



Esthesioneuroblastoma a Rare Tumour of the Sinonasal Vault: A Singular Case Narrative

Sachin Gandhi¹, Shradha Saindani^{2*}, Renuka Mundalik³ and Vishakh Nair³

¹MBBS, MS, FRCS, Consultant at Deenanath Mangeshkar Hospital, Pune, India

²MBBS, DORL, DNB ENT, Junior Consultant at Deenanath Mangeshkar Hospital, Pune, India

³MBBS, DNB ENT, Resident Doctor at Deenanath Mangeshkar Hospital, Pune, India

***Corresponding Author:** Shradha Saindani, MBBS, DORL, DNB ENT, Junior Consultant at Deenanath Mangeshkar Hospital, Pune, India.

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Abstract

Olfactory neuroblastoma (ONB) is a rare head and neck malignancy, accounting for 0.3% of upper aerodigestive tract malignancies and 3% - 6% of the sinonasal tract malignant tumours. It was first described in 1924 by Berger, Luc and Richard. It is a tumour of anterior skull base arising from the neuroepithelium of the olfactory cleft in the superior portion of the nasal cavity. ONB have an indolent course from a slow growing neoplasm to that of a highly aggressive and locally invasive neoplasm with a capacity of regional or distant metastases. Several treatment modalities have been described, given the rarity and recurrence pattern of the tumour, prospective treatment studies are absent. Craniofacial resection with adjuvant radiotherapy (RT) is the treatment of choice for respectable ONB tumours. Now a days in selected cases Endoscopic resection has gained popularity as they prevent facial incisions and craniotomy and is also oncologically sound. We present a case of ONB tumour in a 53 year old male. Patient present with a bleeding mass protruding out of the left nostril. Mass was diagnosed on Contrast enhanced computed tomography (CECT). Biopsy and debulking was planned under general anesthesia. Intraoperative samples were sent for frozen section sampling and procedure was completed once diagnosis was made. Immunohistochemical staining was done. Patient was further referred to Oncologist for Adjuvant Radiotherapy. This condition is quite rare and presentation is also late. So early diagnosis and prompt management improves the treatment outcome and prognosis of the patient.

Keywords: Esthesioneuroblastoma; Olfactory Neuroblastoma; Skull Base Tumour; Endoscopic Resection; Sinonasal Tumour

Introduction

Esthesioneuroblastoma (ENB) represent 3%-6% of all the head and neck tumours [1,2]. Origin is believed to be from the olfactory cleft although there is uncertainty regarding the region the origin of this tumour [3,4]. Other nomenclatures used for ONB are esthesioneuroblastoma, esthesioneurocytoma and neuroendocrine carcinoma [5,6].

The necessity for early diagnosis and treatment for this pathology is owing to its late presentation, aggressive nature and high mortality rates.

Case Report

In this case report we present a case of 53 year old male patient diagnosed as ONB. Patient presented in our out-patient de-

partment (OPD) with chief complaints of Left sided nasal mass, nasal obstruction, epistaxis, left facial pain and headache since 6 months. Diagnostic nasal endoscopy (DNE) was done and a lobulated fleshy mass with ulcerative surface and intermittent areas of necrotic tissue and slough covering the mass was seen filling the left nasal cavity completely and protruding outside the left nasal vestibule. Contrast enhanced computed tomography (CECT) scan was done which showed soft tissue hyperdense mass, enhancing homogenously, originating from the left cribriform area, occupying the left nasal cavity and exerting pressure over the left lateral nasal wall and the turbinates. According to Modified Kadish classification (Box 1), this patient is graded as Stage A. Transnasal Endoscopic Biopsy, frozen section sampling and debulking was planned under general anesthesia after obtaining all the basic blood tests and pre-anesthetic checkup. Intraoperatively adequate biopsy samples were taken and sent for frozen section. Debulking was done using micro-debrider. On Frozen section, neuroendocrine tumour was

diagnosed and samples were processed further for HPE and IHC examination. Haemostasis was achieved using coblator and mass near the skull base was only ablated and scrapping was avoided. Left nasal cavity was packed using 10 cm merocel nasal pack. Nasal pack was removed after 3 days. HPE and IHC confirmed the diagnosis of ONB, Hyams grade 2 (Box 3). Tumour cells were strongly positive for Synaptophysin, Chromogranin A and Calretinin. S-100 protein was marking the sustentacular cells. Patient was further referred to Oncologist for further treatment. Positron emission tomography (PET-CT) was done for staging of the tumour. PET-CT showed FDG avid hyperdense lesion in Left nasal cavity near the cribriform area. No neck nodes or distant metastasis was seen. Patient was started on Neoadjuvant Radiotherapy (RT). After completion of the RT cycles, PET-CT scan was done which showed good response to the treatment. Patient is kept on 6 monthly follow up with DNE and yearly follow up with PET-CT scan.

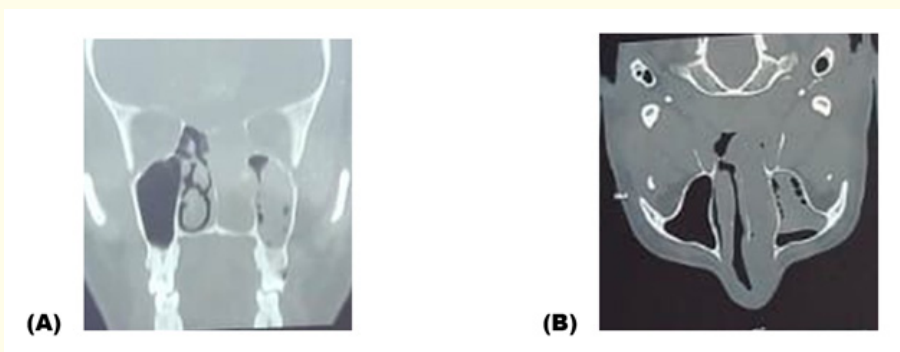


Figure 1: CECT-PNS Coronal (A) and Axial (B) Sections: Hyperdense soft tissue lesion originating from anterior skull base with extension in left nasal cavity with its complete obliteration and compression over the lateral nasal wall.

Box 1: Modified Kadish Classification [7-9]

- **Stage A:** Limited to the nasal cavity
- **Stage B:** Involves the paranasal sinuses
- **Stage C:** Extends outside the sinonasal cavity, including involvement of the base of skull, orbit and intracranial cavity.

Box 2: Dulguerov TNM staging [5,6]

- T1: Limited to the sinonasal cavity excluding the sphenoid sinus
- T2: Involves the cribriform plate or sphenoid sinus
- T3: Involves the orbit or anterior cranial fossa without dural involvement

- T4: Tumors with intracranial involvement
- N1: Any lymph node metastasis
- M1: Any distant metastasis.

Box 3: Hyams' histopathologic grading [10,11]

- **Grade 1:** Well differentiated with lobular preservation, prominent fibrillary matrix, no nuclear pleomorphism, Homer-Wright (HW) rosettes

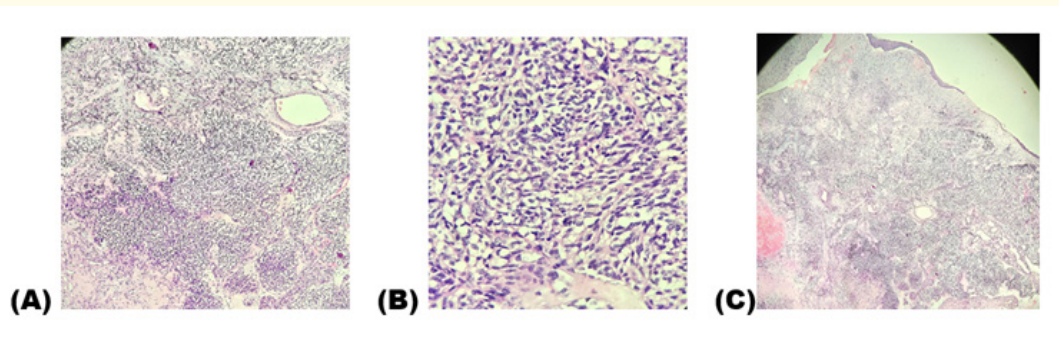


Figure 2: (A), (B) and (C) HPE: Tumour is located in the subepithelial layer. Tumour cells form lobules, nests and sheets with elongated spindle nuclei, fine chromatin and clear cytoplasm.

- **Grade 2:** Low mitotic index, moderate nuclear polymorphism, fibrillary matrix present, HW rosettes
- **Grade 3:** Moderate mitotic index, prominent nuclear polymorphism, low fibrillary matrix, HW rosettes, rare necrosis
- **Grade 4:** High mitotic index, anaplasia, marked nuclear pleomorphism, absence of fibrillary matrix and HW rosettes, frequent necrosis.

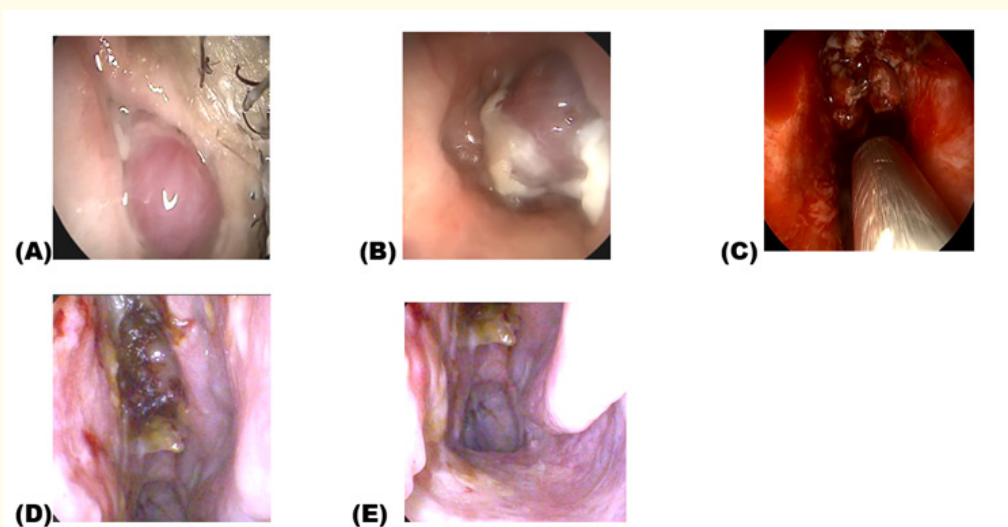


Figure 3: (A) – Preoperative DNE with nasal mass completely obstructing left nasal cavity and protruding outside the vestibule (B) Mass seen through right nasal cavity into the nasopharynx (C) – Intraoperative image (D) & (E) Postoperative and RT DNE (After 3 months) showing regression of the mass with patent nasal passage.

Discussion

ONB is a rare entity accounting for 3%-6% of sinonasal tract malignancy with less number of case reports reported in the literature [1,2]. There is uncertainty with its exact location of origin. Most accepted location being the upper nasal cavity, from the olfactory placodes that undergo replacement by the respiratory mucosa [3,4]. The other sites of origin includes vomeronasal organ, sphenopalatine ganglion and the ganglion of loci. Ectopic origin from paranasal sinus and lower nasal cavity has been reported [4,5]. In our case report, the tumour originated from the cribriform area indicating the site of origin being olfactory neuroepithelium. This type of sinonasal malignancy is encountered in the age group of 45 years-60 years with male preponderance. Presenting symptoms are headache, facial pain, nasal obstruction and epistaxis [5-7]. On DNE, often a reddish gray pedunculated mass with smooth surface that readily bleeds with manipulation is noted [6,7]. On radiological imaging, expansile hyperdense mass, causing extensive bony remodelling destruction of the nasal cavity and the paranasal sinuses should raise suspicion of the aggressive subtype. Magnetic resonance imaging (MRI) is superior to CECT in delineating the extent of tumour, submucosal extension, intracranial, perineural and intraorbital spread [7,8]. There are two major radiological grading systems, Modified Kadish tumour staging and Dulguerov grading system. Amongst the two, Dulguerov grading system correlates more with the survival and recurrence rates as it includes the nodal and metastatic status as well [8-10]. Also, many studies have claimed Dulguerov grading system relates to Hyams staging system [9,10]. Definitive diagnosis can be made only on HPE and IHC. Biopsy should be preferably taken from multiple sites to prevent false negative results and also avoid delay in treatment [11]. Evolution of IHC stains, recently, have made the diagnosis more accurate. ONB arises from basal cells that are mitotically active giving rise to neuronal and sustentacular cells. On light microscopy, ONB are categorised as "small, round and blue cell tumours". Stroma is highly vascularised with nests of cells. Two pattern of rosettes are seen, mostly Homer-Wright or pseudorosettes (30%-50%) and rarely Flexner-Wintersteiner rosette or true rosette (5%) [11,12]. Hyams grading system classifies ONB based on histologic features like architecture, nuclear pleomorphism, rosettes, mitotic activity and necrosis. According to literature Hyams grade 1 and 2 are low grade tumours Hyams grade 3 and 4 are high grade tumours. High

grade hyams tumours have significant impact on survival. Histological grading also plays an important role in narrating the prognosis and treatment outcomes. Low grade tumour can be managed with complete surgical resection and if complete resection is not possible, post-operative adjuvant RT is required [12,13]. But some studies in the literature emphasis on surgical excision along with post-operative adjuvant radiotherapy for all low grade tumours as a standard treatment protocol. It has shown good local control of disease [14]. However, some studies suggest that cases with Kadish stage A and with negative resection margins surgery alone is sufficient as there is considerable complications and morbidity following adjuvant RT. However with advancement of radiation technologies, RT have shown better patient outcomes and minimal toxicity and complications to the critical structures [14,15]. In our case, the tumour was Kadish stage A and Hyams grade 2. Endoscopic surgical excision and postoperative adjuvant RT was done. Following RT patient had minimal symptoms like mucositis and dryness in nose that was managed conservatively. In case of high grade tumour Surgery along with adjuvant or concomitant Chemoradiotherapy (CT/RT) is required [13-15]. Mainstay treatment plan reported in literature is complete surgical resection and followed by adjuvant radiation therapy or concurrent chemoradiotherapy according to the histological and radiological grading. Alternate treatment plan is induction chemotherapy followed by surgery or chemoradiotherapy. Targeted therapy is gaining acceptance in management of head and neck malignancy. Advent of molecular biomarkers and targeted therapies can be promising for high grade of intractable ONB tumours. Targeted therapies currently in use for ONB tumours are Sunitib, Cetuximab, Bevacizumab and Sorafenib. Risks and benefits of these targeted therapies is still under trial. Male sex and advanced disease are poor prognostic factors according to the literature [16].

Conclusion

ONB is a rare group of sinonasal tract malignancy. Presentation of this tumour is often late, with extensive spread of the disease and bony involvement. CECT and MRI imaging is investigation of choice. Multisite biopsy and HPE and IHC examination gives the definitive diagnosis. Evolution of IHC stains increases the accuracy of the diagnosis. Most effective treatment modality for low grade

tumours is complete surgical resection with postoperative RT. For high grade tumours upfront surgery followed by chemotherapy and radiotherapy or Induction chemotherapy followed by surgery and/or chemoradiotherapy are the mainstay treatment options available. Evolution of biomarkers and targeted therapies can be a useful tool in diagnosing and treating this condition.

Declarations

- There was no conflict of interest.
- This manuscript has been read and approved by all the authors and the requirements for authorship have been met. Each author approves that the manuscript represents original work.
- The authors declare that they have no known competing financial or non financial interests or personal relationships that could have appeared to influence the work reported in this paper.
- No funding was received to assist with the preparation of this manuscript.
- The authors have no financial or proprietary interests in any material discussed in this article.
- Ethical Committee Approval was done
- Informed consent was taken.

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