Ewing's Sarcoma of the Rhinomaxillary Complex: A case Report with Review of Literature

Shalini R Gupta, Inderpreet Singh, R K Saran**, Priya Kumar*

Abstract
Ewing's Sarcoma of bone (ESB) is a rare primary malignant tumor of bone, belonging to Ewing's Sarcoma Family of Tumors (EFT) and are neuro-ectodermal in origin. These tumors are characterized histopathologically as small round blue cell tumors (SRBCT) containing cytoplasmic glycogen, cytogenetically by a (t:11;22) or (q:24;12) translocation and molecularly by the presence of EWS and FLI1 fusion transcripts. ESB is primarily a pediatric tumor, uncommon in the Asian population, affecting the axial skeleton and rarely the jaw bones. ESB poses a diagnostic challenge as it shares many features with other malignant tumors whose managements are substantially different. We present the clinical, radiographic histopathological and immuno histochemical features of ESB involving the left rhinomaxillary complex in a young Indian male. We also discuss the differential diagnosis and current treatment modalities in management of ESB.

Key Words
Ewing’s Sarcoma of Bone, Rhinomaxillary Complex, Small Round Blue Cell Tumors

Introduction
Ewing's Sarcoma (ES) was first described by James Ewing in 1921 as a” Diffuse Endothelioma of Bone”. It had been postulated to arise from primitive mesenchymal, reticulum, angioblastic and myelogenous cells of the bone marrow (1,2,3). It is now believed to belong to a larger group of Ewing Sarcoma Family of Tumors that share a common histogenesis from primitive neuroectodermal cells and includes ES of bone (ESB), extraosseous ES, Primitive neuroectodermal tumor (PNET) and Askins tumour (malignant small-cell tumor of the thoracopulmonary region.) (3).

ESB is the second most common primary malignancy of bone after Osteosarcoma but it is relatively rare accounting for 4%-10% of all malignant neoplasms of bone. It is primarily a disease of children and adolescents in the second decade of life. The incidence in males and females is equal up to the age of 13 years, thereafter occurrence in males predominates. It is nine times more common in white children as compared to black children. It is uncommon in Asian population and Orientals. The reason for this striking ethnic distribution could be due to interethnic differences in certain alleles of the EWS gene which is commonly disrupted in these tumors (3,4).

It commonly affects the pelvic bones, long bones of the extremities (femur, tibia, humerus and fibula) and bones of the chest wall. It is rare in the facial bones (1%-2%) and mandible is three times more commonly affected as compared to the maxilla (2,5,6). We present the clinical, radiographic histopathological and immuno histochemical features of a case of ESB involving the left rhinomaxillary complex in a 17 year old Indian male. We also discuss the differential diagnosis and current treatment modalities in management of ES.

Case Report
A 17 year old male reported with history of a slowly enlarging swelling in the left cheek since 4 months. He gave history of trauma to the upper jaw with a cricket ball prior to appearance of the swelling. He complained of left nasal obstruction and slight pain in relation to the swelling. On extraoral examination there was a firm, tender, well defined, 6x6 cm in diameter swelling in the left canine space causing obliteration of the left nasolabial fold and left nasal passage. The overlying skin was adherent to the underlying swelling and there was no paraesthesia / anesthesia in left infraorbital nerve distribution. There was no cervical lymphadenopathy.

From the Department of Oral Medicine & Radiology & *Oral Pathology, Maulana Azad Institute of Dental Sciences, New Delhi, & **Department of Pathology, G B Pant Hospital, New Delhi- India
Correspondence to : Dr. Shalini. R. Gupta, Associate Professor, Oral Medicine & Radiology, Maulana Azad Institute of Dental Sciences, New Delhi
Intraorally a buccopalatal expansion of alveolar bone in relation to maxillary left central incisor to maxillary left premolar was present. The teeth were non tender on percussion, non mobile and had no pulpal symptoms although maxillary left lateral incisor and canine were displaced. The overlying mucosa was non ulcerated, bluish in appearance on the buccal aspect and showed engorgement of underlying capillaries (Fig.1). The Orthopantomograph revealed an osteolytic lesion in the maxillary alveolus in relation to maxillary left central incisor to premolar, with ill defined non sclerotic borders, causing displacement of roots of maxillary left lateral incisor and canine but no evidence of root resorption. The blood investigations revealed Hb-9.8g/dl, TLC 12,450/mm3, ESR- 50mm/hr. Liver function tests, Kidney function test, S. Calcium, S. Phosphorus, Alkaline Phosphatase were within normal limits. Chest and skeletal radiographic survey revealed no abnormality. CECT of the jaws and neck showed infiltrative destructive lesion involving the left maxillary sinus, the overlying skin of the left cheek and the left nasal cavity destroying the inferior nasal concha (Fig.2). An intraoral incisional biopsy was performed under local anesthesia and sent for histopathological analysis. Haematoxylin and Eosin stained sections of the specimen showed a Small Round Blue Cell tumor. Immunohistochemical analysis was done with a panel of markers for SRBCT and the tumor showed strong membrane positivity for CD99 and was negative for S-100, Desmin and HMB-45 (Fig.3). Based on these findings a final diagnosis of Ewing’s Sarcoma of bone was made and the patient was referred to the Head and Neck Oncology Centre where he was treated with Radiotherapy followed by Chemotherapy.

**Discussion**

Locoregional pain is the most common presenting symptom of ESB which may be followed by a palpable mass and is often mistaken for "bone growth" or sport injuries in children. ESB can clinically mimic other malignant lesions like Osteosarcoma, Neuroblastoma and inflammatory conditions like Osteomyelitis. Plain radiography may show tumor related osteolysis, detachment of periostium from the bone (Codman Triangle), periosteal reaction on the form of spicules (sun burst appearance), lamellated type periosteal reaction (onion skin appearance) with adjacent soft tissue involvement. Displacement of tooth follicles or erupted teeth may also occur. Clinically detectable metastases are seen in 25% of ES patients, the most common being the lungs, the bones and the bone marrow. Loco regional lymph node involvement and metastases to the liver or central nervous system are rare. The most precise definition of the local extent of disease can be seen with computed tomography (CT) and the intramedullary portion and the relation of the lesion to adjacent blood vessels and nerves is provided by magnetic resonance imaging (MRI).

Diagnostic staging at presentation is a must for treatment planning and can include CT chest to exclude intrathoracic metastases and 99m - technetium whole body radionuclide bone scans to search for skeletal metastases. Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) has proven to be a highly sensitive screening method for the detection of bone metastases in ESB. Biopsy is the only means to a definitive diagnosis. Bone marrow biopsy can be done to detect microscopic bone marrow metastases which occur in < 10% of patients. ES appear histologically as a small round blue cell tumor (SRBCT). The tumor is composed of a monotonous population of small round cells that have scant faintly eosinophilic to amphophilic
cytoplasm, indistinct cytoplasmic borders, round nuclei with evenly distributed finely granular chromatin, inconspicuous nucleoli and low mitotic activity. It also shows cytoplasmic glycogen which appears as Periodic Acid -Schiff positive diastase digestible granules (2,5). Additionally in 95%-100% of cases, ES express elevated levels of a 32-kDa cell surface sialoglycoprotein p30-32, known as cluster of differentiation 99 (CD99), a Monoclonal Imperial Cancer (research fund)2 (mic2) gene product in a strong, diffuse membrane staining "chain mail pattern" and hence is used as a surrogate marker for their diagnosis (5,6). More than 90% of ES also share a chromosomal translocation (t:11;22)(q:24;12). The rearrangement results in the translocation of the 3' portion of the Friend Leukemia Virus Integration Site 1(fli1) gene from chromosome 11 to the 5' portion of the Ewing Sarcoma gene (ews) on chromosome 22. Molecular detection methods like reverse transcriptase-polymerase chain reaction (RT-PCR) and fluorescence in situ hybridization (FISH) are increasingly being used to detect the presence of EFT specific translocations and are even considered to be the 'Gold Standard' in the diagnosis of ES (8,9). ESB shares many clinical and radiographic features with other SRBCT like metastatic Neuroblastoma, Rhabdomyosarcoma, Retinoblastoma and Lymphoma but the age of presentation may help in differentiation. Other malignancies like Leukemia, Burkitts Lymphoma, Multiple Myeloma, Histiocytosis X, Neuroblastoma, Rhabdomyosarcoma, Retinoblastoma and Lymphoma but the age of presentation may help in differentiation. Other malignancies like Leukemia, Burkitts Lymphoma, Multiple Myeloma, Histiocytosis X, Neuroblastoma, Rhabdomyosarcoma, Retinoblastoma and Lymphoma but the age of presentation may help in differentiation.

Vincristine, Actinomycin D, Cyclophosphamide, Doxorubicin in various combinations in either a high dose intermittent or moderate dose continuous regimen. Modern multimodal therapeutic regimens including combination of chemotherapy, surgery and radiotherapy, can achieve cure rates of 50% and more and a 5-year survival rate of 70%-80% (3,5,11). There is a risk of development of therapy induced secondary malignancies in ES (5%-10%) at 15-20 years from diagnosis (5,12).

**Conclusion**

ESB poses a diagnostic challenge as it shares many of its clinical, radiographic, histopathological and immunohistochemical features with other malignant tumors. The distinction between these tumors is critical as their managements are substantially different which requires a multidisciplinary approach with cautious and continuous follow up.

**References**