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Case Report

EWING'S SARCOMA OF MANDIBLE: A RARE TUMOR AT A RARE LOCATION

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ABSTRACT

Ewing's Sarcoma (ES) is a rare, highly malignant, and poorly differentiated variant of round small cell tumors with the most unfavorable prognosis among all musculoskeletal neoplasms. The histogenesis of ES is still uncertain. However, the latest studies suggest it to be neural crest progenitor cell-derived or neuroectodermally originated primitive neural tissue with various degrees of differentiation [1, 2]. It is an uncommon malignancy of bones (rarely soft tissue) and usually occurs in long bones of children and young adults. ES rarely occurs in the skull (2.3%). But when it does, the maxilla and mandible are its usual primary locations [3]. In this case report, we have presented a rare case of a 4-years old girl with ES of the mandible which was precisely diagnosed and effectively treated using a multi-disciplinary approach. This study aims to spread awareness among physicians to rule out the chances of malignancy in a rapidly growing dental or facial swelling. It also underscores the potential of a better prognosis by timely diagnosing and promptly managing Ewing's Sarcoma in children.

KEYWORDS: Ewing's Sarcoma, Children, Mandible, Small Round Cell Tumor, Oncology,

INTRODUCTION

Identified by James Ewing in 1921, the ES was originally named Diffuse Endothelial Myeloma or Diffuse Endothelioma [4]. Amongst highly lethal malignant tumors, Ewing's Sarcoma (ES) is the sixth most common small round cell tumor [5]. After Osteosarcoma, ES is the second most common malignant neoplasm of bones/soft tissues in children, constituting 10-15% of all primary malignant tumors in the pediatric age group [6]. With the male predominance of 1.5:1, ES is more common in Caucasians than in Asians, and rare in Africans and African Americans. ES most commonly occurs in the second decade of life and rarely occurs in children of age less than 5 years [6, 7]. In 90% of the cases, the cytogenetics of ES reveal translocation of chromosomes either on 11 and 22 or 21 and 22 [8]. The exact pathogenesis of Ewing's Sarcoma is still unknown. The frequency of primary ES malignancy in descending order is: Lower Extremities (45.6%), Pelvis (20.5%), Upper Extremities (12.9%), Axial Skeleton / Ribs (11.8%), and Skull (2.3%) [9]. ES at its usual sites is easy to diagnose, for example, diaphysis of long bones (tibia/femur). However, at the unusual locations (maxilla/mandible), its diagnosis can be incredibly challenging. It usually has a hematological spread but can also have direct extensions to the adjacent bony or soft tissue. Due to its aggressive behavior, metastasis is already present in 14-50% of cases at the time of diagnosis [10]. The malignancy spreads primarily to the lungs (50%), then to the bones (25%), and bone marrow (20%). Metastasis to liver and lymph nodes is uncommon or occurs during the end stage of the

course of ES [11]. Distant metastasis, Age > 15 years, Lesion size > 8cm, Central (pelvis or spine), and poor response to chemotherapy are the poor prognostic factors. The signs and symptoms of ES, such as weight loss, anemia, elevated WBCs, ESR, and LDH, indicate a more extensive disease and a poor prognosis [12].

CASE PRESENTATION

A 4-year-old girl presented to Pediatric Surgical Emergency with rapidly increasing, prominent left lower jaw and neck swelling associated with tooth deformities, persistent low-grade fever, decreased appetite, and difficulty in chewing for 2 weeks. According to the parents, the child was in her usual state of health 2 weeks ago when they noticed a pea-sized swelling in her left submandibular region. She had a history of visits to a dental clinic where she was diagnosed with a periodontal abscess associated with tooth deformity, followed by tooth extraction and a course of oral antibiotics, but the swelling did not subside. It progressively expanded and deformed the other teeth. There was no other significant past medical, surgical, or dental history. There was no history of trauma and no family history of any carcinoma.

Figure 1. Clinical photographs on 5th, 10th, and 14th day of noticeable swelling on the left side of the neck and face

Extra-Oral Examination:

On inspection, there was a 10x8cm asymmetrical swelling in the sub-mandibular region extending from the angle of the mandible to the submental region without crossing the midline. The overlying skin was normal with no discoloration, pigmentation, change in texture, or engorged veins. On palpation, the inspection findings were confirmed. The swelling/mass was oval, non-tender, non-fluctuating, firm to hard, fixed to the underlying structures but not to the overlying skin, normal in temperature, non-pulsatile, non-reducible, having well-defined margins and irregular surface. The transillumination test was negative. There was no regional or generalized lymphadenopathy. On percussion, the affected teeth were found insensitive, and the percussion note on swelling was dull throughout.

On auscultation, there was no audible pulsation or bruit. (Fig.1.1)

Intra-Oral Examination:

The examination of the buccal cavity revealed an irregular, ulcerated mass with a rough lobulated surface extending from the left first premolar to the left retromolar region resulting in the uplifting of the left

half of the tongue and deformity of all teeth on the lower left jaw.

Provisional Diagnosis of Rabdomyosarcoma was made, with a differential diagnosis of Ewing's Sarcoma, Spindle Cell Carcinoma, and Primitive Neuro Ectodermal Tumors (PNET). For the definitive diagnosis and accurate treatment, the following investigations were performed:

Radiological Examination:

The panoramic plain radiograph showed localized osteolytic lesion, cortical erosion, and periosteal reaction resulting in the mottled rarefaction of the angle of the left mandible, visible as moth-eaten, onion peel, or sunray appearance. The empty socket of the previously extracted first left molar tooth and loosened second left molar tooth can also be seen in the figure 2.

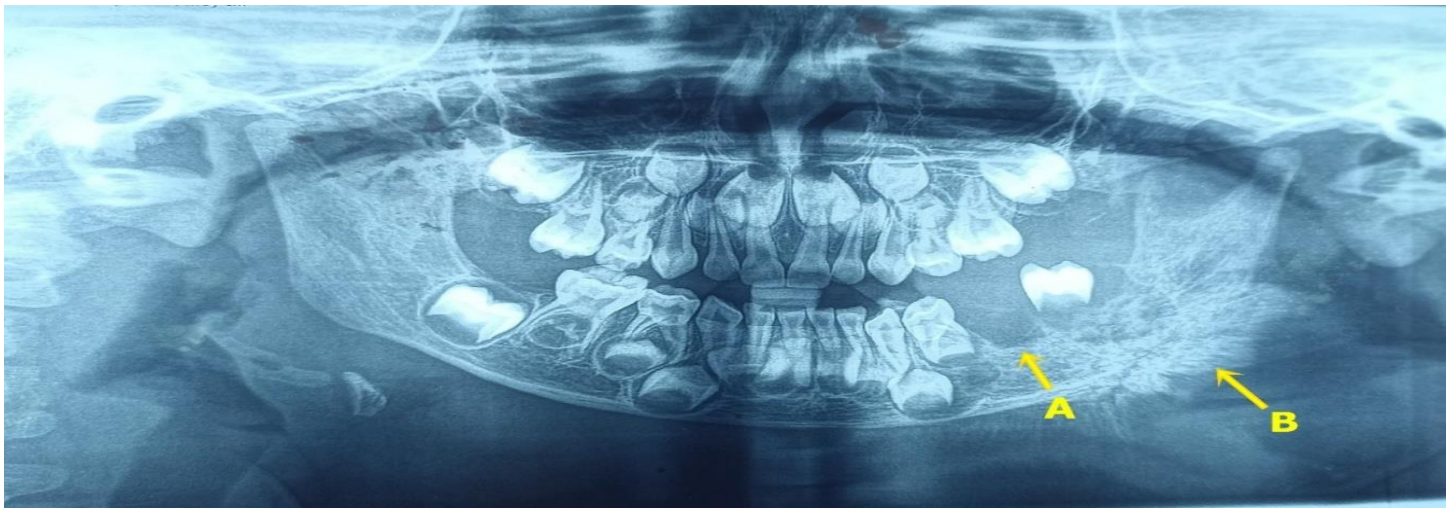

Figure 2. Panoramic Radiograph showing A. an Empty socket of a first molar tooth on lower left jaw, B. Ill-defined, osteolytic mixed lesion involving premolar and molar region of left mandible showing moth-eaten/sunray appearance

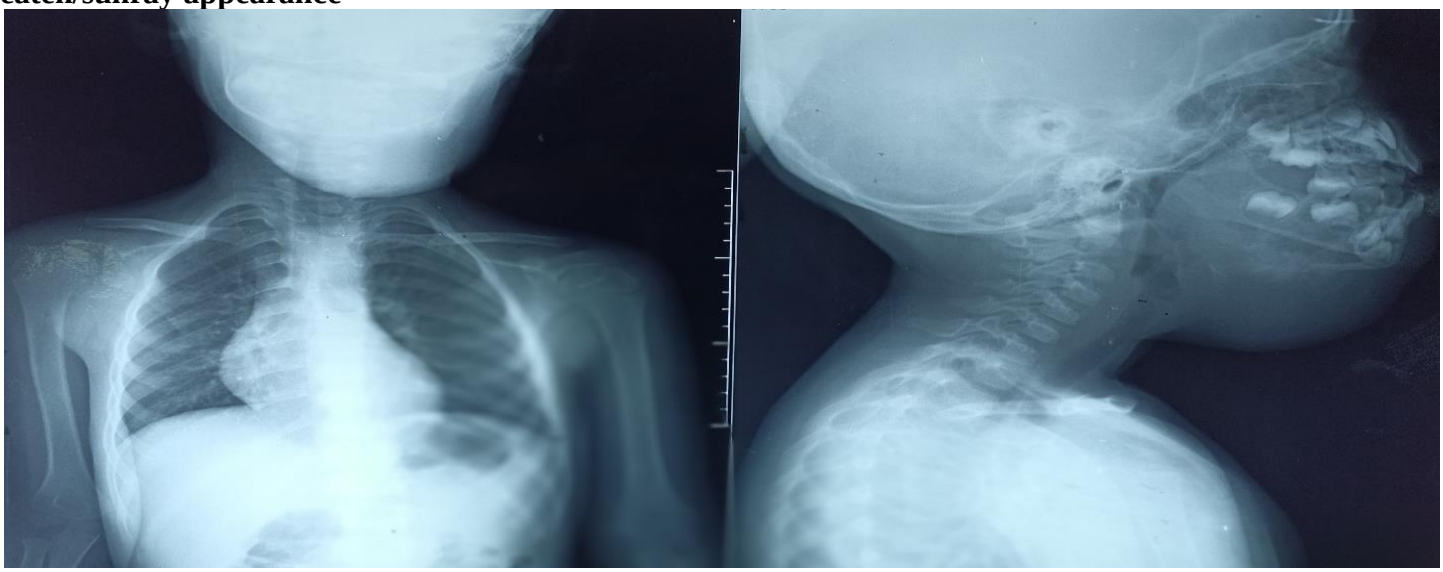

Figure 3. Chest X-ray anteroposterior view: Unremarkable; X-ray head & neck lateral view showing radiolucent soft tissue welling in submandibular and submental region

Computed Tomography (CT) Neck with Intravenous (IV) Contrast showed a soft tissue density, significantly enhancing lesion involving ramus and body of the left hemi-mandible extending; superiorly, to the lower limit of infra-temporal fossa; inferiorly, to the submental region; medially, to the floor of the mouth involving muscles of the left half of the tongue; and laterally, to the soft tissue of left lower cheek.

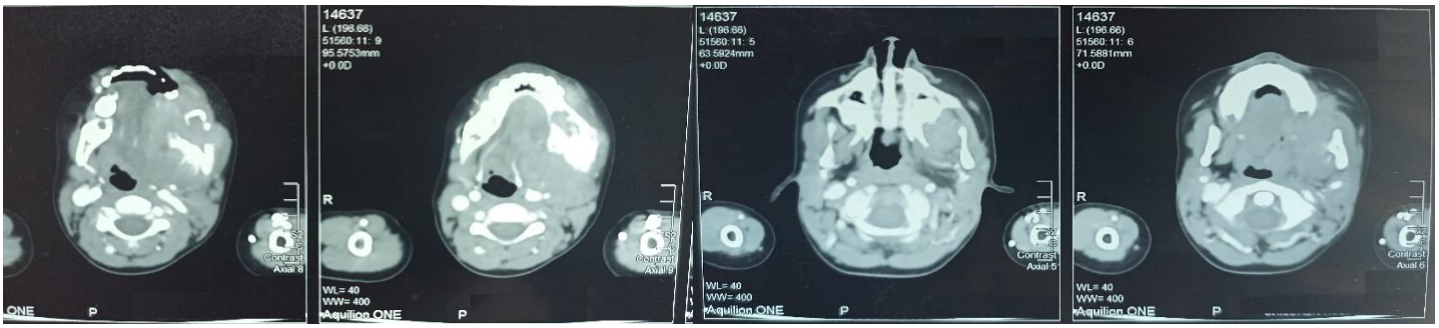

Figure 4. CT neck axial sections showing expansile, lytic lesion in the left mandible with significant enhancement in soft tissue matrix having sunray appearance

CT Chest and Abdomen with IV contrast were unremarkable.

Bone Marrow Trephine Biopsy:

Bone marrow biopsy showed Trilineage Hematopoiesis with no evidence of primary or secondary malignancy.

Whole Body Bone Scan:

The WB body scan showed an inhomogeneous increase in radiotracer uptake in the left lower mandibular bone with bony infiltration, depicting active bone pathology most likely to be metastatic. The lesion was localized as the rest of the scan showed normal tracer distribution in the metaphyseal growth plates of the long bones.

All the above-mentioned investigations suggested a malignant lesion of the left mandible with no metastasis, yet. The Staging System of Musculoskeletal Tumor Society (MSTS) or Enneking System is commonly used for the staging and grading of ES [13]. According to Enneking's staging system, the tumor of this patient was of the A1 category: Compartmentalized, having no metastasis. For the definitive diagnosis of the tumor, histological examination of the tumorous lesion was advised.

Diagnostic Histopathology:

The definitive diagnosis of ES was made after the histological study of the specimen obtained by excision biopsy. Due to Anesthetic and surgical limitations (restricted mouth opening, narrow airway, and possible hindrance by endotracheal intubation in the operative field) temporary/reversible tracheostomy was performed. Excision Biopsy with an attempt to near-to-complete removal of the tumor was performed. The patient underwent radical tumor surgery with total left hemi mandibulectomy and cervical lymph nodes dissection. The surrounding healthy tissue margins were confirmed per-operatively. The sample of excision biopsy sent for histopathological examination confirmed the diagnosis of Ewing's Sarcoma with the positive findings of uniform small round cells with eosinophilic cytoplasm, fine chromatin material, rosette-like structures, round nuclei, focal areas of necrosis, indistinct nucleoli, and cytoplasmic membranes. For cytological examination, CD99, Periodic Acid Schiff (PAS) staining, NKX2.2, Desmin, Vimentin, Neuron-specific Enolase, RT-PCR, and ERG were used. The histology of the excised specimen also confirmed the complete resection of the tumor with no need for re-excision.

Multi-Agent Chemotherapy:

After two weeks of surgery, the patient was introduced to chemotherapy with multiple drugs, including Vincristine, Doxorubicin, Cyclophosphamide, Dactinomycin, and Carboplatin. This neoadjuvant therapy was followed by the reconstruction of the left face and jaw via metallic endoprosthesis. The patient responded well to the treatment and was discharged from the hospital three weeks later, with no active complaint. A follow-up plan was scheduled to keep an eye on recurrence, metastasis, and late complications.

DISCUSSION

After an extensive literature review, it is concluded that the early signs and symptoms of ES may include painful swelling, fever, increased WBC count, ESR, and CRP [10-14]. However, the present case did not develop any such signs. The patient was treated for a dental abscess and underwent left first molar tooth extraction. The accompanying, rapidly expanding radiolucent lesion caused suspicion of malignancy, for which a referral to the pediatric maxillofacial and general surgery department was made. The parents were literate,

concerned, and highly co-operative which made the entire process of early diagnosis-to-management possible.

Ewing's sarcoma is an aggressive malignant disease. This widespread disease is associated with a low survival rate and poor prognosis (<20-30%). However, timely diagnosis of this disease before the occurrence of metastasis can remarkably improve survival, by upto 70%. Just as this present case showed no metastatic spread and responded well to the treatment.

The widely accepted treatment of ES in skull is radical tumor excision with (neo-) adjuvant chemotherapy [15]. ES is also radiosensitive so radiotherapy and/or chemotherapy alone/combined can also be used to treat the disease if and when surgery cannot be performed [16].

It is preferred to perform ablative as well as reconstructive surgery in a single step procedure to reduce operative time, number of surgeries/general anesthesia, and healing time. It also reduces the post-op complications of ablative surgery including scaring, bone fragments displacement, and wound contractions [17]. Even so, a different standard approach was adopted in this present case. Instead of incision biopsy, excision biopsy was performed with the use of a CT scan for the confirmation the location and margins of the tumor. This step significantly reduced the burden of the diseases and the chances of metastasis. Moreover, before the reconstructive surgery, the potential residual tumor fragments were eliminated by neoadjuvant chemotherapy. However, at the time of excision, it was not sure whether this attempt for radical tumor resection would prove to be successful or not. Later, the histopathology report suggested no need for the re-do surgery. So, it can be concluded that standard protocols should be reconsidered and re-evaluated from patient to patient, considering the feasibility and suitability.

CONCLUSION & CLINICAL SIGNIFICANCE

Ewing's sarcoma of the skull is extremely rare. If the patient presents with rapidly growing swelling or radiolucent mass with evident deformity in the oral cavity or jaw, mimicking odontogenic or submandibular abscess, the possibility of the tumor must be ruled out.

CONSENT

At the commencement of this study, written informed consent was taken from the parents for the publication of this case along with relevant investigation results and images. The anonymity of the patient was ensured. A copy of the written consent is also provided to the Editor-in-chief of this journal for review.

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None

CONFLICT OF INTEREST

The authors declare no conflict of interest

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