

Olfactory Esthesioneuroblastoma: A Case Series and Comprehensive Review of the Literature

M. Farina^{1*}, Y. Hanfaoui¹, Y. Hioukan¹, A. Lachgar¹, K. Nouni¹, H. Elkacemi¹, T. Kebdani¹, K. Hassouni¹

¹Department of Radiation Therapy, National Institute of Oncology, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco

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*Corresponding author: M. Farina

Department of Radiation Therapy, National Institute of Oncology, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco

Abstract

Case Report

Esthesioneuroblastoma (ENB), also known as olfactory neuroblastoma, is a rare malignant neuroectodermal tumor of the sinonasal tract thought to arise from the olfactory neuroepithelium. We report a retrospective, descriptive series of six patients with ENB managed at the Radiotherapy Department of the National Institute of Oncology (CHU Avicenne), Rabat, Morocco, between 2020 and 2025, together with a review of the literature. The series included three men and three women aged 21 to 64 years (mean, 40 years). The mean time to consultation was 6 months (range, 2 months to 1 year). Presenting symptoms were mainly sinonasal and ocular, including unilateral nasal obstruction (n = 5), epistaxis (n = 4), ocular signs (n = 4), and sinonasal pain (n = 3). Computed tomography showed Kadish stage C disease in five patients and stage D disease in one. Tumors were Hyams grade I in three cases, grade II in two, and grade III in one. Four patients underwent surgery followed by radiotherapy, delivered with three-dimensional conformal radiotherapy (66–70 Gy) or intensity-modulated radiotherapy. One patient received palliative chemotherapy, and one patient with extensive locoregional disease received symptomatic treatment only. Complete remission was achieved in two patients after 3 years of follow-up; disease progression occurred in one patient, tumor recurrence in two, and one patient died. ENB is frequently diagnosed at a locally advanced stage. Combined surgery and radiotherapy remain the standard curative approach, and multidisciplinary management with long-term surveillance is essential given the risk of late recurrence.

Keywords: Esthesioneuroblastoma, Olfactory neuroblastoma, Sinonasal tumors, Kadish staging, Hyams grade, Radiotherapy, Intensity-modulated radiotherapy, Craniofacial resection.

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INTRODUCTION

Esthesioneuroblastoma (ENB), also known as olfactory neuroblastoma, is a rare malignancy of the head and neck, accounting for approximately 3%–6% of neoplasms arising in the nasal cavity and paranasal sinuses [1]. First described by Berger, Luc, and Richard [2], ENB is a neuroectodermal tumor thought to originate from the olfactory neuroepithelium within the olfactory cleft of the superior nasal cavity, at the level of the anterior skull base [3]. Local tumor extension may involve the paranasal sinuses and skull base, with possible invasion of the orbit, cavernous sinus, and intracranial compartment.

Several therapeutic strategies for ENB have been reported; however, high-level prospective evidence remains limited because of the rarity of the disease and

its characteristic pattern of late recurrence, which necessitates prolonged post-treatment surveillance. The clinical behavior of ENB is heterogeneous, ranging from an indolent, slow-growing neoplasm to an aggressive and locally invasive malignancy with the potential for regional lymphatic and distant metastases. Because of its nonspecific initial symptoms, ENB is often diagnosed at an advanced stage, after substantial local extension has occurred. Nevertheless, advances in surgical techniques, modern radiotherapy, and the incorporation of novel systemic treatments have led to the development of increasingly effective therapeutic strategies and encouraging clinical outcomes [4].

The aim of this study and literature review was to characterize the histopathological and clinical features of olfactory esthesioneuroblastoma, review the principal anatomical and clinical classification systems, identify

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the main prognostic factors, and propose an appropriate multidisciplinary treatment strategy for this rare tumor.

CASE PRESENTATION

The present study is retrospective and descriptive carried out during a 5-year period (2020 to 2025) and based on six observations about olfactory esthesioneuroblastomas compile at the Radiotherapy department of the National Institut of Oncology (CHU Avicenne) of Rabat.

Our series of study included three men and three women, with an age ranging from 21 to 64 years old an average age of 40, and no particular exposing to risk factors were noted.

The average time taken by the patient to consult was 6 months and ranging from 2 months to 1 years, the reason for consultations were mainly the ocular and rhino sinus signs.

Imparticular, a unilateral and nasal obstruction was present in 5 cases, an epistaxis of low abundance resistant to treatment was noted in 4 cases, also, some nasal sinus pains were witnessed in 3 cases. Ocular signs were noted in 4 cases and took the form of exophthalmos for 2 patients, and a low visual acuity for three patients. Some neurological signs consisted of headaches, were noted in one case;

the physical examination, using the nasal endoscopy performed for 5 of our patients, showed a circonferential process of the nasal cavity in 4 cases.

A total filling of the nasal cavity was witnessed in 3 cases and a deviation of the nasal septum to contralateral side in 1 case.

The fundoscopic examination, performed for all our patients, showed signs of vascular damage in 1 case. Besides, the neurological examination indicated a trismus in one case. The examination of lymph nodes showed some palpable cervical lymphadenopathies for 1 patient. A facial CT scan was carried out for our 6 patients and showed a Kadish stage C tumor of nasal

sinus cavities in 5 cases and a Kadish stage D in 1 case. An expansion to the orbital cavities in 2 cases and to the base of the skull in 1 case.

Facial MRI was performed for 3 patients, and the tumor boundaries were extended more than what CT scan showed before.

The diagnosis of olfactory esthesioneuroblastoma was only retained on the basis of the anatomopathological examination of the biopsies. On the microscopique level, the two predominant criteria were a lobular and compact shape. The tumor cells were small with rounded nucleoli.

Cytoplasm was less abundant, without nuclear membrane and with a prominent fibrillated matrix. According to the histologic grading of Hyams three cases were stage I, two others were stage II and one case was stage III.

An extended assessment included a thoraco abdominal CT scan done for 4 patients and also a chest X-Ray for two patients, an abdominal sonography for the two other cases, some lymphadenopathies were found in two patients. Four patients had surgeries from which four by the intranasal approach, and the 4th by open surgery with extended lymph node dissection. A patient was judged for above any treatment due to the important locoregional expansion of the tumor, then she had a symptomatic treatment (Observation N° 2).

The surgical treatment was followed by radiation therapy for 4 patients, 2 received a dose of 70 Gy (using the three-dimensional conformal radiotherapy technique: 3D) and 1 patient received a dose of 66 Gy in 3D, and 1 using conformal radiotherapy with intensity modulation: IMRT (Figures 2-6). One patient had palliative chemotherapy. A complete remission was achieved for two patients after 3 years follow up.

An evolutionary pursuit was noted in 1 case: 3 months after the exclusive surgical treatment. A tumor recurrence occurred in 2 cases, and one patient got out of the hospital and passed away later.

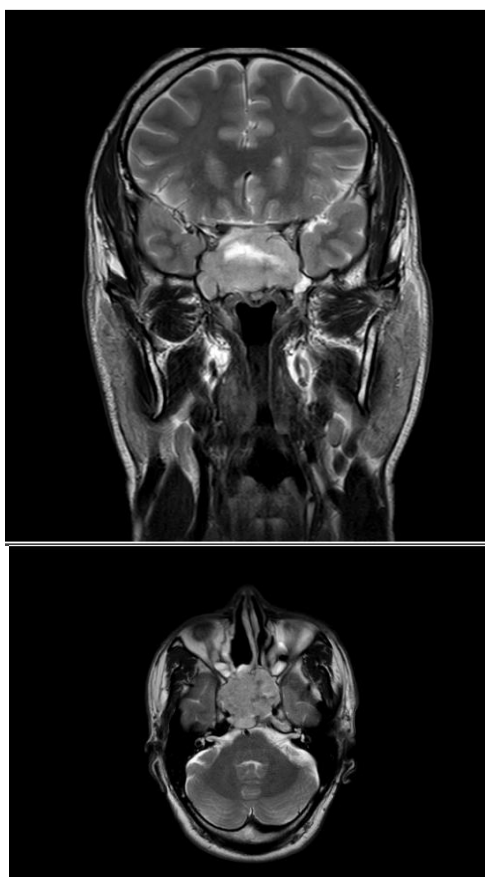


Figure 1 and 2: Sagittal and coronal section of brain MRI in sequence Flair, T2, T1 with contrast injection showing a tumor process

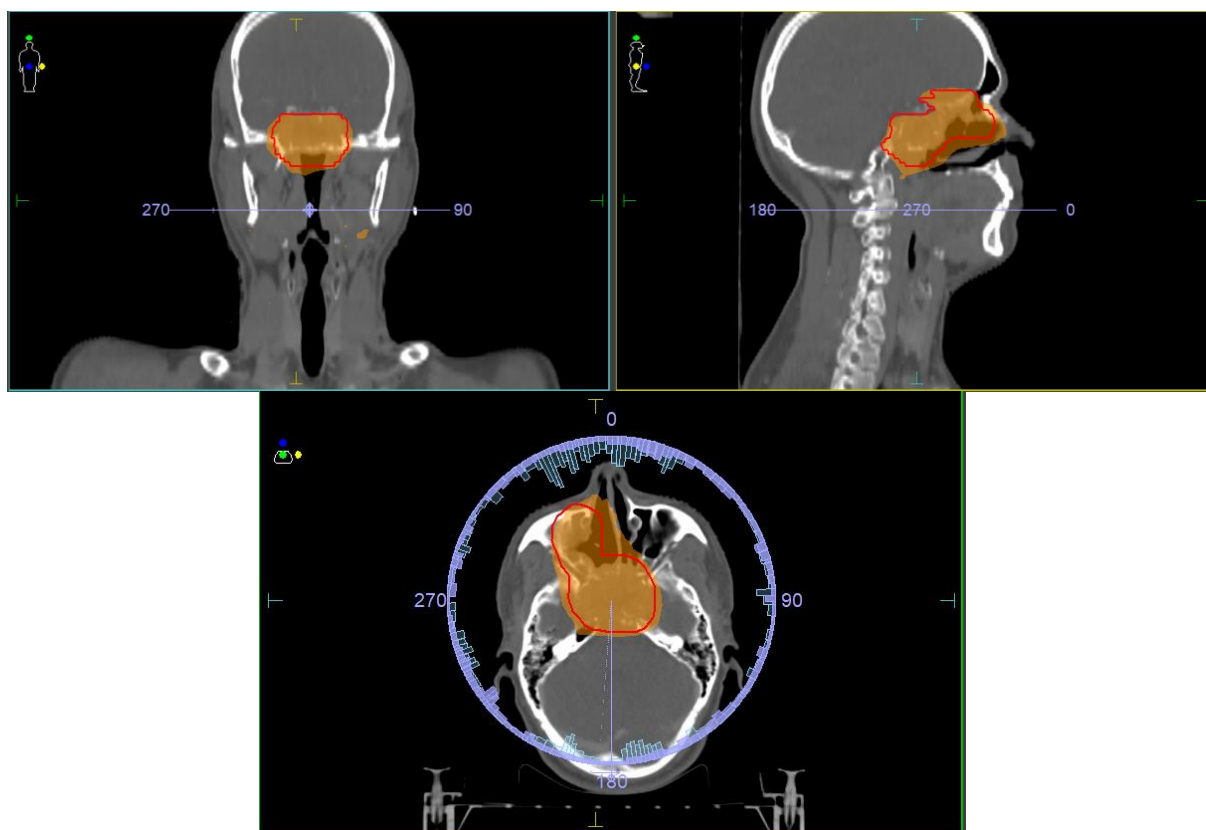


Figure 3 and 4: Dosimetry by the IMRT technique of a patient with Esthesioneuroblastoma

DISCUSSION

Olfactory esthesioneuroblastoma (ENB) was first described by Berger *et al.*. Subsequently, approximately 1,000 cases have been reported in the literature [2]. ENB is a rare malignant sinonasal neoplasm, accounting for approximately 1%–2% of all malignant tumors of the nasal cavity and paranasal sinuses and 3%–6% of all nasal tumors [1–3,5]. The increasing number of cases reported in recent years may reflect improved recognition and diagnosis rather than a true increase in disease incidence [6]. Most published series indicate an approximately equal sex distribution, although a slight female predominance has been reported by some authors [6].

ENB can occur at any age, with two reported incidence peaks: one between 10 and 20 years of age and another between 50 and 60 years [3,5,7]. No definite risk factor has been established. However, previous studies have suggested a possible association with exposure to nitrosamines, wood dust, and certain genetic abnormalities [8].

The initial clinical manifestations of tumors arising from the facial bones, including ENB, are often nonspecific [9]. The symptoms most frequently reported in the literature were similar to those observed in our study [10,11].

Imaging and staging

The radiological assessment of ENB primarily relies on computed tomography (CT) and magnetic resonance imaging (MRI), which provide complementary information [12]. Contrast-enhanced CT, performed in the axial and coronal planes, is particularly useful for evaluating bony involvement. Typically, ENB appears as a relatively homogeneous soft-tissue mass, occasionally containing intratumoral calcifications, with moderate enhancement after contrast administration [5]. CT also contributes to the assessment of tumor extension, including intracranial involvement and invasion of the anterior skull base [2,5]. MRI is valuable for assessing soft-tissue extension, orbital involvement, intracranial spread, and the relationship between the tumor and adjacent neurovascular structures.

Based on the extent of disease, Kadish *et al.*, proposed a three-stage clinical classification [1,2,13]:

- **Stage A:** Tumor confined to the nasal cavity.
- **Stage B:** Tumor involving the nasal cavity and paranasal sinuses.
- **Stage C:** Tumor extending beyond the nasal cavity and paranasal sinuses.

This classification was subsequently modified by Morita. More recently, Dulguerov *et al.*, proposed a more detailed classification based on the TNM system and incorporating findings from CT and MRI [9,13]:

- **T1:** Tumor confined to the nasal cavity and/or paranasal sinuses, with preservation of an air space between the tumor and the cribriform plate.
- **T2:** Tumor contacting or eroding the cribriform plate.
- **T3:** Intracranial extradural extension and/or orbital involvement.
- **T4:** Intracranial intradural extension.

The currently accepted staging systems are the modified Kadish classification described by Morita and the Dulguerov TNM-based classification [7,12]. In our series, radiological staging was performed according to the Kadish classification. Five patients were classified as having stage C disease, whereas one patient had stage D disease.

Diagnosis and treatment

Although imaging findings may strongly suggest the diagnosis of ENB, definitive diagnosis requires histopathological examination [12]. Diagnosis is based on the evaluation of tumor morphology combined with immunohistochemical analysis.

Treatment is determined primarily by tumor resectability and disease extent. For resectable tumors, complete surgical excision with both macroscopic and microscopic tumor clearance, including adequate safety margins, followed by postoperative radiotherapy to the primary tumor bed and appropriate regional lymphatic drainage areas, is generally considered the standard curative approach for sinonasal ENB [12].

No single surgical approach is universally recommended. The choice of approach should be guided by two fundamental objectives [14]: first, achieving adequate exposure and control of all anatomical tumor boundaries, including the cribriform plate; and second, performing an en bloc oncological resection whenever feasible while avoiding tumor fragmentation or transection [14].

In cases of orbital extension, management should be individualized. Most surgeons favor preservation of the globe whenever oncologically appropriate, as orbital exenteration has not consistently been associated with improved overall survival or reduced recurrence rates.

For unresectable tumors, treatment is multimodal and may include first-line chemotherapy, followed by radiotherapy and, when feasible, delayed craniofacial surgery, in accordance with multidisciplinary consensus [5]. Although preoperative radiotherapy has been adopted in some centers, it is not considered the standard approach in most treatment strategies [3,7].

Radiotherapy is directed toward the primary tumor bed and clinically relevant regional lymphatic areas. Depending on the tumor volume and treatment intent, radiation doses ranging from 45 to 60 Gy may be administered [15]. Modern radiotherapy techniques, including intensity-modulated radiotherapy (IMRT), may improve dose conformity and reduce radiation exposure to adjacent critical structures.

Prognosis and follow-up

Olfactory ENB is associated with an unfavorable prognosis, with reported overall survival rates of approximately 50% at 5 years and 30% at 10 years. Local and locoregional recurrence rates may reach 60% [16]. Recurrences may occur either early or several years after initial treatment, supporting the need for lifelong clinical and radiological surveillance.

The prognostic factors associated with ENB remain incompletely defined, largely because of the rarity of the disease and the small sample sizes of most published series. The clinical stage at diagnosis is generally considered the most important prognostic factor. Age, sex, and ethnicity have not consistently been identified as independent prognostic variables. The Hyams histopathological grade also appears to have prognostic significance, with reported survival rates of approximately 56% for low-grade tumors (grades I–II) compared with 25% for high-grade tumors (grades III–IV).

Other relevant prognostic factors include the TNM stage and the treatment modality used. Combined surgery and radiotherapy are generally associated with better survival outcomes than either radiotherapy or surgery alone.

CONCLUSION

Most patients with ENB present with locally advanced disease. Optimal management requires close collaboration among head and neck surgeons, radiation oncologists, medical oncologists, radiologists, and pathologists, from the initial diagnostic work-up through treatment planning and long-term follow-up. Novel therapeutic strategies, including concurrent chemoradiotherapy and dose escalation using advanced radiation techniques such as IMRT and proton therapy, should be prospectively evaluated to determine whether they can improve disease control and survival outcomes in patients with ENB.

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