Oral Oncology 98 (2019) 171–173

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Letter to the editor

Mandible Ewing Sarcoma in a child: Clinical, radiographic and diagnosis considerations

Dear editor

The Ewing Sarcoma (ES) family of tumors (ESFT) is an aggressive form of bone and soft tissue cancer that likely arises from stem or progenitor mesenchymal cells or neuroectodermal cells. Such tumor affects mainly children and teenagers, with a slight male predominance [1–3]. Depending on the degree of neural differentiation, a spectrum of neoplasms of primitive neuroectodermal cells can developed. The Ewing family includes classic ES, which is poorly differentiated small blue round cell tumors (SBRCTs), atypical ES (large cell variant), Primitive Neuroectodermal Tumor (PNET), adamantinoma-like variant, extraskeletal ES, and Askin Tumour (soft tissue tumor localized in the thoracopulmonary region) [4,5]. Its causes are to date unknown and can develop in almost any kind of bone. However, jaw bones account for 5% of the cases of ES, and the mandible is more commonly affected than the maxilla [6]. The objectives of the present study are to both describe a case of ES in a child and discuss the main differential diagnoses and treatment modalities.

A 7-year-old boy was referred to the Oral Diagnosis Center, University of São Paulo, complaining of rapid growth (2 months of duration) in the chin region (Fig. 1A/B). On intraoral examination, an expansion of the vestibular plate in the anterior region of the mandible was observed (Fig. 1C). Cone beam tomography showed a poorly delimited osteolytic lesion measuring around 4 cm of extension located in the anterior region of the mandible. The lesion caused teeth displacement, thin bony septa formation, and a sunburst phenomenon (periosteal reaction) (Fig. 1D). The main diagnostic hypotheses were osteosarcoma, Burkitt's lymphoma, and aggressive central giant cell lesion.

An incisional biopsy was performed, and the histopathological analysis showed sheets of small, round, uniform cells with scant clear cytoplasm, divided into irregular lobules by fibrous strands with indistinct cell membranes and minimal amounts of stroma. Some necrotic areas could be observed. Immunohistochemical reaction was positive for CD99 and S-100 protein, and negative for desmin, FLI1, CD56, CD45, and AEI/AE3. Moreover, Ki-67 was positive in around 20% of the tumor cells. According to clinical, histopathological and immunohistochemistry features, Ewing Sarcoma was diagnosed.

The treatment consisted of 14 chemotherapy cycles of alternate vincristine, doxorubicin, and cyclophosphamide/ifosfamide–etoposide. Mandibular resection and reconstruction with microvascular free fibula flap were performed after the 6th cycle of chemotherapy. Surgical specimen evaluation showed no evidence of residual tumor. After 6 months of the surgery, radiographic features showed consolidation of the fibula and mandible (Fig. 2).

ES represents 4–10% of all malignant bone tumors, being the fourth most common bone malignancy after myeloma, osteosarcoma and chondrosarcoma. However, it is the second bone malignancy in children and young adults. Despite uncertain etiology, 95% of the cases present the same genetic alteration process, which is a chromosomal translocation t (11;22)(q24;q12) [5,7–10]. A total of 71 ES cases of oral cavity has been reported in the English literature, of which 6 were metastatic lesions to oral cavity [8]. Swelling (46%) was the first clinical manifestation, followed by swelling and pain (12.7%). The mandible was affected in 69% of the cases, the maxilla represented 28.2% and the soft tissues, 2.8%. The present case showed an ES affecting the anterior region of the mandible in a 7-YO boy. The lesion presented fast growth that caused facial deformity, and pain was reported during palpation.

Osteosarcoma is the main differential diagnosis of ES. Such tumor is the main malignancy of the bone and affects mainly patients in their first and second decades of life. Moreover, radiographically, both osteosarcoma and ES present as poorly delimited osteolytic lesions [11,12]. In a retrospective study, which evaluated 9411 patients in the age group 0–19 years found only 12 cases neoplasm affecting the mandible, and osteosarcoma was the most prevalent (5 cases) [12]. The "moth eaten" aspect and the periosteal reaction called 'sunburst' can also be observed in both tumors [11,13]. In the present case, cone beam tomography showed a poorly delimited osteolytic lesion, and in parasagittal sections it was possible to observe both the "moth eaten" aspect and the sunburst phenomenon. Margaix-Muñoz et al. [8] showed that dental infections were the main differential diagnoses of ES.

The small blue round cell proliferation is a histological feature common to ES, small cell osteosarcoma (SCO), mesenchymal chondrosarcoma (MCS), lymphoblastic lymphoma (LBL), rhabdomyosarcoma (RMS), neuroblastoma (NB), poor differentiated synovial sarcomas (PDSS), desmoplastic round cell tumors (DRCT), esthesioneuroblastoma (ENB) and blastemal predominant Wilms' tumor (WT). Therefore, immunohistochemistry is the most valuable method for the diagnosis of ES. CD99 (MIC2) and FLI-1, although not specific, are the main markers for ES diagnosis. However, other tumors such as LBL, RMS, SCO, and PDSS can also be positive for CD 99 [14]. The present case was immunoreactive for CD99 and S-100 protein, and negative for desmin, FLI1, CD56, CD45 and AEI/AE3. The ES diagnosis was performed according clinical/radiographic, histopathological and immunohistochemistry features.

The standard treatment for localized head and neck ES consists of adjuvant chemotherapy followed by local surgery. Radiotherapy is not frequently indicated due to its side effects, mainly in children. In the present case, the treatment consisted of adjuvant preoperative chemotherapy and mandibular resection with free fibula flap reconstruction. No tumor was observed in the surgical specimen. Disease prog-

https://doi.org/10.1016/j.oraloncology.2019.08.023
Received 29 July 2019; Received in revised form 28 August 2019; Accepted 29 August 2019
Available online 05 September 2019
1368-8375/

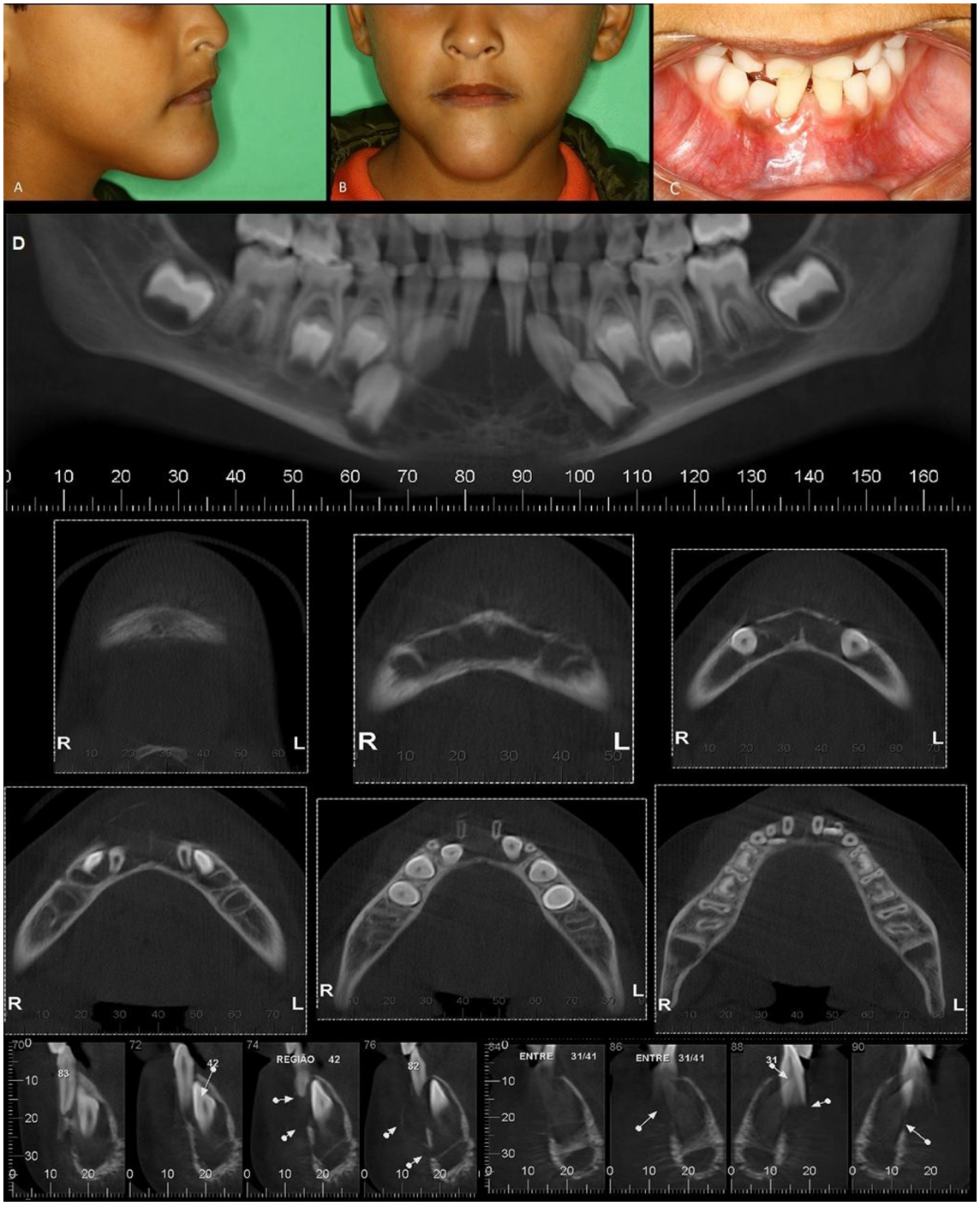

Fig. 1. Extraoral and intraoral view. **A/B:** Growth affecting the chin region, lateral and frontal view. : Displacement of the central lower incisors and enlargement of the anterior mandible region. **D:** Cone beam computed tomography. Panoramic reconstruction shows an osteolytic lesion measuring around 4 cm of extension. Axial sections present disruption of the buccal cortical bone and parasagittal sections show both moth eaten aspect and sunburst phenomenon.

nosis depends on the stage, size and location of the tumor, age of the patient and histological response after chemotherapy. Distant metastases are rare in ES of jaw, in contrast with ES of other anatomic sites that show a strong tendency to develop metastasis [9,15]. Overall survival data on located ES in the head and neck region are presumed to have a better prognosis (80%) compared to ES in other locations (56%) after 3 years of follow-up [5,9]. In patients with distant metastases, the survival rate after 5 years is less than 30% [16].

In summary, ES affecting jawbones is rare. Radiographic features such as sunburst phenomenon can occur, and osteosarcoma is the main differential diagnosis. The treatment for localized ES consists of chemotherapy and radical surgery, and ES of the mandible presents better prognosis than ES of other sites.

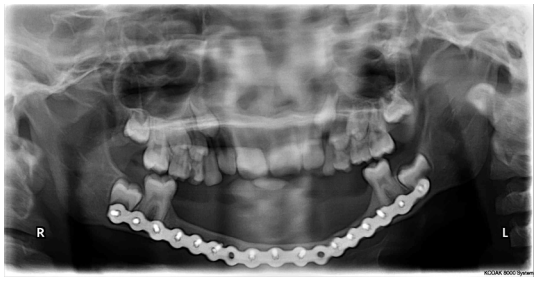

Fig. 2. Panoramic X-ray after 6 months of mandibular resection and reconstruction with microvascular free fibula flap.

Acknowledgment

We would like to thank the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) for Oliveira and Fernandes' scholarships. Fabio A. Alves is research fellow funded by the Brazilian National Council for Scientific and Technological Development (CNPq), Brazil.

References

[1] Kersting N, Kunzler Souza B, Araujo Vieira I, et al. Epidermal growth factor receptor regulation of ewing sarcoma cell function. Oncology 2018;94(6):383–93.
[2] Grier HE. The Ewing family of tumors. Ewing's sarcoma and primitive neuroectodermal tumors. Pediatr Clin North Am 1997;44(4):991–1004.
[3] WHO classification of head and neck tumours 2017;vol. 9:348.
[4] Dou X, Yan H, Wang R. Treatment of an Askin tumor: a case report and review of the literature. Oncol Lett 2013;6(4):985–9.
[5] Bölling T, Hardes J, Dirksen U. Management of bone tumours in paediatric oncology. Clin Oncol (R Coll Radiol) 2013;25(1):19–26.
[6] Qureshi SS, Bhagat M, Laskar S, et al. Local therapy in non-metastatic primary Ewing sarcoma of the mandible and maxilla in children. Int J Oral Maxillofac Surg 2016;45(8):938–44.
[7] Grevener K, Haveman LM, Ranft A, et al. Management and outcome of Ewing Sarcoma of the head and neck. Pediatr Blood Cancer 2016;63(4):604–10.
[8] Margaix-Muñoz M, Bagán J, Poveda-Roda R. Ewing sarcoma of the oral cavity. A review. J Clin Exp Dent 2017;9(2):e294–301.
[9] Yogesh TL, Shetty A, Keswani H, et al. Aggressive high-grade Ewing's sarcoma of maxilla: a rare case report. J Oral Maxillofac Pathol 2018;22(Suppl 1):S48–53.
[10] Fernandez-Pol S, van de Rijn M, Natkunam Y, et al. Immunohistochemistry for PAX7 is a useful confirmatory marker for Ewing sarcoma in decalcified bone marrow core biopsy specimens. Virchows Arch 2018.
[11] Heare T, Hensley MA, Dell'Orfano S. Bone tumors: osteosarcoma and Ewing's sarcoma. Curr Opin Pediatr 2009;21(3):365–72.
[12] de Arruda JAA, Silva LVO, Kato CNAO, Schuch LF, Batista AC, Costa NL, et al. A multicenter study of malignant oral and maxillofacial lesions in children and adolescents. Oral Oncol 2017;75:39–45.
[13] Krishna KB, Thomas V, Kattoor J, et al. A radiological review of Ewing's Sarcoma of mandible: a case report with one year follow-up. Int J Clin Pediatr Dent 2013;6(2):109–14.
[14] Folpe AL, Hill CE, Parham DM, et al. Immunohistochemical detection of FLI-1 protein expression: a study of 132 round cell tumors with emphasis on CD99-positive mimics of Ewing's sarcoma/primitive neuroectodermal tumor. Am J Surg Pathol 2000;24(12):1657–62.
[15] Owosho AA, Ko E, Rosenberg HI, et al. Primary Ewing family of tumors of the jaw has a better prognosis compared to tumors of extragnathic sites. J Oral Maxillofac Surg 2016;74(5):973–81.
[16] Gaspar N, Hawkins DS, Dirksen U, et al. Ewing Sarcoma: current management and future approaches through collaboration. J Clin Oncol 2015;33(27):3036–46.

S.V. Oliveira, L.G. Fernandes
Stomatology Department, School of Dentistry, University of São Paulo, São Paulo, Brazil

L.A.V. Soares Jr.
Dentistry Department, Clinics Hospital, Medical School, University of São Paulo, São Paulo, Brazil

M.F. Moraes
Dentistry Department of ITACI, Clinics Hospital, Medical School, University of São Paulo, São Paulo, Brazil

M.T.A. Almeida
Department of Pediatric Oncology of ITACI, Clinics Hospital, Medical School, University of São Paulo, São Paulo, Brazil

D.S. Pinto Jr.
Stomatoloy Department, School of Dentistry, University of São Paulo, São Paulo, Brazil

F.A. Alves*
Stomatology Department, School of Dentistry, University of São Paulo, São Paulo, Brazil
Stomatology Department, A.C. Camargo Cancer Center, São Paulo, Brazil
E-mail address: falves@accamargo.org.br.

* Corresponding author at: Stomatology Department, AC Camargo Cancer Center, R. Prof. Antônio Prudente, 211 – Liberdade, São Paulo, SP, Brazil.