CASE REPORT

Ewing's Sarcoma of Mandible: A Case Report with Review of Literature

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Abstract

Background: Ewing sarcoma (ES), a rare malignancy, comprises whatever the age, 4–15% of all primary bone tumors. It represents 1% of all malignant tumors in children and is the fourth most common bone malignancy after myeloma, osteosarcoma, and chondrosarcoma.

Case description: A 12-year-old boy came to the Oral Surgery Department of Bretonneau Hospital referred by his dentist with a rapidly evolving swelling in the left mandibula for 6 weeks, which was initially diagnosed as a facial cellulitis. Cone beam computed tomography (CBCT) showed a poorly defined, expansile, and osteolytic tumor on the left side of the mandible. Clinical and radiographic findings were in favor of an aggressive primitive bone tumor. A mandibular biopsy under general anesthesia was performed in the Department of Surgical Oncology at Institut Curie in Paris, revealing an ES.

Conclusion: Mandibular ES can mimic dental infections when swelling is the main clinical manifestation, which can lead to a delayed diagnosis. A correlation between clinical, radiological, histopathological, and immunohistochemical with cytogenetics is needed to confirm the diagnosis. Moreover, smaller tumors have better survival.

Dentists must therefore be aware of the clinical signs of ES in order to quickly refer patients to a specialized department.

Keywords: Case report, Ewing sarcoma, Head and neck sarcoma, Mandibular sarcoma, Pediatric sarcoma.

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Background

Ewing sarcoma (ES) is a scarce malignant tumor that accounts for 4–15% of all primary bone tumors and is the second most common primary bone cancer in infants and children after osteosarcoma. It represents 1% of all malignant tumors in children and he ranks fourth after bone malignancy after myeloma, osteosarcoma, and chondrosarcoma.[1] The incidence, regardless of age, is one case per one million people in the United States. Among patients in their second decade, the incidence in the United States is nine to ten cases per million people.[2] Long bones (58%), pelvis (20%), and ribs (7%) are the most frequent locations. Mandibular localization represents 0.7% of all sites and is most frequently affected than the maxilla.[3] ES was originally described by James Ewing in 1920 as a diffuse endothelioma of bone arising from undifferentiated osseous mesenchymal cells. Olivier Delattre then discovered the expression of the EWSR1/FLI1 fusion transcript by the pathological cells of ES, reflecting the fusion of the EWSR1 and FLI1 genes, responsible for the pathology.[4] It usually occurs from the age of 5 up to 30. The most important prognostic factors include tumor localization or volume and the existence of metastases. As the disease progresses, cortical destruction and invasion of the bone and tissues occur. The common signs and symptoms in the maxillofacial region include swelling, pain, teeth loose, toothache, paresthesia, mucosal ulceration, and trismus.[5] The radiological manifestations of mandibular ES are characterized by sunray-like spicules or an onion-peel pattern periosteal reaction.[6]

Case Description

A 12-year-old boy was referred to the Oral Surgery Department by his dentist because of a rapidly increasing swelling in the left mandible for 6 weeks without any history of trauma or pain. Patient's medical history revealed only a prematurity and he did not take any long-term treatment.

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The extraoral examination revealed a facial asymmetry due to a firm swelling on the left side of the face with diffuse contour (Fig. 1) with a slight hyperesthesia in the territory of the left lower alveolar nerve, without inflammation or argument in favor of a fracture of the facial skeleton. No facial motor deficit nor trismus were found. The cervical palpation revealed a left subangulomandibular adenopathy.

The intraoral examination (Figs 2 and 3) showed a swelling on the left side of the mandible, which reaches the lingual cortex from the canine to the left intermaxillary commissure.

The orthopantomogram radiograph of the mandible (Fig. 4) revealed a poorly defined, osteolysis involving the premolar-molar

region of left side of the mandible, repelling the germ of tooth 38 and tooth 37 presenting a root resorption.

To properly define tumor location and its impact on adjacent structures, a cone beam computed tomography (CBCT) was necessary. CBCT sections showed multiple irregular patchy radiolucent areas mimicking moth-eaten appearance in the internal bone structure (Fig. 5). On CT images, we noticed erosion with a thinning and discontinuity of lingual cortex. Moreover, sunray pattern and radiating spicules, which are typical of ES, were observed on both buccal and lingual cortical bone.

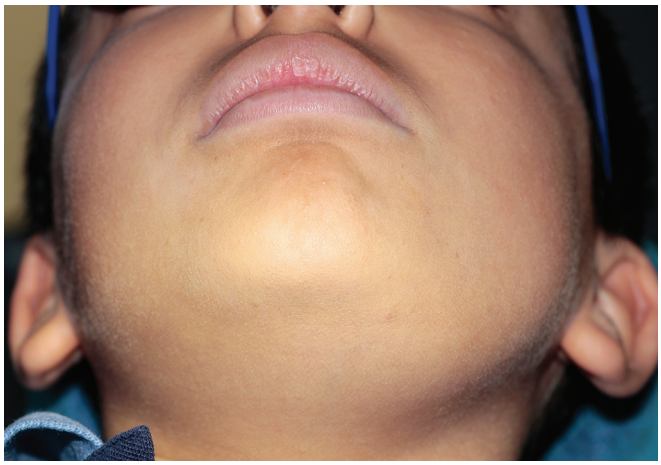

Fig. 1: Extraoral view

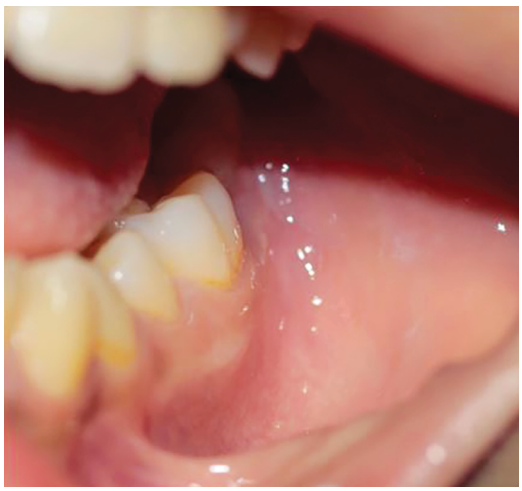

Fig. 2: Intraoral examination—buccal view

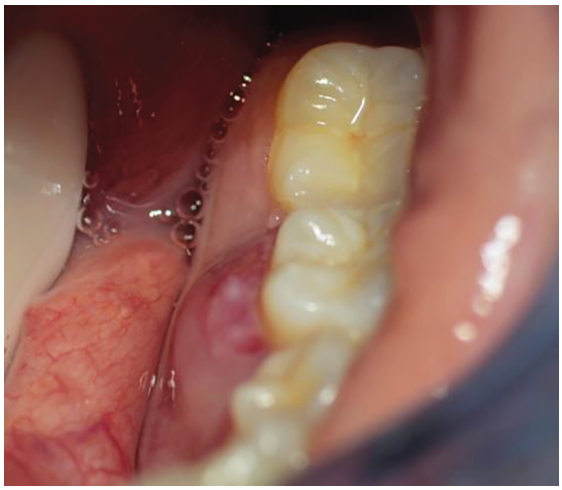

Fig. 3: Intraoral examination—lingual view

This left mandibular lytic tumor was associated with a sunray-like periosteal reaction with lysis of the mandibular canal and of the dental roots of teeth 36, 37, and 38 (Fig. 6) but there was not any considerable cortical expansion.

Based on the clinical and radiological findings, the first hypothesis was in favor of an aggressive primitive bone tumor. The patient was referred to a reference center for cancer, to perform a mandibular biopsy under general anesthesia, a bone marrow aspiration, a magnetic resonance imaging (MRI), a pulmonary CT scan, and a positron emission tomography (PET) scan, to evaluate the primary tumor extension and to exclude metastasis.

The MRI found an expansive tumor of the left mandible, extended to the soft tissues, reaching the symphysis for 2 cm, and associated with a root resorption of teeth 36, 37, and 38. The cortical bone on the lingual side was discontinuous (Fig. 6).

An incisional biopsy was performed, and the specimen was subjected to histopathological examination. The diagnosis of ES was confirmed after histopathological and immunophenotype evaluation of the mucosal biopsy, which found "small round blue cells" and a tumor "with undifferentiated basophilic small round cells" within a desmoplastic stromal reaction (Fig. 7). A genetic analysis was also performed and found an EWSR1/FLI1 fusion, compatible with the diagnosis of ES.

After the multidisciplinary discussion, the patient started the medical treatment according to the Euro Ewing 2012 protocol. The neoadjuvant chemotherapy consisted of five chemotherapy cycles of vincristine, doxorubicin, and cyclophosphamide (VDC) alternating with four chemotherapy cycles of ifosfamide and etoposide (IE). It was followed by a radiotherapy with a total dose of 60 Gy in 30 sessions.

The surgical intervention initially planned after the neoadjuvant chemotherapy would have been a hemimandibulectomy and reconstruction with a fibula-free flap, followed by a radiotherapy depending on the surgical margins. However, regarding the partial positive response to the chemotherapy, and after discussion with the patient and his parents, it was decided to opt for radiotherapy followed by adjuvant chemotherapy (two VDC + three IE).

At the end of the treatment, CBCT scan (Fig. 8) showed complete stability compared to baseline. No clinical sign of tumor progression was observed 15 months after the end of treatment.

Discussion

Ewing sarcoma (ES) is the second most frequent bone tumor after osteosarcoma. It most frequently arises in the long bones.

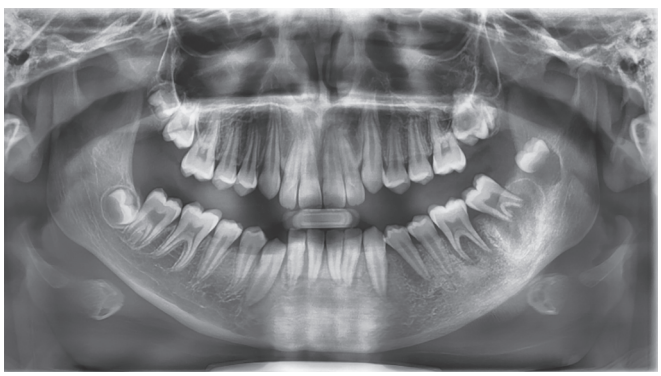

Fig. 4: Orthopantomogram radiograph

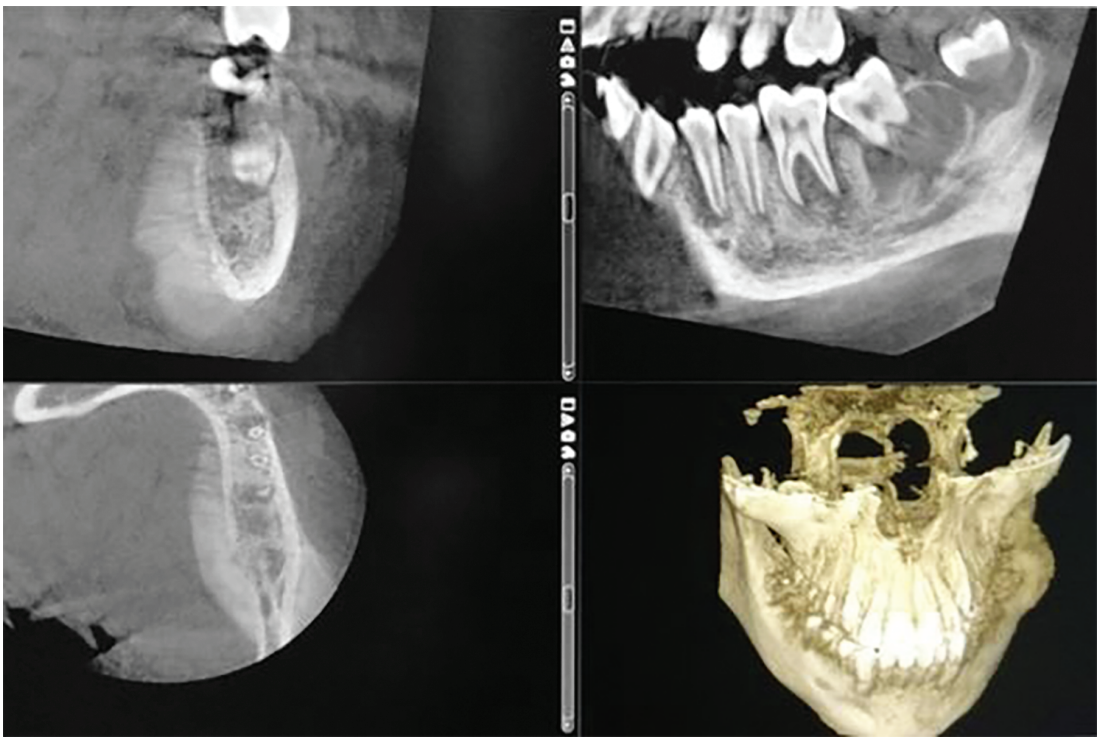

Fig. 5: Baseline CBCT

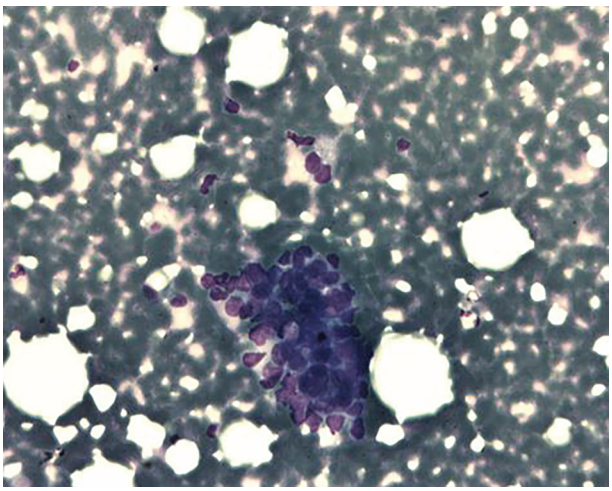

Fig. 6: Cytological examination—sheets of small round cells with inconspicuous cytoplasm

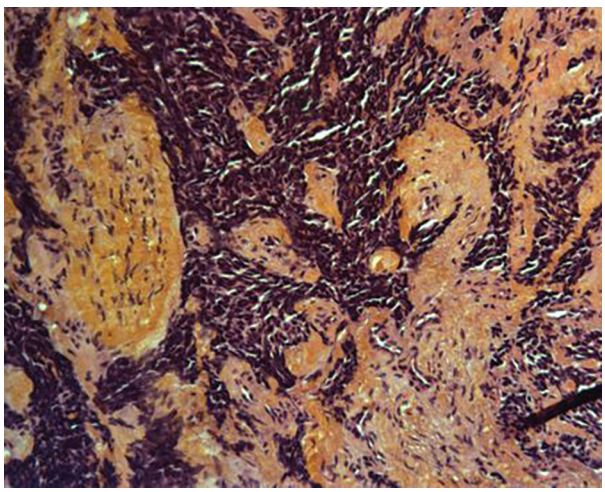

Fig. 7: Anatomopathological examination—proliferation of small undifferentiated basophilic round cells from medium to large size with amphophilic cytoplasm with indistinct boundaries and pepper-and-salt chromatin core, sometimes nucleolated. Mitotic activity is indistinct due to significant crush artifacts. The stroma is fibrous, sometimes desmoplastic, isolating sheets of tumoral cells

Mandibular ES is extremely rare and can mimic odontogenic infection. It mostly affects boys, and the median age is 12.

Clinical symptoms are swelling, pain, and sensory disturbances. In this case, the patient had only swelling causing facial asymmetry without pain or any sensory disturbances.

Computed tomography (CT) and MRI are the best imaging methods to evaluate the tumor.[7] In this case, the tumor was discovered by orthopantomogram radiography and CBCT indicating the eventuality of a malignant process. However, distinguishing ES of the jaw from other jaw tumors such as osteosarcoma, rhabdomyosarcoma, and malignant lymphoma is challenging. In the present case, CBCT showed an osteolytic lesion with the "moth-eaten" appearance and a periosteal reaction called sunburst phenomenon.

The histology of Ewing's sarcoma finds a proliferation of small round cells without bone production. A genetic mutation is sought: the t(11;22) translocation of the EWSR1 gene.[8] Found in 90% of cases, it confirms the diagnosis.

Usually, the treatment for ES in the head and neck region is a combination of radical surgery, chemotherapy, and localized radiotherapy, which may allow long-term survival.[9] Usually, postoperative radiotherapy is indicated in case of positive margins.

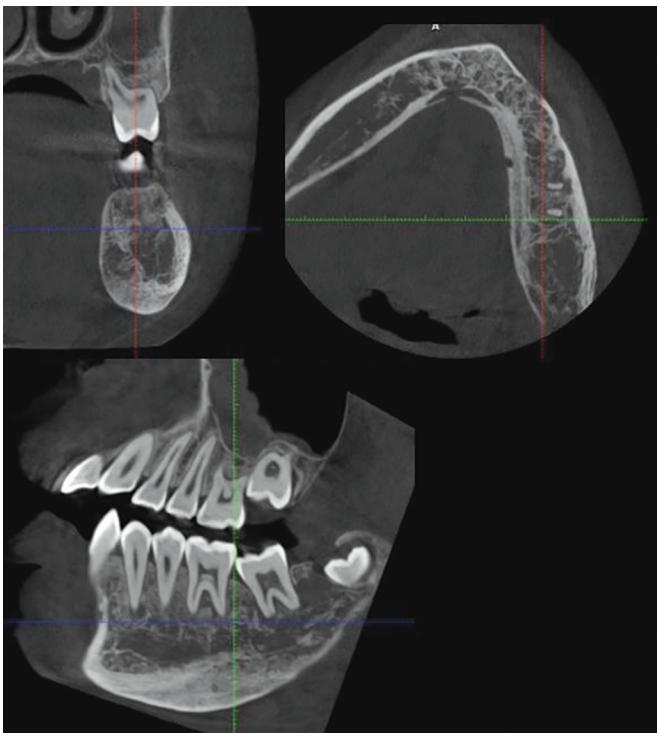

Fig. 8: End of treatment CBCT scan

For mandibular forms, the gold standard surgery consists of a mandibular resection with fibula-free flap reconstruction.[9] However, in children, some authors consider that this extended and heavy surgery is undesirable given the residual growth potential of the mandible, which would be reduced after surgery. However, a systematic review published in 2015 by Zhang et al.[10] found preserved mandibular growth in 50% of patients who underwent this intervention and noted that preservation of the condyle, the starting point of mandibular growth, was a positive prognostic factor. In contrast to this observation, radiotherapy is considered to have a poor prognostic factor for mandibular growth.[10,11] A study published in 2000 by Paulino et al.[12] reported the consequences of radiotherapy on the head and neck region in the treatment of rhabdomyosarcomas. Regarding the oral sphere, there were dental anomalies such as microdontia, hypodontia, and caries. Functional disorders such as trismus, maxillary or mandibular hypoplasia, xerostomia, or even facial asymmetry were reported.

Chemotherapy did not show any significant difference in mandibular growth.

In our case, after explanation of the different therapeutic solutions, it was decided to complete the treatment with external radiotherapy only, regarding the high risk of sequelae that surgery would have caused.

On the CBCT of our young patient, 12 months after the end of radiotherapy, we observed that the root edification of 37 was stopped, the germ of 38 was pushed back into the mandibular angle, and 27 was retained above 26 by the germ of 28. A reaction was also observed in both left and right sinuses (Fig. 8), and there was an ossification of the initial periosteal reaction going from the left mandibular angle to the anterior part of the mandibular body.

Regarding the survival rate, Grevener et al.[13] found no significant difference ($p = 0.75$) between patients with localized disease when comparing the choice of treatment modality (surgery alone versus radiotherapy alone after induction chemotherapy). They concluded that radiotherapy offered an equivalent survival to patients who could not undergo surgery.

Overall survival is about 70% for patients with localized disease.[13] In our case, to date, the disease seems to be under control for our young patient.

Mandibular ES rarely show distant metastasis, unlike ES of other anatomical sites that present a greater risk of metastasis.[14]

Conclusion

Mandibular ES can mimic dental infections when the main clinical manifestation is swelling, which can lead to a delay in diagnosis. A correlation between clinical, radiological, histopathological, and immunohistochemical with cytogenetics is needed to confirm the diagnosis. Smaller tumor without distant metastases has a better prognosis.

Dentists must therefore be made aware of the clinical signs of jaw malignant tumors, including ES, in order to quickly refer patients to a specialized department.

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