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CASE REPORT

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Metastatic olfactory neuroblastoma with unusual solitary metastasis to femur: a case report and literature review

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Abstract

Background Olfactory neuroblastoma (ONB) is a rare malignancy that develops in the nasal cavity, with appendicular skeletal metastases being exceptionally uncommon. We report the case of a middle-aged male with ONB, presenting with an unusual biopsy-confirmed solitary metastasis to the left proximal femur.

Case presentation A 33-year-old male was previously diagnosed with olfactory neuroblastoma in the skull base after initial clinical presentation with progressive left-sided nasal obstruction for six months. He was treated with neoadjuvant chemotherapy, followed by local control via trans-sphenoidal resection in addition to postoperative radiotherapy and adjuvant chemotherapy. Two years later, the patient began experiencing left thigh pain. Radiographic imaging of the left femur revealed an ill-defined lesion in the midshaft with periosteal thickening, suggesting metastatic disease. The lesion caused significant bone destruction, ending up with a non-traumatic pathological fracture. A wide surgical resection of the proximal two-thirds of the femur was performed, followed by endoprosthetic reconstruction to restore structural integrity, joint function, and limb biomechanics. Postoperative management included physical rehabilitation to optimize functional recovery and maintain weight-bearing capacity.

Conclusion This case underscores the importance of early identification of skeletal involvement in ONB, as prompt orthopedic intervention can prevent complications, improve mobility, and contribute to better oncological and functional outcomes. Advanced reconstructive techniques play a pivotal role in achieving durable results in cases involving skeletal metastasis of rare tumors like ONB.

Keywords Olfactory neuroblastoma, Skeletal metastasis, Endoprosthetic reconstruction, Pathological fracture

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Background

Neuroblastomas are predominantly pediatric tumors that originate from the neural crest cells, they are one of the most common malignant solid tumors in the pediatric age group, however, they are extremely rare in adults. While most cases arise from the abdomen specifically adrenal glands, nasal cavity involvement is unusual [1]. Malignant tumors arising from the nasal cavity are relatively rare, with olfactory neuroblastoma accounting for less than 6% of all nasal cavity tumors, with an incidence rate of 0.4 per million [2, 3]. Olfactory neuroblastoma (ONB) is a rare tumor originating from the epithelium of the olfactory nerve in the nasal cavity [4]. It is an aggressive tumor with a high risk of recurrence and metastasis. Patients with ONB typically present with nasal obstruction, nose bleeding, and headache [2]. Management of ONBs requires a multidisciplinary approach, including surgery, radiation, and chemotherapy [5]. In this article, we report a rare case of ONB with metastasis to the left femur complicated with a pathological fracture. The patient voluntarily agreed to publish his relevant medical information and radiological images in a scientific journal for educational purposes, and informed consent was obtained.

Case report

A 33-year-old male who was previously diagnosed with olfactory neuroblastoma in the skull base (Kadish stage C) (Fig. 1) after initial clinical presentation to the otolaryngology clinic with chief complaint of a progressive left-sided nasal obstruction for 6 months, associated with nasal discharge, intermittent facial pressure, hyposmia, and epiphora in his left eye. His past medical history is relevant for ex-smoking as well as primary hypothyroidism and a positive family history of gastrointestinal and hematologic malignancy. After a multidisciplinary tumor board discussion, he was initially treated with neoadjuvant chemotherapy with Cisplatin (25 mg/m^2) and Etoposide (100 mg/m^2) for a total of three cycles with only minimal radiologic response followed by trans-sphenoidal resection in addition to postoperative radiotherapy and adjuvant chemotherapy with four cycles of Taxene (75 mg/m^2).

Two years later, the patient began experiencing intermittent non-specific left thigh pain. Radiographic imaging of the left femur demonstrated an ill-defined lesion in the midshaft with periosteal thickening, raising suspicion of metastatic disease. Further evaluation with Magnetic Resonance Imaging (MRI) revealed a focal lesion in the proximal third of the femoral shaft, characterized by heterogeneous enhancement, measuring approximately 8 cm, and accompanied by a periosteal reaction (Fig. 2). Whole-body fluorodeoxyglucose-positron emission tomography (FDG-PET) confirmed a hypermetabolic expansile bony lesion in the left proximal femur, with no evidence of additional lesions elsewhere. Open biopsy was subsequently performed and a histopathology analysis by a specialized pathologist confirmed the diagnosis of metastatic round cell tumor consistent with olfactory neuroblastoma (Hyam grade 3) (Fig. 3). Tumor cells exhibited strong positive staining for synaptophysin, chromogranin, and CD56. The proliferative marker (Ki67) was positive in 15–20% of the tumor cells (Fig. 4). Which indicated an intermediate proliferative potential, thus neoadjuvant chemotherapy was administered to reduce the proliferative index of the tumor prior to surgery.

Unfortunately, the patient subsequently had a minor trauma and he sustained a pathologic fracture at the bone lesion and biopsy site (Fig. 5). The patient was temporarily stabilized with skin traction and scheduled for surgical limb salvage intervention. Following a multidisciplinary tumor board discussion, a wide surgical resection of the proximal two-thirds of the femur with proximal femur modular endoprosthetic reconstruction was performed by an orthopedic oncologist (Fig. 6). His postoperative course was uneventful and he commenced rehabilitation protocol with partial weight-bearing and muscle-strengthening exercises as per our standard protocol. He has a very good functional outcome and was ambulating full weight bearing during his routine surveillance follow-up visits at 3, 6, and 9 months.

Discussion

ONB, also known as esthesioneuroblastoma, originates from the olfactory nerve [6]. It predominantly occurs during the second and sixth decades of life, with no sex predominance. Patients with ONB typically present with nonspecific symptoms, including nasal obstruction, epiphora, headache, and other more aggressive symptoms, such as blurred vision, recurrent epistaxis, and hyposmia, depending on the tumor invasion of the surrounding structures. Thus, an early diagnosis and management are crucial to prevent permanent complications [7]. ONB is an aggressive tumor, with 40% of the patients eventually developing metastasis [8]. However, effective primary treatment and local tumor control can significantly reduce the incidence of metastasis. Cervical lymph nodes were the most common sites of metastasis, followed by the spine and lungs. No significant difference in the overall survival rate based on the site of distant metastasis [9]. Nevertheless, metastasis to long bones in extremities similar to our case is extremely rare, and it was only reported once in the literature [10].

The diagnosis of olfactory neuroblastoma requires a high amount of clinical suspicion as it can mimic many benign conditions. Computed tomography (CT) and Magnetic Resonance Imaging (MRI) are essential for

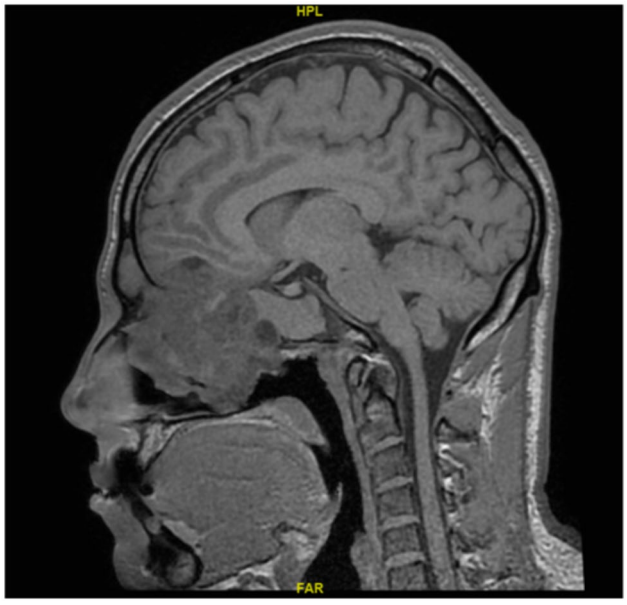

Fig. 1 Magnetic resonance image of the paranasal sinus (sagittal view)

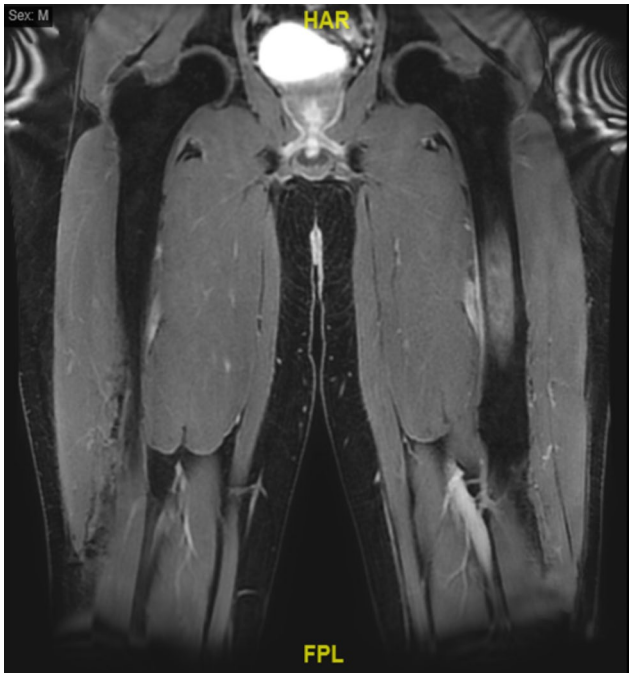

Fig. 2 Magnetic resonance image of the femur (coronal view)

the precise visualization of the nasal cavity and paranasal sinus, although the diagnosis cannot be made without histological confirmation. Rhinoscopy is crucial for performing a biopsy and to assess the tumor extent [11]. The histological grading of ONB was described by Hyams in 1988 and was divided into four grades [12]. In our case, the patient had Hyamm grade 3 ONB, which is considered high-grade with a 5-year survival rate of 25% [13]. Moreover, staging using the modified Kadish system classifies olfactory neuroblastomas into four stages: stage A, where the tumor is confined to the nasal cavity only; stage B, when the tumor extends to the paranasal sinus; stage C, when the tumor involves the intracranial cavity, skull base, orbit, or cribriform plate; and stage D, when there are regional or distant metastases. Our patient initially had Kadish stage C, however, after the diagnosis of the distant metastasis to the left femur, he was classified as Kadish stage D, which unfortunately has a 10-year survival rate of 13.3% [14, 15]. Given the rarity of these tumors, no standard management protocol has been established. Treatment options include surgical resection, radiotherapy, and chemotherapy. Traditionally, surgical resection through an open craniofacial approach was the only option. However, due to the high risk of complications, an endoscopic endonasal approach has been introduced, with a lower complication rate and a shorter hospital stay as compared to those of the open approach [16].

Radiotherapy also plays a crucial role in managing olfactory neuroblastoma, despite some controversy regarding the approach of the radiotherapy. Yin and Elkon suggested that radiotherapy alone is sufficient for treating Kadish stages A and B [17, 18], while Duo et al. reported that surgical resection followed by adjuvant radiotherapy for Kadish stages C and D improved the overall survival rate [19]. However, Broich et al. suggested that surgical resection combined with radiotherapy should be administered for all stages of ONB [20]. Notably, ONB is a chemosensitive tumor, and chemotherapy is mainly administered preoperatively to reduce the proliferative index (Ki67), followed by surgical resection and adjuvant radiotherapy [21]. In our case, the patient received three cycles of neoadjuvant chemotherapy, underwent trans-sphenoidal resection, and adjuvant radiotherapy, with an additional four cycles of chemotherapy. In a similar reported case, a patient had ONB with multiple bone metastases involving the humerus, thoracic vertebrae, lumbar vertebrae, and femur was treated with only three cycles of chemotherapy (two cycles of cyclophosphamide and one cycle of pirarubicin), which resulted in symptomatic relief; however, there were no significant changes in the tumor size on MRI [10].

Conclusions

In conclusion, this case report aims to describe a very rare case of metastatic ONB with long bone involvement and to review the current available literature. Early diagnosis of ONB requires a very high index of suspicion and aggressive management with systemic as well as local modalities are crucial to minimize local recurrence, distant metastasis and improve the overall survival rate.

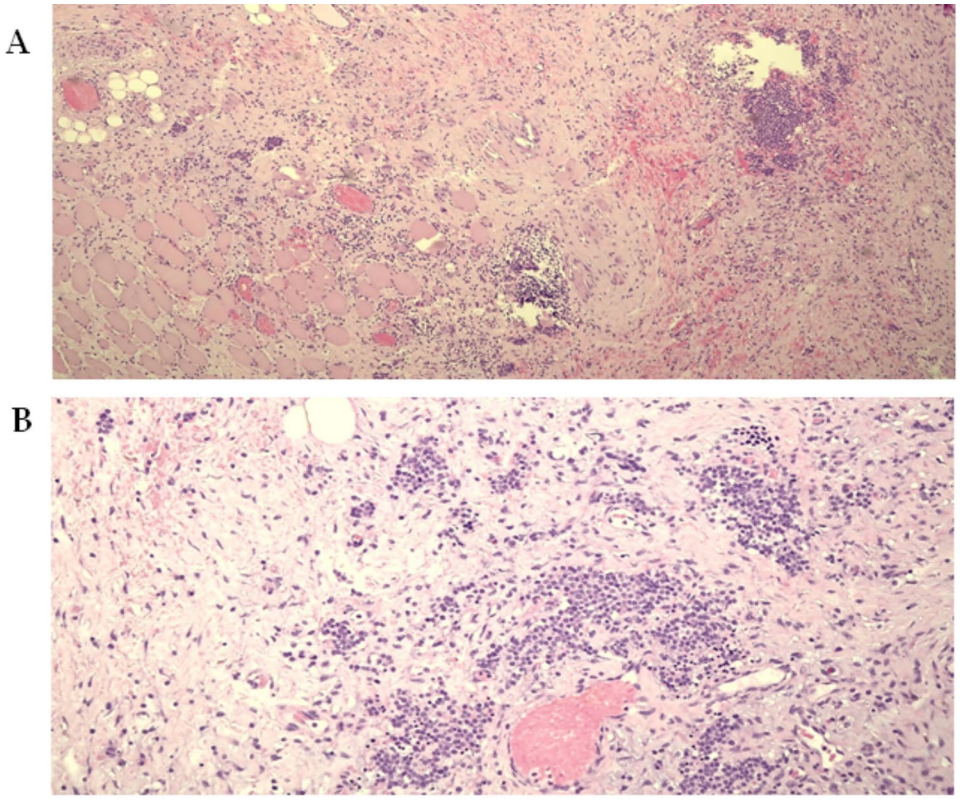

Fig. 3 Histopathology of biopsy sections. (**A**) Low power view 40x. Nests and lobules of monotonous tumor cells infiltrating the fibroadipose tissue are observed. (**B**) Intermediate power view 100x. The image shows round nuclei, indistinct nucleoli, and scant cytoplasm, along a vascular-rich to hyalinized stroma. It also features a fibrillary neural matrix solid growth pattern, marked mitotic activity, and necrosis. No neuropil is observed

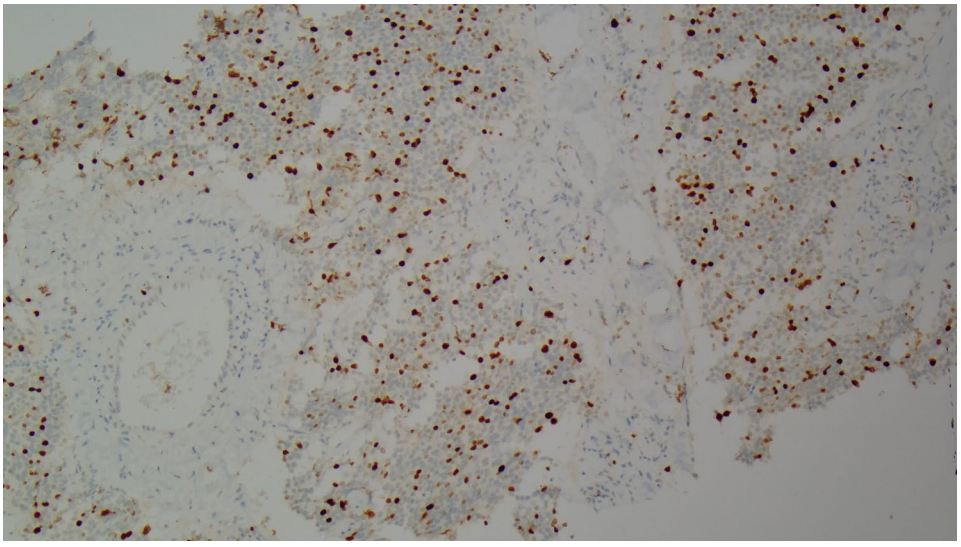

Fig. 4 Intermediate power view (200x) of the immunohistochemistry section demonstrating Ki67 expression. The Ki67 proliferation index shows 15–20% proliferation

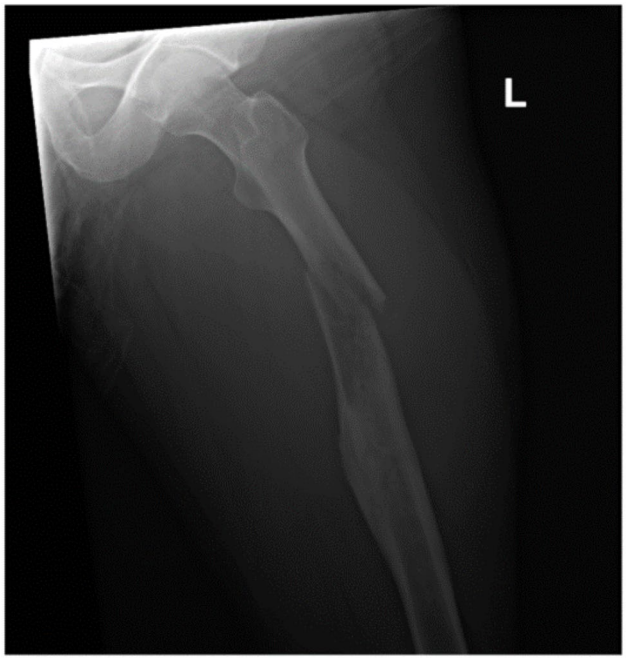

Fig. 5 Radiograph of the left femur (anteroposterior view)

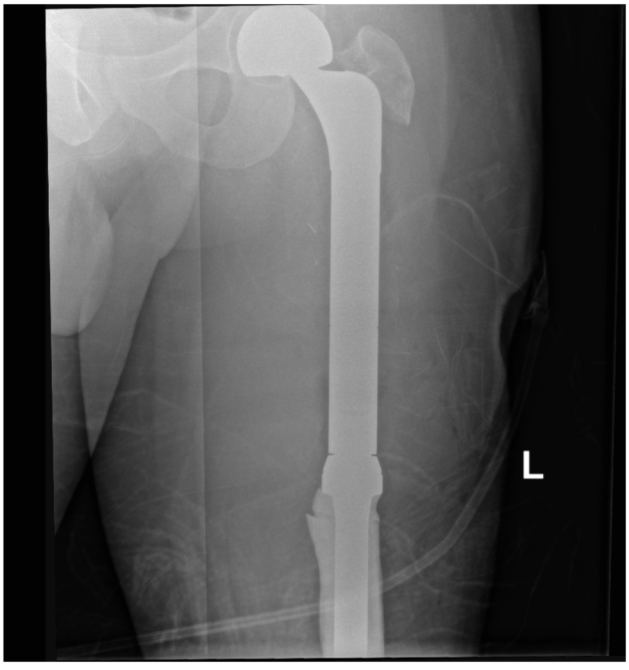

Fig. 6 Radiograph of the left femur (anteroposterior view)

Abbreviations

ONB	Olfactory neuroblastoma
CT	Computed tomography
MRI	Magnetic Resonance Imaging
FDG-PET	Fluorodeoxyglucose - positron emission tomography

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Not applicable.

Author contributions
Abdulrahman Alaseem, Mishari Alanez, Ahmed Altuwaimi, Ibrahim Alshaygy, Motaz AlAqeel, and Waleed Albishi wrote the main manuscript text, and Fahad Almehrij and Saeed Bahabri prepared Figs. 1, 2, 3, 4 and 5. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
At our institution, Institutional Review Board approval is not required for case reports. Written informed consent was obtained from the patient to publish this paper.

Consent for publication
Written informed consent was obtained from the patient to publish this paper.

Competing interests
The authors declare no competing interests.

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References

1. Swift CC, Eklund MJ, Kraveka JM, Alazraki AL. Updates in diagnosis, management, and treatment of neuroblastoma. Radiographics. 2018;38:566–80. https://doi.org/10.1148/rg.2018170132.
2. Zhong W, Wang C, Ye W, Wu D. Primary olfactory neuroblastoma of the nasopharynx: A case report. Ear Nose Throat J. 2023;102:NP19–23. https://doi.org/10.1177/0145561321989436. Epub 2021 Jan 21. PMID: 33474978.
3. Tosoni A, Di Nunno V, Gatto L, Corradi G, Bartolini S, Ranieri L, et al. Olfactory neuroblastoma: diagnosis, management, and current treatment options. Front Oncol. 2023;13:1242453. https://doi.org/10.3389/fonc.2023.1242453.
4. Faragalla H, Weinreb I. Olfactory neuroblastoma: a review and update. Adv Anat Pathol. 2009;16:322–31. https://doi.org/10.1097/PAP.0b013e3181b544cf.
5. Mody MD, Saba NF. Multimodal therapy for sinonasal malignancies: updates and review of current treatment. Curr Treat Options Oncol. 2020;21:4. https://doi.org/10.1007/s11864-019-0696-4.
6. Valli R, De Bernardi F, Frattini A, Volpi L, Bignami M, Facchetti F, et al. Comparative genomic hybridization on microarray (a-CGH) in olfactory neuroblastoma: analysis of ten cases and review of the literature. Genes Chromosomes Cancer. 2015;54:771–5. https://doi.org/10.1002/gcc.22288.
7. Fiani B, Quadri SA, Cathel A, Farooqui M, Ramachandran A, Siddiqi I, et al. Esthesioneuroblastoma: A comprehensive review of diagnosis, management, and current treatment options. World Neurosurg. 2019;126:194–211. https://doi.org/10.1016/j.wneu.2019.03.014.
8. Mori R, Sakai H, Kato M, Hida T, Nakajima M, Fukuda T, et al. Olfactory neuroblastoma with spinal metastasis: case report. No Shinkei Geka Neurol Surg. 2007;35:503–8.
9. Marinelli JP, Janus JR, Van Gompel JJ, Link MJ, Foote RL, Lohse CM, et al. Esthesioneuroblastoma with distant metastases: systematic review & meta-analysis. Head Neck. 2018;40:2295–303. https://doi.org/10.1002/hed.25209.
10. Zhou Q, Li Z, Liu B, Zhao L, Tian B, Wang L, et al. Occult olfactory neuroblastoma presenting with multiple bone metastases: a case report. Medicine. 2020;99:e22630. https://doi.org/10.1097/MD.0000000000022630.
11. Ghaffar S, Salahuddin I. Olfactory neuroblastoma: a case report and review of the literature. Ear Nose Throat J. 2005;84:150–2. https://doi.org/10.1177/014556130508400311.
12. Rao KR, Upadhya IB. A review on Esthesioneuroblastoma. Indian J Otolaryngol Head Neck Surg. 2022;74(Suppl 2):1584–90. https://doi.org/10.1007/s12070-021-02726-2.
13. Dulguerov P, Allal AS, Calcaterra TC. Esthesioneuroblastoma: a meta-analysis and review. Lancet Oncol. 2001;2:683–90. https://doi.org/10.1016/S1470-2045(01)00558-7.

14. Konuthula N, Iloreta AM, Miles B, Rhome R, Ozbek U, Genden EM, et al. Prognostic significance of Kadish staging in esthesioneuroblastoma: an analysis of the National Cancer database. Head Neck. 2017;39:1962–8. https://doi.org/10.1002/hed.24770.
15. Jethanamest D, Morris LG, Sikora AG, Kutler DI. Esthesioneuroblastoma: a population-based analysis of survival and prognostic factors. Arch Otolaryngol Head Neck Surg. 2007;133:276–80. https://doi.org/10.1001/archotol.133.3.276.
16. Hagemann J, Roesner J, Helling S, Jacobi C, Doescher J, Engelbarts M, et al. Long-term outcome for open and endoscopically resected sinonasal tumors. Otolaryngol Head Neck Surg. 2019;160:862–9. https://doi.org/10.1177/0194599818815881.
17. Yin ZZ, Gao L, Luo JW, Yi JL, Huang XD, Qu Y, et al. Long-term outcomes of patients with esthesioneuroblastomas: A cohort from a single institution. Oral Oncol. 2016;53:48–53. https://doi.org/10.1016/j.oraloncology.2015.11.021.
18. Elkon D, Hightower SI, Lim ML, Cantrell RW, Constable WC, Esthesioneuroblastoma. Cancer. 1979;44:1087–94. https://doi.org/10.1002/1097-0142(197909)44:3<1087::aid-cncr2820440343>3.0.co;2-a.
19. Duo GS, Feng JL, Zhang ZY, Wang LJ. Survival impact of postoperative radiotherapy in patients with olfactory neuroblastoma: 513 cases from the SEER database. Cancer Radiother. 2022;26:663–9. https://doi.org/10.1016/j.canrad.2021.12.006.
20. Broich G, Pagliari A, Ottaviani F. Esthesioneuroblastoma: a general review of the cases published since the discovery of the tumour in 1924. Anticancer Res. 1997;17:2683–706.
21. Sun Y, Zhang SR, Wang MJ, Huang Q, Cui SJ, Yang BT, et al. Neoadjuvant chemotherapy in the treatment of locally advanced olfactory neuroblastoma in 25 cases. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi chin. J Orl Head Neck Surg. 2023;58:425–30. https://doi.org/10.3760/cma.j.cn115330-20230115-00026.

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