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Clinical Paper
Head and Neck Oncology

Local therapy in non-metastatic primary Ewing sarcoma of the mandible and maxilla in children

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Abstract. Ewing sarcoma (ES) of the jaw bones comprises a small fraction of ES at all sites. Due to their rarity, a specific policy for local treatment is lacking. The aim of this study was to evaluate the local therapy for ES and recommend measures to individualize treatment options. Patients with primary non-metastatic ES of the jaw bones treated between August 2005 and February 2015 were analyzed. All patients received primary induction chemotherapy, following which lesions amenable to resection based on specific radiological criteria were resected; those with unresectable lesions were offered definitive radiotherapy. The maxilla was the primary site in 13 patients and the mandible in eight. The median age of patients was 11.6 years (range 5–17 years). Overall, surgery was performed in 17 patients and definitive radiotherapy was used in four patients. Postoperative radiotherapy was administered to 12 patients and was avoided in five patients with 100% tumour necrosis. The 3-year overall survival, event-free survival, and local control were 68.1%, 63.6%, and 80.2%, respectively. Mandible primary and a histological response to chemotherapy were significant prognostic factors. The stratification of patients based on radiological criteria aids in selecting local therapy. In eligible patients, surgery with contemporary reconstruction results in optimal oncological and functional outcomes. Surgery also has the added advantage of identifying patients who may not need radiotherapy.

Key words: head and neck cancer; Ewing sarcoma; mandible; maxilla; surgery; reconstruction; radiotherapy; chemotherapy.

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Ewing sarcoma (ES) of the jaw bones accounts for 1.8–5.2% of ES at all sites.[1–3] Although the role and impact of primary chemotherapy is well established in ES, the management of local disease remains inconsistent. Lesions of the jaw represent a distinct surgical challenge, with the possibility of functional impairment and cosmetic inadequacy.[4] Similarly, radiation for jaw lesions is restricted due to the proximity of critical structures, which may compromise the delivery of effective radiation therapy.[2] As data specific for jaw ES are limited and varied treatments are offered, a definitive and uniform policy for local treatment is lacking.[1–7] Generally, radiotherapy is reserved for large lesions that are considered unresectable. At the same time, due to concerns related to the surgical defect and the need for reconstruction, surgery is also relatively contraindicated. A randomized controlled trial comparing those with a similar extent of disease treated with surgery or radiotherapy

may perhaps resolve this issue. However, this seems unlikely since ES of the mandible and maxilla is rare. Hence, the evaluation of a case series may help in determining the appropriate treatment. The case series presented herein includes updated data for a few patient cases that have been reported previously, in order to have a sufficient number of patients to evaluate treatment outcomes and to identify risk factors.[4]

The aim of this study was primarily to evaluate the local therapy of ES and recommend measures to individualize treatment options in a given clinical scenario for patients with ES of the jaw.

Materials and methods

Patients with primary non-metastatic ES of the mandible or maxilla treated between August 2005 and February 2015 were selected from a prospectively maintained institutional database. All patients had undergone a comprehensive clinical evaluation and a core biopsy for confirmation of the diagnosis. Patients who underwent a surgical exploration elsewhere had their biopsy result reviewed at the study centre. Diagnosis was established based on histomorphology and immunohistochemical analysis. Translocation studies were performed in equivocal cases. All patients underwent investigations to exclude metastatic disease, including a whole-body technetium bone scan, chest computed tomography (CT) scan, bone marrow aspiration, and biopsy. A whole-body positron emission tomography (PET) scan was also performed in some patients ($n = 13$). Every patient case was discussed at a multidisciplinary tumour board meeting for treatment planning.

Radiology

CT or magnetic resonance imaging (MRI) was performed for all patients to evaluate the primary tumour and to assess the response to induction chemotherapy. A PET scan was performed for patients receiving definitive radiotherapy in order to assess the local response. A large volume tumour was defined as a neoplasm equal to or more than 5 cm in the greatest dimension, and a small volume tumour as one with a greatest dimension of less than 5 cm.

Chemotherapy

All patients were treated according to the institutional chemotherapy protocol for ES, which included two courses of VIE couplet (vincristine, ifosfamide, and etoposide), followed by two courses of VAC couplet (vincristine, doxorubicin, and cyclophosphamide) administered every 3 weeks as neoadjuvant/induction chemotherapy.[7] Following local therapy to the primary tumour, maintenance therapy was administered, consisting of 10 courses of chemotherapy administered every 3 weeks (four courses of VAC, two courses of VIE, and four courses of VCD (vincristine, cyclophosphamide and actinomycin D) with actinomycin D substituted for doxorubicin after a total dose of 360 mg/m^2). Vincristine was administered weekly throughout the chemotherapy schedule.

Local therapy

An absence of specific criteria on imaging, together with the possibility of achieving negative surgical margins, formed the basis of the selection of patients for surgery (Figs. 1–3). The tumour was considered unresectable if there was (1) deep infiltration of the infratemporal fossa or base of the skull, (2) involvement of the posterior ethmoid and sphenoid sinus, or (3) extensive soft tissue and skin infiltration.

Lesions amenable to surgery were resected. Patients with unresectable lesions were offered definitive radiotherapy. The surgical technique used has

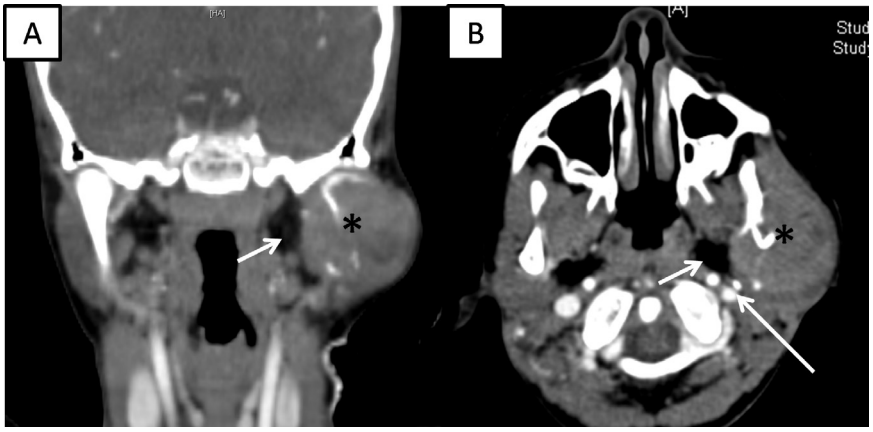

Fig. 1. Coronal (A) and axial (B) CT images showing a destructive lesion in the vertical ramus of the mandible, with an associated mass in the masticator space. The short arrows show the preserved parapharyngeal space; the long arrow shows the uninvolved carotid space. There is no destruction of the temporal bone or any intracranial extension.

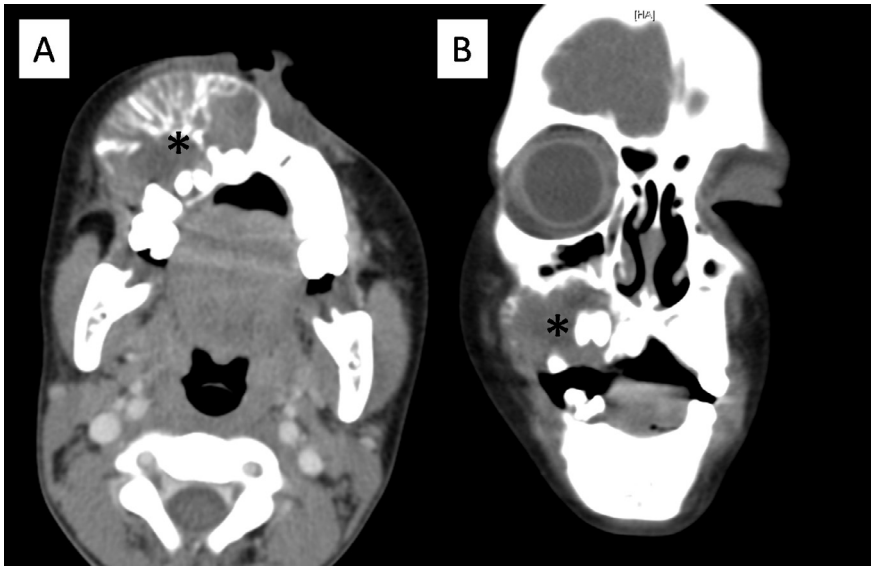

Fig. 2. Axial (A) and coronal (B) CT images showing an expansile lesion in the right side of the maxilla (*) limited to the upper alveolus, with a modelling deformity of the maxillary sinus. There is no infiltration of the infratemporal fossa.