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Case Report

A rare case of Ewing's sarcoma of the maxillary sinus ☆

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ABSTRACT

Ewing's sarcoma is generally an aggressive, poorly differentiated bone and soft tissue tumor affecting children and young adults, it accounts for 4%-6% of all primary bone tumors and primary facial locations occur in only 1%-4% of all cases, primarily in the mandible and calvaria. Involvement of the paranasal sinuses is rare. Here we report the case of an 11-year-old girl with no medical, surgical, or traumatic history, who presented for 1 month and progressive evolution of swelling of the left cheek, associated with pain, nasal obstruction, rhinorrhea, and a slight weight loss not quantified. A craniofacial computed tomography (CT) scan showed a mixed lytic and condensing lesional tissue process centered on the left maxillary sinus, heterogeneously enhanced after contrast injection, lysing the walls of the sinus extended to the homolateral nasal cavity and slightly infiltrating the adjacent soft tissues. An incisional biopsy was performed and the pathological study proved that it was Ewing's sarcoma. She was put on neoadjuvant chemotherapy using 6 courses of vincristine, doxorubicin, ifosfamide, etoposide which resulted in a partial regression of the tumor size by 50%. Then the patient was put on combined chemotherapy and radiotherapy. A follow-up CT scan after 6 courses of vincristine, actinomycin, cyclophosphamide, and 17 sessions of radiotherapy showed lesion stability. Maxillary Ewing's sarcoma is a rare and aggressive tumor. Therefore, early diagnosis, combination therapy, and long-term follow-up are suggested in such cases to improve the survival rate.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Introduction

Ewing's sarcoma, a member of the Ewing family tumors (EFT), stands as the second most prevalent malignancy affecting the bone and soft tissues among children, adolescents, and young adults [1,2]. This category encompasses various subsets of tumors, including Ewing's sarcoma of bone (ESB), extraosseous Ewing's sarcoma (EES), peripheral primitive neuroectodermal tumors of bone (pPNET), and small cell malignancies of the thoraco-pulmonary region (Askin's tumor). These tumors share a neuroectodermal origin, and their histopathologic subclassification relies on the level of neuronal differentiation they exhibit [3]. Overall, Ewing's sarcoma accounts for 4%-6% of all primary bone tumors [3].

Although rare, primary facial involvement occurs in only 1%-4% of Ewing's sarcoma cases, typically affecting the mandible and calvaria. In contrast, paranasal sinus and skull base involvement represent exceptionally uncommon locations for these tumors [4]. In this report, we present a noteworthy case of Ewing's sarcoma originating in the maxillary sinus of an 11-year-old girl.

Case report

An 11-year-old girl presented with an unusual swelling on her left cheek that she first noticed a month ago. The swelling had progressively grown in size, causing her pain, left nasal obstruction, rhinorrhea, and unexplained weight loss. Moreover, there was no relevant medical or family history, nor any reported incidents of trauma.

During a physical examination, a hard, well-defined left para-nasal enlargement, measuring roughly 4 × 3 cm and extending into the infraorbital region, were discovered. No notable abnormalities were found during the other examinations, which included ophthalmologic, auricular, oral, and cervical checks.

A full biological workup was performed. The results revealed no significant abnormalities. A craniofacial CT scan was ordered and revealed a tissue lesion with lytic (destructive) and condensation features. The lesion was centered in the left maxillary sinus and appeared poorly limited with irregular contours. After contrast injection, the lesion showed heterogeneous enhancement. Its dimensions were 43 × 39 × 41 mm (Fig. 1). The process observed had various effects on the surrounding structures: it raised and thinned the floor of the left orbit, lysed the floor of the maxillary sinus and the alveolar bone, exposing the roots of opposing teeth. It invaded the soft palate and lysed the anterior, posterior, and lateral walls of the maxillary sinus. In addition, slight infiltration of the jugal soft tissues was noted, as well as invasion of the homolateral papyraceous lamina into the left nasal fossa and septum (Fig. 2). Importantly, the CT scan did not reveal lymph node enlargement or cervical adenopathy.

Seeking a definitive diagnosis, an incisional biopsy was performed using the functional endoscopic sinus surgery (FESS) technique. The subsequent anatomopathological study of the surgical specimen confirmed a diagnosis of Ewing's sarcoma.

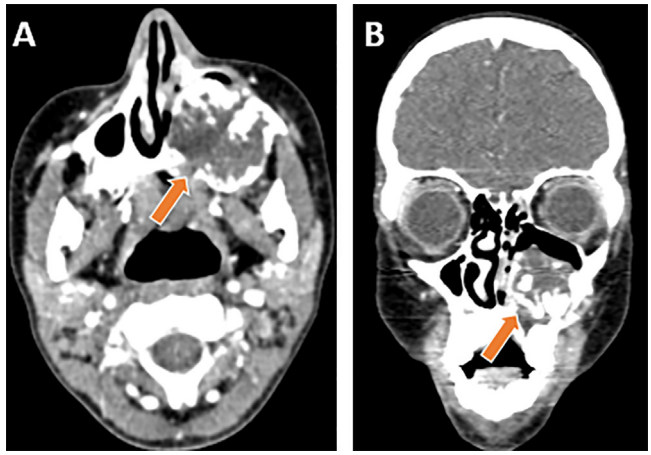

Fig. 1 – Craniofacial CT in axial (A) and coronal (B) sections in the parenchymal window showing a lytic and osteocondensing tissue lesion process centered on the left maxillary sinus, heterogeneously enhanced after injection of contrast medium, extended to the homolateral nasal cavity and septum, and discretely infiltrated the adjacent soft tissues.

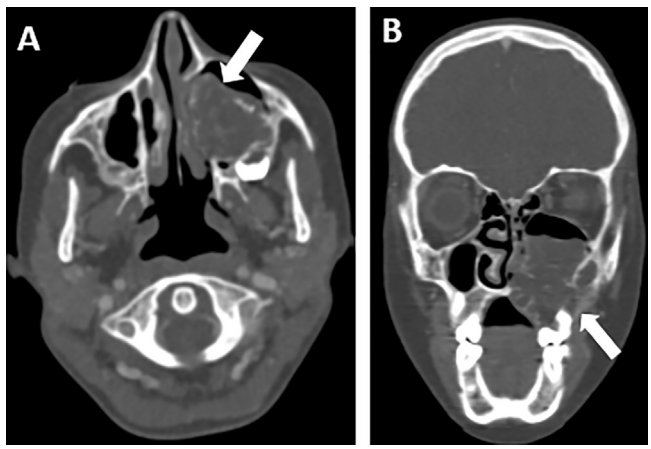

Fig. 2 – Craniofacial CT scan in axial and coronal section in the bone window showing uplift and thinning of the left orbital floor, lysis of the floor of the maxillary sinus and alveolar bone with exposure of the opposing tooth roots, invasion of the soft palate, lysis of the anterior, posterior, and lateral walls of the maxillary sinus, and lysis of the homolateral papillary lamina invading the left nasal fossa and septum.

The histological examination unveiled a tumor characterized by a proliferation of round cells, arranged in either a diffuse or alveolar architecture. These cells varied in size from small to medium and occasionally formed rosettes or pseudo-rosettes. Notably, the cells exhibited sparse basophilic cytoplasm and hyperchromatic anisokaryotic nuclei, along with increased mitotic activity. Furthermore, they strongly expressed the anti-CD99 antibody, confirming the diagnosis of Ewing's sarcoma (Fig. 3). To assess the potential extent of the disease, a

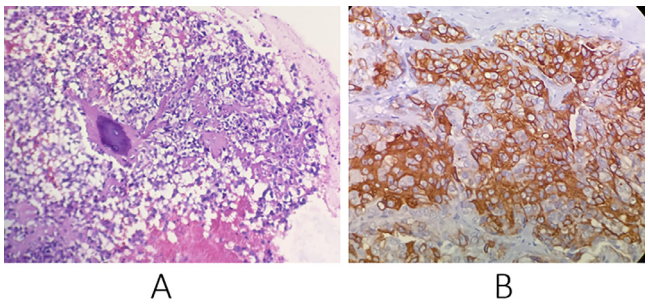

Fig. 3 – (A): Partially necrotic small round blue cell tumor (HE x 100), (B): Intense and diffuse positive staining of tumor cells by anti CD99 antibody (IHC x 200).

thoraco-abdomino-pelvic CT scan was performed, which revealed no signs of distant metastasis.

Following diagnosis, the patient was rapidly referred to the pediatric oncology department for neoadjuvant chemotherapy. The treatment plan was in line with the EURO-EWING 99 protocol for non-metastatic Ewing's sarcoma. Over a 5-month period, the girl received 6 courses of vincristine, doxorubicin, ifosfamide, etoposide (VIDE). A craniofacial CT scan performed during the follow-up period showed a 50% regression in the size of the left maxillary lesion compared with the initial scan (Fig. 4). Consequently, the patient was prescribed a combined therapeutic approach comprising chemotherapy and radiotherapy. She underwent 6 additional courses of vincristine, actinomycin, cyclophosphamide (VAC), excluding actinomycin during the 2nd and 3rd doses due to concomitant radiotherapy. Simultaneously, she underwent 17 sessions of radiotherapy spanning 6 weeks. A follow-up CT scan demonstrated stability in the lesion of the left maxillary process, indicating a positive response to the prescribed treatment regimen.

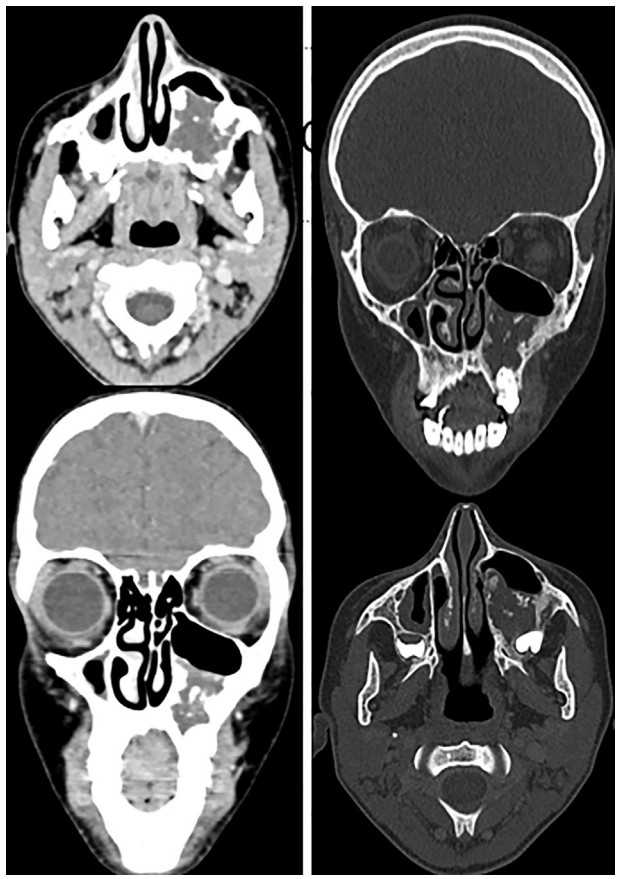

Fig. 4 – Axial and coronal sections of a craniofacial CT scan in the parenchymal and bone window showing an estimated 50% regression in size of the lesional process of the left maxillary sinus compared with the initial CT scan.

Discussion

The EFT family comprises several types, including Ewing's sarcoma of bone (ESB), extraosseous ES (EES), peripheral primitive neuroectodermal tumor of bone (pPNET), and malignant small cell tumor of the thoraco-pulmonary region (Askin's tumor). These neoplasms share similar histopathological, ultrastructural, and immunohistochemical features, suggesting a common neuroectodermal origin [5]. Additionally, cytogenetic studies have identified a consistent karyotypic change: t(11;22) (q24;q12). This finding confirms that "ES" and "PNET" represent a single entity, with Ewing's sarcoma being the most primitive and undifferentiated member of the spectrum, while PNET represents a more neurally differentiated counterpart [6].

According to a comprehensive study by Cotterill et al. [7], primary Ewing's sarcomas of the head and neck are considered rare, accounting for only 3.8% of reported cases. However, in other studies, the prevalence of bone and soft tissue Ewing's sarcomas in the head and neck region varies from 1% to 7% of all locations, with children accounting for up to 18% of cases. Among these head and neck cancers, primary sinonasal neoplasms are considered the most exceptional subgroup in terms of rarity [8,9].

The most frequently observed clinical presentation of the condition is a rapidly enlarging mass, often accompanied by pain [10]. In some cases, additional symptoms such as paresthesia, tooth loss, and ulceration of the mucosa above the mass have been reported. It is possible for a tumor in the maxillary sinus to remain undetected until it extends beyond the nasal cavity and into the oral cavity, resulting in symptoms such as nasal obstruction, rhinorrhea, epistaxis, and destruction of the palate [4]. This delayed detection often leads to a late diagnosis, with patients presenting with locally advanced or even metastatic tumors [11]. In our specific case, the patient initially presented with a progressively increasing painful swelling in the cheek area.

Computed tomography (CT) is the preferred radiological technique for investigating bone tissue sarcomas. Common CT findings include cortical bone expansion, erosion, and subsequent destruction, often accompanied by a spiculated or laminated periosteal reaction with an "onion skin appearance" in long bones. However, such onion skin or sunburst-like periosteal reactions are extremely rare in jaw lesions [6,12]. Magnetic resonance imaging (MRI) is also an essential tool in

the diagnostic process as it aids in the evaluation of lesion extension into adjacent soft tissues, provides valuable information for diagnosis, and allows monitoring of tumor response to chemotherapy [13]. Additionally, diagnostic tools such as MRI, CT scan, technetium-99m scan, and bone marrow samples can be employed to identify distant metastases [11]. In our specific case, no metastasis was detected.

Distinguishing Ewing's sarcoma from other tumors originating in the sinonasal tract on the basis of clinical and radiological assessments alone can prove difficult. The National Comprehensive Cancer Network (NCCN) guidelines for bone cancer stipulate that a conclusive diagnosis is based on examination of tissue samples by histological, immunohistochemical, and cytogenetic analysis obtained from a biopsy. Biopsies can be taken by needle puncture or during surgery [11]. In our particular case, an incisional biopsy was performed using the functional endoscopic sinus surgery (FESS) technique.

The medical literature describes several potential differential diagnoses for small round blue cell tumors in the sinonasal tract. These include rhabdomyosarcoma, lymphoma, poorly differentiated carcinomas, melanoma, olfactory neuroblastoma, and EFT [14].

Immunohistochemical analysis often reveals strong, diffuse membrane expression of CD99 in neoplastic cells, with a significant proportion of cases showing nuclear expression of FLI-1. However, myogenic and hematolymphoid markers are generally absent [15]. In our particular case, immunohistochemical study revealed small blue cells immunoreactive for vimentin, CD99, and FLI-1, but negative for CK, S-100, and desmin. In EFT, the most common cytogenetic marker for Ewing's sarcoma is the translocation t(11,22)(q24;q12), which accounts for over 85% of cases. Other translocations involving the Ewing sarcoma locus on chromosome 22, such as t(21,22)(q22;q12) and t(7,22)(p22;q12), have also been observed [5,15].

Therapeutic approaches for Ewing's sarcoma include surgical resection, chemotherapy, and radiotherapy. An optimal treatment plan typically includes a combination of surgical excision and modern chemotherapy or radiotherapy [14,16]. Adjuvant chemotherapy has significantly improved the overall survival of EFT patients since its initial use in the early 1970s. Large-scale studies have reported 5-year survival rates of up to 70% and 10-year survival rates of around 50% [17,18]. Radical surgery is not considered the primary treatment modality for Ewing's sarcoma. Current standard treatment begins with chemotherapy unless contraindicated. Patients generally undergo 4-6 cycles of neoadjuvant chemotherapy, even when the tumor appears resectable. This approach eliminates micro-metastatic disease and facilitates more effective local disease control with large negative margins [11]. Changes in tumor size and the appearance of new lesions are used to assess response to chemotherapy, categorizing it as complete response, partial response, stable response, or progressive disease [16]. The role of radiotherapy in local control in patients who have achieved complete remission after surgery and chemotherapy has been the subject of debate in the literature. Some authors oppose its use after surgery with large clear margins [11]. However, if histological examination of a resected tumor reveals more than 10% viable tumor cells, postoperative chemoradiotherapy can be administered to control local recurrence [19].

Prognostic factors such as patient age, tumor location, staging, and size play a crucial role in predicting outcomes. Patients under 15 years of age without metastases have a better prognosis, with a 5-year survival rate of 55% compared to 22% in cases with metastases [16].

Conclusion

Primary Ewing's sarcoma in the head and neck region is a rare occurrence, and when it arises in the sinonasal location, it becomes even more infrequent. The diagnosis of this condition presents a challenge that demands comprehensive correlation among clinical, radiological, histological, immunohistochemical, and cytogenetic evaluations. It is worth noting that Ewing's sarcoma located in the head and neck, including the maxilla and sino-nasal tract, generally exhibits a more favorable prognosis compared to other disease locations. To prevent local recurrence and achieve improved survival rates, a multidisciplinary approach is essential, incorporating an effective treatment plan involving chemotherapy and surgery or chemoradiotherapy.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Author contributions

All authors contributed equally to this work.

Patient consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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