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(CASE REPORT)

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Olfactory Neuroblastoma: A case report of a rare tumor and a brief review of the literature

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Abstract

Olfactory neuroblastoma (ONB) is a rare neoplasm originating from the olfactory neuroepithelium. Due to its rarity and diagnostic challenge, it requires a multidisciplinary diagnostic and management approach. Our patient is a 49-year-old male with no previous history of malignancy who presented with recurrent epistaxis, diplopia, facial edema, anosmia, and a protruding mass from his right nostril. Imaging studies showed a heterogeneously enhancing mass (4.2 x 3.5 x 3.8 cm) in the right superior nasal cavity extending through the skull base and causing displacement of the right frontal lobe. A multidisciplinary tumor board discussion led to an endoscopic biopsy of the tumor before proceeding with chemotherapy, transcranial resection of the tumor, and postoperative radiation. Pathology results indicated the tumor was positive for synaptophysin, chromogranin, NSE, and S100 and negative for cytokeratin, EMA, LCA, desmin, and myogenin, confirming a grade II ONB without lymphovascular invasion. The patient had no evidence of tumor recurrence at 36 months of follow-up. He continues to have hyposmia, frontal headaches, and right eye epiphora from nasolacrimal duct injury, which have all been managed conservatively. Overall, the patient has a good functional status and intact cognitive abilities following tumor resection. This case highlights the importance of recognizing variable presentations of rare tumors, especially in patients with low-risk factors, and of appropriately managing them to achieve optimal patient outcomes.

Keywords: Olfactory neuroblastoma; Neuroepithelium; Multidisciplinary; Surgery; Radiation Therapy; Chemotherapy

1. Introduction

Olfactory neuroblastoma (ONB), also called esthesioneuroblastoma, is a relatively rare type of malignancy that originates from the olfactory neuroepithelium in the superior part of the nasal vault. [1] Although few cases were reported with a sinonasal origin, ONB remains a significant condition because, on most occasions, patients initially present with nonspecific symptoms of a benign condition. [2] This presentation results in a significant delay in referral to a specialist, leading to complications such as invasion of the skull base, orbit, or the brain. The prognosis is directly dependent on the stage of presentation. [2]

Symptoms may include unilateral nasal obstruction, intermittent epistaxis, rhinorrhea, facial headache, and a reduced

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sense of smell. [1] A diagnosis must incorporate endoscopic examination, radiographic evaluation, and histopathological characterization. [3] Definitive diagnosis is dependent on tissue biopsy findings, recognizing the growth of small to moderate-sized neuroblastic cells within a neurofibroblastic background, attended by the presence of Homer-Wright rosettes, in addition to neuroendocrine features and IHC studies characteristic of ONB. [4]

Staging systems such as Kadish remain widely used to describe anatomic extent and guide treatment planning and prognosis. The histologic grading further refines risk stratification. [5] Treatment is typically multimodal and best directed by disease stage and grade. Surgery, via open craniofacial approaches but now also endoscopically via the endonasal route when safely possible, is typically the major component of treatment. [6] Surgery is usually followed by radiation, whereas chemotherapy is considered in more advanced disease, particularly involving high-grade tumors. [7] [8] Long-term follow-up is required, particularly for a tumor which is known to recur many years posttreatment.

In this report, we present a 49-year-old male with progressive nasal obstruction and epistaxis who developed diplopia and facial edema, leading to the diagnosis of ONB with intracranial and orbital extension. This case highlights the importance of diagnostic pointers in such an uncommon tumor.

2. Case presentation

2.1. Clinical presentation

A 49-year-old male presented to the emergency department because of recurrent epistaxis requiring nasal packing, progressive diplopia in upward gaze, and striking facial swelling. Symptoms began with unilateral nasal obstruction and intermittent epistaxis (8 months) that he attributed to seasonal allergies; he self-treated using over-the-counter decongestants with no relief of the symptoms. Symptoms had worsened slowly over 3 months prior to presentation with persistent right-sided nasal congestion, anosmia, and blood-tinged rhinorrhea. He had right-sided facial pain and a right-sided headache. About 2 weeks before the current presentation, a mass was apparent in the right nostril. Empiric antibiotic therapy for possible sinusitis was not effective. The nasal mass, cranial nerve involvement, and unremitting symptoms prompted his primary care physician to refer him to an urgent ENT consultation for advanced imaging and diagnosis.

2.2. History and physical examination

The patient was a 25-year-old woodworker with exposure to hardwood dust regularly. He denied prior head and neck radiation, chemical exposures, and nasal polyps. He reported controlled hypertension with amlodipine. No history of previous malignancy. His cannabis use was recreational, and he denied alcohol abuse and immunosuppressive diseases. His mother had breast cancer and passed away aged 62 years; his father had prostate cancer. There was no family history of head and neck cancers, neuroendocrine tumors, or genetic cancer syndromes.

On physical examination, the patient was in good condition but appeared in obvious distress. A 3 cm polypoid mass that occupied the right nasal cavity and was reddish-gray and friable, with active oozing, was seen in the anterior rhinoscopy. The mass was seen to arise at the superior nasal vault. There were right-sided proptosis and limitation of upward gaze, indicating orbital floor involvement with mild periorbital edema, but no changes in visual acuity. Cranial nerve check revealed a loss of sensation in his right V2 field. There was no protrusion of the hard palate. The nasopharyngeal involvement was not observed, and a flexible nasopharyngoscopy showed the extension of the mass posteriorly. No palpable lymphadenopathy was detected in the neck. Olfactory nerve assessment was positive for right-sided anosmia. There were no other cranial nerve abnormalities**.**

2.3. Radiographic studies

CT paranasal Sinuses (with contrast) showed a heterogeneously enhancing mass in the right superior nasal cavity and ethmoid air cells with an erosion of the cribriform plate and fovea ethmoidalis. The 1.5 cm intracranial mass extended from the skull base and pushed the right frontal lobe aside. There was partial medial orbital wall erosion extending to the medial extraconal space. The mass led to opacification of the right maxillary, ethmoid, and frontal sinuses. Peripheral calcifications within the tumor were observed.

MRI of the brain and facial bones (with gadolinium) showed a lesion with moderate T1 and inhomogeneous T2 signal intensity and uneven enhancement. A peculiar dumbbell shape of the mass was observed with a narrowing of the waist at the cribriform plate. The intracranial extension depicted a mass effect of the right gyrus rectus and the surrounding vasogenic edema. No characteristic dural tail or meningioma enhancement pattern was observed. A hypercellular tumor was suggested by diffusion restriction. There were no other intracranial lesions detected.

Radiological differentiations diagnosis included: Olfactory neuroblastoma (Esthesioneuroblastoma): -Most likely due to cribriform origin, dumbbell, and calcifications. Sinonasal undifferentiated carcinoma (SNUC) - Aggressive tumor, but generally not invaded intracranially at this point. Neuroendocrine carcinoma - Could resemble it, but tends to have more destructive bone changes. Lymphoma - Less likely due to characteristic dural tail or hyperostosis, and Meningioma - Unlikely. The patient's tumor extended through the cribriform plate by intracranial and orbital extension, so it was stage C Kadish Stage. This stratification was important for treatment planning as Stage C disease usually receives multimodal therapy in the form of surgery, chemotherapy, and radiation.

2.4. Tumor board discussion

The case was discussed in the multidisciplinary head & neck tumor board in the presence of neurosurgery, otolaryngology, medical oncology, radiation oncology, neuroradiology, and pathology. As the tumor size was 1.5 cm, there was intracranial extension, and the radiographic appearance was highly indicative of olfactory neuroblastoma, the team discussed the options of biopsy and upfront resection. It was feared that endoscopic biopsy could result in serious bleeding and inadequate tissue that could not be analyzed on a molecular level. Nonetheless, the opinion was initially for endoscopic biopsy to establish diagnosis before treatment planning, as management varied widely for olfactory neuroblastoma (esthesioneuroblastoma), SNUC, and other sinonasal malignant tumors. Endoscopic cautious examination with interventional radiology was to be undertaken in case of embolization. The tumor board recommended preoperative biopsy for possible consideration of neoadjuvant therapy.

2.5. Tissue diagnosis

Several friable fragments of tan-pink tissue were endoscopically biopsied, measuring approximately 1.2 cm in aggregates, with hemorrhages and necrosis. Microscopically, the sections showed a highly cellular neoplasm in lobules separated by fibrovascular stroma, resulting in classical Zellballen-like organoid structures. The tumor cells were small to medium-sized, with hyperchromatic round nuclei, fine, minced-salt-and-pepper chromatin, indistinct nucleoli, and scanty cytoplasm. Homer-Wright rosettes (neuroblastic rosettes) were identified as composed of tumor cells organized around a central neuropil with no lumen. Mitotic activity was high with 12 mitoses per 10 high-power fields, and the background was focally calcified and necrotic.

Pathological differential diagnosis included sinonasal undifferentiated carcinoma (SNUC), which was ruled out, as there was evidence of a neurofibrillary matrix and rosettes. Neuroendocrine carcinoma: Lacks Homer-Wright rosettes, different IHC profile. Rhabdomyosarcoma: Young age is typical, with a different immunoprofile—pituitary adenoma: characterized by its unusual location and distinct architecture. IHC studies showed positive results for Synaptophysin (intense, diffuse), Chromogranin (focal), NSE, S100 (sustentacular cells at the lobule periphery), and CD56. The following markers were negative: Cytokeratin (CK CAM 5.2, AE1/AE3), EMA, LCA, Desmin, and Myogenin. ONB was confirmed by high synaptophysin expression, chromogranin expression, the presence of S100-positive sustentacular cells, and a negative epithelial marker. (Figure 1 A, B, C, D) The tumor histologic grade of Hyam was Grade II (moderate nuclear pleomorphism, increased mitotic activity, and the presence of rosettes and a distinguishable neurofibrillary matrix). Molecular testing was not performed.

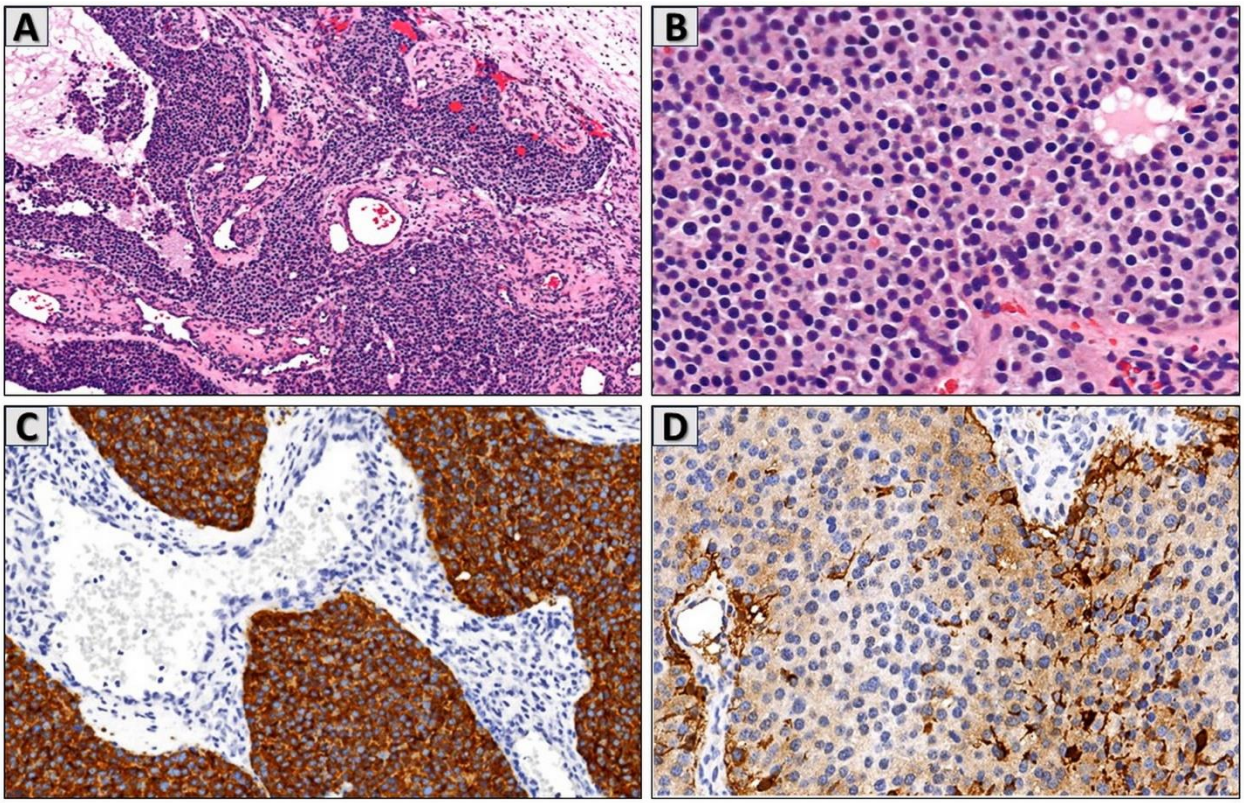
2.6. Treatment regimen

Following the biopsy diagnosis, neoadjuvant therapy started with three courses of cisplatin and etoposide. The treatment resulted in a 50% decrease in tumor size on a repeat MRI. A combined endoscopic endonasal with bifrontal craniotomy to undergo craniofacial resection was performed. The operation was successful, and gross total resection was attained, and negative margins were confirmed on the frozen section. Skull base reconstruction was performed with the help of a pedicled nasoseptal flap and pericranial flap. A CSF leak that occurred temporarily was controlled with lumbar drainage, which complicated the postoperative course but resolved. The final pathology confirmed the biopsy diagnosis of ONB, grade II, and with clear margins (nearest margin 3 mm). Lymphovascular invasion was not found.

Adjuvant intensity-modulated radiation therapy (IMRT) was applied 6 weeks after surgery. The treatment was acceptable, with mucositis and fatigue manageable.

2.7. Follow-up and outcome: Surveillance and monitoring of the patient were conducted using MRI of the brain/sinuses and CT of the chest after 4 months, then every 6 months during the first 2 years. At 36 months follow-up, the patient had no signs of local recurrence or distant metastases. He had constant hyposmia and minor frontal headaches that were medically managed. After 6 months, he returned to modified work without significant dust

exposure. Three years after the diagnosis and treatment, the neuropsychological examination revealed no abnormal cognitive ability. Quality-of-life measurement showed normal functional status, with an ECOG performance status of 1.



1A: Low power view showing cellular neoplasm in lobules separated by fibrovascular stroma (H&E X20); **1B:** High power view showing small to medium-sized tumor cells with hyperchromatic round nuclei (H&E X40); **1C:** Tumor cells positive for synaptophysin; **1D**: Tumor cells showing sustentacular cells at the lobule periphery, positive for S-100

Figure 1 Microscopic examination and immunohistochemistry of the olfactory neuroblastoma

3. Discussion

3.1. Background (History, epidemiology, and WHO classification)

ONB, also known as esthesioneuroblastoma or esthesioneuroepithelioma, was first described by Berger and colleagues in 1924. ONB is a malignant neoplasm arising from the olfactory neuroepithelium in the superior nasal cavity and anterior skull base. [3] [9] In the subsequent decades, the tumor has been given different names, and its origin has been a subject of debate. However, modern clinicopathologic studies and IHC support that it originates from olfactory neuroepithelial progenitor cells. [1]

ONB is rare, with an estimated incidence range of approximately 0.2–0.4 per million to 0.4-1.0 per million population per year, and accounts for roughly 2-6% of intranasal malignant cases. [2] [3] ONB cases have been reported in individuals of all ages, but peak in middle-aged adults (40 to 70). However, there is no consistent or clear overall tendency for a specific sex. [1] [5] In many cases, the first presenting symptom is a nasal obstruction, epistaxis, and anosmia. In later stages, headaches develop, more severe orbital or intracranial extension accompanied by neurologic symptoms, which reflect the tumor's aggressive local behavior. Late diagnosis is common since the early symptoms mimic those of a benign paranasal sinus condition. [2] [3]

Prognosis typically depends on the stage and the histologic grade. Various classification systems are documented in the medical literature. These include the modified Kadish classification (A-D), Dulguerov TNM, and AJCC adaptations. The initial Kadish stage has historically been associated with survival and local control and is still widely used. [5] [10] [11] In terms of histology, pathologists have used the Hyams system since the 20th century, and it is still the most popular grading system. It classifies tumors based on architecture, mitotic activity, degree of pleomorphism, rosette formation, and necrosis. [11] Many scholars, however, opt to simplify Hyams into high (grade III-IV) and low (grade I-II) groups for prognostic implications. [3] [11] Even so, the latest WHO updates on the classification of the tumors of the head and

neck area (5th edition) advocate for a hybrid approach in classifying the tumors. This hybrid approach can be achieved by using macroscopy, microscopy, immunoprofiling, and available molecular data. [12]

Molecular data warrant the classification of ONB as a distinct malignant neuroectodermal tumor of the olfactory epithelium within the head and neck region. It is distinguished from other neuroendocrine and neuroectodermal tumors of the sinonasal region by its unique composite morphological, IHC, and molecular features. [3] ONB arises from neuronal progenitor cells (Globose Basal Cells, GBCs) in the olfactory epithelium. Its molecular profile often reflects a block in neuronal maturation, mimicking the gene expression of these progenitor states (msGBC/npGBC). [13] Molecular profiling helps distinguish ONB from olfactory carcinoma and identify high-risk features. [13]

Management is multimodal, entailing surgery coupled with radiotherapy or chemotherapy. Recent studies consistently show that endoscopic and endoscopic-assisted craniofacial techniques are successful for properly selected tumors. [2] [3]

3.2. Pathogenesis, pathophysiology

ONB is a rare malignancy of the sinonasal tract, and its pathogenesis is a subject of ongoing research. The cell of origin is believed to be the olfactory neuroepithelium, a specialized tissue located in the superior nasal cavity responsible for the sense of smell. [14] [15] This origin is supported by the tumor's typical location at the cribriform plate and its expression of neural and neuroendocrine markers. The patient's primary symptom of anosmia is a direct pathophysiologic consequence of the tumor's growth within and destruction of the neuroepithelium. [15]

Molecular and genetic analyses of olfactory neuroblastoma have not yet identified a single characteristic mutation, but several alterations have been implicated in its development. [1] Dysregulation in signaling pathways such as Notch, Hedgehog, and Wnt/β-catenin has been observed, which are crucial for neural crest development and differentiation. [13] [15] Overexpression of growth factors such as EGFR and PDGF, and mutations in tumor suppressor genes such as TP53, have been reported in some cases, contributing to uncontrolled cell proliferation and tumor growth. [1] [13] The tumor's local spread, as seen in this case, occurs through direct extension. Its origin in the superior nasal vault allows it to easily erode the thin cribriform plate to gain intracranial access and invade the adjacent orbits through the lamina papyracea. This direct invasion explains the patient's diplopia and V2 sensory loss.

Histopathologically, the tumor's neuroblastic origin is reflected in its characteristic features. The formation of lobules separated by a fibrovascular stroma, creating a "Zellballen" pattern, is a classic finding. [1] The presence of Homer-Wright rosettes further confirms its neural differentiation. The expression of synaptophysin, chromogranin, and CD56 is an IHC hallmark of its neuroendocrine nature. At the same time, the S100-positive sustentacular cells at the periphery of the lobules are consistent with the structure of normal olfactory tissue. [4]

3.3. Comparative analysis of our case with the existing literature.

3.3.1. Clinical presentation and radiological findings

Several features of our case align closely with previously reported cases of ONB. Our patient was a 49-year-old male, which is consistent with epidemiologic data. Yin Z. reported that ONB exhibits a unimodal age distribution, most commonly presenting in adults aged 50-60 years. [16] Likewise, Brisson's long-term retrospective analysis found that the majority of ONB patients are male (59%). [8] Clinically, our patient exhibited hallmark symptoms frequently described in the literature, including unilateral nasal obstruction, intermittent epistaxis over several months, right-sided anosmia, diplopia, proptosis, and facial edema. [7] [8] [17] Notably, while facial edema has been described, its pronounced severity in this case was particularly striking. [8]

On physical examination, a classic mass occupying the nasal cavity and arising from the superior nasal vault was identified, consistent with typical ONB presentation. [7] The mass measured 1.5 cm, appeared reddish-gray and friable, and demonstrated active oozing with posterior extension. ONB is a locally aggressive tumor capable of invading adjacent structures, including the skull base and orbits, and metastasizing in 20–48% of cases. [7] Our patient had no palpable cervical lymphadenopathy. The most common reported metastatic sites of ONB include cervical lymph nodes (10–33%), bone, and lungs. [18] Radiographically, imaging findings in our case were consistent with those reported in the literature. A characteristic "dumbbell" configuration with constriction at the cribriform plate was also present, a classic radiologic feature described by Thompson et al. [4]

Among the existing staging systems, the Kadish classification remains the most widely used. It includes three stages: Stage A, disease confined to the nasal cavity; Stage B, extension into the paranasal sinuses; and Stage C, extension beyond

the paranasal sinuses. [4] Given the tumor's intracranial and orbital involvement, our patient met the criteria for Kadish Stage C.

3.3.2. Diagnosis (Pathology, immunohistochemistry, and molecular findings)

Our case demonstrates a diagnostic picture highly compatible with ONB, consistent with current literature. Establishing the diagnosis of ONB requires correlating the history, physical examination, and CT/MRI findings for qualitative evaluation and staging. [7], all of which were undertaken in our patient. Full-body CT and PET scans are also recommended to assess the extent of systemic disease, as noted by Bradley et al. [19] A biopsy is mandatory and is typically performed after imaging. [7] Despite the variability in histologic appearance across the numerous sinonasal tumor histologic types, several key microscopic features remain characteristic of ONB. [7] This variability underscores the need to confirm the preliminary diagnosis using IHC studies, which has become routine practice. The microscopic findings in our case are consistent with the reported literature. [20] The tumor was already diagnosed without the need to perform molecular testing.

3.3.3. Management and outcomes

The primary goals in managing ONB are complete tumor eradication, preservation of surrounding critical structures, avoidance of perioperative complications, and long-term prevention of recurrence. Local recurrence remains one of the most significant challenges in ONB management. [21] Treatment strategies typically include surgery, radiation therapy (RT), and systemic chemotherapy, used alone or in combination depending on tumor stage and patient factors. [21]

Surgery is a fundamental component of ONB treatment. Achieving negative margins (R0 resection) and, to a lesser extent, R1 resection is an independent predictor of both overall survival and event-free survival. [22] The two principal surgical approaches are the traditional transcranial (open) approach and, more recently, the endoscopic endonasal approach. Due to the rarity of ONB, large-scale comparative studies are limited, making direct comparison between open and endoscopic outcomes challenging. [7] However, a systematic review and pooled analysis of 226 patients reported no difference in survival outcomes between endoscopic and open surgery for T1 and T2 sinonasal malignancies. [28]

In 2019, the International Consensus Statement on Endoscopic Skull Base Surgery recommended endoscopic surgery for Kadish stage A and B tumors. Kadish C tumors may be approached endoscopically only when clear negative margins can be obtained. Conversely, Kadish C tumors with orbital involvement, lateral extension beyond the orbital axis, or involvement of the hard or soft palate or the midface are recommended for management with an open approach. [22] Ultimately, the decision regarding surgical technique must consider tumor size, tumor location, patient comorbidities, and the surgical team's expertise. Most importantly, the approach should allow complete resection with negative margins and enable robust skull-base reconstruction. The tumor in our patient was removed using a combined endoscopic endonasal and bifrontal craniotomy to undergo craniofacial resection.

RT is another cornerstone of ONB management. Over the years, various radiation strategies have been evaluated, ranging from elective RT for early-stage disease to pre- and postoperative RT combined with chemotherapy for advanced cases. [7] [23]. A retrospective SEER-based study found that postoperative RT (PORT) did not improve overall survival in Kadish A or B disease; however, in advanced stages (Kadish C and D), postoperative RT significantly improved outcomes. Five- and ten-year overall survival rates were 70.7% and 53.4% with PORT, compared to 42.6% and 29.5% without PORT. [24] While some studies recommend surgery plus RT primarily for higher-stage disease (Kadish C and D) [23] [25], others have argued in favor of multimodal therapy across all stages. [7] In our patient, adjuvant intensity-modulated radiation therapy (IMRT) was applied 6 weeks after surgery

Induction chemotherapy (IC) can be employed in cases with locally advanced disease. Its goals include tumor debulking to facilitate organ preservation, especially of the eye and brain, and reducing the risk of distant metastasis. [1] Patients with more advanced tumors, particularly Kadish C disease, appear to benefit most from treatment regimens incorporating surgery and postoperative RT. [7] In select high-risk patients, concurrent chemoradiation (CT-RT) with cisplatin after surgery may enhance local control. [26] [27] demonstrated in a cohort of 138 non-metastatic ONB patients that surgery followed by CT-RT resulted in the best prognosis when compared with surgery alone or surgery plus RT.

Our patient received three cycles of cisplatin and etoposide as neoadjuvant treatment and had a 30% reduction in tumor volume with significant tumor shrinkage on repeat MRI. He later completed treatment with multimodal therapy and definitive surgical resection in the form of a combined endoscopic endonasal approach with bifrontal craniotomy for craniofacial resection. Gross total resection was obtained, and negative margins were confirmed on both frozen section

and final pathology. The tumor was determined as Hyams Grade II with a closest margin of 3 mm. He then underwent IMRT adjuvant radiotherapy six weeks after this surgery. Treatment was well tolerated with controllable mucositis and fatigue.

4. What have we learned from this case?

This case offers several important learning points. The most important diagnostic teaching point is that even when such patients with ONB present with symptoms that seem innocent, i.e., "seasonal allergies," especially those that persist and are unilateral, one must maintain a high index of suspicion for malignancy. The 8-month gap between the first and second stages, having progressive nasal obstruction, epistaxis, and anosmia, also reflects that olfactory neuroblastoma can be an insidious disease. The presence of neurologic symptoms (e.g., facial pain, diplopia, or sensory deficits) is a major red flag that warrants expedited referral for advanced imaging and specialist consultation, as it indicates that the disease has possibly progressed to central skull base invasion.

This case further underscores the importance of a multidisciplinary tumor board in guiding treatment for rare tumors. The first discussion of resection versus needle biopsy illustrates the clinical challenge faced in balancing the need for definitive tissue diagnosis against the dangers of bleeding and of obtaining a nondiagnostic sample. Chemoradiation with neoadjuvant chemotherapy, leading to interval reductions in tumor size and downstaging before a combined craniofacial resection, is one of the most effective therapies for increasing the chances of gross total excision with negative margins, which remains an important prognostic factor.

In addition, this case demonstrates that good long-term survival can be achieved in advanced (Kadish Stage C) disease when aggressive multimodal therapy is applied. The patient's disease-free follow-up after 3 years and his good quality of life indicate that neoadjuvant chemotherapy, radical surgery, and adjuvant radiation combined can be effective. This result defies the traditional poor prognosis associated with intracranial extension and should motivate physicians to adopt a curative-intent approach in such cases. It demonstrates that, despite an advanced initial disease stage, a positive outcome is achievable and helps mold future practice by recommending thorough, aggressive management from the outset.

Abbreviations

- Olfactory neuroblastoma (ONB),
- Radiation therapy (RT);
- Intensity-modulated radiation therapy (IMRT);
- Immunohistochemistry (IHC)

5. Conclusion

We present the case of a 49-year-old male with advanced olfactory neuroblastoma to highlight the diagnostic and therapeutic complexities of this rare sinonasal malignancy. This case is valuable to the medical community because it illustrates a classic, albeit delayed, presentation in which common symptoms masked a locally advanced tumor. It underscores the critical importance of early and thorough investigation of persistent unilateral nasal complaints. Furthermore, this report demonstrates the successful implementation of a modern, multidisciplinary treatment paradigm, including neoadjuvant chemotherapy, combined craniofacial resection, and adjuvant radiation, resulting in excellent oncologic outcomes and preservation of quality of life, even in the presence of intracranial extension. By sharing this experience, we aim to increase clinicians' and pathologists' awareness, reinforce diagnostic red flags, and contribute to the evidence supporting aggressive, multimodal therapy as the standard of care for achieving long-term survival in patients with this challenging disease.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors make the following declarations:

- Payment/services information: All authors have declared that they received no financial support from any organization for the submitted work.
- Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might be interested in the submitted work.

Statement of ethical approval

Ethical review and approval were not required for this study involving human participants. The paper has been sufficiently anonymized to maintain the patient's confidentiality.

Data access statement

All relevant data are included in the paper.

Author contributions

All authors contributed equally to producing this manuscript.

Statement of informed consent

Consent for the publication of this case was obtained from the patient.

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