Case Report

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An atypical Esthesioneuroblastoma of the sphenoid sinus: a case report

Safaa Touihmi, MD[a,*], Ichraq Horrane, MD[a], Ilham Rkain, MD[a]

Introduction and importance: Esthesioneuroblastoma (ENB) is a rare tumor, arising from the olfactory epithelium. It manifests as an aggressive tumor in the superior aspect of the nasal cavity. Sinonasal symptoms are the most common. The cervical lymph nodes ensue in nearly 10% of cases and hematogenous metastases are rare. The diagnosis is histological. This tumor is staged using the Kadish et al System. The imaging techniques, using both computed tomography (CT) and MRI provides all the important information required for treatment modality. Today, the standard multimodal treatment combining external craniofacial resection, radiotherapy, and chemotherapy has improved long-term survival.

Case presentation: A 27-year-old male patient with no medical history, complained of a headache, a unilateral right nasal obstruction, epistaxis, and anosmia for 2 months. Nasal endoscopy showed a pinkish-gray mass filling the right nasal cavity. An enhanced-contrast CT scan was performed and objectified a mildly enhancing extensive mass of the sphenoid sinus with bone erosion of the left wall of the sinus and intracranial involvement. An intranasal biopsy was performed, resulting in a histopathological diagnosis of olfactory neuroblastoma. Our case was staged as stage C according to the Kadish staging. The tumor was inoperable, the patient had chemotherapy, radiotherapy, and pain management.

Clinical discussion: ENB is an aggressive malignant tumor derived from the specialized olfactory neuroepithelium of the upper nasal cavity. Several published reports confirm ectopic cases of ENB throughout the nasal cavity and the central nervous system. Because sinonasal malignant lesions are rare and difficult to distinguish from their benign counterparts. ENBs appears as a soft, glistening, polypoidal, or nodular mass covered by intact mucosa or as friable masses with ulceration and granulation tissue. A radiological, CT scan through the skull base and paranasal sinuses with intravenous contrast should be performed. ENBs are solid, enhancing nasal cavity masses that may manifest erosion into nearby osseous. MRI provides better discrimination between tumor and secretions and optimal assessment of orbital, intracranial, or brain parenchymal involvement. The biopsy is the next important step in securing a diagnosis. Classic treatment strategies of ENB are based on surgery or radiotherapy as unique modalities or a combination of surgery and radiation therapy. More recently, chemotherapy has been introduced in the therapeutic armamentarium since ENB has proven to be chemosensitive. The elective neck dissection remains controversial. Long-term follow-up is mandatory for patients with ENB.

Conclusion: While most ENBs originate in the superior nasal vault and present with typical symptoms of nasal obstruction and epistaxis in the late stages of the disease, uncommon manifestations should be considered as well. Adjuvant therapy should be considered in patients with advanced disease and unresectable disease. A continuing follow-up period is needed.

Keywords: case report, chronic nasal obstruction, esthesioneuroblastoma, malignant tumor of the nasal cavity, olfactory neuroblastoma

Introduction

Berger and colleagues first described Esthesioneuroblastoma (ENB) or olfactory neuroblastoma in 1924, generally manifesting as an aggressive tumor in the superior aspect of the nasal cavity near the cribriform plate along the superior septum, and at the superior turbinate[1]. It represents 3–6% of all intranasal tumors. ENBs have a bimodal age of onset in the second and sixth decades of life, and the sex distribution is approximately the same[2,3]. Sinonasal symptoms are the most common, they simulate the clinical picture of chronic rhinosinusitis inflammatory disease, and thus this tumor can be misdiagnosed, and consequently the treatment is delayed[4]. The cervical lymph nodes ensue in nearly 10% of cases; hematogenous metastases are rare but may occur in bone, bone marrow,

[a]Department of Otorhinolaryngology and Head and Neck Surgery Department, University Hospital of Tangier, Tetouan-Al hoceima

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*Corresponding author. Address: Abdelmalek Essaadi University, Faculty of Medicine and Pharmacy, Tangier, Oujda 60900, Morocco. Tel: +00212633622093, E-mail: Safaatouihmi.st@gmail.com (S. Touihmi).

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lung, or skin. Recurring symptoms must not be ignored, the tumor recurrence is very frequent. This tumor is staged using the Kadish et al System (1976). The imaging techniques, using both computed tomography (CT) and MRI, is the golden standard in offering the information for the tumor's extension and thus the treatment planning. Today, the standard multimodal treatment combining external craniofacial resection, radiotherapy, and chemotherapy has improved the long-term survival rate for tumors previously considered nontreatable. However, local recurrence rates are high and are reported to be between 58 and 62%[5]. Several published reports confirm the ectopic cases of ENB, in this article, we add to the literature another case of an atypical ENB of the sphenoid sinus that was presented and managed in the ENT department of the University Hospital.

This case report has been reported in line with the Surgical CAse REport (SCARE) Criteria.

HIGHLIGHTS

- Emphasize the challenge confronted in diagnosing the tumor clinically and by imaging, as there is no typical clinical presentation, or specific radiological features for the esthesioneuroblastoma.
- The sphenoid sinus is a rare origin of the tumor.
- The diagnosis is retained by pathological examination of the lesion sample.
- The rarity of the tumor often leads to a delayed diagnosis.
- The surgery can be complicated.
- A multimodal therapeutic protocol is a heavy but good alternative especially in young patients.

Case presentation

We report the case of a 27-year-old male patient, a married engineer with no children. The patient had no personal significant features, especially no history of smoking, alcohol consumption or respiratory tract infections, allergies or discontinued medication and no history of head and neck surgery. No inheritable conditions or health problems were found in the family history. The Young patient was referred by the family physician for a persistent headache increasing over a year, which was treated as chronic rhinosinusitis,with nasal steroids and *analgesics, the patient showed no improvement*. The appearance of a unilateral right progressive nasal obstruction, epistaxis, and anosmia for two months urged the family physician into referring him to our department. The left nasal cavity was filled with a firm pink-gray mass, with an irregular overlying surface, revealed in the nasal endoscopy and seen after cleaning the discharge. His vision in both eyes was normal, and his eye movement was unrestricted. Examination of the oral cavity is unremarkable. There is no lymphadenopathy and the general examination was unremarkable. Systemic examination was also normal. A polypoid chronic rhinosinusitis was initially suspected, but the unilateral clinical symptomatology and localization of the mass made it mandatory to firstly rule out , or not, a malignant disease. The blood examination revealed a hemoglobin level of 12,1g/dl, a white blood cell count of 7650 cell/mm3, and a serum; C-reactive protein level of 3,5 mg/l. TA nasosinusal and cerebral enhanced-contrast CT scan was performed and objectified a mildly enhancing mass of the sphenoid sinus with bone erosion of the left wall of the sinus and intracranial involvement and intralesional calcifications. The lesion also involved the ethmoid sinuses from the nasal septum to the nasal cavity (Fig. 1).

The radiological features of the mass confirmed the malignant nature of the lesion. A histopathological confirmation was needed and for this matter, an intranasal biopsy, under local anesthesia, was performed, resulting in a histopathological diagnosis of olfactory neuroblastoma. This biopsy was realized, in the operating room, by the second-year intern supervised by the department senior, the biopsy was well tolerated by the patient, and a pain-free, low-abundance nosebleed was stopped by 5 min of digital compression. Our case was staged as stage C according to the Kadish staging and T4NOMO according to the Dulguerov staging. The patient was evaluated by a multidisciplinary cancer board committee, where it was determined the tumor was inoperable. As a result, the committee suggested palliative chemotherapy, radiotherapy, and pain management. Primary radiotherapy was offered, and the patient received a total of 5940 cG y to the involved areas (the last 540 cG y was administered as a sinus boost), and also followed by platinum-based chemotherapy consisting of Cyclophosphamide, Doxorubicin, and Vincristine for six cycles. After a 6-month follow-up, the patient presented no further clinical progression of the tumor, the blood tests showed no chemotherapy-related toxicity, and the imaging by paranasal and cerebral CT scan showed a slight regression of 15% of the tumor's size, The tumor partially responded to radiation and chemotherapy but was still not surgically resectable. Given the patient's tolerance to the therapeutic protocol, the decision was to maintain chemotherapy with regular follow-ups every 6 months with clinical examination and imaging and blood tests.

Clinical discussion

ENB is an aggressive malignant tumor emerging from the specialized olfactory neuroepithelium of the upper nasal cavity; it represents 3% of all endonasal neoplasms, and the sex distribution is approximately the same[2,3]. According to the published studies, the tumor revealed a bimodal age distribution; in the second, and fifth decade[6,7]. The tumor may extend submucosally and consequently invades the paranasal sinuses, nasal cavity, and the surrounding structures, the tumor can also cross the cribriform plate, invade the brain, or seed the cerebrospinal fluid[2,7]. Considerable published articles confirm the ectopic origin cases of ENB throughout the nasal cavity and the central nervous system, These published articles demonstrate cases with a primary origin in the posterior nasal septum, the nasal inferior meatus, the maxillary sinus the pterygopalatine fossa, the sella turcica, the petrous apex, and the sphenoid sinus as was the case with our patient[1,8]. Given their rarity and the clinical presentation resemblance between benign and malignant lesions, the diagnosis of nasosinusal malignant lesions can be challenging and eventually delayed. The tumor's evolution remains considerably insidious, and patients are often not examined until they present with nasal obstruction, headache, nasal pain, excessive lacrimation, epistaxis, anosmia, and visual symptoms that occur when the orbit is invaded and include diplopia, vision loss, proptosis, and epiphora[8]. Intracranial is often asymptomatic. Generally,

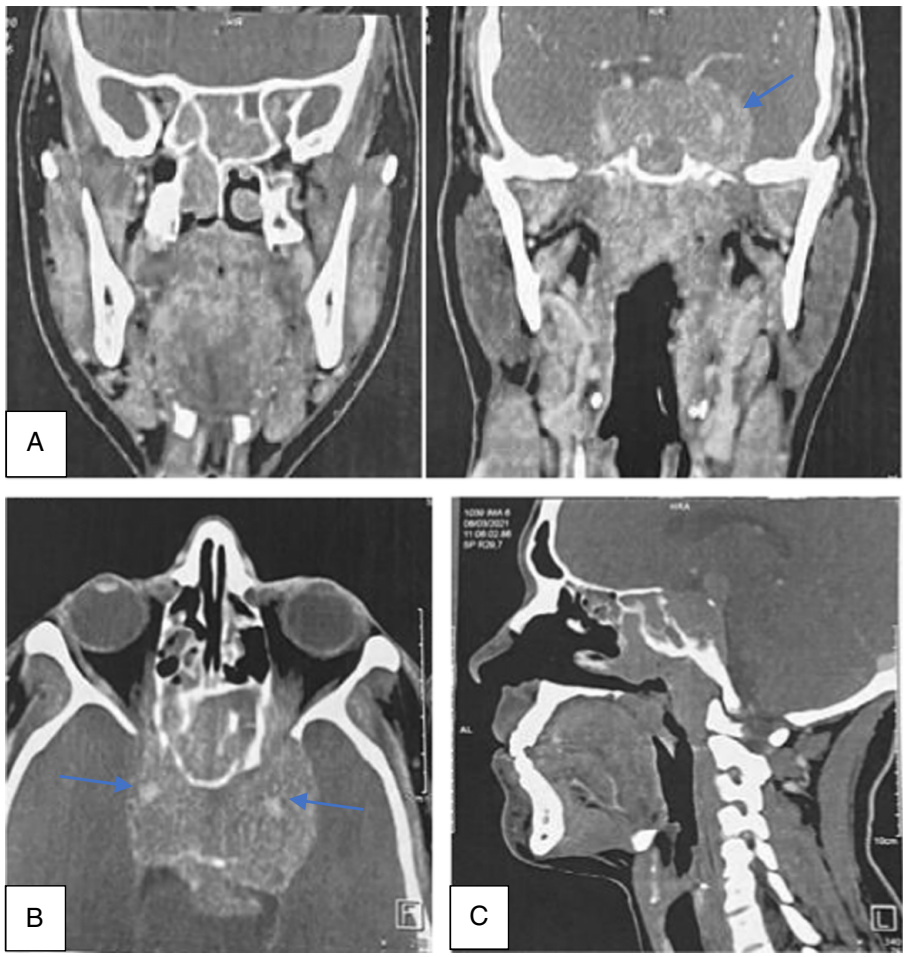

Figure 1. Enhanced computed tomography scan of the skull base and paranasal sinuses; coronal (A), axial (B), and sagittal slices (C) showing mildly enhancing mass of the sphenoid sinus with intralesional calcifications (blue arrows) and bone erosion intracranial involvement and extending to the ethmoid sinuses the nasal septum to the nasal cavity.

ENBs appear as a soft, glistening, polypoidal, or nodular mass covered by intact mucosa or as friable masses with ulceration and granulation tissue[9,10]. The ENB metastasis to cervical lymph nodes has a standard pattern, disseminating first to level II nodes, the levels I, III, and retropharyngeal nodes could also be involved. Given the tumor's aggressive behavior and hematologic spread, the recurrent disease can sometimes be first recognized in areas far away from the primary site[11]. ENB metastasis most commonly occurs in the lungs and bones, followed by the liver, spleen, scalp, breast, adrenal gland, and ovary, and also in rare sites such as the thoracic spine, spinal cord, parotid, and the trachea[1,12,13].

The combined use of (CT) scan through the skull base and paranasal sinuses and (MRI) techniques is the golden standard for offering the information for the tumor's extension and thus the treatment planning. In the CT scan, the tumor appears as solid and enhancing nasal cavity masses, bone erosion of adjacent structures, such as the orbital plate, the ethmoid bone, the cribriform plate, and the fovea ethmoidal could also be encountered. A CT scan is the optimal modality for evaluating bony involvement. In MRI, the tumor appears as hypointense and isointense or hyperintense to gray in respectively T1-and T2-weighted images. This imaging technique provides better discrimination between tumor and secretion and optimal assessment of orbital and intracranial or brain parenchymal involvement[14]. Intralesional calcification observed on neuroimaging can be considered pathognomonic for ENB, and the presence of cysts along the intracranial margins of Kadish Stage C lesions in which there is intracranial extension also yields a definitive diagnosis.

ENB is staged by the Kadish system, this classification has a prognostic value and divides lesions into three stages: stage A (tumor is limited to the nasal fossa); stage B (tumor extends to the paranasal sinuses); and stage C (tumor extends beyond the paranasal sinuses). The Dulguerov system uses the TNM classification and includes the imaging data, it considers the early invasion of the cribriform plate in the T2 stage, and separates intracranial but extradural tumors from true brain involvement[15,16].

After the adequate examination on physical examination and imaging, the biopsy is the next important step to confirm the diagnosis. The histological grading system for ENB was described by Hyams in 1988[10]. This system scores mitotic activity, nuclear polymorphism, amount of fibrillary matrix, rosette formation, and amount of necrosis seen. The histological diagnosis of esthesioneuroblamas is determined using a combination of light microscopic appearance, and a battery of immunohistochemical stains, (chromogranin, synaptophysin, S-100 protein, and neuron-specific enolase). The authors of genetic and molecular

studies have shown that ENB is a member of the Ewing sarcoma and PNET family[1].

The treatment options of ENB include surgery, radiotherapy, and more recently, chemotherapy, these options could be used exclusively or combined. Chemotherapy has been introduced as a therapeutic option since ENB has proven to be chemosensitive and responsive to platinum-based agents and the most commonly used regimen includes cyclophosphamide with vincristine. Surgical removal of the tumor and postoperative radiotherapy is the basic therapeutic strategy of the ENB. Surgical treatment requires one bloc resection of the tumor with negative surgical margins. Endoscopic surgery can be realized in selected cases. Craniofacial resection has become the best surgical procedure for achieving safe, en-bloc resection of the disease. Radiotherapy is systematically recommended, even after the resection of early stages of lesions with negative surgical margins[15,17]. Chemotherapy is reserved for unresectable or recurrent tumors as it was in our case, and for metastatic cases. In unresectable lesions, multimodality treatment including, preoperative chemotherapy and radiotherapy with local resection in an attempt to attain locoregional control and increase the chance of survival may be considered[18]. Therapeutic neck dissection is no controversy; however, no consensus is yet present about prophylactic elective neck dissection[6]. The tumor recurrence is very frequent and can develop soon after an aggressive treatment or several years later. The authors believe that embolic metastasis, such as seen intracranially can explain the recurrence. Another theory includes the possible development of a second primary (i.e. 'field of cancerization') or potential transformation because of the tumor signaling[7]. In our case, unfortunately, the tumor's stage was very advanced, and we could not evaluate the surgical efficiency of the surgical treatment. Close and long-term follow-up is mandatory for patients with ENB, with clinical exams, nasal endoscopy, and anatomic imaging. The authors recommend examination every 3–6 months with a CT scan and/or MRI for surveillance for 2 years, which can be extended to 6–12 months afterward for 10 years, or indefinitely. According to the literature , Hyams grade, lymph node metastasis, Kadish stage, and extent of resection are proven to be the main prognosis factors[17].

Conclusion

While most ENBs originate in the superior nasal vault and present with typical symptoms of nasal obstruction and epistaxis in the late stages of the disease, uncommon manifestations should be considered as well. ENB should be kept in the differential of masses throughout the nasal cavity, paranasal sinuses, and surrounding anatomical locations. A patient with a history of prior ENB can also have a recurrence in distant locations. Adjuvant therapy should be considered in patients with advanced disease and unresectable disease. An extended follow-up period is required for these patients.

Ethical approval

Hereby, I Safaa Touihmi consciously assure that for the manuscript Primary tuberculosis of the pyriform sinus: case report, the following is fulfilled:

(1) This material is the authors' own original work, which has not been previously published elsewhere.
(2) The paper is not currently being considered for publication elsewhere.
(3) The paper reflects the authors' own research and analysis in a truthful and complete manner.
(4) The paper properly credits the meaningful contributions of coauthors and co-researchers.
(5) The results are appropriately placed in the context of prior and existing research.
(6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.
(7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Patient perspective

Finding out about my disease and how insidious it has been evolving I was frustrated, however, I was ready to hear about the alternatives, and so far I am not decepointed.

I. Safaa Touihmi, state that the work has been reported in line with the SCARE 2020 criteria[19].

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Author contributions:

S.T.: writing, study concept of the paper; I.H.: helping in the clinical study of the case; I.R.: supervising.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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References

[1] Senchak A, Freeman J, Ruhl D, *et al*. Low-grade esthesioneuroblastoma presenting as siadh: a review of atypical manifestations. Case Rep Otolaryngol 2012;2012:1–6.
[2] Oskouian RJ, Jane JA, Dumont AS, *et al*. Esthesioneuroblastoma: clinical presentation, radiological, and pathological features, treatment, review of the literature, and the University of Virginia experience. Neurosurg Focus 2002;12:1–9.
[3] Sepúlveda I, Herrera Á, Delgado C, *et al*. Esthesioneuroblastoma: a case report and review of the literature. Int J Odontostomat 2012;6:285–9.

[4] Buohliqa L, Upadhyay S, Nicolai P, *et al*. Possible esthesioneuroblastoma metastasis to paranasal sinuses: clinical report and literature review: possible esthesioneuroblastoma metastasis to paranasal sinuses. Head Neck 2016;38:E32–6.
[5] Carey R M, Godovchik J, Workman AD, *et al*. Patient, disease, and treatment factors associated with overall survival in esthesioneuroblastoma: factors associated with ENB survival. Int Forum Allergy Rhinol 2017;7:1186–94.
[6] Alotaibi H A, Priola S M, Bernat A-L, *et al*. Esthesioneuroblastoma: summary of single-center experiences with focus on adjuvant therapy and overall survival. Cureus 2019.
[7] Michel J, Fakhry N, Santini L, *et al*. Nasal and paranasal esthesioneuroblastomas: clinical outcomes. Eur Ann Otorhinolaryngol Head Neck Dis 2012;129:238–43.
[8] Sethi B, Kumar Y, Mishra J, *et al*. Esthesioneuroblastoma arising from the middle meatus. J Cancer Res Ther 2013;9:99.
[9] Fiani B, Quadri SA, Cathel A, *et al*. Esthesioneuroblastoma: a comprehensive review of diagnosis, management, and current treatment options. World Neurosurg 2019;126:194–211.
[10] Dublin A, Bobinski M. Imaging characteristics of olfactory neuroblastoma (esthesioneuroblastoma). J Neurol Surg Part B Skull Base 2015;77:1–5.
[11] Shukla R, Singh P, Senthil S, *et al*. Esthesioneuroblastoma: a case report. 5.
[12] Banuchi V E, Dooley L, Lee NY, *et al*. Patterns of regional and distant metastasis in esthesioneuroblastoma: metastatic disease in esthesioneuroblastoma. Laryngoscope 2016;126:1556–61.
[13] Unal A, Ozlugedik S, Tezer M S, *et al*. An atypical esthesioneuroblastoma of the inferior nasal cavity and maxillary sinus: report of a case. Tumori J 2006;92(no. 5):440–3.
[14] Ow T J, Bell D, Kupferman M E, *et al*. Esthesioneuroblastoma. Neurosurg Clin N Am 2013;24:51–65.
[15] Chadha S, Pannu K K. Esthesioneuroblastoma: a case report. Indian J Otolaryngol Head Neck Surg 2011;63:44–6.
[16] Hollen T R, Morris CG, Kirwan JM, *et al*. Esthesioneuroblastoma of the nasal cavity. Am J Clin Oncol 2015;38:311–4.
[17] Rao K R, Upadhya I B. A review on esthesioneuroblastoma. Indian J Otolaryngol Head Neck Surg 2021;74. doi: 10.1007/s12070-021-02726-2
[18] Kumar R. Esthesioneuroblastoma: multimodal management and review of literature. World J Clin Cases 2015;3:774.
[19] Agha R A, Franchi T, Sohrabi C, *et al*. The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84:226–30.