Int J Clin Exp Med 2017;10(3):5510-5513
www.ijcem.com /ISSN:1940-5901/IJCEM0038253

*Case Report*

# Primary extraskeletal Ewing sarcoma in the olfactory sulcus misdiagnosed as olfactory neuroblastoma: a case report with review of literature

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Received November 6, 2016; Accepted January 18, 2017; Epub March 15, 2017; Published March 30, 2017

**Abstract:** Extraskeletal Ewing sarcoma (EES) is an aggressive malignancy with low incidence that occurs in the soft tissues of the lower extremities, paravertebral tissues, and chest wall. Few EES cases in the head and neck region have been reported. In this paper, we presented a case of EES that occurred in the olfactory sulcus with similar presentation as olfactory neuroblastoma. To our knowledge, this is the first case of EES in this region. Furthermore, we analyzed the clinical features of EES and reviewed existing literature.

**Keywords:** Extraskeletal Ewing sarcoma, olfactory sulcus, nasal tract

## Introduction

Ewing sarcoma (ES) is a poorly differentiated and aggressive malignancy that frequently develops within bones, especially in the long bones of the extremities. Different from the skeletal form, extra skeletal Ewing sarcoma (EES) has low incidence and mainly occurs in the soft tissues of the lower extremities, paravertebral tissues, chest wall and retroperitoneum [1, 2]. Few cases along the nasal tract or the head and neck region have been documented in the literature. In the current study, we reported a case of primary EES in the olfactory sulcus, which was initially suspected as olfactory neuroblastomain a 19-year-old male patient who presented with epistaxis. We aim to increase the significance of understanding the morphological features of EES, which might help in the accurate diagnosis and appropriate management of EES patient.

*Case presentation*

A 19-year-old male patient was admitted to our department with epistaxis as the only symptom. He presented no significant medical background and family history. No abnormal findings were revealed throughout the physical examination and laboratory tests. CT scan reveals soft tissue density placeholder in the sphenoid sinus (**Figure 1A-C**), while no evidence in any other area of the whole body. After preoperative preparation, nasal endoscopic surgery was performed. During the surgery, soft neoplasm was observed in the left olfactory sulcus area (**Figure 1D**). The tumor expanded posteriorly to the superior turbinate and the ostiumsphenoid sinus. The neoplasm was initially suspected to be an olfactory neuroblastoma as shown by endoscopy, considering the position and the appearance. However, biopsy showed Des(-), myogenin(-), LCA(-), CD99(+), Fli-1(+-), CD34(-), CD56(+), CgA(-), Syn(-), Ki-67(15%+), PAX-5(-), PCK(+) (**Figure 2**). Fluorescence in situ hybridization showed the ectopia of the EWSR1 gene, and these findings confirmed the diagnosis of ES. After the surgery, the patient was admitted to the Department of Oncology and subjected to Vincristine-Adriamycin-Cisplatin (VAC) chemotherapy. After one year of follow up, the patient has finished six cycles of chemotherapy and remains free of recurrence to date.

## Discussion

EES belongs to the Ewing sarcoma family of tumors (ESFT), and was first described by Tefft

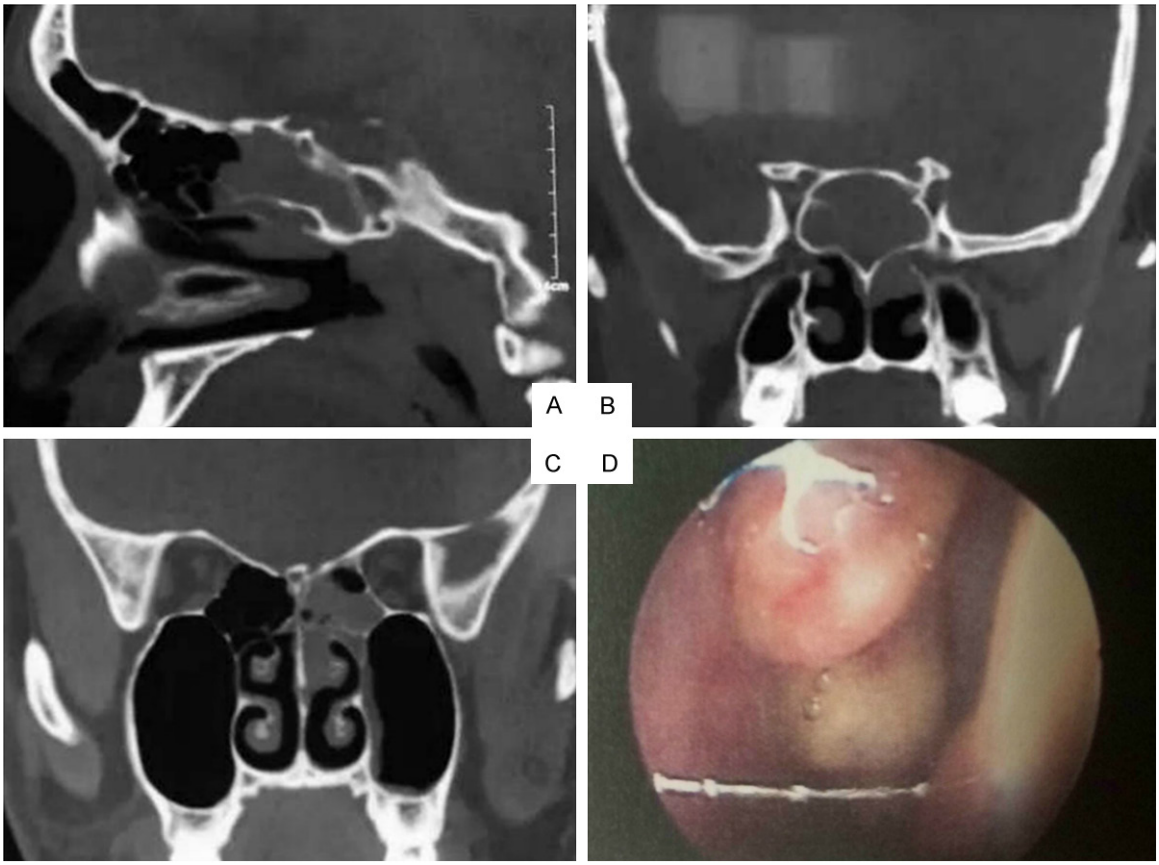


**Figure 1.** CT scans (A-C) showed soft tissue shadows in the sphenoid sinus, ethmoid sinus and nasal tract. Nasal endoscopy (D) demonstrated the neoplasm in the olfactory sulcus.

in 1969 [3]. Since Angerwall and Enzingerfirst proposed the term "extraskeletal Ewing sarcoma" in 1975 [4], a few isolated cases or small series of EES have been reported. EES mainly occurs in the soft tissues of the lower extremities, paravertebral tissues, chest wall and retroperitoneum [1, 2]. To our knowledge, only extremely limited cases of EES in the nasal tract have been reported in literature. In this paper, we reported the first EES case that occurred in the olfactory sulcus.

Due to the rarity of EES, its clinical manifestation is not specific, and is based on the position of its occurrence. Epistaxis is one of the most common manifestations of diverse groups of nasal tumors, as similarly presented in our case. Other common symptoms may include and are not limit to nasal obstruction and anosmia. In aggressive malignancies, like EES, early metastasis occurs through the blood. Some EES cases exhibit lymph node involvement, which is identified as an independent adverse prognostic factor [5].

The early diagnosis of EES is of great significance considering its early metastasis. Given its the diverse manifestations, the diagnosis of EES may also require several ancillary techniques, such as medical images and pathological methods. Tumors are typically isointense to hyperintensein T1-weighted MRI images and hyperintensein T2-weighted images. Smaller tumors are tend to be homogeneous, but the heterogeneity on unenhanced and contrast-enhanced images is the norm for larger tumors, relating to hemorrhage and internal necrosis [6, 7]. Upon CT scan, tumors similarly show heterogeneous enhancement with hypoattenuating areas, which correspond to necrosis and high-density foci in cases of hemorrhage. Calcification is atypical, occurring in about 10% of tumors upon presentation [7-9]. Pathological methods are the gold standard in tumor diagnosis. Unfortunately, there is no specific immunohistochemical marker for EES. Although CD99 expression is not specific, its diagnostic value in EES is important. Other tumors, such as lymphoblastic lymphoma, poorly differenti-

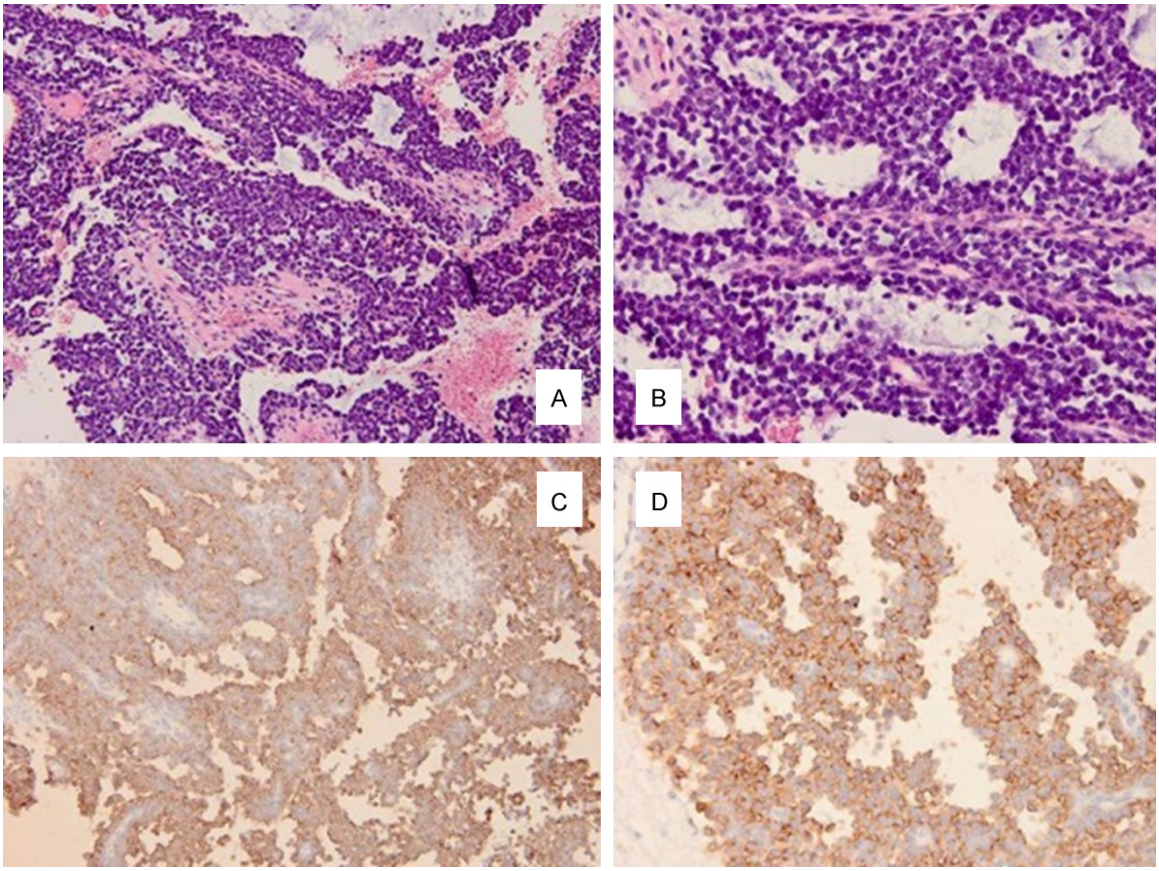


**Figure 2.** Immunostaining of tumour samples. The tumour is composed of broad sheets of small round cells with scant clear cytoplasm and coarse chromatin. Hematoxylin and eosin staining, magnification (A) ×200; (B) ×400. The tumour has a high mitotic index and the tumour cells are diffusely positive for CD99 magnification (C) ×200; (D) ×400.

ated synovial sarcoma, and rhabdomyosarcoma, may also show positive staining in response to the CD99 antigen. As a result, negativestaining for other markers (chromogranin, synaptophysin, neurofilament, S-100 protein, rosette formation,and neurofibrillary matrix) ensures the diagnostic accuracy [10]. The combination of CD99 and NKX2.2, a transcriptional target of EWSR1-FLI1, is highly specific for the diagnosis of EES [11]. Moreover, the majority of EES patients have t(11;22)(q24;q12), which is the fusion between the 5' end of the EWS gene from chromosome band 22q12 with the 3' portion of the *11q24 FLI1* gene, a member of the ETS family of transcription factors. This EWS fusion protein blocks the differentiation of pluripotent marrow stromal cells. Other cases might have t(21;22)(q22;q12), in which EWA is fused EWS to a closely related ETS gene, ERG from chromosome band 21q22. These findings can also be helpful in our diagnosis [12, 13].

Early diagnosis and effective resection are essential treatment approach for EES. Moreover, chemical and/or radical therapies have significant roles in treatment. The most effective chemotherapy regimens include ifosfamide, cyclophosphamide, doxorubicin, etoposide, vincristine and dactinomycin. These chemotherapy drugs work well for ES and ESS, especially for the eradication of microscopic or overt metastatic diseases. Response rates to induction chemotherapy are routinely high, and show complete and partial responses in up to 90% of cases. In additional, radical therapy is also widely accepted. Resection of the primary lesion is preferred to radiotherapy alone for local disease control because of late recurrence [14, 15]. Generally, EES, an aggressive tumor with a high incidence of local recurrence and distant metastasis, is more common in men than in women, particularly during the first 2-3 decades of life [2].

The successful management of EES requires the cooperation of both surgery and postoperative oncological therapy, including radical and chemical methods. Different groups of nasal tumors may present similar appearances and manifestation, and may not differ in surgical approach. However, given the malignancy of EES, its early and correct diagnosis and identification are of great significance to patients' long-term prognosis and should receive considerable attention from be pathologist and oncologist, as well as physicians and surgeons.

In conclusion, EES is an aggressive tumor with highincidences of local recurrence and distant metastasis. The rare presentation of EES in the nasal tract, for example in the olfactory sulcus, does occur, and should therefore receive more attention. A multimodality treatment that consists of adequate surgical resection, aggressive chemotherapy, and radiotherapy is recommended for EES management. Despite the low incidence of EES, we should emphasize the importance of its careful evaluation, early diagnosis, and appropriate management.

## Disclosure of conflict of interest

None.

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