Case Report

A Rare Case of Sinonasal Carcinoma-Olfactory Neuroblastoma

https://doi.org/10.47210/bjohns.2025.v33i1.193

Vishal K. Magdum,[1] Aishwarya A. Kachare,[1] Rahul S. Gosavi,[1] Manali P Joshi[1]

ABSTRACT

Introduction

Over the past decade, the pathology of un differentiated sinonasal malignancies has undergone extensive study, leading to significant advancements in the depiction and histopathological classification of various entities. These entities are now recognized as subsets of "sinonasal undifferentiated carcinomas (SNUC)" and poorly differentiated unclassified carcinomas. Typically, these malignancies are detected at later stages, by which time they have often invaded the facial and cranial regions. Olfactory neuroblastoma, which arises from the olfactory neuroepithelium with neuroblastic immature differentiation, is one such malignancy.

Case Report

We present a case involving a left-sided nasal mass with blood-tinged discharge that obscured the nasal cavity. Previous biopsies had been inconclusive. Imaging revealed a large heterogeneous mass with bone erosions and extension into the intraorbital and intracranial regions. The patient underwent an endoscopic nasal biopsy.

Discussion

This case presents a rare instance of olfactory neuroblastoma,illustrating diagnostic difficulty due to overlapping features with other sinonasal tumors, highlighting the critical role of histopathology and immunohistochemistry and exceptional response to palliative therapy in advanced-stage disease.

Keywords

Esthesioneuroblastoma, Olfactory; Neuroectodermal Tumors; Recurrence; Immunohistochemistry

Sinonasal undifferentiated carcinoma (SNUC) is a rare and highly malignant tumor that occurs in the nasal cavity and/or paranasal sinuses. It was first described by Frierson et al. in 1986.[1]

In contrast, olfactory neuroblastoma (ONB) is a neuroectodermal tumor originating from the olfactory neuroepithelium in the nasal cavity, representing 1-2% of all intranasal tumors.[2] Although SNUC and olfactory neuroblastoma appear histologically similar, the later generally has a better prognosis. Immunohistochemistry plays a crucial role in establishing a definitive diagnosis. Due to the nonspecific nature of early symptoms and the rarity of the tumor, 70% of patients are diagnosed at an progressed stage,[3] with cases seldom submitted for consultation, further highlighting the diagnostic challenges for these tumours.

Currently, there are no standardized guidelines for their diagnosis and therapeutic management. Multimodal treatment, including chemotherapy (CT) and radiotherapy (RT), or a combination of both, is necessary. In this patient, endoscopic excision of the nasal mass was performed, followed by post-diagnosis radiotherapy due to the high incidence of locoregional recurrence.

1 - Department Of ENT, Sanjeevan Medical Foundation Ent Post Graduate Training Institute, Miraj, Maharashtra

Corresponding author:
Dr. Aishwarya A. Kachare
email: kachareaish2015@gmail.com

Case Report

A 68-year-old man , belonging to low socioeconomic status sought care to the ENT outpatient department with a six-month history of an enlarging left nasal mass accompanied by intermittent epistaxis and progressive nasal obstruction. There were no associated complaints of sneezing, headache, post-nasal drip, facial pain or cervical lymphadenopathy. He had undergone 3 to 4 previous biopsies that were inconclusive, showing only granulation tissue and chronic inflammation with a suspected infectious etiology. These findings were confirmed via diagnostic nasal endoscopy. A probe test was performed to assess the mass's characteristics and mobility, revealing it to be smooth and friable, without bleeding on touch. The mass was attached to the lateral wall of the nose, sparing the septum.

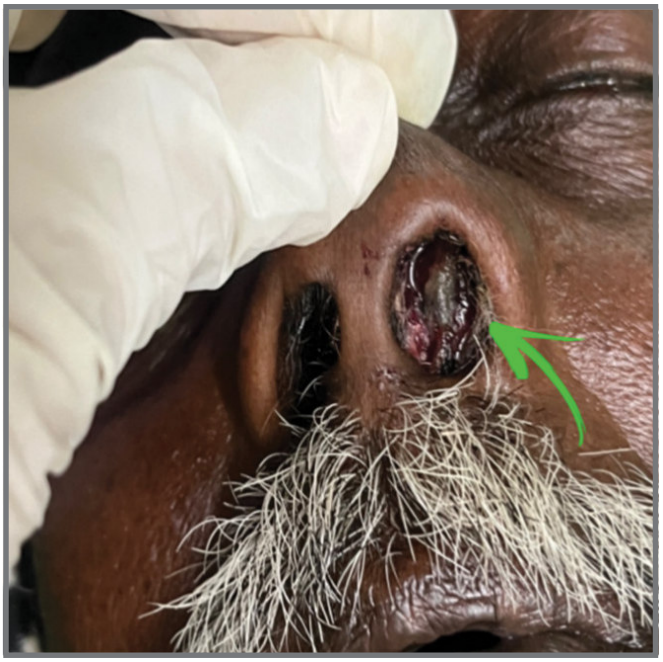


Fig. 1. Clinical examination revealed a solitary, smooth, friable mass with blood-tinged discharge, filling and obstructing the left nasal cavity and causing displacement of the septum towards the contralateral side.

Radiological Investigations

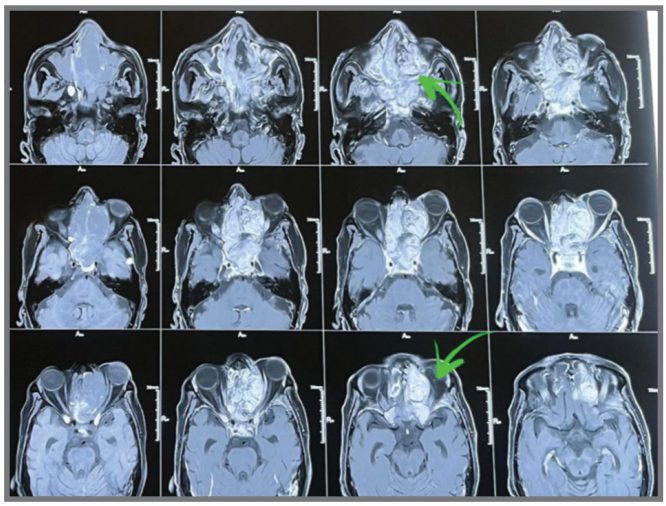
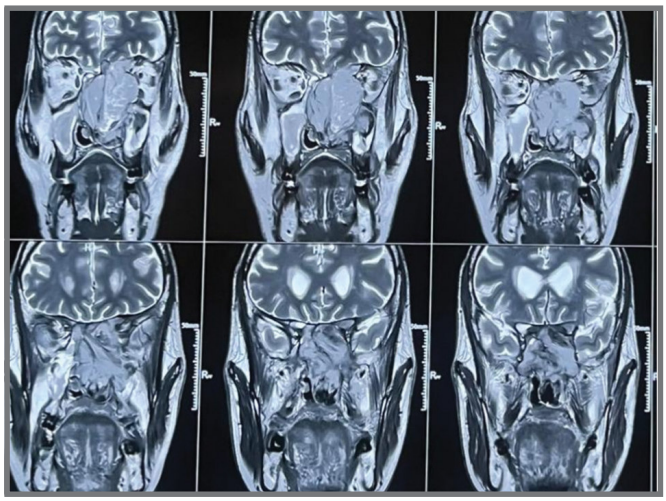


Fig. 2. MRI PNS WITH ORBIT- 2 (A) AXIAL VIEW- shows a large heterogeneously enhancing lesion eroding the nasal septum, with extension into adjacent sinuses (left frontal, maxillary, ethamoid and sphenoid) intracranial involvement (Eroding cribriform plate), and invasion of the orbit's extraconal compartment (lamina papyreacae).



2 (B) CORONAL VIEW

Given the clinical presentation and inconclusive results from previous biopsies, it was decided to perform an endoscopic biopsy from a deeper site to obtain a more definitive diagnosis. The patient underwent an endoscopic biopsy of the left nasal mass under general anesthesia.

The histopathology report described a tumor composed of round and spindle cells with hyperchromatic nuclei and scanty amphophilic cytoplasm. The stroma showed myxoid changes with scattered primitive spindle-shaped mesenchymal cells, suggesting a high-grade undifferentiated carcinoma. Immunohistochemistry revealed that the tumor cells expressed CK, EMA, synaptophysin (focally), and MIC-2, consistent with a malignant round cell tumor and olfactory neuroblastoma. Taking into consideration the patient's age, financial situation, and the advanced stage of the disease, surgical approach was not advised, PET CT scan was recommended. However, the patient opted to proceed with palliative treatment instead.

The patient underwent postoperative intensity-modulated radiotherapy with a total dose of 60 Gy delivered over six weeks. He had remained disease-free for six months and continues to attend regular follow-ups.

Discussion

Olfactory neuroblastoma originates from specialized neuro-epithelial olfactory cells, which are likely the progenitors of neuroendocrine carcinomas of the sinonasal tract. These olfactory cells are typically located in the superior aspect of the nasal cavity, including the superior nasal concha, upper part of the nasal septum, and cribriform plate of the ethmoid. Specific sites of origin for this malignant neural crest-derived tumor include Jacobson's vomeronasal organ , the sphenopalatine ganglion, the ectodermal olfactory placode, the ganglion of Loci, and the olfactory neuroepithelium located at the cribriform plate and the superomedial surface of the superior turbinate. ONB can develop at any age (2–94 years), but it most commonly shows a double-peaked age distribution in the 2nd and 6th decades of life,[4] without a gender predilection.Patients from the lowest socioeconomic status (SES) group were nearly 85% more likely to present with advanced-stage olfactory neuroblastoma compared to those in the highest SES group, reflecting delayed access to specialized care. While the use of multimodal therapy did not vary significantly across SES tiers, race was strongly linked to treatment differences: Black patients were over 60% less likely than White patients to receive multimodal treatment. This suggests that, despite an apparent parity in treatment across SES levels, racial disparities persist independently.[5] The most common presentation includes unilateral nasal obstruction and epistaxis, while less common symptoms are sneezing, rhinorrhea, headache regional metastases most commonly involve the cervical lymph nodes, and cervical nodal involvement is well-established as one of the most significant prognostic factors affecting survival.

Since the tumor involves the olfactory epithelium, anosmia is not a common complaint. Grossly, olfactory neuroblastoma appears as a soft polypoid mass covered in mucosa with a glistening surface. It can range in size from a small nodule less than 1 cm to a mass that occupies the entire nasal cavity, with potential extension into adjacent paranasal sinuses, nasopharynx, orbit, and sometimes the cranial vault.

From a practical standpoint, ONB's often lack distinguishing features, making them difficult to differentiate from other nasal tumors based on appearance alone. Imaging, particularly CT or MRI, is crucial for accurate diagnosis and assessment. While ONB does not exhibit specific radiological characteristics, MRI is superior in evaluating suspected invasion of the skull base, orbit, and perineural tumor spread .[6] On MRI, the tumor typically appears isodense on T1-weighted imaging and hyperintense on T2/STIR sequences, with findings such as bony erosions and intracranial or intraorbital extensions. Angiographic techniques have no role in the diagnostic or therapeutic workup of ONB, as it is typically not a highly vascular tumor.

Fluorodeoxyglucose (FDG) positron emission tomography (PET) is frequently utilized in patients with advanced disease, particularly for assessing treatment response ,conventional imaging for staging and restaging esthesioneuroblastoma, detecting nodal and distant metastases as well as local recurrence not visible on MRI or CT.

The Kadish system is the most widely used classification for categorizing the anatomical extent of ONB, despite the existence of other staging approaches.[7]

This system originally defined three categories but was later expanded by Morita et al. to include cervical and distant metastases as an additional stage, creating the "modified Kadish" staging system.[8] Separately, in 1992, Dulguerov et al. introduced a T-staging framework focusing on radiological findings.[9]

Table I : Modified Kadish System

STAGE	EXTENSION
A	Confined to nasal cavity
B	Involvement of one or more paranasal sinuses
C	Extension beyond the nasal cavity and paranasal sinuses involving cribriform plate, skull base, orbit or intracranial cavity
D	Regional lymph node metastasis

The **Hyams grading system** is widely used for tumor classification and prognostication based on histopathological features.[10] Higher-grade tumors are associated with a worse prognosis. As the grade increases, diagnosis often becomes challenging, frequently necessitating ancillary studies for confirmation.

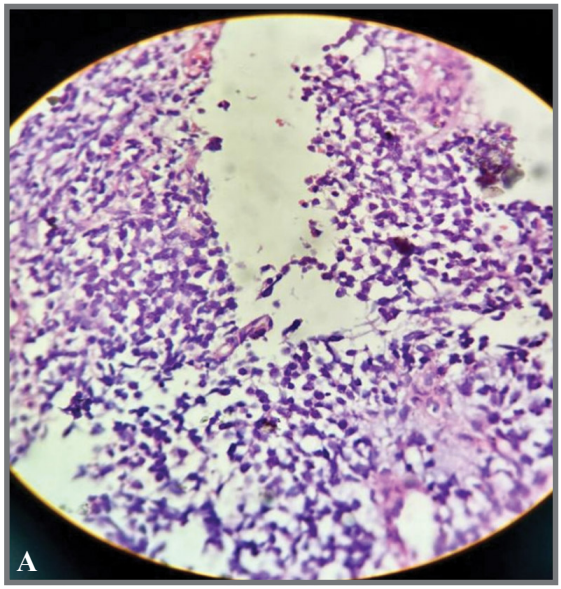


Fig. 3. Photomicrographs of hematoxylin and eosin stains 100x fig3(a) shows interconnecting rosettes with hyperchromatism and 100x

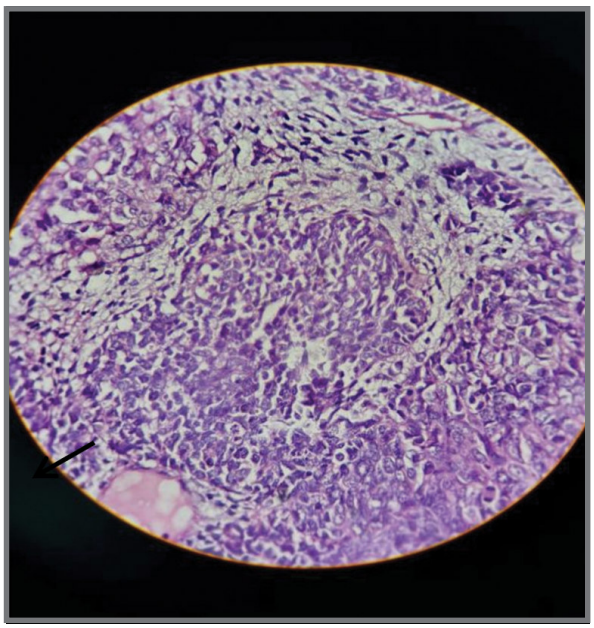


Fig. 3. (b)-shows flexner winterstenier rosettes -duct like spaces lined with non-ciliated columnar epithelial cells arranged around a central lumen

Immunohistochemistry findings for ONB include positivity for Synaptophysin (focal), Neuron-Specific Enolase (NSE), Chromogranin, CD56, S-100, neurofilament protein (NFP), and cytokeratins (e.g., AE1/AE3). The small, round tumor cells are typically positive for these markers, whereas peripheral cells exhibit S-100 positivity. Nuclear immunoexpression of INI-1 and RB1 is retained in tumor cells.

Treatment utilises a combination of surgery, external beam radiation, and chemotherapy these modalities. The primary objective in ONB surgery is achieving a negative margin resection when feasible, which can be accomplished via an open approach or endoscopic resection. For tumors involving the skull base, treatment plans are typically developed and implemented collaboratively between the otolaryngologist and neurosurgeon. A 2017 study by Harvey et al. compared open transcranial resection to endoscopic resection of ONB, reporting favorable survival outcomes for patients undergoing endoscopic resection.[11] Postoperative complications including orbital, vascular, and intracranial injuries, can lead to cerebrospinal fluid leaks, meningitis,

Table II: Hyams Grading System

MICROSCOPIC FEATURES	GRADE 1	GRADE 2	GRADE 3	GRADE 4
Architecture	Lobular	Lobular	+/-lobular	+/-lobular
Pleomorphism	Absent	Present	Prominent	Marked
Mitosis	Absent	Present	Prominent	Marked
Necrosis	Absent	Absent	Present	Prominent
Rosettes	Homer -wright	Homer-wright	Flexner-winterstenier	Flexner-winterstenier
Calcification	Variable	Variable	Absent	Absent
Neurofibrillary matrix	Prominent	Present	Prominent	Marked

and high recurrence rates, particularly after endoscopic ONB resection. However, this approach preserves olfaction and vital structures. Advances in radiation techniques have further minimized toxicity and protected nearby critical anatomy.

Radiation therapy, in both neoadjuvant and adjuvant settings, has been studied for the definitive treatment of ONB. Radiation therapy is recommended for high-grade tumors, as well as for borderline resected, residual, or recurrent low-grade tumors. The conformational radiation techniques currently employed include Intensity-Modulated Radiation Therapy (IMRT). IMRT is particularly recommended as it provides better protection for nearby structures and tissues. This technique allows the radiation dose to conform more precisely to the three-dimensional (3D) shape of the tumor by modulating the intensity of the radiation beam in multiple small volumes.

In a study by Mori et al.,[12] a multimodal therapeutic approach combining radiation therapy with precise treatment planning based on CT simulation achieved excellent outcomes. The 5-year overall survival (OS) and relapse-free survival (RFS) rates were reported to be 88% and 74%, respectively. Adjuvant radiation therapy is indicated for Kadish stage B and C tumors.

The resectability of locally-advanced esthesioneuroblastoma may be improved by chemotherapy, which is a treatment option for individuals with incurable local illness.

However, it is employed for locally advanced or metastatic disease. Currently, the preferred chemo-therapy regimen involves administering cisplatin (33 mg/m² daily) and etoposide (100 mg/m² daily) for three consecutive days.[13]

Conclusion

Following a multidisciplinary evaluation, the patient underwent a minimally invasive endoscopic resection of the visible tumor. Post-procedural pathology confirmed a diagnosis of moderate-grade olfactory neuroblastoma (ONB), with disease characteristics and extension consistent with Kadish stage C and a high-grade classification per the Hyams system. Ten days later, the patient was scheduled to receive adjuvant external beam radiation therapy (RT). Post-treatment follow-up includes regular MRI scans and nasal endoscopy to monitor for recurrence, with an emphasis on the absence of clinical or radiological lymph nodes.

References

1. Frierson Jr HF, Mills SE, Fechner RE, Taxy JB, Levine PA. Sinonasal undifferentiated carcinoma: an aggressive neoplasm derived from schneiderian epithelium and distinct from olfactory neuroblastoma. The American journal of surgical pathology. 1986 Nov 1;10(11):771-2.
2. Thompson, L. D. (2009). Olfactory neuroblastoma. Head and neck pathology, 3, 252-259.

3. Kleihues P, Louis DN, Scheithauer BW, Rorke LB, Reifenberger G, Burger PC, Cavenee WK. The WHO classification of tumors of the nervous system. Journal of Neuropathology & Experimental Neurology. 2002 Mar 1;61(3):215-25
4. Yin Z, Wang Y, Wu Y, Zhang X, Wang F, Wang P, et al. Age distribution and age-related outcomes of olfactory neuroblastoma: a population-based analysis. Cancer Manag Res (2018) 10:1359–64
5. Sharma RK, Irace AL, Overdevest JB, Turner JH, Patel ZM, Gudis DA. Association of race, ethnicity, and socioeconomic status with esthesioneuroblastoma presentation, treatment, and survival. OTO Open (2022)
6. Ahmad A, Branstetter IV BF. CT versus MR: still a tough decision. Otolaryngologic Clinics of North America. 2008 Feb 1;41(1):1-22
7. Kadish S, Goodman M, Wang CC. Olfactory neuroblastoma—a clinical analysis of 17 cases. Cancer. 1976 Mar;37(3):1571-6
8. Morita A, Ebersold MJ, Olsen KD, Foote RL, Lewis JE, Quast LM. Esthesioneuroblastoma: prognosis and management. Neurosurgery. 1993 May 1;32(5):706-15
9. Dulguerov P, Calcaterra T. Esthesioneuroblastoma: The UCLA Experience 1970-1990. The Laryngoscope. 1992 Aug;102(8): 843–9
10. Goshtasbi K, Abiri A, Abouzari M, Sahyouni R, Wang BY, Tajudeen BA, Hsu FPK, Cadena G, Kuan EC. Hyams grading as a predictor of metastasis and overall survival in esthesioneuroblastoma: a meta-analysis. Int Forum Allergy Rhinol. 2019 Sep;9(9):1054-1062
11. Harvey RJ, Nalavenkata S, Sacks R, Adappa ND, Palmer JN, Purkey MT, Schlosser RJ, Snyderman C, Wang EW, Woodworth BA, Smee R. Survival outcomes for stage matched endoscopic and open resection of olfactory neuroblastoma. Head & neck. 2017 Dec;39(12):2425-32
12. Mori T, Onimaru R, Onodera S, Tsuchiya K, Yasuda K, Hatakeyama H, Kobayashi H, Terasaka S, Homma A, Shirato H. Olfactory neuroblastoma: the long-term outcome and late toxicity of multimodal therapy including radiotherapy based on treatment planning using computed tomography. Radiation oncology. 2015 Dec;10:1-9.
13. Bhattacharyya N, Thornton AF, Joseph MP, Goodman ML, Amrein PC. Successful treatment of esthesioneuroblastoma and neuroendocrine carcinoma with combined chemotherapy and proton radiation: results in 9 cases. Archives of Otolaryngology–Head & Neck Surgery. 1997 Jan 1;123(1):34-40.