dengue fever. Hence, multidisciplinary approach should be carried out while treating such patients.*

Key words: *Esthesioneuroblastoma, Lymphoma, Rhabdomyosarcoma, Melanoma.*

Section – ENT

INTRODUCTION

The entity described as 'esthesioneuroepitheliome olfactif' by French authors (Berger *et al* 1924) was subsequently termed olfactory nueuroblastoma and esthesioneuroblastoma by American workers (Hutter et al 1963).[1,2] These rare tumors taking origin from olfactory neuroepithelium, present a challenging differential diagnostic situation, are aggressive in behaviour and notoriously recalcitrant. Neuroepithelium is composed of the supporting cells, sensory receptor cells and basal cells. The basal cells are mitotically active and are presumably the progenitor of the olfactory neuroblastoma(ONB). It accounts for 3% of all intranasal tumors. A Clinicopathological study of esthesioneuroblastoma is presented in view of its rarity.

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METHODS

A prospective study was conducted between Feb 1998 to Feb 2004 in the Department of ENT, JNMC, AMU Aligarh. All the five patients taken up for study proved histopathologically to be cases of esthesioneuroblastoma. Patient demographics, tumour histological findings, presenting signs and symptoms, staging (Kadish & Dulguerov), postoperative complications, adjunct therapy and recurrence was examined.

RESULTS

The study was conducted in the Department of Otorhinolaryngology at J.N.M.C. A.M.U Aligarh. Five patients were taken up for study and one was discarded after it turned out to be malignant melanoma. The average age of presentation was 51 years, with male preponderance of 4:1. Of the five patients, three presented with unilateral nasal obstruction (60%) and two with epistaxis (40%). Proptosis was present in one patient. Anosmia, headache and pain were other associated symptoms. Average duration of presentation was three months. There was no past history of nasal bleeding, tuberculosis or any other contributory signs and symptoms. General examination revealed pallor in four patients (80%) and all had asthenic build. Local examination (anterior rhinoscopy) showed the

lateral displacement of the nasal septum & telecanthus with proptosis of the right eyeball in one patient. Reddish gray polypoidal growth postero-superior to middle meatus was noted in three patients and in two patients the mass was completely filling the nasal cavity. On probing it bled & had attachment superiorly. Lymph node was found in only one case (20%). Radiological study of nose & PNS were done. X-ray PNS showed fullness of right maxillary sinus (Fig. 1). CT scan PNS showed erosion of lateral nasal wall on right side, homogeneous density in the right ethmoidal region, erosion of lamina papyracea and retroorbital density (Fig 2) in one patient. CECT in four other cases showed that the disease was confined to the nasal cavity. Punch biopsy was taken in all cases & send for histopathological examination. Histopathological sections revealed a richly cellular neoplasm, consisting of small cells slightly larger than lymphocytes with round to oval mitotically inactive nuclei, sharp nuclear membranes and finely granular chromatin. The cytoplasm was scanty. The cells were arranged in diffuse and compact sheets and clusters, in focally fibrillary background (Fig. 3). Rosettes both true (Homer –Wright) and false were seen. A diagnosis of esthesioneuroblastoma was assigned.

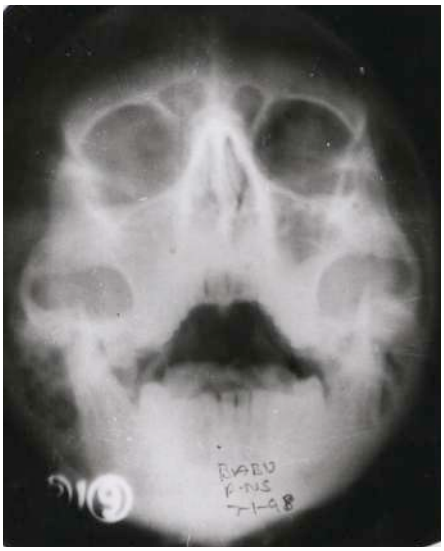

Figure 1: X-ray showing fullness of right maxillary sinus

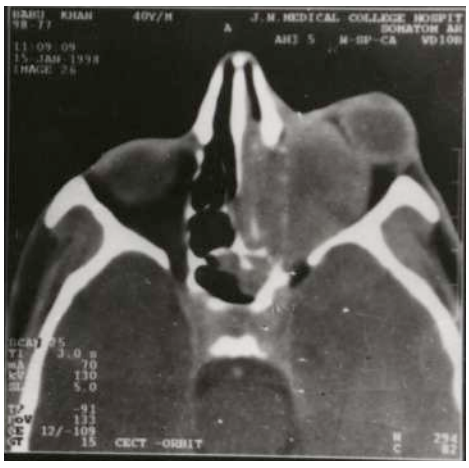

Figure 2: CT scan showing homogenous density in right ethmoidal

Tumour markers were assessed in doubtful cases which further confirmed diagnosis. All the cases were planned & combined modality therapy was undertaken. This included bitemporal coronal incision in two cases. Moures incision with Lynch extension in two cases & Moures with supraciliary and subciliary extension for the removal of the eyeball. Postoperative radiation therapy was given in all cases. All patients are under follow-up except one.

Figure 3: Photomicrograph showing small cells arranged in sheets and clusters, with fibrillary background. (Haematoxylin & Eosin x 125)

Table-1 Showing the patients with Esthesioneuroblastoma (ONB)

Patient	Age(yrs)/Sex	Presenting features	Stage (Kadish)	Treatment
1	50/M	U/L Nasal Obstruction Proptosis	C	Combined Modality
2	60/F	U/L Nasal Mass, Epistaxis	B	Combined Modality
3	45/M	Anosmia, Headache	C	Combined Modality
4	48/M	U/L Nasal Obstruction Epistaxsis	A	Combined Modality
5	52/M	U/L Nasal Obstruction Pain	B	Combined Modality

DISCUSSION

The unique anatomic location in the sinonasal area that is roof of nasal cavity to mid nasal septum and superior turbinate makes this tumor particularly vulnerable to diagnostic fallacy, not only clinically, but even to the histopathologist. Growths like lymphoma, rhabdomyosarcoma, malignant melanoma and sinonasal carcinoma form a group of small blue-celled imposters, which can closely simulate an esthesioneuroblastoma (Devaney K et al 1996).[3] This tumor differs from many other round cell malignancies in being chiefly an adult infliction with median age at presentation being about 50 years (Jethanamest D et al 2007) and with no definite predilection for either sex (Tajudeen B A et al 2014)).[4] However some authors have reported occurrence at any age with bimodal occurrence in second and sixth decade (Lester D. R. Thompson 2009).[5] Unilateral nasal

obstruction (71%) and epistaxis (46%) are the most common symptoms. Anosmia, pain and proptosis occur in 21% of patients each (Dulguerov et al 1992).[6]

Lymph nodes are involved in only 29% at presentation i.e. 14/48 cases (M.C. Howell et al 2011).[7] In our study lymph node metastasis was found in 20% (1/5 cases). Level 2 nodes were involved in one case i.e. upper jugoludigastric lymph node at the time of diagnosis. Kadish (1976) clinical staging system for ONB depends on whether disease is confined to the nasal cavity (stage A) or nasal cavity and paranasal sinuses (stage B) or extends beyond these sites (stage C). In 1992 Dulguerov *et al*[6] proposed a new staging system for ONB, which had higher correlation between stage and duration of disease free survival, although statistical significance was not reached. Recently, the Hyams histological grading system has emerged as a promising prognostication tool that offers an added value to stage which addresses prognosis and biology in esthesioneuroblastoma i.e. stage verus grade (Saade RE et al 2015).[8]

Radiographically both CT and MRI are pertinent as tumor displays a variety of imaging characteristics and aggressiveness. The expansile tendency of olfactory neuroblastoma is characterized by bowing of the sinus walls. The density, signal and enhancement characteristics are non-specific. Olfactory neuroblastoma should be suspected in all ages following identification of a mass in the superior nasal cavity demonstrating both expansile and destructive growth patterns (Pickuth D et al 1999).[9] On gross or macroscopic examination, the tumor is generally polypoid, soft pink to red brown and hemorrhagic. An origin from neuroectodermal elements of the olfactory membrane or the primordial olfactory placode is postulated (Obert G J *et al* 1960). The presence of fibrillary component in histopathalogic section, visualization of true and pseudorosettes and in unresolved situations immunohistochemical demonstration of neurone specific enolase (NSE), chromogranin, synaptophysin nuerofilaments and S-100 usually leads to diagnostic discrimination (Haas I et al 2003).[10] In corollary malignant lymphomas display no neuritic or fibrillary structure, have characteristic peri-cellular reticulin staining and show positivity for leucocyte common antigen (CD45), monoclonal immunoglobulins or T-cell receptor gene rearrangements. Tumors with myoid differentiation (rhabdomyosarcomas) show characteristic cross striations with phosphotugstic acid haematoxylin and immunohistochemical positivity of myoglobin, myosin and alpha-actinin (Schupman R et al 1986).[11] Melanoma cells usually are sufficiently pleomorphic for easy recognition, in addition to showing intracellular, and extra cellular melanin, where doubt persists resolution may be achieved through a positive DOPA reaction, ultrastructural demonstration of melanosomes, premelanosomes and positivity for S- 100 protein, HMB-45 and melan-A (Thompson et al 2003).[12] The undifferentiated sinonasal carcinoma shows a characteristic lymphoepitheliomatous morphology, at least focally, and is positive for keratin. Accurate diagnosis of esthesioneuroblastoma is of undiluted importance because of the usually worse prognoses of other malignancies of sinonasal area. Encouraging results have been obtained by stereotactic radiosurgery in recurrent ONB as noninvasive option (Van Gompel JJ et al 2014). And for the recurrent tumor, in-situ or distant resurgence can be detected by measuring urinary homovanillic acid and vanillyl mandelic acid, in cases where these metabolites are elevated at the time of primary diagnosis (Candito M et al 1992).[13] Dias et al (2003)[14] in their study used different treatment protocols to analyse prognostic factors (Fisher Exact Test & Log-rank test) and survival rate (Kaplan-Meier method). Kadish classification was best for predicting disease free survival. Cranofacial resection (CFR) with postoperative radiotherapy provided excellent disease free survival rate (86%) compared with other therapeutic options (Ow. T J *et al* 2013).[15] In our study, two cases underwent craniofacial resection with neck dissection in one case. Postoperative radiotherapy was given in all cases which took care of the retropharyngeal lymph nodes also. Poor prognosis was associated with distant metastasis and lymph node involvement. Stamberger et al in 2000 have highlighted that the combination of two minimally invasive therapies ie endoscopic sinus surgery and stereotactic radiosurgery provides a reliable new approach to the treatment of a series of ONB that offers excellent quality of life, less injury to the patients, fewer side effects and fewer long term adverse effects than other treatment strategies. Five-year survival according to Kadish was 90% for stage A, 71% for stage B & 47% for stage C.

CONCLUSION

From the above results, the authors concluded that hepatic and renal involvement occurs in patients suffering from dengue fever. Hence, multidisciplinary approach should be carried out while treating such patients.

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