CASE REPORT

Ewing's Sarcoma of Mandible: A Case Report with Review

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Abstract

Aim: To make dentists and pedodontists aware of a possible outcome of a rapidly growing swelling.

Background: Ewing's sarcoma is a rare aggressive variant of small round cell tumors and is an uncommon malignancy that occurs usually in childhood. It constitutes 10–15% of all primary malignant tumors and represents the second most common malignant bone tumor occurring in children and young adults.

Case description: We report a case of Ewing's sarcoma in an 11-year-old male child who reported with a rapidly progressing swelling in the left mandibular posterior region. Panoramic view and computed tomography showed characteristic moth eaten and sun-ray appearance. Fine-needle aspiration cytology revealed a small round cell tumor. Since the exact diagnosis is hard to achieve before biopsy, the condition poses a difficult diagnostic dilemma for the clinician. Histopathology was performed for the accurate diagnosis.

Conclusion: Dentists and pedodontists should develop a high index of suspicion in diagnosing cases with rapidly enlarging intraoral or extraoral swellings as early and correct diagnosis may improve clinical management and survival for patients with this disease.

Clinical significance: Our case report is an attempt to help the dental community in developing familiarity with the clinical presentation of Ewing's sarcoma.

Keywords: Computed tomography, Ewing's sarcoma, Mandible, Small round cell tumor.

International Journal of Clinical Pediatric Dentistry (2019): 10.5005/jp-journals-10005-1665

Background

Ewing's sarcoma is included in a diverse group of non-epithelial neoplasms with predominantly neural features (neuroectodermal). Ewing's sarcoma is sixth most common highly lethal malignant small round cell tumor of bone and soft tissues and is found to be poorly differentiated and aggressive in behavior biologically.[1] Primary malignant tumors of the jaws are rare, and especially, the diagnosis and treatment of Ewing's sarcoma can be challenging.[2] It constitutes 10–15% of all primary malignant tumors and represents the second most common malignant bone tumor occurring in children and young adults.[3]

The small round cell tumors of childhood include neuroblastoma, the Ewing family of tumors (ESFT), rhabdomyosarcoma, lymphoma, and desmoplastic small round cell tumor.[4] This group of small round cell tumor is malignant, highly aggressive, and seen under the microscope as a monotonous proliferation of small cells with scanty cytoplasm.[5]

Ewing's sarcoma (ES) was first described by James Ewing in 1920 as a diffuse endothelioma of bone.[6] It arises from undifferentiated osseous mesenchymal cells affecting mainly adolescents and young adults, usually occurring between the ages of 10 and 20.[7,8] It is rarely seen before the age of 5 and after the age of 30. Males are slightly more commonly affected than females with a ratio of 1.5:1.[1] It has also been described in siblings, although this is very rare.

It is still debatable whether it is of endothelial origin, from immature reticulum cells or primitive mesenchymal cells of bone marrow, or of neural origin.[9] It primarily affects the skeletal system and accounts for 4–10% of all types of bone cancers in long bones. Lower extremities, pelvis, upper extremities, axial skeleton, ribs, and head and neck region are the most common locations affected in descending order.[3] The femur is the most frequently affected site, with the tumor usually arising in the midshaft region.

The occurrence of ES in the head and neck region is unusual and accounts for less than 3% cases.[10] Ewing's sarcoma originating in the maxillofacial region usually involves the mandible and less frequently the maxilla. Major prognostic factors include site, tumor volume, and the presence of metastases.[11] As the disease advances, it causes cortical destruction and spreads and invades the periosteum and soft tissues.[12]

The radiological features of Ewing's sarcoma in the mandible are characterized by a periosteal reaction in the form of sun-ray spicules or the "onion- skin" pattern of the periosteal reaction of the jaws.[7]

The following case report is presented to highlight the clinical appearance and radiological features including computed tomography and histopathological findings in Ewing's sarcoma of the mandible affecting an 11-year-old boy.

Case Description

An 11-year-old male child presented to the Department of Oral Medicine and Radiology with a rapidly enlarging swelling on left lower jaw since one month. There was no history of trauma or

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How to cite this article: Ahuja US, Puri N, Gupta D, *et al.* Ewing's Sarcoma of Mandible: A Case Report with Review. Int J Clin Pediatr Dent 2019;12(5):470–474.

Source of support: Nil

Conflict of interest: None

pain associated with the swelling. Also, no secondary or sensory changes could be elucidated. His past dental/medical history was unremarkable.

The extraoral examination revealed facial asymmetry due to a diffuse swelling on the left side of the face, which extended superoinferiorly from infraorbital margin to the lower border of the mandible measuring approximately 6 × 5 cm in its greatest dimensions. The anteroposterior extent of the swelling was from the corner of the mouth till the pinna of the ear (Fig. 1). The skin over the swelling appeared to be normal with uniformly blending borders. Swelling was firm-to-hard in consistency and was non-tender on palpation. No discontinuity was noted in the lower border of the mandible. There was neither local rise in temperature over the swelling nor fixity to the underlying structures. Lymph node examination revealed solitary, enlarged, unilateral, fixed, firm to hard left submandibular lymph node.

The intraoral examination disclosed a large mass extending from the distal of left second premolar to the retro molar area expanding both buccally and lingually. The swelling was approximately 5 × 4.5 cm in size, well defined, and irregular in shape with a rough lobulated surface. The mucosa over the swelling appeared slightly ulcerated (Fig. 2).

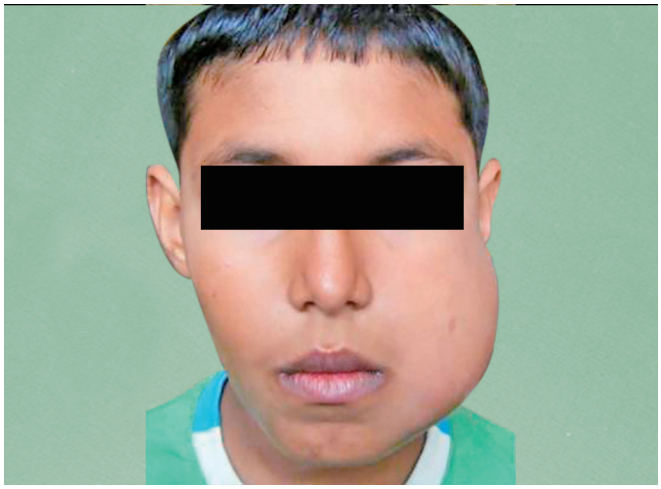


Fig. 1: Extraoral clinical photograph showing oval swelling on left side of face

On palpation, the inspectory findings were confirmed. The swelling was nontender and variable in consistency ranging from soft to firm, nonfluctuant, nonreducible, compressible, and non-pulsatile. The teeth in the affected area were not sensitive to percussion and grade 1 mobility could be demonstrated in 37.

The radiographic examination of the mandible revealed ill-defined, osteolytic, mixed, radiolucent, and radiopaque lesion involving premolar–molar region of left side body of mandible, extending from distal of erupting 34 to angle of the mandible on panoramic radiograph. A normal trabecular pattern was disrupted in the affected area, simulating moth-eaten appearance. The lamina dura was found to be discontinuous in the involved teeth. A considerable root resorption was seen in 73, 74, 75. Severe crestal and inter-dental bone loss in relation to 36 and 37 was evident (Fig. 3).

As a part of regular investigations of maxillofacial swellings, the patient was subjected to ultrasonography to check the vascularity and nature of the lesion. The ultrasonographic findings revealed an isodense large soft tissue mass in the involved area measuring approximately 56 × 56 mm in size. Ultrasonography also showed erosion and periosteal reaction of mandible. The mass was associated with increased vasculitis with arterial flow on color Doppler ultrasonography (Fig. 4). Enlarged submandibular lymph nodes were also observed.

In order to precisely know the location, anatomical relation of the tumor, its effect on surrounding structures, and any evident metastases, computed tomography (CT) was advised. CT sections showed an ill-defined, expansile, osteolytic lesion in the body of the mandible on left side with a significant enhancing soft tissue matrix. Multiple irregular patchy radiolucent areas mimicking moth-eaten appearance were noted in the internal structure. Erosion, irregular thinning and discontinuity of both buccal and lingual cortex on CT images were evident. The characteristic sun ray pattern or the radiating spicules were noticed on lingual cortex. No considerable cortical expansion was observed (Fig. 5).

Based on the clinical and radiological appearance, a provisional diagnosis of malignancy of left body of the mandible was given. A complete hemogram was performed, which showed anemia, leukocytosis, and increased erythrocyte sedimentation rate. An increase in the serum levels of alkaline phosphatase and C-reactive proteins was also observed.

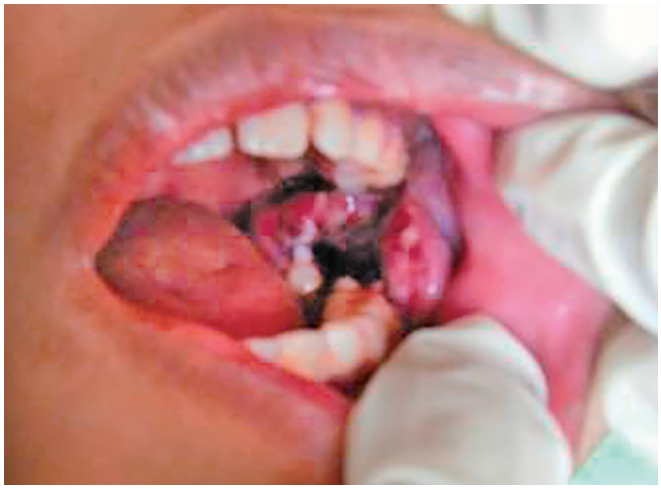


Fig. 2: Intraoral clinical photograph showing swelling and lesion on left side

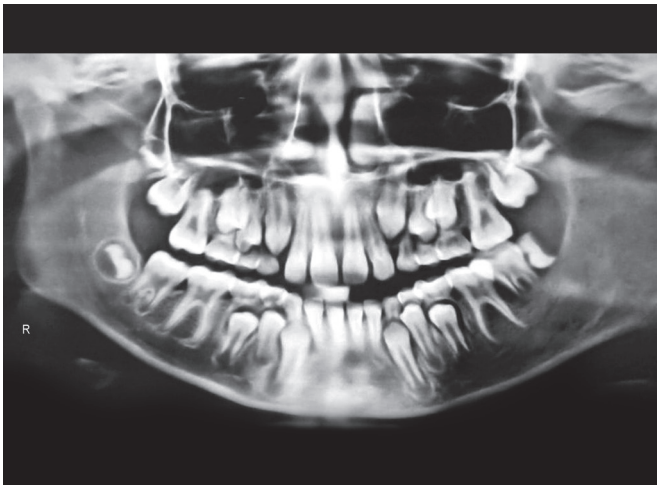
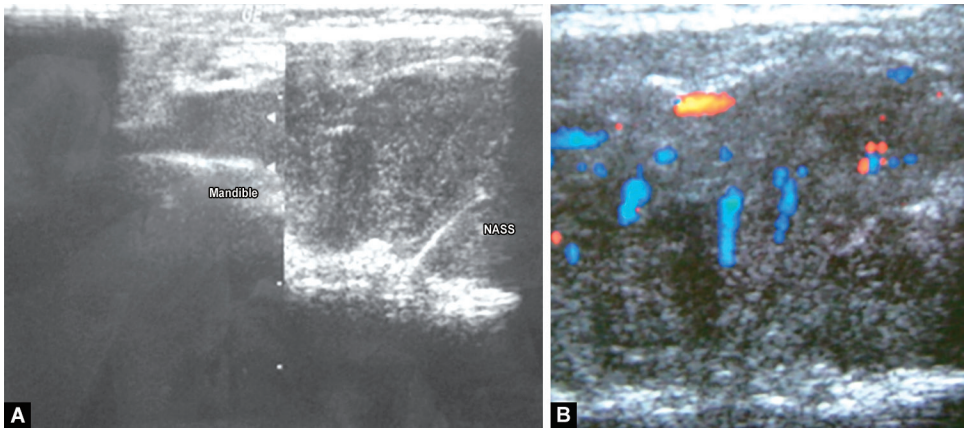
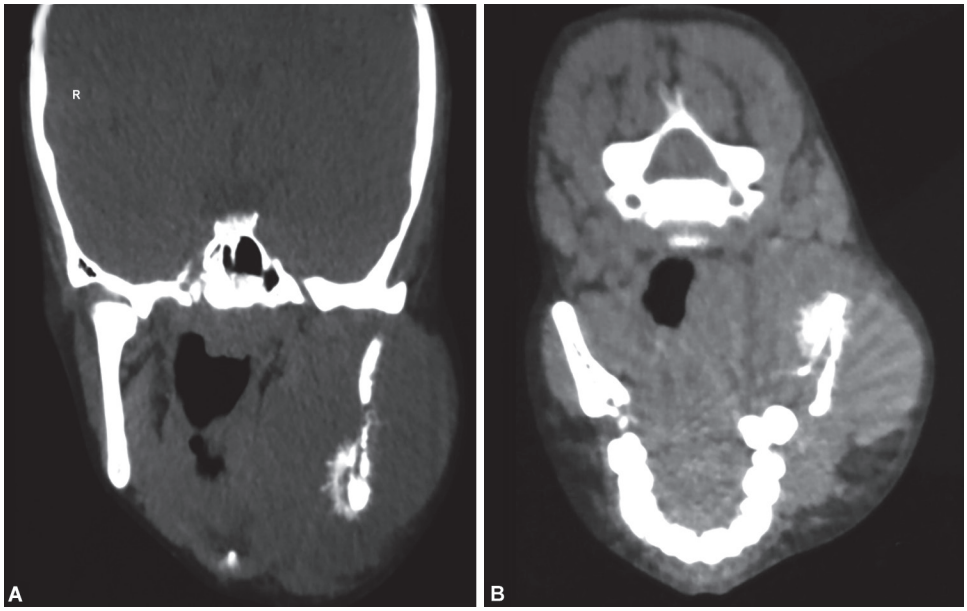


Fig. 3: Panoramic radiograph showing ill defined, osteolytic mixed lesion involving premolar–molar region of left body of mandible



Figs 4A and B: Ultrasonography revealing isodense large soft tissue mass in mandible



Figs 5A and B: CT coronal and axial section shows expansile, lytic lesion in left body of mandible with significant enhancing soft tissue matrix having sunray appearance

Fine needle aspiration cytology of the lesion showed a highly cellular smear with tumor cells arranged in groups of loosely cohesive cell as well as scattered singly. Individual cells were small, dark having round-to-ovoid nuclei, dark chromatin, and scanty cytoplasm. Few cells were large with moderate cytoplasm, round-to-ovoid nuclei, and granular chromatin. The background show formed elements of blood suggestive of small round cell tumor. We performed incisional biopsy of the pathology under local anesthesia to establish a definitive diagnosis.

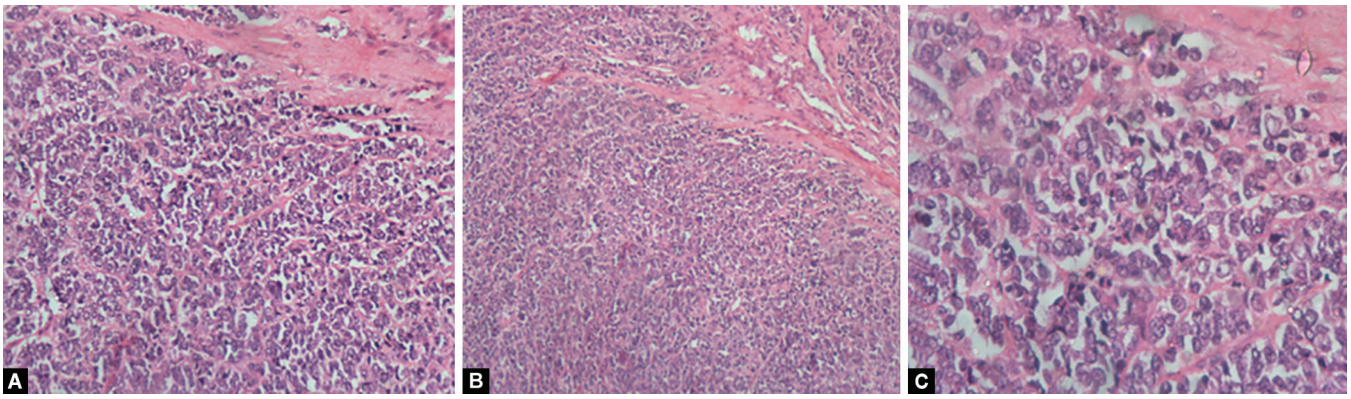
Confirmatory diagnosis of Ewing's sarcoma was made after histopathological evaluation of biopsy specimens. The features observed during microscopic examination were sheets of uniform small round cells arranged in diffuse pattern with indistinct outline, scanty cytoplasm, well-defined nuclear outline with round-to-oval nucleus, and inconspicuous nucleoli. Mitotic figures were not prominent (Fig. 6).

The standard treatment options for localized ES are surgical excision, radiotherapy, chemotherapy, or combination of all. The patient was referred to regional cancer centre where surgery for the tumor resection was performed under general anesthesia. The surgical specimen consisted of a portion of the mandible and the teeth involved in the tumor. In this case, patient underwent adjuvant chemotherapy treatment with vincristine, and cyclophosphamide at the Regional Cancer Centre.

Discussion

ES is a malignant neoplasm that primarily affects the long bones of the extremities with nearly 50% of reported cases involving the femur and pelvis. It exhibits a marked predilection for whites and is rarely seen among blacks. Ewing's sarcoma of the jaws is rare and accounts for less that 3% cases.[10]

Ewing suggested the hemangiogenic origin, due to the presence of desmosomal-type structures and basement membrane-like material or alkaline phosphatase activity, although there is no clear evidence of a vascular origin.[12] The origin of this tumor was unclear until recently, when electron microscopic and immunohistochemical analyses suggested that it is of neurogenic origin. ES tumors often express a balanced translocation involving the EWS gene on chromosome 22 and a member of the ETS family of transcription factors.[13]



Figs 6A to C: Histopathology slides showing round cells arranged in sheets, round nucleus with vascular chromatin and prominent nuclei with abundant clear cytoplasm

The disease is more prevalent in males and usually affects in the second and third decades of life. The bones of the pelvic girdle and the lower extremities are the most common sites of disease. The other sites include vertebrae, ribs, skull, small bones of the hands and feet, and jaws. The disease is believed to start in the Haversian canals, subperiostially, or in the medulla.[14]

Ewing's sarcoma most often presents as destructive, expansile, and mottled radiolucency, which mostly produces a laminated or onion skin periosteal reaction. Some authors believe that radiographic appearance of "onion skinning" is a characteristic of Ewing's sarcoma of the bone.[14] The radiographic differential analysis of Ewing's sarcoma of the mandible consists of osteogenic sarcoma, osteomyelitis, neuroblastoma, lymphosarcoma, histiocytosis X, rhabdomyosarcoma, and metastatic carcinoma.[15]

Although periosteal bone reaction is also evident in other pathologies, the presence of a large soft tissue mass intraorally in the present case helped differentiation of Ewing's sarcoma from osteomyelitis and eosinophilic granuloma. The age of the patient ruled out the possibility of neuroblastoma, which is usually encountered in less than 5 years of age.[16] Histopathologically, Ewing's sarcoma is composed of small, poorly differentiated cells with medium size, round or oval nuclei exhibiting a fine chromatin pattern, small nucleoli, and scanty cytoplasm. The intracytoplasmic glycogen can be demonstrated by PAS stain in 75% of the cases of ES, but that is not considered to be conclusive as presence of glycogen can be observed in other small round cell tumors also.[10] Oberlin O considered the embryonic reticulum cell of bone marrow as the basic tumoral element, because of the presence of dark cells as maturating reticulum cells.[17] Some authors considered the dark cells to represent degenerative changes of the principal cell.

Accurate diagnosis of ES is crucial for the most appropriate clinical management of patients. Adequate clinical information and the recognition of the morphological, radiological, immune-cytochemical, and sometimes ultra structural features of ES and ESFT are all required for its differential diagnosis from other small round cell tumors of childhood, such as neuroblastoma, rhabdomyosarcoma, Hodgkin's lymphoma, other primitive neuroectodermal tumors, desmoplastic small round cell tumor, poorly differentiated synovial sarcoma, and small cell osteosarcoma.[3]

Pathologies, most commonly mistaken histologically for Ewing's sarcoma, include eosinophilic granuloma, malignant lymphoma, and metastatic neuroblastoma. Eosinophilic granuloma shows the presence of "histiocytic" features, in the form of eosinophilic cytoplasm with oval or indented nucleus. Malignant lymphomas contains lymphoid cells, intermixed with round cell components of varying size with usually negative PAS stain, and positive reticulin stain.[18]

Currently, ES is treated in a multidisciplinary manner including chemotherapy, surgery, and radiotherapy. Even in a small area of Ewing's sarcoma, multiple therapy modalities are required due to the high risk of metastasis.[19] The treatment strategy for ES is characterized by multidisciplinary collaboration between pediatric oncologists, medical oncologists, radiation oncologists, and orthopedic surgeons. Approximately only 10% of the patients with Ewing's sarcoma survived before the introduction of chemotherapy as a management modality, which has now been drastically improved with 75% survival rates in patients with localized tumors.[20] Pre- and postoperative intensive systemic chemotherapy with multiple anticancer drugs is the standard treatment modality for ES. Preoperative chemotherapy eliminates any micro-metastases, decreases tumor load, and helps in selecting postoperative anticancerous drugs.

If radiographic assessment indicates difficulty in surgical excision, preoperative radiotherapy can be administered. Some authors have the opinion that radiotherapy is not required in patients responding well to preoperative chemotherapy and have been adequately excised surgically. However, the cases poorly responding to anticancerous drugs and inadequately excised should be considered for radiotherapy.

The treatment outcomes of ES have improved recently but late complications and secondary malignancies remain the major risks. This necessitates the long-term follow-up in the patients with ES in order to detect secondary malignancies, any recurrences or relapses, muscular or skeletal problems, and any other complications.

Conclusion and Clinical Significance

Ewing's sarcoma is characterized by specific clinical, imaging, and histological features. For a proper understanding and an early diagnosis of such cases, a thorough analysis and a long-term follow-up is required. It is a rare malignancy that may affect the facial bones of young individuals. The present case highlights the clinical appearance and findings of various imaging modalities for the diagnosis of this rare tumor. Any fast growing swelling in young patients with ulcerated intraoral appearance should be evaluated considering Ewing's sarcoma as a differential diagnosis. All the general dentists and in particular pedodontists should be well aware of its clinical appearance and radiographic findings as the

early diagnosis and intervention of Ewing's sarcoma is critical due to its poor prognosis and tendency to metastasize.

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