Ewing’s Sarcoma of the Mandible: A Rare Case Report and Review of Literature

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CASE REPORT

ABSTRACT

Ewing’s sarcoma is a small, round and blue cell malignancy that most commonly arises in the skeleton of adolescents and young adults. Although it may appear in any bone, it is more common in the axial skeleton, rarely involving the jaws (1-2% incidence mostly in the mandible). In this article, we are reporting a rare case of Ewing’s sarcoma of mandible in an 18-year-old female patient with the typical radiographic appearance of spiculated bone formation.

Keywords: Ewing’s sarcoma, Small round cell tumor, ES/PNET.

INTRODUCTION

Ewing’s sarcoma was first described by James Ewing in 1920 as a diffuse endothelioma of bone. Ewing’s sarcoma constitutes 6 to 8% of all primary malignant tumors and represents the third most common osseous neoplasm after osteosarcoma and chondrosarcoma. Ewing’s sarcoma is genetically and histologically distinctive small round cell sarcoma of bone, and it constitutes 1% of all malignant tumors in children. It is a notoriously aggressive and destructive malignancy of bone arising from marrow mesenchymal stem cells. Since then, it has been documented as a distinct malignancy of primitive mesenchymal stem cells that have undergone a unique reciprocal translocation of chromosomes 11 and 22.

CASE REPORT

An 18-year-old female patient reported to the Department of Oral Medicine and Radiology (Govt Dental College and Hospital, Afzalgunj, Hyderabad) with swelling in right lower side of the jaw since one year. Initially, swelling was small and progressive rapid growth was observed in last 6 months, later paresthesia of right lower lip was noticed. Extraoral examination revealed diffuse swelling present on the right side of angle and body of mandible extending into submandibular region crossing midline. Overlying skin is stretched and shiny with venous prominence (Fig. 1). It is soft to hard in consistency. Intraoral examination revealed buccal and lingual cortical plate expansion and mobility in relation to 45, 46, 47 and 48. There was lingually and buccally displaced 47 and 48 respectively (Fig. 2).

Fig. 1: Extraoral photograph showing large submandibular swelling
Orthopantomograph (OPG) and lateral skull radiographs showed mixed radiolucent-radiopaque lesion with ill-defined ragged borders extending from 45 to posterior border of ramus of mandible, with spiculated bone formation at the right angle of mandible. OPG also showed root resorption of 48 (Figs 3 and 4).

Computed tomography (CT) revealed osteolytic and osteoblastic lesions involving ramus and angle of right mandible with large soft tissue component and new bone formation. Periosteal reaction observed in ramus of right mandible, suggestive of osteosarcoma (Fig. 5). Skeletal scintigraphy given an impression of bony swelling of right mandible with osteoblastic components and possible necrosis. No distant skeletal metastasis seen.

Histopathological examination showed fragments of a cellular lesion along with fibrous tissue and bone. The lesion is comprised of monomorphous round cells with round to oval nuclei having scanty cytoplasm (Fig. 6). The nuclei showed dispersed chromatin, inconspicuous nucleoli, and mitotic activity is seen. The lesion also shows prominent, collapsed thin-walled vessels.

Immunohistochemistry showed strong membrane positivity noted in the tumor cells for CD99 and negative for LCA. Features are consistent with ES/PNET (Ewing’s peripheral neuroectodermal tumor) mandible.

**DISCUSSION**

Ewing’s sarcoma belongs to the Ewing sarcoma family of tumors (ESFT), which comprises a group of small round cell neoplasms of neuroectodermal origin and includes the primitive neuroectodermal tumors. ESFT may arise in osseous or nonosseous sites and in multiple locations, including the soft tissues anywhere in the body, such as the paravertebral and thoracic areas. There is considerable clinical and histologic overlap between this tumor and primitive neuroectodermal tumor. Most investigators now believe that ES and PNET are different morphological expression of one tumor type.

Ewing’s Sarcoma can affect any bone but the most common sites are the lower extremity (45%), followed by the pelvis (20%), upper extremity (13%), axial skeleton and ribs (13%) and face (2%). Facial skeletal quite rare with mandible being the most commonly affected bone. Approximately 90% of the reported cases occurring in the mandible have been primary lesions and 10% have been metastases.

It is mostly seen in patients younger than 20 years (80%). The peak age of occurrence is in the teenage years (50%). It practically never occurs in black individuals. Young men are affected slightly more often than young women (1.4:1).

ES clinically usually presents with the well-known inflammatory complex of fever, pain, swelling, paresthesia and leucocytosis. History of fever is not a constant feature. Pain varies from moderate to very severe, is often intermittent in character and is more marked at night. Pain in other parts of the skeleton is the earliest indication of metastasis. Enlargement of the nearest draining lymph nodes is often present.

The most frequent radiographic findings described were permeative bone destruction and the presence of an adjacent soft tissue mass. ES of the jaws presents similar radiographic features to involvement of the peripheral skeleton. These include: (1) A permeative destructive pattern characteristic of the small round cell tumor, (2) periosteal reaction was seen in over half of the cases. The laminated type of periosteal reaction is difficult to demonstrate in the jaws because of the complex anatomy, (3) adjacent soft tissue involvement is a very common
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Finding in ES. Dental elements were involved in 75% of the cases in the form of displacement of the tooth follicle or erupted permanent teeth.⁹

Some reports indicate that the radiological features of ES in the mandible are characterized by a periosteal reaction in the form of sunray spicules, whereas others have described an onion skin pattern of periosteal reaction in ES in the jaws.⁷

The radiologic differential interpretation of ES of the mandible consists of osteogenic sarcoma, neuroblastoma, lymphosarcoma, histiocytosis X, rhabdomyosarcoma, osteomyelitis and metastatic carcinoma. The presence of a large soft tissue mass aided differentiation of Ewing’s tumor from osteomyelitis and eosinophilic granuloma. The age of the patient ruled out the possibility of neuroblastoma, which is common in less than 5 years age group. However, radiology is not totally reliable guide to diagnosis and histopathological examination is necessary to confirm the nature of the tumor.¹⁰

The differential diagnosis of ES is one of exclusions because it has no specific markers. All small, round, blue cell tumors of childhood, such as primary bone sarcomas, rhabdomyosarcomas, lymphomas, neuroblastomas and primitive neuroectodermal tumors should be considered.¹¹

The diagnosis is established by biopsy, in which the tumor is seen as layers of small round cells, similar to lymphocytes but larger. Mitotic cells are rare, intercellular stroma is scarce and a large portion of the tumor may be necrotic. Tumor cells placed around a clear central area forming rosettes may be seen, resembling Homer-Wright rosettes, typical of neuroblastomas. Intracytoplasmic glycogen is a definitive aspect, but not pathognomic because it is also present in other tumor cells, such as osteosarcomas, rhabdomyosarcomas and neuroblastomas.¹²

Recent immunoperoxidase and cytogenic studies indicate that PNET and ES are the same entity showing varying degrees of neuroectodermal differentiation and they are categorized into a group known as the Ewing family of tumors. CD 99/MIC2 is a cell surface glycoprotein found in virtually all ES and PNET. But it is also detected in other small round cell tumors, such as T-lymphoblastic lymphoma, poorly differentiated synovial sarcoma, small cell osteosarcoma, rhabdomyosarcoma, desmoplastic round cell tumor, small cell carcinoma and Merkel cell carcinoma and it should be used as part of a panel of immunostains, given its lack of complete specificity.¹³

More than 90% of cases show a characteristic translocation t (11; 22) (q24; q12) resulting in the fusion of the EWS and FLI-1 genes. This gene rearrangement causes a fusion product which functions as an oncogenic aberrant transcription factor with structural variability and potentially prognostic impact.¹⁴

The prognosis of ES is poor because of multiple metastases most commonly to the bone, lung, lymph node and liver, which may occur within a few months after the onset of the tumor.¹⁵ Poor prognostic factors are patients below 10 years of age, pelvic lesions, presence of systemic symptoms, large tumor volume (> 200 ml), high mitotic rate, filigree pattern in histopathological sections and poor response to chemotherapy. Ewing’s sarcoma of the mandible has got better prognosis than long bones since facial sites are diagnosed earlier.²

Between 20 and 25% of the patients are diagnosed with metastatic disease (10% lung, 10% bone/bone marrow, 5% combination or others). A chest CT scan is required to rule out lung or pleural metastases. The assessment for bone and bone marrow metastasis is to include 99m Tc bone scintigraphy, to detect osseous metastasis, and light microscopical examination of bone marrow aspirates and biopsies taken at sites distant from the tumor. Positron-emission tomography (PET) scanning for bone metastases and PCR techniques to investigate for bone marrow metastases are sensitive methods currently under evaluation.¹⁶

With surgery or radiotherapy alone, 5-year survival is <10%. With treatment in current multimodality trials including chemotherapy, survival is 60 to 70% in localized and 20 to 40% in metastatic disease. Bone metastasis confers a poorer outcome than lung/pleura metastases (less than 20% compared with 20 to 40% 5-year survival). All current trials employ 3 to 6 cycles of initial chemotherapy after biopsy, followed by local therapy and another 6 to 10 cycles of chemotherapy usually applied at 3 weeks intervals. Treatment duration is thus 8 to 12 months. Agents considered most active include doxorubicin, cyclophosphamide, ifosfamide, vincristine, dactinomycin and etoposide. Protocols that have proved to be most effective
include at least one alkylating agent (ifosfamide or cyclophosphamide) and doxorubicin. Radiotherapy is applied at doses of 40 to 45 Gy for macroscopic disease. Most relapses occur in the first 3 years of follow-up; late relapses have rarely been observed even after 15 years or longer. Follow-up intervals should be 2 to 3 months during the first 3 years, 6 months until 5 years and at least once yearly thereafter.16

**CONCLUSION**

In general, Ewing’s sarcoma is a rare malignancy that may affect the facial bones of young individuals. Even with an isolated area of ES, the risk of metastasis is so great that it may warrant multiple therapy modalities. In case of suspected cases, an evaluation of the lesion should be carried out using plain films, CT, MRI, bone scan and biopsy. After treatment, it is mandatory to provide suitable prosthesis, so that these young patients lead a quality life.

**REFERENCES**