EWING'S SARCOMA OF MANDIBLE: A CASE REPORT

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Recent years have seen a remarkable change in the perception of histogenesis and classification of round cell sarcomas (RCS). Ewing's sarcoma (ES) is one of these which typically arises in the long bones however is rare in the jaws. It shows the most unfavorable prognosis of all primary bone malignancies with the 5 year survival rate of 10%. It metastasizes very soon by haematogenous route to lungs, liver, brain and other bones. Problem lies with the histological diagnosis of the tumor as it is undifferentiated or anaplastic and simulates other round cell tumors affecting the children and adolescent. The present case is of a 7 year boy diagnosed as Ewing's sarcoma on the basis of classic clinical, radiological, cytopathological and histopathological findings.

Key words: Ewing's Sarcoma, Extra-osseous Ewing's Sarcoma, Primitive neuroectodermal tumor, Round cell tumor.

Ewing's sarcoma is a highly lethal small round cell tumor, first described by James Ewing in 1921. It typically arises in the bone and accounts for 6-10% of bone malignancies.[1] Though the extraosseous forms are rare, Angervall and Enzinger described it as ES of soft tissues. 90% of the lesions occurs between 5 to 30 years of age with the peak being 2nd decade. It is approximately twice as common in males as in females and is uncommon in blacks. Swelling of affected bone with intermittent pain is often the earlier sign and symptom. The bones commonly affected are the long bones of the extremities, although the skull, clavicle, ribs and shoulder may be involved. Jaw involvement is uncommon and ranges from 1-13%. Among the jaws mandible is more commonly affected than maxille. Parasthesia and loosening of teeth are common findings while, low grade fever, leukocytosis and increased ESR are other findings which may be present. Radiographically it is an irregular, lytic, ill defined radiolucent lesion. Appearance of jaw swelling is rapid along with intra oral mass which may soon become ulcerated. [1-7]

Case report

A 7 year old boy reported to the Department of Oral and Maxillofacial Pathology, MDCRC, Indore; with a chief complaint of swelling in the left side of lower jaw since 4 months with intermittent dull pain and intermittent low grade fever. He had no history of trauma and no relevant medical problem. Extra oral examination revealed a single diffused swelling of approximately 5 x 3 cm on the left side of the lower jaw with normal overlying skin. Anteroposteriorly it extended from the right side of chin to the left side till middle of body of mandible while supero- inferiorly the extension was from the angle of mouth till inferior border of the mandible involving it (Fig–1). Palpative findings revealed slightly tender swelling with hard consistency without rise of local temperature. Intra oral examination showed a single, well defined lobulated swelling of size 3x2 cm involving the alveolar ridge, extended from 32 to 75 region (Fig 2). The overlying mucosa was red dish in colour, 32 was displaced and 73, 74 were missing and had history of exfoliation 2 months back. OPG revealed a destructive ill defined radiolucency from 42 to 36 while 32 and 75 and tooth germs of 33 and 35 were seen floating in the radiolucency with thinning of inferior border of the mandible and superio-inferior expansion in 33 region. The follicle of 33 was destroyed and tooth was displaced to the inferior border (Fig.3). Occlusal radiograph showed buccal expansion with typical sunray appearance in molar region whereas in ante-

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rior part it showed smooth convex hazy radio-opacity, however lingual cortex was intact (Fig.4). The haematological and biochemical investigation showed 10gm/dl haemoglobin level, 9750cells/mm^3 leukocyte count, 100mg/dl RBS and 0.6mg/dl serum creatinine. Intraorally 1ml blood tinged watery fluid was obtained on FNAC. Cytopathology revealed highly cellular stroma spread on serous background. The tumor cells were either scattered or arranged in clusters admixed with numerous RBC. They were round to oval with dense round nuclei filling the whole cell without cytoplasmic rimming. Few cells also showed prominent nucleoli (Fig.5). However haematoxylin and eosin (H&E) stained section on incisional biopsy revealed clusters of round darkly staining cells with scanty cytoplasm separated by few connective tissue septae. Few isolated as well as clusters of clear cells were also noted. The cell outline was indistinct with well defined, hyperchromatic nuclei and showed increased mitotic activity. Focal areas of necrosis and large hemorrhagic areas too were noted with areas of extra cellular eosinophillic secretions (Fig-6).

A histological diagnosis of Ewing's sarcoma was made. Patient was immediately referred to cancer hospital for radical surgical excision along with chemotherapy and radiation therapy. Whole body CT scan and chest x-ray was also advised to rule out any distant metastasis. Inspite of earnest efforts, the patient could not be traced for recall.

Discussion:

Cancer accounts for the major cause of death in Indian children, next to infection and malnutrition. Leukemia is the most common malignancy, accounting for approximately 30% of all childhood cancers. Approximately 35,000 – 40,000children develop cancer each year in India. Because of the major advances in the diagnosis, multi-modal therapy, development of rationale use of combination chemotherapy and improved supportive care, the cure rate in childhood cancer has increased tremendously and over 60% of all childhood cancers are now curable. In some cancers, the cure rate is nearing 90%.[8] However bone tumors being diverse in their gross and morphologic features are critical to accurately diagnose and treat. As a group they can affect any bone at any age and can be simple to fatal in its biologic behavior.[3] ES is a very lethal primary bone malignancy that metastasises very soon to the lungs and causes diagnostic difficulties due to its undifferentiated anaplastic nature.[9] Although it is non osteogenic and cell of origin is controversial, the impression of origin from the immature reticulum cells is recently confirmed by electron microscopy.[10] Histologicaly it shares a convenient umbrella term 'small round cell tumors' which include several defined entities as well as some tumors that morphologically fit within the group but cannot be further characterized.[11] Similarly the term small round cell malignant tumors (SRCMT) describes a group of undifferentiated pediatric bone tumors.2 Recently a single biologic entity Ewing's sarcoma family of tumors (ESFT) has been proposed and accepted. The entity includes ES, extra osseous Ewing's sarcoma (EES) and Primitive Neuroectodermal Tumor (PNET).[12] The suggested cell of origin include endothelial, pericytic, bone marrow, osteoblastic, mesenchymal and more recently is settled for primitive neuroectodermal cells. All the three entities are linked together by a common origin and by a common cytogenetic translocation abnormality t (11;22) (q24;q12). This suggests a phenotypic spectrum in these conditions varying from undifferentiated ES to PNET positive for Homer – Wright rosettes and neural markers (neuron specific enolase, S-100).[13] Histologically ESFT differ from the other round cell tumor mostly from their indistinct cellular outline and the dendritic processes. ES and PNET have some differences like ES has more pale cytoplasm, have open nuclei with finer chromatin in contrast to PNET, all of which are features of neuronal differentiation. Also mitotic figures, necrosis and endothelial hyperplasia is more common in PNET. [14] Cytological findings of ES are well described in various literatures14 and were clearly noted in the present case. The findings differ greatly from other sarcomas like metastatic rhabdomyosarcoma as its cells are tadpole shaped, metastatic neuroblastoma shows

neurofillaments and rosettes, metastatic small cell carcinoma shows keratin, small cell osteosarcoma shows osteoid and fibrosarcoma shows cellular but spindles shaped cells. Lymphoma shows lymphoglandular bodies and PNET shows lot of rosettes and granular chromatin. Histopathologically ES is explained as extremely cellular neoplasm composed of solid sheets without any distinct pattern. In some cases variable sized nests are separated by fibrovascular septa creating a lobular pattern. The cells themselves are small and round with sacnty cytoplasm and relatively large round/ovoid nuclei with dispersed chromatin and hyperchromasia. The cell borders are indistinct. Large areas of necrosis and haemorrhage are also commonly present.[1,5] All these features are predominantly seen in present case. Now various cytogenetic studies help in specific diagnosis of ES but characteristic translocation is seen in gene EWS/FLI-1(t(11;22) (q24q12)).[15,1,4] Monoclonal antibodies to the fusion gene protein product are termed CD99.1 Few researchers state that CD99 is also positive in other tumors like synovial sarcoma, mesenchymal chondrosarcoma, alveolar rhabdomyosarcoma whereas ES in some cases may not show t(11;22) translocation. Although cytogenetic analysis can detect a wide variety of chromosomal translocation, it is time consuming and the success rate is quite variable. 50% of the time it cannot provide an answer.2 Ultimately it comes routine clinico-pathologic correlation which plays a major role in the diagnosis. In the present case clinical, radiological, cytological and histopathological features were correlated and a final diagnosis of ES was made. Treatment of ES is multi modal and involves chemotherapy and surgery which has increased the survival rate to 75% .16-19

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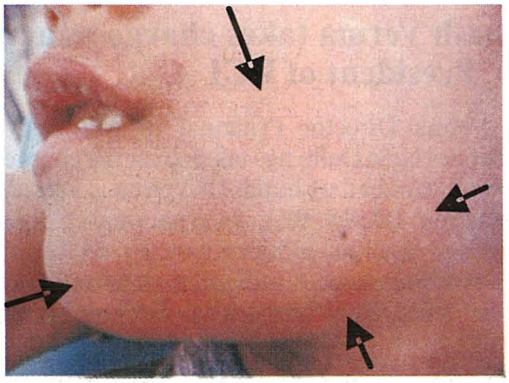


Fig.1.Diffused swelling on left side of face involving inferior border of mandible.a

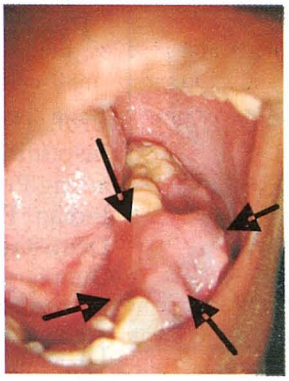


Fig.2.Lobed swelling on the left alveolus extending from 32 to 36.

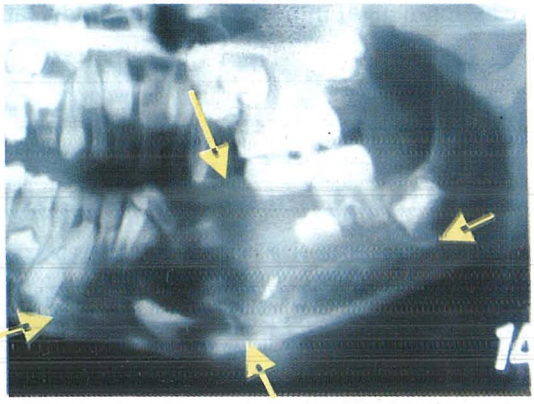


Fig.3.Ill defined destructive radiolucency from 42 to 36 along with superoinferior expansion of mandible at 33

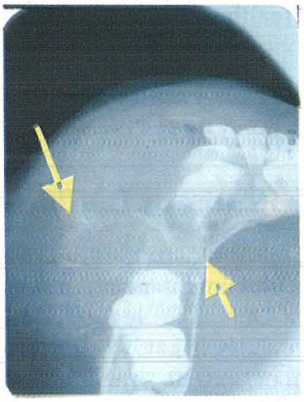


Fig.4.Buccal cortical expansion showing typical sunray appearance with intact lingual cortex.

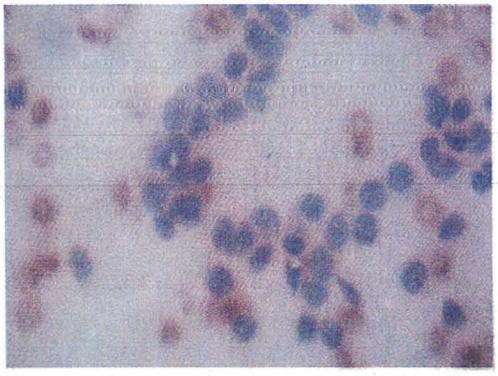


Fig.5.FNAC smear with clusters of small round cells having dark large nucleus and scanty cytoplasm interspersed with RBCs. (H&E stain 100X)

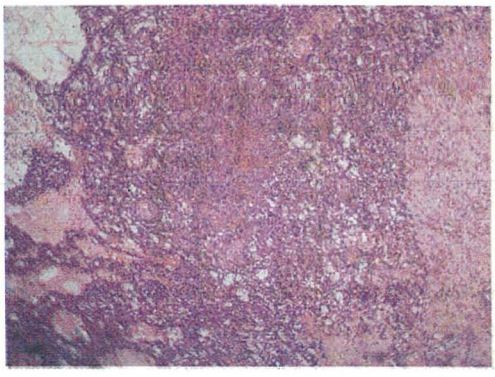


Fig.6. Round to oval cells with indistinct cellular outline and ill defined hyperchromatic nucleus filling the whole cell.(H&E stain 100X)