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Case Report

Primary extraskeletal Ewing sarcoma of the sinonasal tract: a rare case report and review of the literature

Li-Ding Yao[1], Jin-Long Tang[2], Liang-Ji Lu[1], Mohammad-Farez Sayfoo[3], Xiu-Liang Zhu[1]

[1]Department of Radiology, The Second Affiliated Hospital, Zhejiang University School of Medicine, No.88 Jiefang Road, Hangzhou 310009, Zhejiang, China; [2]Department of Pathology, The Second Affiliated Hospital, Zhejiang University School of Medicine, No.88 Jiefang Road, Hangzhou 310009, Zhejiang, China; [3]Zhejiang University School of Medicine, No.866 Yuhangtang Road, Hangzhou 310058, Zhejiang, China.

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Abstract: Purpose: Extraskeletal Ewing sarcoma (EES) is a rare, round-cell malignant neoplasm that mostly manifests as a large and bulky soft-tissue mass. EES is most commonly found in the paravertebral region, extremities, chest wall, retroperitoneum, pelvis and hip. EES can occur in the head and neck. However such locations are considered to be rare for this type of malignant neoplasm. Methods: We report a 41 years female diagnosed with EES, and performed a brief review about the clinical features and diagnostic strategies of the EES. Results: The CT and MRI examination reveals a mass in the nasal cavity and paranasal sinuses, and the pathological examination supported the diagnosis of EES. Conclusions: Primary Ewing's sarcoma must be considered when the expansile nasal mass is detected with extensive invasion into adjacent structures and bony destructive changes, although which is a very rare condition.

Keywords: Ewing sarcoma, extraskeletal, sinonasal tract

Introduction

Extraskeletal Ewing sarcoma (EES) is a rare, round-cell malignant neoplasm that is histologically indistinguishable from the more common osseous Ewing sarcoma [1, 2]. Both EES and Ewing sarcoma are derived from the same neuroectodermal cells that share the same cytogenetic marker, with translocation of chromosomes t(11;22)(q24;q12) [3]. The medical terminologies "peripheral primitive neuroectodermal tumor" (PNET) and "Askin tumour" (thoracopulmonary PNET) are no longer used. This is because, in terms of histological appearance and morphology, PNET and Askin Tumour are identical to EES. Consequently, for the sake of simplicity and clarity, the two terms mentioned above are avoided [4]. Tefft et al [5] first described this tumor in children with paravertebral soft tissue masses.

Symptoms are non-specific and typically depend on the location of the tumor. EES are most commonly diagnosed via computed tomography (CT) and magnetic resonance imaging (MRI). The final diagnosis of EES requires a comprehensive analysis on the histopathology, immunoprofile and interphase fluorescence in situ hybridization (FISH) results. EES could exist in any part of the human body, but it is less likely to occur in the head and neck [6, 7]. In this study, we present a case of EES found in the nasal cavity and paranasal sinuses, which invaded to the orbits and anterior cranial fossa.

Case report

A 41-year-old woman was admitted to The Second Affiliated Hospital Zhejiang University School of Medicine (Hangzhou, China) in November 2014, complaining of headache, blurred vision and diplopia for 1 month. The symptoms had become more intense, and anosmia presented for 4-5 days. Physical examination revealed right exophthalmos. Laboratory tests exhibited no pathological changes or abnormalities.

A paranasal sinuses computerized tomography (CT) examination was performed, which

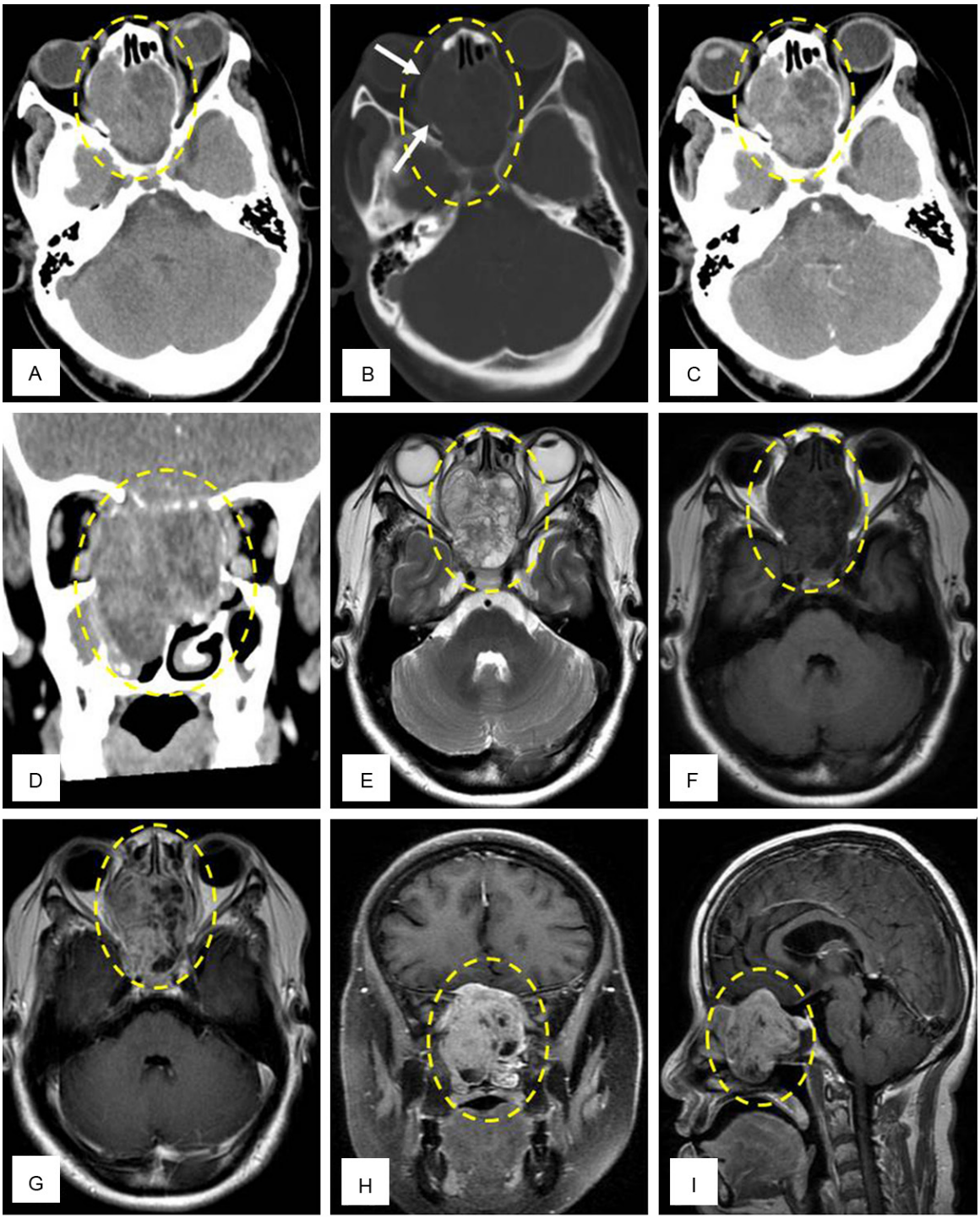

Figure 1. Computed tomography imaging (A-D) and magnetic resonance imaging (E-I) features of EES. A contrast-enhancement paranasal sinuses CT examination revealed that a large mass (yellow dashed circle) with an irregular shape located in the nasal cavity and paranasal sinuses. The mass is heterogeneous isodensity compared to the muscle, with hypoattenuating areas corresponding to necrosis (A). This tumor invaded the adjacent bones (arrows), causing absorption of destruction (B). By contrast (C, D), the mass had mild enhancement. It is heterogeneously hyperintense on T2 weighted images (E) and hypoisointense on T1 weighted images (F). On post-contrast T1-weighted MR image (G-I), heterogeneous enhancement of the mass is noted. The lesion extended to the orbits, coming into contact with the medial rectus muscles and optic nerves. The mass extended beyond the skull, and occupied the anterior cranial fossa, displacing and compressing the frontal lobes.

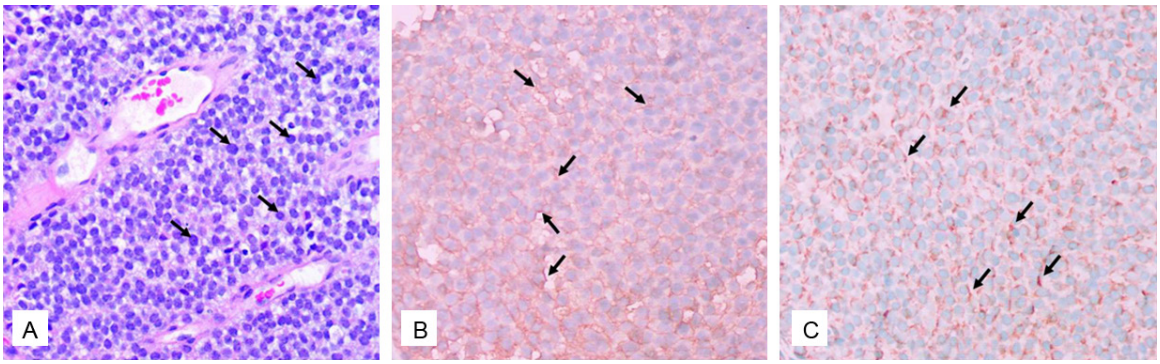

Figure 2. Pathologic features of tumour samples. (A) The tumor shows small, round, malignant cells (arrows) with hyperchromatic nuclei, scant cytoplasm, and brisk mitotic figures (Hematoxylin and eosin staining; magnification, ×400). (B) The tumour cells (arrows) show a strong membranous CD99 staining pattern (Immunohistochemistry; magnification, ×400). (C) The tumour cells (arrows) show diffusely positive for vimentin (Immunohistochemistry; magnification, ×400).

revealed a large mass with an irregular shape locating in the nasal cavity and paranasal sinuses. The mass was noted to display heterogeneous isodensity, when compared to the muscle, with hypoattenuating areas corresponding to necrosis (**Figure 1A**). The size of the mass was approximately 39 mm × 52 mm. The mass eroded the maxillary, ethmoid and sphenoid sinuses, infiltrating the middle portion of the nasal septum, extending to the posterior region of the nasal cavities, and affecting the hibateral turbinates except the left inferior turbinate. The mass involved the adjacent bones, causing absorption of destruction (**Figure 1B**). By contrast, the mass had mild enhancement (**Figure 1C**, **1D**).

Subsequently, the patient underwent a head magnetic resonance (MR) examination, which showed heterogeneous hyperintensity on T2 weighted images (**Figure 1E**) and hypointensity on T1 weighted images (**Figure 1F**) and with apparent post-contrast enhancement (**Figure 1G-I**). The mass showed a relatively well-defined margin, which involved the adjacent tissues, especially the medial rectus muscles and optic nerves. It must also be noted that the mass extended beyond the skull, and occupied the anterior cranial fossa, displacing and compressing the frontal lobes. Other MR imaging feature found here was the presence of Serpentine high-flow vascular channels, which had low signal intensity presented.

Eventually, the patient underwent surgical removal of the tumor. Histologically, the tumor consisted of small, round, malignant cells with hyperchromatic nuclei, scant cytoplasm, and brisk mitotic figures (**Figure 2A**). Immunohistochemical studies revealed that the tumour cells were diffusely positive for CD99 (**Figure 2B**) in a membranous pattern and diffusely positive for vimentin (**Figure 2C**). Furthermore, FISH revealed a t(22;12) translocation. Thus the diagnosis of EES was established.

After excision of the tumor, the patient received radiotherapy and chemotherapy. At 15 months follow up, she was asymptomatic with no evidence of distant or local relapse.

Literature search

We performed a PubMed search for all cases of EES of the sinonasal tract up to December 2017 (**Table 1**).

Discussion

EES is a rare, round-cell malignant neoplasm that mostly manifests as a large and bulky soft-tissue mass [1, 32]. Most cases of EES occur during the second or third decade of life [33, 34]. However, based on an analysis of the Surveillance, Epidemiology and End Results Program (SEER) database between 1973 and 2007, Applebaum et al [35] found patients with EES have a higher mean age, but also a bimodal distribution with EES more commonly found in those older than 35 and less than 5 years compared with skeletal tumors. The most commonly reported locations of EES are the paravertebral region (32%), lower extremities (26%), chest wall (18%), retroperitoneum (11%), pelvis

Table 1. Summary of previously reported cases of patients with Ewing's sarcoma of paranasal sinuses

Study	# of Cases	Age/gender	Immunohisto-chemistry (CD99)	Treatment	Clinical outcome
Fernandez CH et al, [8] 1974	2	NA	NA	Chemoradiation	NA
Strong LC et al, [9] 1979	3	NA	NA	Chemoradiation	DOD-1 months, NED-48 months NED-276 months
Pontius KI et al, [10] 1981	1	39/Female	NA	Chemoradiation	NED-24 months
Whang-Peng J et al, [11] 1987	1	22/Male	NA	Surgery + postop radiation	AWD-29 months
Csokonai LV et al, [12] 2001	1	19/Male	NA	Surgery + postop radiation	NED-12 months
Böör A et al, [13] 2001	1	20/Female	+	Surgery + chemoradiation	NED-12 months
Aferzon M et al, [14] 2003	1	14/Female	+	Surgery + chemoradiation	NED-6 months
Alobid I et al, [15] 2003	1	23/Female	+	Chemoradiation	NED-59 months
Wexler LH et al, [16] 2003	1	9/Female	NA	Chemotherapy + surgery	NED-36 months
Windfuhr JP et al, [17] 2004	1	7/Male	+	Surgery + chemoradiation	NED-17 months
Coskun BU et al, [18] 2005	1	16/Female	+	Chemoradiation	NED-12 months
Infante-Cossio P et al, [19] 2005	1	17/Male	+	Chemotherapy + surgery	NED-96 months
Kawabata M et al, [20] 2008	1	12/Male	+	Chemoradiation	NED-20 months
Thariat J et al, [21] 2008	1	10/Male	NA	Chemotherapy + surgery	NED-15 months
Whaley JT et al, [22] 2009	2	9/Female	NA	Chemoradiation	NED-12 months
		17/Male	NA	Chemoradiation	Dead at 29 months
Gray ST et al, [23] 2009	2	15/Female	+	Surgery + chemoradiation	NED-23 months
		17/Male	+	Chemoradiation	Chemoradiation
Hafezi S et al, [24] 2011	14	Female (7, 13, 15, 18, 22, 35, 45, 69, 70); Male (13, 25, 33, 34, 54)	+ (14 cases)	Chemoradiation (3 cases); Surgery (2 cases); Surgery + postop radiation (1 case); Chemotherapy (1 case); NA (7 cases)	NED-4, 6, 21, 26, 128 months; DOD-17 months; DOD with breast mets-14 months; AWD with lung mets1 month; NA (6 cases)
Yeshvanth SK et al, [25] 2012	1	15/Female	+	Chemotherapy + surgery + radiotherapy	NED-12 months
Li M et al, [26] 2013	1	39/Female	+	Radiotherapy + chemotherapy	NED-32 months
Jeong BY et al, [27] 2013	1	42/Male	NA	Surgery + chemotherapy	NED-106 days
Negru ME et al, [28] 2015	1	33/Male	+	Chemotherapy + chemoradiation	NED-15 months
Lepera D et al, [29] 2016	2	31/Male	+	Surgery + chemoradiation	AWD-3 years
		26/Female	+	Chemoradiation	Chemoradiation
Lombardi D et al, [30] 2017	5	31/Female	NA	Chemoradiation	NED-139 months
		36/Female	NA	Chemoradiation	NED-110 months
		36/Female	NA	Surgery + chemoradiation	NED-70 months
		48/Male	NA	Surgery + chemoradiation	DOD-100 months
		25/Female	NA	Chemoradiation	NED-118 months
Suzuki T et al, [31] 2017	1	23/Male	+	Surgery + chemoradiation	NED-30 months

NA, not available; *NED,* no evidence of disease; *DOD,* dead of disease; *AWD,* alive with disease at last follow up; *Mets,* metastasis.

and hip (11%), and upper extremities (3%) [4]. It is a rare occurrence that EES appears in the head and neck. A study discovered that only 6 out of 70 (8.5%) patients with EES locating in the head and neck [32]. Furthermore, there are a few reports of EES involving the sinonasal tract.

The imaging features of EES on contrast-enhanced CT or MRI can be generally characterized as bulky heterogeneous masses with frequent local invasion or a mass effect to adjacent organs. Although these tumors generally showed a relatively well-defined margin, tending to displace adjacent structures, local invasion to adjacent organs was also frequently observed. In particular, local invasion was common in tumors of the abdomen, pelvis, and thorax [32]. The case reported here is consistent with these reports. We found that the tumor mainly displaced adjacent structures, but also invaded the nasal septum, turbinates and skull, occupying the anterior cranial fossa.

On CT, the attenuation of the mass is similar to that of muscle. The majority of tumors showed heterogeneous enhancement with hypoattenuating areas corresponding to necrosis and high-density foci in cases of hemorrhage [7, 32]. Relative to muscle, these tumors are typically hypointense to isointense on T1-weighted images and hyperintense on T2-weighted images. The tumor mostly has prominent heterogeneous enhancement following the intravenous administration of gadolinium, indicating hemorrhage and internal necrosis. An additional imaging feature of MR imaging of EES is the presence of serpentine high-flow vascular channels, which has low signal intensity with all pulse sequences. This feature was also identified in our report.

The final diagnosis of EES was based on the histopathology, immunoprofile and FISH results. Histologically, these lesions demonstrate crowded sheets of small round blue cells. They share a karyotype abnormality with translocation involving chromosomes 11 and 22. This translocation between the long arms of chromosomes 11 and 22 (t[11;22][q24;q12]) is present in approximately 90% of these lesions [3, 4]. Successful treatment of EES requires multidisciplinary management combination of neoadjuvant chemotherapy, surgical resection, and radiation therapy [4, 34]. With respect to previous cases, it must be noted that The prognosis of EES is poor, with a high incidence of local recurrence and distant metastasis. Applebaum et al found that patients with localized EES have an unfavorable prognosis prior to two years from initial diagnosis, but then the outcomes for EES are significantly better [35].

In conclusion, one can confirm that EES of the sinonasal tract is a rare phenomenon. Moreover, the presentation of the case of a 41-year-old woman with an EES in the nasal cavity and paranasal sinuses is significant as confirmation by histologic analysis, histochemical stains, immunohistochemistry, and FISH were readily performed. This shows the different techniques used to identify EES. CT and MRI are very useful for delineating tumor extent, identifying distant metastases, predicting resectability and for guiding surgical management. The purpose of this case is to alert radiologists and prompt clinicians to bear in mind that although the presence of EES in the sinonasal tract is rare, it must still be included in the differential diagnosis of sinonasal mass lesions. Prompt operation should be performed in order to correctly establish the diagnosis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiu-Liang Zhu, Department of Radiology, The Second Affiliated Hospital of Zhejiang University School of Medicine, No.88 Jiefang Road. Hangzhou 310009, Zhejiang, China. Tel: +86-571-8820-8439; Fax: +86-571-8820-8439; E-mail: zhuxiul@zju.edu.cn

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