

Ewing's Sarcoma of the Mandible with Extensive Bony Metastasis in a Young Male: A Case Report

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ABSTRACT

Ewing's Sarcoma Family of Tumours (ESFTs) comprises locally aggressive, undifferentiated small round blue-cell tumours of neuroectodermal origin, predominantly seen in adolescents. These tumours arise from non random chromosomal translocations involving the Ewing's Sarcoma (EWS) gene. ESFTs in the mandible are uncommon. A 14-year-old male patient presented with a painless swelling in the right jaw. Plain radiographs, ultrasonography, contrast-enhanced Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) revealed a large, partially well-defined, highly vascular soft tissue mass in the right mandibular region. It measured approximately 80×82×75 mm (anteroposterior x transverse x craniocaudal), with both solid and cystic components. The mass was destroying the underlying right temporomandibular joint, head, ramus and posterior body of the right hemimandible, including extensive sunray-type bony spiculations. There were multiple lytic lesions in the skull and facial bones, as well as, altered marrow signal intensity in the calvarium, bilateral humeri and clavicles, and cervical and thoracic vertebrae, indicating a locally aggressive tumour with extensive metastasis into the bones and marrow. The diagnosis was confirmed by histopathology, which showed fibrocollagenous tissue infiltrated by sheets of small round cells with scanty eosinophilic cytoplasm and prominent nuclei. Management typically involves a combination of chemotherapy, radiation and surgery. However, metastatic Ewing's Sarcoma has a poor prognosis.

Keywords: Head and neck radiology, Jaw swelling, Mandibular sarcoma, Primitive neuroendocrine tumour

CASE REPORT

A 14-year-old male patient presented to the Department of General Surgery with a swelling in the right parotid region that had developed spontaneously over the last year. In the past six months, it had shown rapid growth. There were non specific episodes of fever reported. Upon examination, the swelling was hard and fixed to the underlying bone, involving the right infratemporal region and the area over the ramus of the right hemimandible. The overlying skin was smooth, without venous prominence [Table/Fig-1,2]. The intraoral examination was unremarkable, except for some white patches over the gingivobuccal space [Table/Fig-3].



[Table/Fig-1]: Frontal clinical picture showing the swelling involving the right infratemporal region, the area over the ramus of the right hemimandible up to the angle.



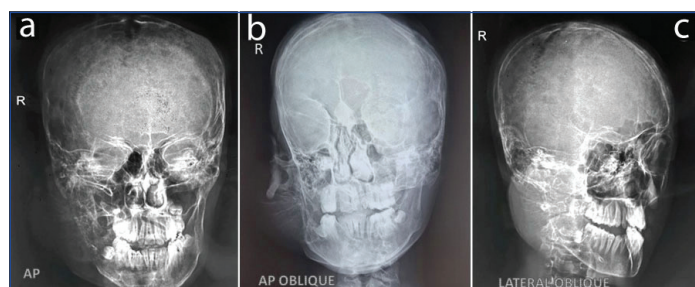
[Table/Fig-2]: Lateral clinical picture showing the swelling involving the right infratemporal region, the area over the ramus of the right hemimandible up to the angle.



[Table/Fig-3]: Intraoral picture was unremarkable except for some white patches over the gingivobuccal space.

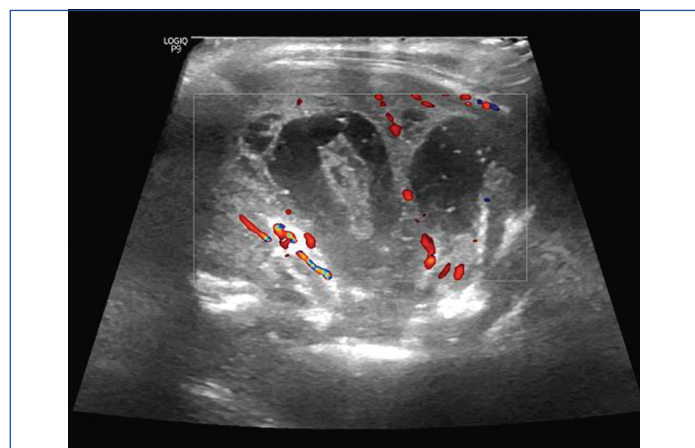
A Complete Blood Picture (CBC) revealed normocytic normochromic anaemia and a raised Erythrocyte Sedimentation Rate (ESR). He was then referred to the Department of Radiodiagnosis for further evaluation.

A prompt radiograph of the skull revealed a large soft-tissue mass in the right infratemporal region with erosion of the underlying mandibular ramus and a sunburst type spicular periosteal reaction [Table/Fig-4a-c]. Multiple radiolucent lesions were noted in the calvaria.

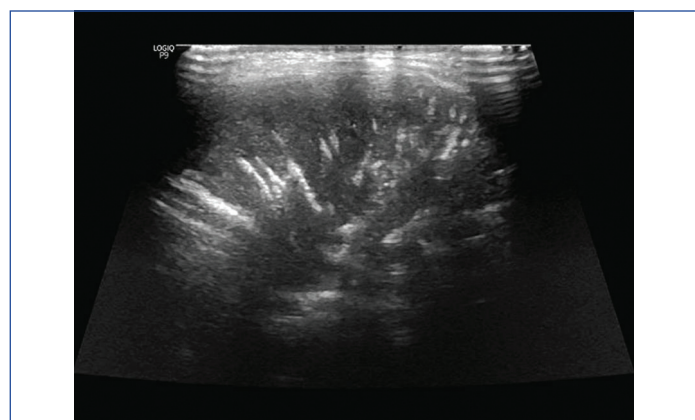


[Table/Fig-4]: Plain radiographs of the skull in a) Anteroposterior (AP); b) AP oblique and c) Lateral oblique showed a large soft-tissue mass involving the right infratemporal region with erosion of the underlying mandibular ramus up to the angle of mandible along with sunburst type of radiating spicular periosteal reaction. Multiple lucent lesions were seen in the calvaria.

Ultrasonography of the local area showed a large, hypoechoic, heterogeneous, predominantly solid Space-occupying Lesion (SOL) over the right hemimandible, with a few cystic spaces containing moving echoes. Colour doppler revealed increased vascularity within the solid portions of the SOL [Table/Fig-5]. The SOL displayed echogenic bony spiculations in a radial distribution [Table/Fig-6].



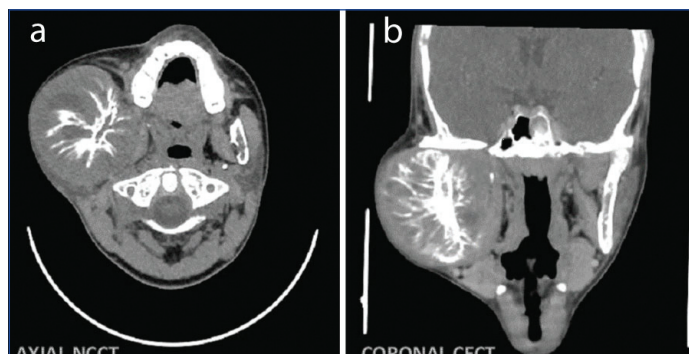
[Table/Fig-5]: Ultrasonography with colour doppler showed the large hypoechoic heterogeneous SOL having internal cystic spaces with moving echoes in the cystic areas and increased vascularity in the solid areas.



[Table/Fig-6]: Ultrasonography of the SOL showed echogenic bony spiculations distributed in a radial fashion.

Contrast-enhanced Computed Tomography (CECT) of the face and neck region revealed a large, expansile, heterogeneously enhancing soft-tissue lesion involving the right hemimandible and

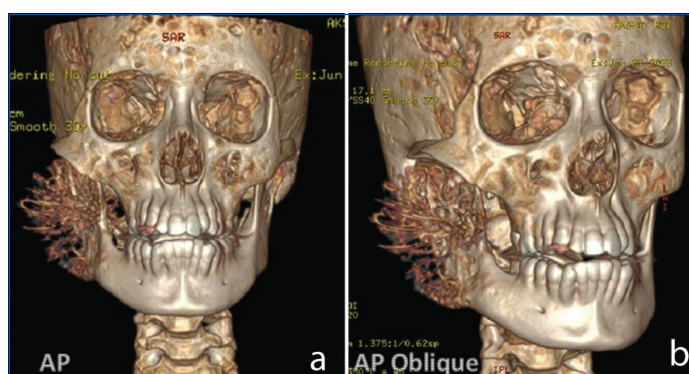
the muscles of mastication. It measured approximately 80x82x75 mm (anteroposterior x transverse x craniocaudal). There was erosion of the right temporomandibular joint, head, ramus and the posterior part of the mandible body, with extensive sunburst-type spiculated periosteal reaction [Table/Fig-7a,b]. Multiple lytic lesions were also seen in the calvaria [Table/Fig-8]. A 3 Dimensional (3D)-CT reconstruction of the face and neck provided a more accurate depiction of the abnormalities [Table/Fig-9a,b].



[Table/Fig-7]: Axial section of a) Plain CT and b) Coronal reconstruction of CECT of the face and neck showed the presence of a large expansile heterogeneously enhancing soft-tissue lesion involving the right hemimandible causing erosion of the right temporomandibular joint, head, ramus and some portion of the posterior part of body of the right hemimandible with extensive sunburst type of spiculated periosteal reaction.



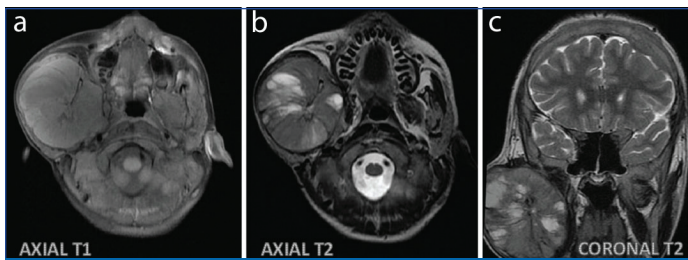
[Table/Fig-8]: CECT of the brain in axial section showed multiple lytic lesions in the calvaria.



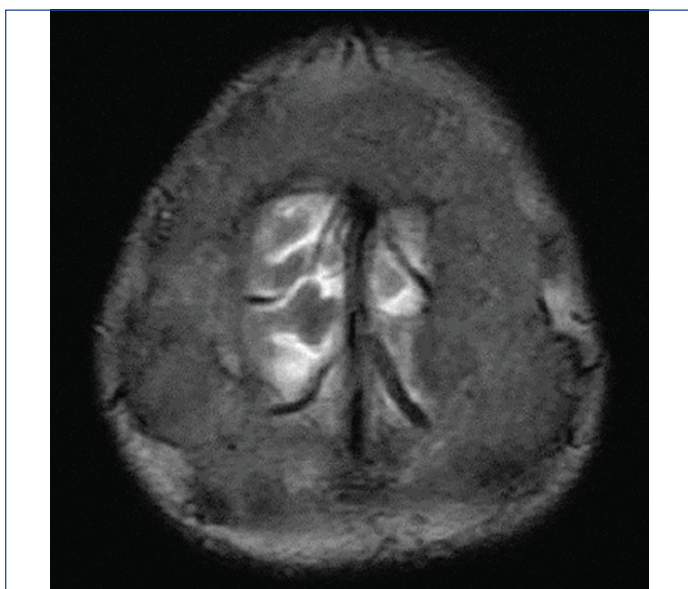
[Table/Fig-9]: The lytic lesions were better visualised in the 3D reconstructed computed tomography images in a) Anteroposterior (AP) and b) AP Oblique. These images better demonstrated the destruction of the right hemimandible and the spiculated periosteal reactions.

Magnetic Resonance Imaging (MRI) of the brain and neck demonstrated a large, relatively well-defined, heterogeneous signal intensity solid-cystic SOL in the right masticator space, with loss of fat planes with the muscles of mastication [Table/Fig-10a-c]. The solid portion of the mass was isointense on T1-weighted images (T1WI) and relatively hyperintense on T2-weighted images (T2WI).

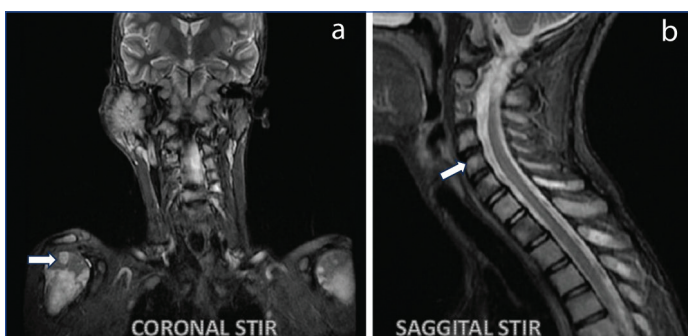
The internal cystic areas were hypointense on T1WI and showed Cerebrospinal Fluid (CSF) like hyperintensity on T2WI. There was also a loss of fatty marrow signal in the calvaria and altered signal intensity in the diploic space [Table/Fig-11]. Short T1 Inversion Recovery (STIR) sequences showed multiple lesions with altered signal intensity in the bilateral heads of the humeri, clavicles, and the cervical and thoracic vertebrae [Table/Fig-12a,b].



[Table/Fig-10]: T1WI in the a) Axial plane, b) T2WI in the axial plane and c) Coronal plane showed a large well-defined expansile complex solid-cystic, predominantly solid SOL at the right ramus of the mandible involving the right masticator space. The solid portion was isointense on T1WI and hyperintense on T2WI. The internal cystic portions were hypo-intense on T1WI and showed CSF-like hyper-intensity on T2WI.



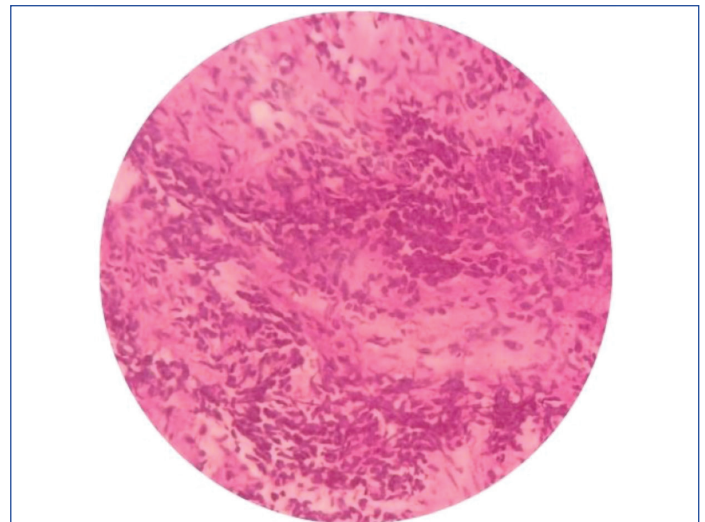
[Table/Fig-11]: T2 weighted Fluid-attenuated Inversion Recovery (FLAIR) MRI in the axial section demonstrated loss of fatty marrow signal in calvaria with altered signal intensity in the diploic space.



[Table/Fig-12]: STIR sequence revealed multiple altered signal intensity lesions (solid arrows) in the a) Bilateral head of the humerus and b) Cervical and thoracic vertebrae.

Histopathology confirmed Ewing's Sarcoma (ES). The samples exhibited fibrocollagenous tissue infiltrated by sheets of small round cells with scanty eosinophilic cytoplasm and prominent nuclei. No osteoid matrix was observed [Table/Fig-13]. Immunohistochemistry (IHC) was positive for Cluster of Differentiation (CD) 99.

The patient is currently undergoing combination chemotherapy with vincristine, doxorubicin and cyclophosphamide, along with radiotherapy. A hemimandibulectomy with mandibular reconstruction is planned. However, the prognosis for patients with extensive bone and marrow metastasis remains extremely poor.



[Table/Fig-13]: Histopathological image from the biopsy of the mass revealed the presence of fibrocollagenous tissue infiltrated by sheets of small round to oval shaped cells with very scanty eosinophilic cytoplasm and prominent nucleus. No osteoid matrix was noted (H&E, 10x).

DISCUSSION

The ESFTs are among the most common primary bone malignancies in adolescents, ranking second only to osteogenic sarcomas [1]. The majority of ESFT cases exhibit metadiaphyseal involvement in the long bones, with the femur being the most commonly affected. Primary ES of the jaw is an extremely rare occurrence, accounting for about 1% of all ES cases, due to the scarcity of haematopoietic marrow in the jaw bones. In the jaw, the mandible is affected twice as often as the maxilla. The ramus, angle and posterior body are the most common locations for tumours in the mandible [2-4]. Arafat A et al., studied 17 cases of ES of the jaw and found that, of the nine cases where the tumour arose from the mandible, six involved the posterior body and ramus [5]. In the present case, the tumour primarily affected the ramus and the posterior part of the body.

Ewing's Sarcoma (ES) was first described by the American pathologist James Ewing as a diffuse endothelioma of bone. ES and Primitive Neuroectodermal Tumours (PNETs), which were previously thought to be two separate pathologies, are now classified within the same spectrum of Ewing Sarcoma Family Tumours (ESFTs) [6]. This group includes locally aggressive, undifferentiated small round blue-cell tumours of neuroectodermal origin, comprising both osseous and extraosseous ES, atypical ES (large-cell variant), adamantinoma-like variants, PNETs (also known as ES/PNET), and Askin tumours (small, blue, round-cell tumours of the thoracopulmonary region). PNETs occurring outside the Central Nervous System (CNS) are referred to as peripheral PNETs (pPNETs or ES/pPNETs) [7].

More than three-quarters of patients with ESFTs present before the age of 20 years and exhibit a slight male predominance with a ratio of 1.4:1 [2]. Laboratory investigations may reveal anaemia, leukocytosis and a raised ESR. In cases of ES of the mandible, swelling is the most common symptom, followed by pain, paraesthesia, and loose teeth [5]. Histopathologically, ES is characterised by uniform small round cells with scanty clear to eosinophilic cytoplasm, rounded nuclei with inconspicuous nucleoli arranged in a sheet-like pattern. Immunohistochemistry (IHC) most commonly shows positivity for CD99, followed by vimentin [8].

Gorospe L et al., reported a case of mandibular ES that revealed an ill-defined, permeative soft-tissue mass in the right hemimandibular ramus with permeative bony destruction and loss of fat planes with the muscles of mastication, along with displacement of the right parotid gland [9]. These findings are consistent with the present case.

The most common radiological feature is the presence of permeative bone destruction associated with a soft-tissue mass. A spiculated

periosteal reaction is often observed. Wood RE et al., reviewed 105 cases and reported that the onion-peel type of lamellated appearance was not a common feature of ES in jaw bones, likely due to their complex anatomy [10]. In the case discussed here, the onion-peel appearance was not observed; instead, a radially arranged spiculated periosteal reaction was very vividly demonstrable. According to de Santos LA and Jing BS, displacement of the adjacent tooth is quite common, but this was not seen in the current case [11]. A plain radiograph of the local area is usually the initial investigation performed. Ultrasound (USG) is important for determining the vascularity of the lesion and differentiating solid areas from cystic ones. CT and MRI assist in more accurate delineation of the tumour, evaluation of the adjacent soft tissue, vascular involvement, and the search for metastatic lesions. MRI is the preferred method for staging and monitoring the effects of therapy. The lesion is usually hypointense to isointense compared to the adjacent muscles on T1WI and exhibits inhomogeneous signal intensity on T2-weighted imaging (T2WI) due to the presence of necrotic and haemorrhagic areas. Gadolinium contrast injection aids in better differentiation of the tumour extent and its margins from adjacent normal tissues [9]. The typical sunray type of spiculated periosteal reaction, the presence of a soft-tissue mass and permeative bone destruction are also seen in osteosarcomas. The mixed (blastic-lytic) type of osteosarcoma can mimic ES. However, osteosarcoma of the jaw usually occurs beyond 30 years of age, whereas ES, both appendicular and in the jaw, is typically seen in individuals below 20 years. Osteosarcoma may additionally show new bone formation in the adjacent soft tissue [11].

Other small round cell tumours, such as metastatic neuroblastomas and rhabdomyosarcomas, can mimic ES both radiologically and histopathologically, as all of these are round-cell tumours. However, the age of incidence for these tumours is mostly below five years [11]. Histiocytosis X is usually well-defined, unlike ES. Eosinophilic granuloma classically shows the presence of floating teeth within an area of bone destruction on a radiograph [11]. Metastatic carcinoma of the mandible is usually seen in the older age group, and there would typically be a history of a primary tumour, elsewhere. The typical periosteal reaction would not be seen here [11].

The presence of metastasis is an indicator of poor prognosis. Treatment aims at managing the primary site using a combination of surgery and chemoradiotherapy, as well as, preventing and treating metastatic lesions. However, the chances of recurrence are high.

The 5-year survival rate for disseminated ES with extensive bone and marrow metastasis is just 5-10% [12].

CONCLUSION(S)

Any swelling of the jaw in a young patient should immediately undergo radiological analysis, as it could be a rare presentation of an aggressive tumour like Ewing's sarcoma, as in the present case. Common metastasis sites should be examined. Prompt radiographs, ultrasound, CECT, and MRI should be performed. Histopathology helps to confirm the diagnosis.

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