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Olfactory Neuroblastoma Masquerading As Benign Nasal Disease: A Case Report

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ABSTRACT

Background:
Olfactory neuroblastoma is a rare neuroendocrine malignancy of the sinonasal tract that frequently mimics benign nasal disease. Clinical features such as nasal obstruction, epistaxis or anosmia may overlap with inflammatory conditions. These overlapping clinical features require a high index of suspicion for early diagnosis and intervention. Advances in imaging, including 68Ga-DOTATATE PET-CT, have improved staging accuracy by targeting somatostatin receptor expression. Patients diagnosed at an early-stage disease can be managed by endoscopic resection often supplemented with adjuvant radiotherapy to optimize local control.

Case Report:
A 66-year-old African woman presented with a two-year history of progressive unilateral nasal obstruction and intermittent epistaxis. She was initially treated as a case of benign nasal polyp. Postoperative histopathology unexpectedly revealed Hyams Grade 2 olfactory neuroblastoma. Nasal endoscopy demonstrated a mass in the left middle meatus and CT imaging confirmed a well-defined lesion confined to the nasal cavity without bony erosion. 68Ga-DOTATATE PET-CT showed moderate tracer uptake without metastatic spread classifying the tumour as Kadish Stage A. The patient subsequently underwent endoscopic resection of the residual tumour, with histologically clear margins. Adjuvant intensity-modulated radiotherapy (60 Gy in 30 fractions) was administered to reduce recurrence risk while minimizing toxicity to adjacent optic structures. At 12-month follow-up, she remained disease-free with minimal treatment-related side effects.

Conclusion:
This case underscores the diagnostic challenges involved in management of olfactory neuroblastoma. It further highlights the importance of advanced imaging in cases presenting with persistent nasal masses. Endoscopic resection when combined with targeted radiotherapy offers excellent local control in cases diagnosed at an early-stage.

Keywords: Chromogranin, DOTATATE PET-CT, Esthesioneuroblastoma, INSM1, Olfactory Neuroblastoma, Synaptophysin

INTRODUCTION

Olfactory neuroblastoma (esthesioneuroblastoma) is a rare neuroendocrine malignancy originating from the olfactory epithelium, first described by Berger et al. in 1924.[1] Accounting for less than 3% of sinonasal tumors, it poses diagnostic challenges due to nonspecific symptoms and histologic resemblance to other small round blue cell tumors.[2] Typical presentations such as nasal obstruction, epistaxis, and anosmia often lead to misdiagnosis as benign conditions like nasal polyps or sinusitis.[3] Diagnosis relies on histopathology showing small round cells with salt-and-pepper chromatin and immunohistochemical positivity for synaptophysin, INSM1, and chromogranin.[2] Advanced imaging with 68Ga-DOTATATE PET-CT has improved staging and localization by exploiting somatostatin receptor expression.[4] Endoscopic resection with or without adjuvant radiotherapy remains the preferred treatment for early-stage disease, offering excellent disease control and functional outcomes.[5]

CASE REPORT

A 66-year-old African female with no significant comorbidities presented with a two-year history of progressive left nasal obstruction, intermittent epistaxis, and post-nasal drip. She was initially diagnosed with a benign nasal polyp and underwent endoscopic excision in the left nasal fossa. Postoperative histopathology revealed Hyams Grade 2 olfactory neuroblastoma.

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On nasal endoscopy, a fleshy mass was identified occupying the left middle meatus. The patient did not have any other significant systemic symptoms or relevant past medical history.

Cross-sectional CT imaging of the paranasal sinuses showed a soft tissue density lesion in the left nasal cavity centered in the middle meatus and olfactory cleft, without bony erosion or extension into the cribriform plate or orbit (Figure 1).

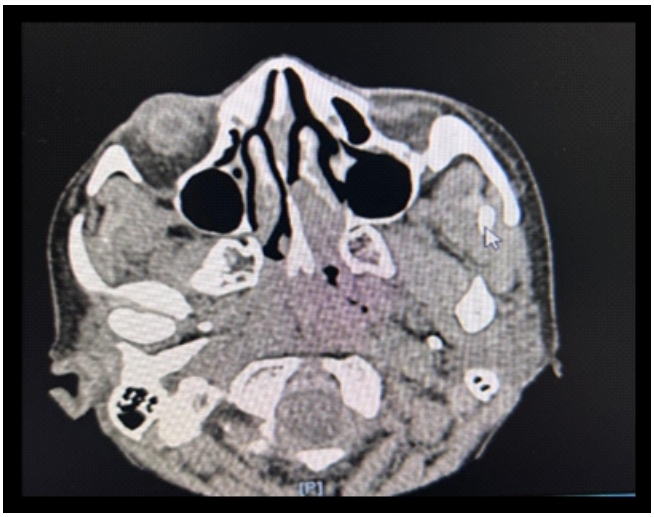

Figure 1. CT scan of paranasal sinuses depicting a well-defined mass in the superior left nasal cavity abutting but not breaching the cribriform plate, with no intracranial extension.

Microscopically, the tumour showed small round blue cells with salt-and-pepper chromatin and Homer Wright pseudo-rosettes. Immunohistochemistry was positive for neuroendocrine markers (synaptophysin, chromogranin, INSM1) and negative for cytokeratin and S100, distinguishing it from sinonasal undifferentiated carcinoma or melanoma. 68Ga-DOTATATE PET-CT demonstrated moderate radiotracer uptake in the lesion without evidence of regional or distant metastases, confirming localized disease.

Kadish staging classified the tumour as Stage A (limited to the nasal cavity), and Hyams grading was Grade 2 (low-to-intermediate grade) with an anticipated 5-year survival of 80–90% but a moderate recurrence risk (10–30%). The patient underwent excision and biopsy of the residual tumour with endoscopic resection. Intraoperative inspection revealed the tumour arose from the olfactory cleft without involving the cribriform plate, and histopathological examination confirmed negative margins. Adjuvant radiotherapy was delivered at 60 Gy in 30 fractions by intensity-modulated radiotherapy (IMRT). This schedule was chosen due to the 10–30% recurrence rate of Hyams Grade 2 tumours and the need to limit radiation dose to neighbouring optic structures which is an important benefit of IMRT Post-treatment follow-up consisted of nasal endoscopy, showing healed mucosa without evidence of residual disease and Grade 1 mucositis which was managed symptomatically without treatment interruption. These findings support the effectiveness of combined endoscopic resection and IMRT for local control with preservation of tolerability.

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DISCUSSION

The diagnostic process for olfactory neuroblastoma is challenging, with the tumour often being masqueraded by benign polyps both on radiology and histology, thus requiring repeated biopsy with immunohistochemistry (INSM1) when there remains clinical suspicion. DOTATATE PET-CT has been found superior to FDG-PET because of its specificity for targeting somatostatin receptor expression, enabling more accurate tumor localization and staging. Therapeutically, endoscopic resection is now the norm for Kadish A/B tumours, with 5-year survival rates of 85–90%, and open craniofacial methods being reserved for advanced (Kadish C) disease. Radiotherapy protocols also continue to advance, with standard doses of 55–65 Gy now questioned by recent evidence that 50 Gy can be adequate for Hyams G1–2 tumours with clear margins; proton therapy further optimizes outcomes by decreasing orbital toxicity markedly. Molecular breakthroughs are transforming the landscape, with IDH2 inhibitors (e.g., enasidenib) under evaluation for IDH2-mutant disease and DLL3-targeted therapy (e.g., tarlatamab) being promising in relapse. These findings as a whole highlight the need for multidisciplinary collaboration to maximize diagnostic and treatment approaches to this rare cancer.

Endoscopic resection is currently the treatment of choice for Kadish A/B olfactory neuroblastoma, with high rates of disease control and less morbidity than with conventional open craniofacial techniques.[5,6] Nicolai et al. have described five-year survival rates of up to 90% with endoscopic treatment, particularly when clear margins are obtained.[6] A meta-analysis by Rawal RB et al emphasized the importance of multidisciplinary collaboration and supported endoscopic techniques for early-stage sinonasal malignancies for its lower complication rates.[7] Craniofacial resection is typically reserved for advanced cases with intracranial involvement.[8]

Radiation therapy remains a mainstay of olfactory neuroblastoma management, particularly in intermediate or high-grade tumours or when surgical margins are uncertain. The NCCN guidelines recommend a dose of 55–65 Gy.[9] But newer evidence from current research indicates that reduced doses (about 50 Gy) can be adequate for low-grade (Hyams I–II) tumours with R0 resection, reducing radiation-associated toxicity. Proton beam therapy has been revealed to decrease optic and brain toxicity in skull base cancers compared to photon therapy, with Mehta et al. reporting

decreased visual injury rates in olfactory neuroblastoma patients treated with protons.[10]

Olfactory neuroblastoma can simulate other small blue round cell tumours, thus histopathologic assessment is imperative. Typical characteristics involve small round cells with salt-and-pepper chromatin, fibrillary stroma, and Homer Wright rosettes.[11]

Differentiation is supported by immunohistochemistry, wherein INSM1, synaptophysin, and chromogranin are positive, while cytokeratin and S100 are generally negative in Olfactory neuroblastoma.[12]

Chemotherapy has limited proven application in Olfactory neuroblastoma, especially in the early stages.[13] The GETTEC group identified no survival benefit with chemotherapy in Kadish A/B patients. Neoadjuvant regimens are, however, being investigated for advanced, unresectable, or recurrent disease.[14] Molecular profiling has also identified new therapeutic targets. IDH2 mutations in olfactory neuroblastoma can be treated with anadenia, and DLL3-targeted therapy is under investigation in clinical trials for recurrent disease.[15]

CONCLUSION

This case highlights the diagnostic challenges of olfactory neuroblastoma, which often mimics benign nasal conditions, underscoring the importance of histopathological accuracy and multidisciplinary management. Treatment continues to evolve, with molecularly targeted therapies such as IDH2 inhibitors and DLL3-directed agents showing promise for recurrent or advanced disease. Ongoing research and prospective trials are essential to refine chemotherapy protocols and develop personalized treatment strategies for this rare malignancy.

ETHICAL CONSIDERATION:

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The patient's identity has been anonymized to protect confidentiality, and all clinical details have been presented without identifying information.

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Conflict of interest : None.

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Author Contribution:- ZA: Conceptualized the study, collected and analyzed patient data, drafted the original manuscript, and revised subsequent versions. Served as corresponding author. **AAA:** Assisted in data collection and analysis, contributed to manuscript writing (case presentation and investigations sections), and reviewed final drafts. **AA**: Provided expert oncological guidance, critically reviewed the manuscript (particularly treatment and discussion sections), and approved the final version for submission.

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