

Ectopic olfactory neuroblastoma - complete response to chemotherapy following a late recurrence: A case report

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Abstract. Olfactory neuroblastoma, also known as esthesioneuroblastoma, is a rare type of cancer that originates in the nerve tissue of the olfactory epithelium, located in the upper part of the nasal cavity. The present study reports the case of a female patient who was 35 years old at the time of diagnosis in 2013, with an ectopic olfactory neuroblastoma (Hyams grade III, Kadish stage B) in the right sphenoid sinus, associated with the paraneoplastic syndrome of inappropriate antidiuretic hormone secretion (SIADH). Following transnasal endoscopic surgical resection and adjuvant intensity-modulated radiotherapy (60 Gy) in 2014, the SIADH resolved and the patient achieved complete remission. After a 10-year latency period, in April 2024 the patient developed a late, destructive local recurrence (5.3x4.7 cm) with extension to the maxillary sinus and right orbit. Given the technical limitations for salvage surgery and the refusal of re-irradiation, a multidisciplinary committee approved the administration of 6 cycles of systemic chemotherapy with cisplatin (75 mg/m²) and etoposide (100 mg/m²) every 21 days. Treatment began in June 2024 and concluded in September 2024. Treatment was well tolerated, with only grade 1 nausea and transient grade 2 myelosuppression. Close follow-up with contrast-enhanced head and neck CT in December 2025 confirmed the complete clinical and radiological response, demonstrating the total absence of the tumor lesion. As of February 2026, the patient remains asymptomatic and disease-free. The present case highlights the rarity of ectopic sphenoid location, the usefulness of SIADH as an indirect biomarker and the high chemosensitivity of

high-grade variants in late recurrences, justifying prolonged and indefinite follow-up.

Introduction

Olfactory neuroblastoma (esthesioneuroblastoma) is a rare malignant neuroectodermal neoplasm arising from the neuro-epithelium of the upper portion of the nasal cavity. Unlike classic pediatric neuroblastoma, it primarily affects adolescents and adults. The 5-year overall survival rate for patients with olfactory neuroblastoma ranges between 60 and 80%, though prognosis drops significantly for those presenting with advanced-stage or metastatic disease (1). Olfactory neuroblastoma accounts for 3-6% of all tumors of the nasal cavity. Although typically orthotopic, <10% of cases correspond to ectopic neuroblastomas, which originate in sites where olfactory neural crest cells do not normally reside, presumably due to aberrant migration during embryonic development. Among ectopic locations, the paranasal sinuses (ethmoid, maxillary and sphenoid) are the most common, and they are also reported in the nasal septum, the sellar region and the nasopharynx. Tumors with ectopic presentation are usually characterised by a more locally invasive behaviour than their orthotopic counterparts (2).

Due to its neuroendocrine nature, olfactory neuroblastoma possesses the ability to synthesise vasopressin. Consequently, syndrome of inappropriate antidiuretic hormone secretion (SIADH) has been identified as a paraneoplastic manifestation in 2% of patients worldwide. However, this paraneoplastic association increases markedly in ectopic variants, affecting ≥18% of patients and manifesting concomitantly with the tumor or preceding it by several years (3). Clinically, initial symptoms are usually nonspecific and include unilateral nasal obstruction, persistent rhinorrhea, epistaxis or visual and orbital disturbances in advanced stages, coexisting with euvolemic hyposmolar hyponatraemia in functional cases (4).

The standard approach to olfactory neuroblastoma is based on a multimodal regimen combining endoscopic or open surgery with adjuvant radiotherapy, reserving chemotherapy for advanced or initially unresectable stages. Despite therapeutic advances and an overall 5-year survival rate of ~80%,

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long-term locoregional recurrence rates remain high, occurring in ~30% of patients (4).

A distinctive biological feature of this tumor is its insidious course and its propensity for markedly late relapses, even a decade after achieving complete remission, which warrants prolonged and indefinite clinical and imaging surveillance. Progression to the orbit or adjacent structures and high histological grade (Hyams grades III and IV) notably worsen the prognosis. In cases of recurrence or high-grade disease, the tumors demonstrate high chemosensitivity, with cisplatin- and etoposide-based regimens being the most widely validated first-line systemic therapies (5).

The present case describes a rare tumor in adults with its ectopic presentation in an unusual location, the right sphenoid sinus. Furthermore, associated SIADH is identified in a minimal percentage of patients with neuroblastoma. Finally, although relapses typically occur several years later and show a poor response to chemotherapy, the present case relapsed very late (10 years) but exhibited a complete response to standard chemotherapy with cisplatin and etoposide, representing an exceptionally rare clinical scenario that is poorly documented in the international medical literature.

Case report

A 35-year-old female patient was admitted to the Department of Internal Medicine, Princess Marina Hospital (Gaborone, Botswana) in December 2013. The patient had no notable medical history; however, they reported a history of malaise, muscle weakness, cramps and recurrent global headaches of ≥ 2 years in duration. Clinical interview and physical examination revealed right-sided nasal obstruction, dysosmia and dysgeusia of ≥ 1 year in duration. Serum chemistry revealed sodium levels between 130-134 mmol/l during euvolemic states (normal range: 135-145 mmol/l), leading to a definitive diagnosis of SIADH.

In January 2014, the patient underwent a contrast-enhanced CT scan of the paranasal sinuses at initial presentation. Fig. 1A shows a sagittal view demonstrating a heterogeneous enhancing mass occupying the right sphenoid sinus (5.3x4.2x4.4 cm), extending into the ipsilateral ethmoid air cells, nasal cavity, and maxillary sinus (green arrows). Fig. 1B shows a sagittal view depicting the ectopic tumor location within the sphenoid body and its relationship to the skull base, with no evidence of macroscopic intracranial extension (green arrows). Fig. 1C illustrates an axial view showing an expansive mass in the right sphenoid sinus, which causes bony wall opacification and remodeling, as well as a leftward deviation of the nasal septum due to mass effect (green arrows).

The contrast-enhanced CT scan of the neck showed a symmetrical nasopharynx without well-defined lesions. The mucosal surfaces of the upper aerodigestive tract, larynx and base of the tongue appeared symmetrical and without notable findings. The parotid and submandibular glands were normal and the thyroid gland appeared symmetrical without well-defined nodules. The carotid and jugular vessels, as well as the deep suprahyoid and infrahyoid cervical spaces, showed no abnormalities. No suspicious cervical lymph nodes were visualized. The central skull base was intact and the cervical

vertebrae, spinal cord and lung apices showed no notable findings (data not shown).

An endoscopic incisional biopsy was performed (January 2014), taking a small sample from the most accessible part of the tumor in the nasal cavity, away from the cribriform plate and the sphenoid sinus to avoid causing a cerebrospinal fluid leak. Immunohistochemical staining showed positivity for synaptophysin, S-100 and neuron-specific enolase (NSE), as well as a Ki-67 cell proliferation index of 15%, while it was negative for CD99, epithelial membrane antigen and cytokeratins (MNFI16). This information is based on the primary pathology report. Once the diagnosis of olfactory neuroblastoma was confirmed, definitive excision was performed.

In February 2014, after assessing the tumor's relationship with the carotid artery and optic nerve, a transnasal endoscopic surgical resection was performed. Given the absence of intracranial involvement, the sphenoid ostium was directly visualized and the tumor was excised while preserving the integrity of the anterior skull base. A wide sphenoidotomy was then performed to ensure a clear mucosa, along with reaming of the remaining bone to remove any tumor nests, aiming for negative microscopic margins. Serum sodium levels returned to normal 48 h after tumor excision.

Microscopic examination allowed for the analysis of multiple fragments of grayish-white tissue, measuring 3x2x1 cm in total. Upon sectioning, the surface was solid and white, with a lacy appearance and some bright white areas. A total of five representative blocks were processed. Microscopic examination of the sections revealed a tumor composed of irregular, circumscribed tumor nests separated by fibrotic stroma, with some areas exhibiting a diffuse pattern. Histological examination was performed using standard hematoxylin and eosin staining on formalin-fixed, paraffin-embedded tissue sections to evaluate cellular morphology and architectural patterns. A total of five representative tissue blocks were processed. Tissue sections (3-4 μ m thickness) were deparaffinized in xylene (two changes, 10 min each) and rehydrated through a descending graded ethanol series (100, 95 and 70%, 5 min each) down to distilled water. Nuclear counterstaining was carried out with Mayer's hematoxylin for 3-5 min, followed by rinsing in running tap water for 5 min to allow blueing. Sections were briefly differentiated in 1% acid alcohol, washed and counterstained with 1% eosin Y solution for 1-2 min for cytoplasmic and stromal contrast. Finally, the slides were dehydrated through ascending grades of ethanol, cleared in xylene and mounted with synthetic resin under glass coverslips for microscopic examination.

The neoplastic cells had small, round nuclei with chromatin ranging from coarse to fine punctation and scant cytoplasm. The tumor presented a fibrillar intercytoplasmic background, and both Flexner and Homer-Wright rosettes were identified (Fig. 2). Due to the loss of architecture, nuclear pleomorphism, frequent necrosis and high mitotic rates with sparse neuropil, it was classified as Hyams grade III (4). The final histopathological diagnosis was olfactory neuroblastoma (C72.2). The diagnostic code corresponds strictly to the International Classification of Diseases, Tenth Revision (ICD-10) nomenclature for malignant neoplasms of the olfactory nerve. The absence of microscopic dural invasion confirmed Kadish stage B (4).

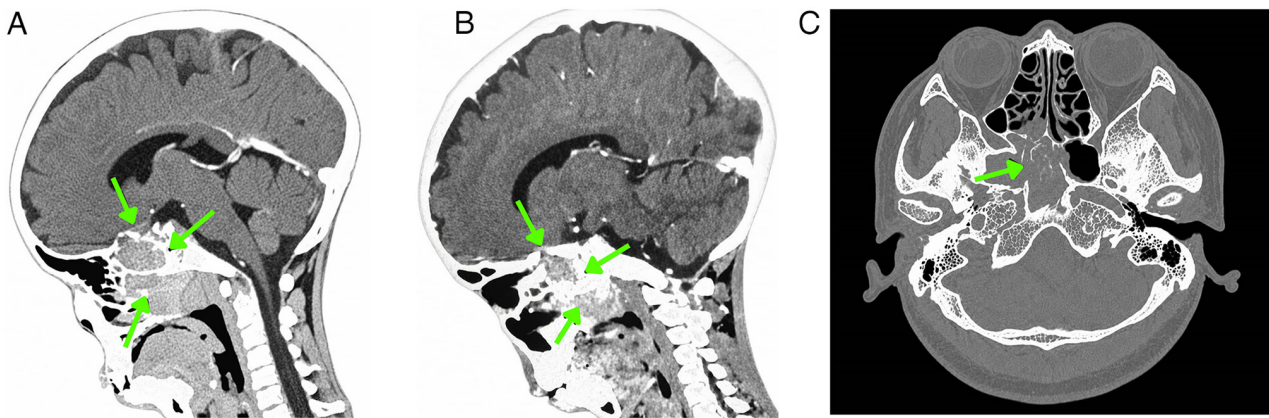


Figure 1. Contrast-enhanced CT scan of the paranasal sinuses at initial presentation (January 2014). (A) Sagittal view showing a heterogeneous enhancing mass occupying the right sphenoid sinus (5.3x4.2x4.4 cm) and extending into the ipsilateral ethmoid air cells, nasal cavity, and maxillary sinus (green arrows). (B) Sagittal view depicting the ectopic tumor location within the sphenoid body (green arrows), demonstrating its relationship to the skull base without evidence of macroscopic intracranial extension. (C) Axial view illustrating an expansive mass in the right sphenoid sinus causing bony wall opacification and remodeling (green arrows), along with leftward deviation of the nasal septum due to mass effect.

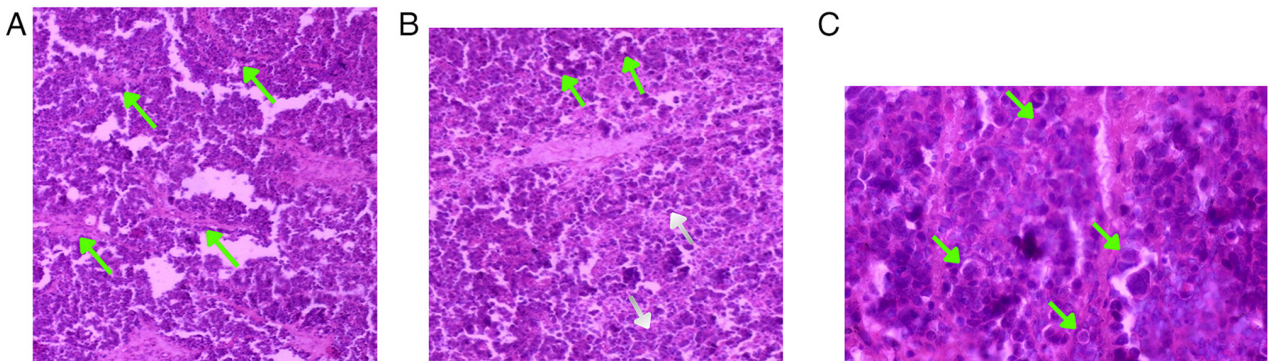


Figure 2. Optical microscopy images with H&E staining from a biopsy sample of the sphenoid sinus tumor mass obtained prior to definitive treatment (January 2014). (A) Low-power view (magnification, x100; scale bar, 100 μ m) showing irregular, well-circumscribed cellular nests (green arrows) separated by a delicate fibrous stroma. (B) High-power view (magnification, x400; scale bar, 50 μ m) depicting a fibrillary background with identified Homer-Wright rosettes (white arrows) and Flexner-Wintersteiner rosettes (green arrows). (C) High-power view (magnification, x400; scale bar, 50 μ m) demonstrating nuclear pleomorphism (green arrows) with a high mitotic index and prominent mitotic figures (green arrows).

Finally, treatment was completed with adjuvant radiotherapy using intensity-modulated radiation therapy (IMRT), 60 Gy, which allowed the dose to be concentrated in the sphenoid body and ethmoid air cells, protecting the optic nerves and optic chiasm. Adjuvant radiotherapy commenced in March 2014 (6 weeks postoperatively). A total dose of 60 Gy was delivered in 30 daily fractions (2.0 Gy/session, 5 days per week), concluding in April 2014 after a 6-week treatment period.

No notable adverse effects were reported after radiotherapy. Follow-up CT and MRI scans with contrast showed no evidence of tumor lesions. The patient remained under otolaryngology follow-up every 3 months for 2 years, then every 6 months for 3 years and annually thereafter. Blood tests and imaging studies were repeated every 6 months for 5 years, including head and neck CT or MRI, complete blood count and liver, kidney and thyroid function tests every 6 months (Table SI).

However, in April 2024, the patient returned to the Princess Marina Hospital (Gaborone, Botswana), presenting spontaneously with persistent rhinorrhea and self-limiting epistaxis.

Fig. 3 presents contrast-enhanced CT scans of the paranasal sinuses acquired in April 2024, confirming tumor relapse. The images demonstrate a complex, heterogeneous calcified mass, measuring 5.3x4.7 cm, centered within the right nasal cavity. Coronal and sagittal views, provided in Fig. 3A and B, reveal extensive involvement of the ethmoid sinuses. Critically, these views, combined with the axial image in Fig. 3C, show multi-compartmental direct extension of the tumor. Specific features include significant invasion and partial obliteration of the right maxillary antrum, alongside clear encroachment into the medial aspect of the right orbit, highlighting the locally aggressive nature of the recurrence.

In May 2024, a late local recurrence was diagnosed. Given the lack of available human and technological resources for salvage surgery, the refusal of the patient to receive further radiation therapy and considering the high risk of microscopic metastases and the chemosensitivity of high-grade neuroendocrine tumors, it was decided to administer 6 cycles of cisplatin [75 mg/m² intravenously (IV), day 1] and etoposide (100 mg/m² IV, days 1, 2 and 3) every 21 days, which began in June 2024.

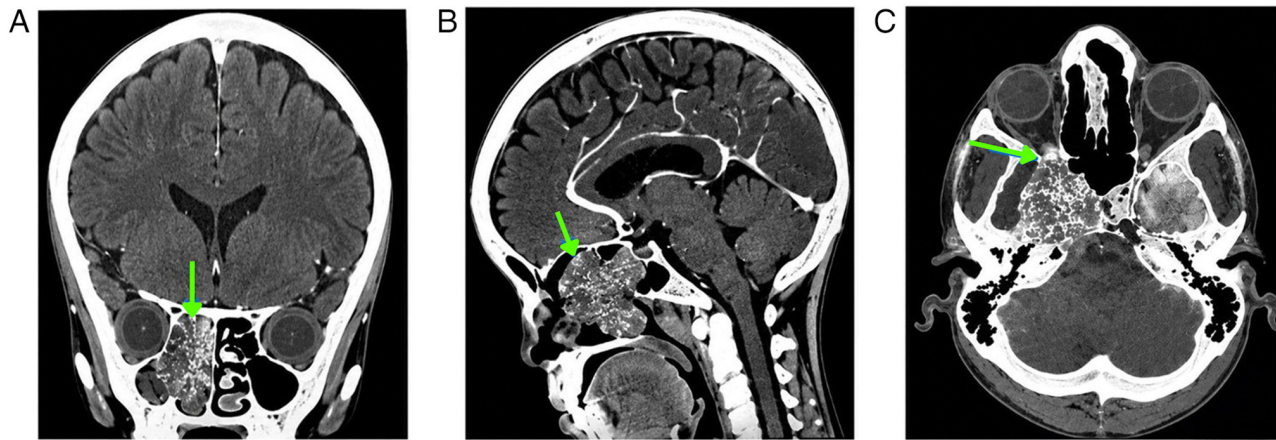


Figure 3. Contrast-enhanced CT scan of the paranasal sinuses demonstrating tumor relapse (April 2024). (A) Coronal view showing a new heterogeneous calcified mass (5.3x4.7 cm) in the right nasal cavity (green arrows). (B) Sagittal view depicting tumor extension into the ethmoid sinuses with invasion of the maxillary antrum (green arrows). (C) Axial view illustrating the calcified mass with invasion and opacification of the maxillary antrum (green arrows).

Despite the well-documented toxicity profile of the cisplatin and etoposide regimen, which is often associated with severe side effects, the good tolerance of the patient throughout the 6 cycles resulted only in the occurrence of grade 1 nausea and grade 2 myelosuppression. Both events were transient and of short duration, allowing for effective management through the timely initiation of supportive treatment. Following standard protocols, the emetic symptoms were controlled with conventional antiemetics. On day 1 (the highly emetogenic combination phase), intravenous premedication consisted of a triple-agent antiemetic regimen comprising a 5-HT₃ receptor antagonist (ondansetron, 8 mg IV), a neurokinin-1 (NK₁) receptor antagonist (fosaprepitant, 150 mg IV) and dexamethasone (12 mg IV). For days 2 and 3 (the continuation of etoposide), daily prophylactic antiemetic coverage included intravenous ondansetron (8 mg IV once daily) along with oral dexamethasone (8 mg daily). Delayed emesis protection on day 4 was maintained using oral dexamethasone (8 mg once daily). Throughout all 6 treatment cycles, rescue medication with metoclopramide (10 mg orally or IV as needed every 8 h) was available, achieving effective emetic control with no grade ≥ 2 adverse gastrointestinal events reported. The haematological toxicity responded favourably and predictably, avoiding interruptions or dose reductions and reinforcing the success of the therapeutic regimen. The patient demonstrated a favourable clinical and radiological response, completing the last cycle in September 2024. They were subsequently monitored closely with clinical and radiological follow-up every 12 weeks.

The most recent head and neck CT scan was performed in December 2025, showing complete absence of the lesion described as a recurrence in April 2024. The brain parenchyma, ventricles, sulci and basal cisterns appeared normal, with no focal mass lesions or abnormal enhancement after contrast administration; the orbits and cranial bones also appeared normal. The neck, the larynx, pharynx and postnasal drip were normal; the thyroid and salivary glands appeared normal without notable cervical lymphadenopathy. The infrahyoid muscles, prevertebral soft tissues and cervical spine showed no abnormalities (Fig. 4). As of

the date of the present report (February 2026), the patient remained asymptomatic.

Discussion

Olfactory neuroblastoma is a rare malignant neuroendocrine neoplasm that classically originates in the olfactory neuroepithelium of the nasal cavity roof, specifically in the cribriform plate, superior turbinate and superior nasal septum. However, the biological behaviour of this entity becomes considerably more complex when it occurs in ectopic locations, with the sphenoid sinus being one of the most unusual anatomical variants (5). In the present case, the initial tumor mass predominantly occupied the right sphenoid sinus. The presence of ectopic neuroepithelial tissue in the paranasal sinuses is attributed to abnormalities in the embryological migration of the olfactory placode or to the persistence of pluripotent cell remnants along the craniofacial developmental pathways. From a biological standpoint, ectopic olfactory neuroblastomas tend to exhibit silent and expansive growth due to the laxity of the air cavities that house them, which explains why severe obstructive or neurological symptoms usually manifest late, when the tumor has already reached critical dimensions or caused notable local bone destruction (6). In the patient of the present study, the Hyams grade III tumor showed marked local aggressiveness, eroding adjacent structures and extending into the ethmoid air cells and olfactory sulcus. However, despite its locally expansile growth pattern, no microscopic dural invasion was identified at initial presentation, indicating that the tumor remained confined to the extracranial compartment.

In the context described, it is important to emphasise that the histopathological characterisation of this neoplasm should not be limited to the identification of structural neuroendocrine markers, but rather requires the incorporation of molecular prognostic tools, among which the Ki-67 cell proliferation index is fundamental (7). The present case showed positivity for synaptophysin, chromogranin, S-100, NSE and had a Ki-67 cell proliferation index of 15%. It has been considered that the omission of Ki-67 would have deprived the patient of a critical factor for stratifying the biological behaviour of the tumor. An

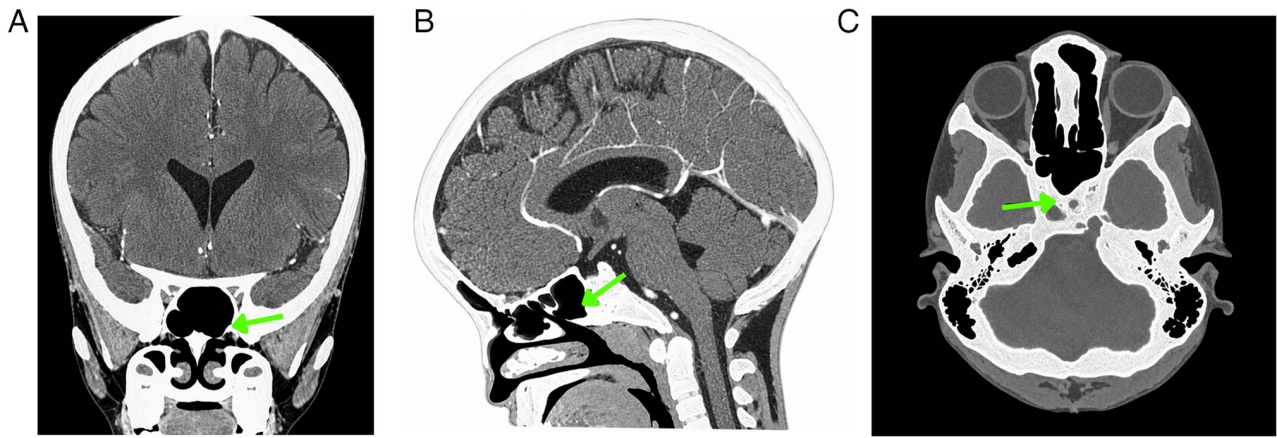


Figure 4. Contrast-enhanced CT scan of the paranasal sinuses in the follow-up evaluation (December 2025). (A) Coronal view showing complete resolution of the initial lesion in the ethmoid sinus (green arrows), compared to the baseline study. (B) Sagittal view showing complete resolution of the initial lesion in the maxillary sinus (green arrows), compared to the baseline study. (C) Axial view showing complete resolution of the initial lesion in the sphenoid sinus (green arrows), compared to the baseline study.

elevated Ki-67, at thresholds of $\geq 10\%$, correlates with lower progression-free survival, more locally invasive behaviour and a greater propensity to develop local recurrences or distant metastases, characteristics shared by high-grade ectopic variants (7). In the present case, classified as a Hyams grade III, the determination of Ki-67 served as an indicator of tumor aggressiveness and additional justification for its high sensitivity to cytotoxic regimens based on cisplatin and etoposide after late relapse.

Furthermore, due to its ectopic location in the sphenoid sinus and its morphology of small, round, blue cells, the histopathological differential diagnosis required differentiation from other malignant nasosinusal neoplasms. The absence of immunoreactivity for cytokeratins (MNFI16) and CD99 was the cornerstone that allowed the exclusion of small cell neuroendocrine carcinoma, which shows cytokeratin positivity in a paranuclear droplet pattern, and Ewing sarcoma (diffuse and strong membranous expression of CD99). Likewise, the negativity for cytokeratins ruled out undifferentiated sinonasal carcinoma, an aggressive entity that often overlaps morphologically with Hyams grade III, but which retains epithelial markers. Furthermore, the positivity for the S-100 protein in the periphery of the tumor nests, which identifies the sustentacular cells, along with the background of intercytoplasmic neuropil and the Homer-Wright and Flexner rosettes, allowed it to be differentiated from an amelanotic sinonasal melanoma or an alveolar rhabdomyosarcoma (4).

The Hyams grade III classification was based on an evaluation of its cytological characteristics, which place this neoplasm within the high-grade category. Unlike grades I and II, where a distinct lobular architecture and prominent fibrovascular stroma are preserved, the examination revealed a loss of architecture with the presence of irregular tumor nests and areas of diffuse or subtle growth patterns. Cytologically, the cells exhibited moderate to severe nuclear pleomorphism with chromatin variations and scant cytoplasm, accompanied by reduced background neuropil compared to low-grade lesions. Finally, the determining criteria for consolidating grade III corresponded to a high mitotic rate and the presence of foci of tumor necrosis, parameters that differentiate this stage

from grade IV, where necrosis is prominent, pleomorphism is extreme and neurofibrillary differentiation or rosette formation disappears completely (8).

In another context, it should be noted that the clinical presentation of this tumor can be accompanied by paraneoplastic syndromes due to its classic neuroendocrine differentiation, with SIADH being one of the most notable and clinically relevant systemic manifestations (9). In the present study, SIADH manifested insidiously with a chronic history of malaise, muscle weakness, cramps and recurrent global headaches, associated with persistently low serum sodium levels in a euvolemic state. The ectopic secretion of arginine vasopressin by these neoplastic cells disrupts water homeostasis in the renal collecting tubules, promoting excessive water reabsorption that culminates in dilutional hyponatraemia. From a prognostic perspective, the coexistence of SIADH in patients with skull base tumors can complicate perioperative management and increase the risk of severe cerebral oedema if not carefully managed (10). However, an important clinical and diagnostic observation is that SIADH acts as an indirect functional tumor marker; in the present study, the normalization of serum sodium just 48 h after surgical resection confirmed the success of tumor cytoreduction and the eradication of the ectopic hormone production source.

Although SIADH and the associated dilutional hyponatraemia were the principal neuroendocrine and electrolyte disturbances of the patient at presentation, the management of high-grade neuroendocrine tumors also requires consideration of other metabolic complications associated with tumor progression and cell lysis, such as paraneoplastic hypercalcaemia. Hypercalcaemia in advanced or recurrent skull base malignancies can derive from both local osteolysis due to bone invasion of the paranasal sinuses and from tumor secretion of parathyroid hormone-related protein (11). Complications arising from uncontrolled hypercalcaemia are multisystemic and serious, ranging from renal dysfunction mediated by the induction of nephrogenic diabetes insipidus and vasoconstriction of the afferent arteriole, to cardiac conduction abnormalities with shortening of the QT interval and risk of ventricular arrhythmias. Likewise, at the level of the central

nervous system, hypercalcaemia exacerbates neurological symptoms, inducing lethargy, progressive mental confusion, profound neuromuscular weakness and, in key phases, coma, which can mask or mimic symptoms derived from the tumor mass at the base of the skull or from a possible orbital recurrence (11).

Evidence indicates that the neoplasm in the present study is distinguished from most carcinomas of the sino-nasal region by its propensity for very late recurrences, a biological feature documented in the international literature. While common epithelial neoplasms usually recur within the first 5 years after definitive treatment, olfactory neuroblastoma can remain in a prolonged latency state, with relapses reported even 10, 15 or 20 years after initial management (12). In the present case, the patient experienced a local recurrence 10 years later, after successfully completing a combined regimen of endoscopic surgery and adjuvant IMRT. The prevalence of recurrences in long-term follow-up series ranges from 30-50% of cases, and a marked proportion of these are classified as very late. This behaviour underscores the inadequacy of 5-year follow-up protocols for this disease, justifying the need for lifelong clinical and imaging surveillance, alternating CT and MRI scans to detect tumor reactivation in time.

Furthermore, the pathophysiology underlying such prolonged tumor recurrence rests on contemporary concepts of tumor latency and permissive microenvironments. Following the initial multimodal treatment in 2014, which combined transnasal endoscopic resection with bone drilling and 60 Gy radiotherapy, quiescent tumor stem cells likely persisted in the deep microscopic margins of the sinonasal region or in the surrounding connective tissue. These cells possess advanced cellular DNA repair mechanisms and a low replication rate, making them resistant to ionising radiation and programmed cell senescence. Latent oncogenesis implies that these cells enter a G₀ cell cycle arrest, evading immune surveillance through the downregulation of major histocompatibility complex molecules and the expression of immune checkpoint ligands (13). Over the course of a decade, the progressive accumulation of new secondary somatic mutations, genomic instability and local epigenetic changes, influenced by post-radiation stromal fibrosis and chronic tissue hypoxia, could have altered the biological balance, triggering tumor angiogenesis and proliferative reactivation that may have ultimately given rise to the new heterogeneous and calcified mass identified in 2024.

Finally, when comparing the clinical course of the patient with reported recurrence cases, correlations and discrepancies emerge. In the literature, disease-free survival in late-relapse series averages between 7-12 years, placing the 10 years observed in the present case at the core of this chronological range (11,12). Regarding the site of relapse, the literature indicates that isolated local recurrences in the nasal cavity and ethmoid sinuses are the most common, followed by cervical lymph node metastases and distant spread to the lung, bone and liver (13). The patient presented with a destructive local recurrence involving the right nasal cavity and ethmoid sinuses with extension to the right orbit, an aggressive pattern of local spread consistent with historical cases of high histological grade. Clinically, while numerous cases present

with neurological symptoms due to intracranial invasion, the patient of the present study only exhibited persistent rhinorrhea and self-limiting epistaxis, with no evidence of extension to the anterior cerebral fossa in tomographic studies, which gave them a more favourable risk profile in terms of resectability, although with an ominous prognosis without timely oncological intervention.

In the present case, the decision-making process regarding the relapse was conditioned by logistical, technical and structural limitations of the hospital, which unequivocally determined its clinical course. Although guidelines suggest a second salvage surgery for operable local recurrences (14), the reality at the time of diagnosis presented a restrictive scenario; the hospital neither had the specialized human resources with subspecialty in endoscopic skull base surgery, nor the essential equipment (intraoperative neuronavigation systems and endoscopy towers with instruments for orbitomaxillary tumor reaming) necessary for a second transnasal endoscopic resection and a wide salvage sphenoidotomy with secure margins. Furthermore, the conditions of the public health network and inter-institutional agreements made it impossible to refer the patient to another healthcare centre that had these services. Given this scenario and the refusal of the patient to undergo re-irradiation, systemic chemotherapy became established as the only real, viable and ethically justifiable alternative of active oncological treatment to stop the progression of the disease.

The choice of platinum and epipodophyllotoxins was based on the chemosensitivity of high-grade neuroendocrine tumors. The use of 6 cycles of cisplatin and etoposide administered every 21 days replicated the salvage therapy protocols described in the international medical literature for Hyams grade III/IV olfactory neuroblastoma (15). Reviewing historical series, the overall response rate to combination chemotherapy in the context of recurrences ranges from 40-70%, with complete response being a less frequent but documented event in selected cases (16). The complete tumor remission achieved, evidenced by the CT scan of August 2024 with the disappearance of the heterogeneous orbitonasal mass, places the present case within the group of exceptional responders to systemic cytotoxic agents. Analogous reported cases have shown that macroscopic eradication of recurrent disease using cisplatin/etoposide can offer prolonged progression-free survival, provided that strict follow-up is maintained (16).

Upon confirmation of the recurrence, therapeutic decision-making presented a highly complex challenge. Given the impossibility of performing another surgical treatment and the refusal of the patient to undergo another cycle of radiotherapy, a comprehensive approach became essential. For these reasons, the present case was discussed within a tumor board composed of a clinical oncologist, a radiation oncologist, a radiologist, a histopathologist, an internist, an otolaryngologist, a maxillofacial surgeon, a social worker and a psychologist.

This deliberation allowed for the analysis not only of biological criteria but also of the psychological and social circumstances of the patient. The joint evaluation was the cornerstone that ethically justified the choice of chemotherapy as the viable alternative, achieving an optimal consensus that resulted in the aforementioned outcome.

A limitation of the present study is that the immunohistochemical evaluation described relies solely on the original

institutional pathology reports. Retrievable histological image files or tissue slides were unavailable for direct re-evaluation, which precluded independent verification of the representative staining patterns.

In conclusion, the present case represents an extraordinarily unusual and scientifically valuable manifestation within nasosinusal neoplasms, describing an olfactory neuroblastoma of ectopic origin in the right sphenoid sinus. The emergence of this tumor outside its usual orthotopic zone in the nasal vault poses complex diagnostic challenges, demonstrating a biological behaviour of silent but locally aggressive growth that can be confused with other malignant neoplasms of the skull base without rigorous immunohistochemical confirmation.

The unique nature of this presentation is underscored by its paraneoplastic association with SIADH. This neuroendocrine dysfunction, triggered by the autonomous production of vasopressin by ectopic tumor cells, served as an indirect biological marker of treatment response, and its complete biochemical resolution correlated directly with successful initial surgical cytoreduction. The presence of SIADH underscores the need for a multidisciplinary clinical approach to mitigate severe metabolic risks during the course of the disease.

Finally, the most remarkable aspect of the present case lies in the development of a late locoregional recurrence after a decade of clinical and imaging latency, followed by complete and sustained remission with cisplatin- and etoposide-based salvage systemic chemotherapy. This scenario documents the high chemosensitivity of high-grade variants to standard cytotoxic regimens, even in the face of advanced relapses with orbital invasion. This behaviour also deviates from traditional short-term oncological follow-up protocols, justifying the need for lifelong surveillance in these types of tumors.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

JEPR led the study, performed the final drafting and handled manuscript submission. EASG selected the case and provided the clinical data. MCGC performed the CT scan image analysis. MCMS collaborated with data acquisition (histopathological data). GCNZ drafted the manuscript and worked on data analysis and interpretation. IEF and ALS conducted the literature review. IEF made substantial contributions to the conception and design of the work, as well as to data acquisition. ALS, in addition to participating in data acquisition, contributed to the analysis and interpretation of the data. JEPR and EASG confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the images and associated medical case information.

Competing interests

The authors declare that they have no competing interests.

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