

Esthesioneuroblastoma: a case report

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ABSTRACT

Esthesioneuroblastoma (olfactory neuroblastoma) is an uncommon neuroectodermal tumor. Its biological activity ranges from indolent growth to local recurrence and rapid widespread metastasis. Treatment options consist of surgical resection followed by radiation therapy for primary lesions and the addition of chemotherapy for advanced, recurrent, or metastatic lesions. Patients often present with nasal obstruction, rhinorrhea, recurrent epistaxis, hyposmia, or anosmia. We report a case of esthesioneuroblastoma involving bilateral nasal cavity leading to bilateral nasal obstruction, epistaxis and proptosis of the right eye associated with decreased visual acuity on that eye and loss of smell. A diffuse nontender, 6x6 cms swelling with illdefined margins was seen over the nasal bridge, extending superiorly to glabella and laterally to right maxillary region. X-ray PNS showed soft tissue mass in the nasal cavity with destruction of nasal septum, intense periosteal reaction with destruction of right maxillary wall and extension to right orbit. CT scan of paranasal sinuses showed 8.5x4.9x 7.8 cms irregularly marginated heterogeneous iso- to hyper dense soft tissue mass lesion with extensive adjacent bony destruction and spiculated periosteal reaction involving bilateral nasal cavity and anterior cranial fossa. Biopsy from right nasal mass showed neuroblastoma. The patient received radiotherapy and chemotherapy. The modified Kadish staging system, lymph node status, treatment modality, and age are useful predictors of survival in patients who present with esthesioneuroblastoma. Excellent outcomes for esthesioneuroblastoma are achievable. Long-term follow-up is necessary because of the extended interval for recurrent disease; unlike most sinonasal malignancies, surgical salvage is possible.

Keywords: Esthesioneuroblastoma, olfactory neuroblastoma, nasal cavity, bilateral nasal mass.

Esthesioneuroblastoma (olfactory neuroblastoma) is an uncommon neuroectodermal tumor that originates from the olfactory sensory epithelium in the upper nasal fossa at the level of the cribriform plate represents up to 5.0% of malignant tumors of the nasal cavity. First described by Berger *et al* in 1924, almost 1000 cases have been published. The probable origins reported for this tumor include the sphenopalatine ganglion, the vomeronasal organ of Jacobson, the neuroepithelial cells of the olfactory membrane, the ectopic olfactory epithelium in the nasal mucosa, and the amine precursor uptake and decarboxylation cells.¹ The sex distribution is roughly equal.² The incidence peaks between 11 and 20 years old and again between 51 and 60 years old.¹ These lesions can be easily missed because the presenting symptoms mimic those of benign tumors of the nose. They are often discovered incidentally during septoplasty or polypectomy.³ Patients present with nonspecific symptoms of nasal obstruction (70.0%) and epistaxis (50.0%); less common symptoms include headache, pain, visual disturbances, and anosmia (<5.0%). Owing to the nonspecific nature of the presenting symptoms, patients often have a long history prior to diagnosis.⁴ Clinical presenting symptoms depend on the site of the

tumor origin and invasion to adjacent structures. For example, tumors involving the orbital area generally present with epiphora, decreased visual acuity and proptosis.⁵ We report a clinical presentation with bilateral nasal obstruction due to olfactory neuroblastoma (ONB) involving bilateral nasal cavity leading to bilateral nasal obstruction, epistaxis and proptosis of the right eye associated with decreased visual acuity and loss of smell.

CASE REPORT

A 28 yrs old male, a tent decorator and resident of Varanasi, presented to Radiotherapy OPD with the chief complaints of blocked nose with mass in both nostrils for 1 year, nasal bleeding for 6 months, swelling of the nasal bridge for 4 months and bulging of right eye for 3 months. Past history and family history are insignificant. Patient was on homeopathic treatment with no improvement. He was apparently well 1 yr back, when he started complaining of bilateral blocked nose which was associated with bilateral pinkish nasal mass (right > left) and nasal bleeding for 6 months which occurred daily and of significant amount which was relieved by lying down. He also noticed a rapidly increasing



Fig. 1(A)



Fig. 1(B)



Fig. 1(C)

Fig 1(A) and (B) Before treatment: Fusiform swelling over the nasal bridge, extending superiorly to glabella and laterally to right maxillary region with mild proptosis of right eye and lateral deviation. **Fig. 1(C)** After treatment: The tumour size reduced after treatment was started.

swelling over nasal bridge for 3 months and bulging of right eye with decreased vision and associated headache and neck pain. On physical examination, general examination was unremarkable. Systemic examination was also unremarkable except for the smell sensation which was lost. On local examination, a diffuse 6x6 cms fusiform swelling (Fig.1A, B and C) with illdefined margins was seen over the nasal bridge, extending superiorly to glabella and laterally to right maxillary region. It was nontender and there was no rise in local temperature. Fleshy mass was visible in both nostrils with mild proptosis of right eye and mild lateral deviation. The mass was associated with purulent nasal discharge. Eye movements were normal but visual acuity was decreased. Examination of the oral cavity is unremarkable. There is no lymphadenopathy. Complete blood count, renal function test, liver function test are within normal limit. X-ray Paranasal sinuses (PNS) shows soft tissue mass in the nasal cavity with destruction of nasal septum, intense periosteal reaction with destruction of right maxillary wall and extension to right orbit. Lateral view of the skull was unremarkable. CT scan of paranasal sinuses (Fig.2. A and B) showed 8.5x4.9x 7.8 cms irregularly marginated heterogeneous iso- to hyper dense soft tissue mass lesion with extensive adjacent bony destruction and spiculated periosteal reaction involving bilateral nasal cavity and anterior cranial fossa suggestive of angiosarcoma versus esthesioneuroblastoma. Mass extended superiorly involving bilateral frontal lobe with adjacent multiple cystic areas and cribriform plate destruction. Inferiorly the mass was limited by hard palate, however cortical thinning or break at places were seen. Posteriorly it extended through choana to nasopharynx and destruction of anterior sphenoid sinus wall extending into sinus. Laterally cortical break (permeation) was seen bilaterally on the medial wall of maxillary antral wall and medial orbital wall extending into medial orbital extraconal compartment with lateral displacement of right globe and maxillary antrum at places and anteriorly the mass

extended to soft tissue along the plane of nose and frontal peri calvaria through destruction of frontal bone and nasal bone. Extensive speculated type periosteal reaction was seen. Nasal septum was destroyed. Chest X-Ray (PA) shows right sided cervical rib. Biopsy from right nasal mass (Fig. 3) showed monomorphic malignant round cell tumour with occasional rosette formation compatible with neuroblastoma. Patient received one cycle of Vincristine, Actinomycin D, Adriamycin and Cyclophosphamide. Patient was planned for radiotherapy and received 2 # of 400 cGy as emergency treatment for pain. Patient received radiation (500 cGy/ 25#) and weekly and Vincristine and cyclophosphamide.

DISCUSSION

The incidence of esthesioneuroblastoma, an uncommon malignant neoplasm of the upper nasal cavity, is low. A relatively small number of cases have been reported in a variety of heterogeneous series that span long periods.¹ Olfactory neuroblastoma is a locally extensive malignancy and frequently directly invades the skull base, orbit, and adjacent soft tissue from the typical "cribriform" site. Distant and regional metastases are present in 14.0-38.0% of cases at the time of diagnosis, and the cervical lymph nodes, lung and bone are the most commonly involved sites.⁵ Symptoms are unspecific and common to most tumors and benign diseases of the nasal cavity – unilateral nasal obstruction and epistaxis are the most frequent ones.⁶

The ONB should be differentiated from other malignant tumors in anterior skull base. CT and MRI are helpful to identify the margin and spread approaches of the tumor. On CT scan, the tumor usually present with a heterogeneous mass, sometimes with focal necrosis or calcification. The paranasal sinuses and anterior skull base are often destroyed, while the clivus is intact. On a T₁-weighted MRI image, the ONB shows isointense, while in a T₂-weighted image, it shows hyperintense, which is significantly different from the mucosal fluid. The tumor can be heterogeneously enhanced with

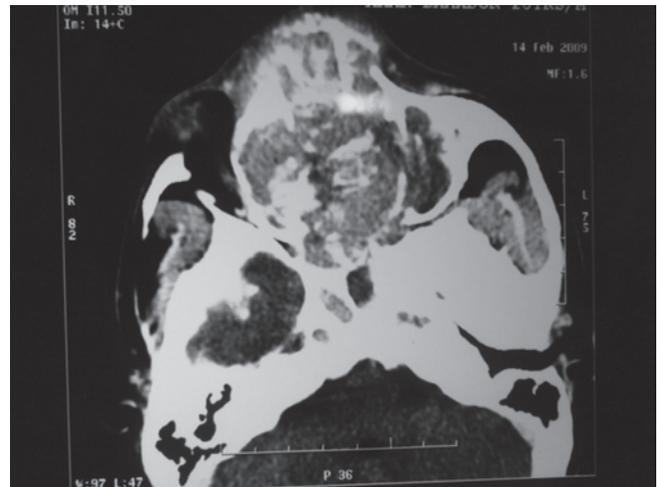


Fig . 2. Computed tomography (CT) coronal image of PNS: (A) Without contrast and (B) With contrast : Heterogeneous iso- to hyper dense soft tissue mass lesion with extensive adjacent bony destruction and spiculated periosteal reaction involving bilateral nasal cavity and anterior cranial fossa.

Gadolinium injection. The signals are homogeneous with patching hyperintense or punctiform hypointense when necrosis or calcification occurs. Extensive cerebral edema may appear when the tumor invades into the sellar area.⁷

Several staging systems have been developed with variable prognostic utility. Kadish system has been the most commonly used staging system with strong prognostic correlation.⁸ Kadish's classification divides the tumors in three stages: A (tumors restricted to the nasal cavity), B (tumors involving the nasal cavity and paranasal sinuses) and C (tumors extending to beyond the paranasal sinuses -orbit, skull base or metastasis).⁶

Esthesioneuroblastomas can be usefully graded using a scheme developed by Hyams, based on histologic features using 4 grades based upon lobular architecture, fibrillary matrix, rosettes, calcification, mitoses and necrosis. This system has been found to correlate with

prognosis in most studies. It was found that grade I patients had a uniformly good outcome whereas grade IV behaved considerably worse. Grade I and II are well-differentiated tumors and are relatively easily identified, whereas grade III and IV are sometimes difficult to differentiate from other high-grade tumors of the sinonasal tract such as sinonasal undifferentiated carcinoma or sinonasal neuroendocrine carcinoma, thereby affecting the number of patients in different grades. It is, however, important to differentiate ONB from non-ONB neuroendocrine tumors of the sinonasal region because of better overall survival and local control of the former.⁸ Diagnosis of this tumor may initially be difficult, and it has been referred to as "the great imposter." Many tumors may mimic an esthesioneuroblastoma. Specific tumors to be aware of include inverting papilloma, squamous cell carcinoma, adenocarcinoma, sinonasal undifferentiated carcinoma, hemangioma, and metastatic carcinoma. Certainly, in addition to imaging, the diagnosis must be made definitively through histopathology.⁹ The tumor shows a relatively homogenous population of small round cells set in a variable fibrillary stroma and forms part of the differential diagnosis of round cell lesions of the head and neck region. The presence of a fibrillary intercellular background in conjunction with the presence of Homer – Wright rosettes in an upper nasal neoplasm is considered to be diagnostic of olfactory neuroblastoma.¹⁰ Homogeneous small cells in a rosette or pseudorosette formation characterize a well-differentiated esthesioneuroblastoma, whereas an undifferentiated esthesioneuroblastoma consists of anaplastic hyperchromatic small cells with little cytoplasm. The latter may be difficult to diagnose; therefore, further studies in the form of electron microscopy and immunohistochemical staining should be performed.⁹

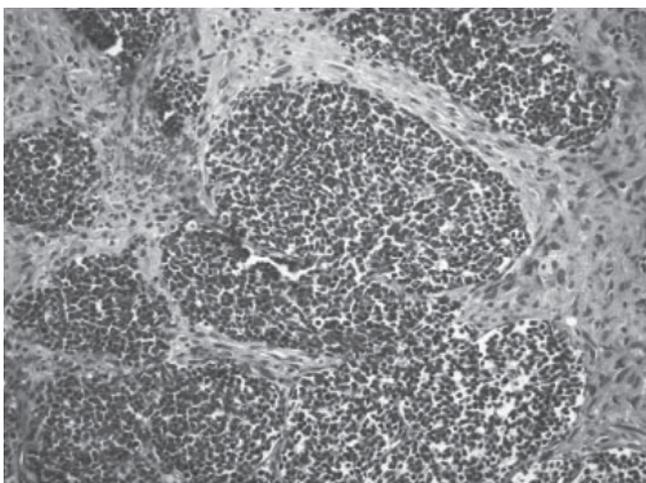


Fig. 3. Microscopic picture of Esthesioneuroblastoma : The tumor consists of large islands of small cells with hyperchromatic nuclei showing a vesicular pattern and scant cytoplasm. Mitotic activity is brisk. (Hematoxylin and eosin stain)

Owing to the “small, round, blue-cell” nature of the neoplasm, the differential diagnosis is quite broad; it includes melanoma, rhabdomyosarcoma, sinonasal undifferentiated carcinoma, lymphoma, Ewing’s sarcoma, pituitary adenoma, plasmacytoma, paraganglioma, and primitive neuroectodermal tumor. Clinical and demographic findings can help make distinctions, as can pertinent immunohistochemical reactions to synaptophysin, chromogranin, neuron-specific enolase (NSE), neurofilament protein (NFP), S-100 protein, keratin, CD45RB, desmin, CD99, and HMB45. Olfactory neuroblastomas are usually positive with synaptophysin, chromogranin, NSE, NFP, and S-100 protein.⁴

With regard to treatment, the combination of surgery and radiotherapy is the most frequent approach and offers the highest cure rates, but definitive radiotherapy as a nonsurgical treatment is also used. However, despite definitive local treatment, local recurrence and distant metastases are often reported with the latter observed in 25.0-50.0% of cases. Chemotherapy is therefore often also implemented in patients with recurrent or metastatic ONB.² Dulguerov *et al* more recently performed a metaanalysis of publications between 1990 and 2000, detailing treatment of esthesioneuroblastoma. The treatment modalities analyzed were surgery alone; surgery and radiotherapy (RT); RT alone; a combination of surgery, RT, and chemotherapy; RT and chemotherapy; and chemotherapy alone. Statistical analysis compared the different treatment modalities against the approach with the highest average survival (surgery and RT). They identified 26 studies that described 390 patients with esthesioneuroblastoma. Overall survival at 5 years was 41.0%, with data extracted from 24 publications. They found that the combination of surgery and RT was the most frequently used treatment (44.0%) and was associated with the best average survival results (65.0%). Survival results were 48.0% for surgery alone, 37.0% for RT alone, 40.0% for chemotherapy alone, and 51.0% for RT plus chemotherapy. They concluded that combination surgery and RT seemed to be the optimal approach to treatment, with single-modality treatment being reserved only for a patient with a small tumor located well below the cribriform plate. The role of elective neck treatment for esthesioneuroblastoma remains controversial. The incidence of cervical metastases in recent publications has ranged from 17.0% to 33.0%. Furthermore, the presence of palpable lymph nodes at presentation has been a poor prognostic factor for survival (eg, the 5-year survival was 0% in patients in whom nodes were present and 65.0% in those in whom they were absent).¹¹

When treated with aggressive surgical therapy such as

craniofacial en bloc tumor resection, in conjunction with adjuvant therapy of radiation with or without chemotherapy, esthesioneuroblastoma can be a curative disease with local control of the disease. Dulguerov and colleagues reported a 5-year survival rate of 45.0%. Others have reported a survival rate as high as 70.0% with a local recurrence rate of 30.0%.

Prognosis depends on the stage and grade of the disease. Negative prognostic factors are age (more than 50 years at presentation), female gender, tumor recurrence, and metastasis.¹ Compared with other sinonasal malignancies, the prognosis of ONB is much better, with a disease-free survival at 5 years of more than 80.0%.¹² In a review of 97 cases between 1967 and 1977, Elkon *et al* found a favorable 3-year overall survival rate in patients with stage A or B disease (88.9% and 83.3%, respectively), while patients with stage C disease had only a 52.9% survival rate at 3 years. Recently, the University of Virginia Health System updated a series of 50 cases and reported higher disease-free survival rates of 86.5% and 82.6% at 5 and 15 years; all patients received multimodality treatment including craniofacial resection, radiotherapy, and chemotherapy for stage C disease.¹³

Postoperative complications have been reported in 15.0-40.0% of cases. Major complications include cerebrospinal fluid leakage, frontal lobe abscess, intracranial hemorrhage, and infection.¹⁴

An excellent outcome can be achieved with an aggressive approach. Although no standard treatment protocol has been established, we strongly believe a multidisciplinary approach with judicious use of craniofacial resection and Intensity-modulated radiation therapy is an excellent treatment paradigm for these tumors. We believe that chemotherapy is best used to treat advanced or recurrent disease.

REFERENCES

1. Prakash Sampath P, Park MC, Huang D, Deville C, Cortez S, Chougule P. Esthesioneuroblastoma (Olfactory Neuroblastoma) with Hemorrhage: An Unusual Presentation. *Skull Base* 2006; 16: 169-74.
2. Kiyota N, Tahara M, Fujii S *et al*. Nonplatinum-based chemotherapy with irinotecan plus docetaxel for advanced or metastatic olfactory neuroblastoma. *Cancer* 2008; 112: 885-91.
3. Argiris A, Dutra J, Tseke P, Haines K. Esthesioneuroblastoma: The Northwestern University experience. *Laryngoscope* 2003; 113: 155-60.
4. Thompson LDR. Olfactory neuroblastoma. *Ear Nose Throat J* 2006; 85: 569-70.
5. Chan LP, Wang LF, Tai CF, Wu CC, Kuo WR. Huge Sphenoid Sinus Olfactory Neuroblastoma: a case report. *Kaohsiung J Med Sci* 2009; 25: 87-92.

6. Araújo RP, Gomes EF, Menezes DB, Ferreira LM, Rios AS. Rare nasosinusal tumors: Case series and literature review. *Rev Bras Otorrinolaringol* 2008; 74: 307-14.
7. Li-wei Z, Ming-shan Z, Ji Q *et al.* Management of intracranial invasive olfactory neuroblastoma. *Chin Med J* 2007; 120: 224-7.
8. Sharma S, Sharma MC, Johnson MH, Lou M, Thakara A, Sarkar C. Esthesioneuroblastoma – a clinicopathologic study and role of dna topoisomerase alpha. *Pathol Oncol Res* 2007; 13: 123-9.
9. Lee A, Goldstein DP, Irish J, Gentili F, Perez-Ordenez B. Noncontiguous Bilateral Esthesioneuroblastoma: A Case Report. *Skull Base* 2007; 17: 405–8.
10. Ayoub A, Hiari MA. Olfactory Neuroblastoma: a case report. *J Romanian Military Services* 2005; 12: 48-50.
11. Loy AH, Reibel JF, Read PW, Thomas CY, Newman SA, Jane JA. Esthesioneuroblastoma. *Arch Otolaryngol Head Neck Surg* 2006; 132: 134-8.
12. Bellizzi AM, Bourne TD, Mills SE, Stelow EB. The Cytologic Features of Sinonasal Undifferentiated Carcinoma and Olfactory Neuroblastoma. *Amer J Clin Pathol* 2008; 129: 367-76.
13. Jethanamest D, Morris LG, Sikora AG, Kutler DI. Esthesioneuroblastoma. *Arch Otolaryngol Head Neck Surg* 2007; 133: 276-80.
14. Castelnuovo PG, Delu G, Sberze F, Pistochini A, Cambria C, Battaglia P. Esthesioneuroblastoma: Endonasal Endoscopic Treatment. *Skull Base* 2006; 16: 25-9.