The Journal of Laryngology & Otology
September 2003, Vol. **117,** pp. 736–738

Ewings' sarcoma of the mandible

Juan L. Quesada, M.D., Juan M. Alcalde*, M.D., Juan M. Espinosa*, M.D., Rafael García-Tapia, M.D.*

Abstract
Ewings' sarcoma involving the facial bones is rare although it is the second most frequent bone malignancy. For the diagnosis a biopsy is needed. Currently the treatment is the combination of chemotherapy and radiotherapy with surgery indicated in only a few instances. We report a case of Ewing's sarcoma of the mandible and describe its clinicopathologic features and the treatment of this disease.

Key words: Sarcoma, Ewings; Mandible

Introduction

Ewing's sarcoma is an undifferentiated round-cell tumour, first described by James Ewing in 1921. It occurs most frequently in adolescents between the ages of 10 and 15 years. It usually involves the long bones of the extremities and the pelvic bones. Involvement of the facial bones is rare and is reported in one to four per cent of cases.[1–9] The diagnosis is made from the clinical and radiological features and also by the histological analysis of the tumour. The multidisciplinary treatment of Ewing's sarcoma has improved the survival from less than 15 per cent to more than 50 per cent of cases.[3,7,9]

Case report

A 14-year-old girl was first seen in August 1994 with paresthesis in the left half of the lower lip. She was diagnosed with Bell's palsy and a course of steroids and anti-inflammatories was begun. After that she presented an ipsilateral firm and painful submandibular mass. A sialography was then performed with a normal result and the treatment was restarted. In September she noticed a parotid gland swelling and trismus. She was diagnosed of parotiditis and treatment with antibiotics and anti-inflammatories was prescribed. As she did not improve echography was performed with no changes seen. When a simple tomograph was done, a lytic lesion with Codman's triangle was seen at the mandibular angle. Computer tomography (CT) of the parotid gland showed a soft tissue mass that involved the subtemporal fossa and eroded the mandibular angle. A fine needle biopsy made the diagnosis of round cell tumour and a biopsy give the diagnosis of round cell tumour compatible with Ewing's sarcoma. She then came to our centre for evaluation and treatment.

The patient received two pre-operative courses of cyclophosphamide (750 mg/day), doxorubicin (30 mg/day) and methotrexate (18 mg/day) for three days and vincristine (2 mg/day) for two days at a 21-day interval and two more of cyclophosphamide, D-actinomycin (0.75 mg), bleomicin (14 mg) for three days and vincristine (2 mg) for two days at a 21-day interval. One month after the treatment she underwent a partial left hemimandibulectomy including the masseter muscle. The coronoid process and the head of the mandible were spared.

After surgical treatment she received five more courses with cyclophosphamide, doxorubicin, methotrexate for three days and vincristine for two days at a 21-day interval and four with cyclophosphamide, doxorubicin, methotrexate bleomicin for three days and vincristine for two days. She also received 58.8 Gy to the left hemimandible and parapharyngeal soft tissue.

Microscopically, fragments of bone and muscle showed an infiltrative tumour consistent of small and uniform cells with scanty cytoplasm and darkly staining nuclei. Neoplastic cells formed small clusters and strands growing within the marrow spaces among trabecular. Occasionally, the tumour showed a peripheral pattern, with cells surrounding small blood vessels. There were some foci of

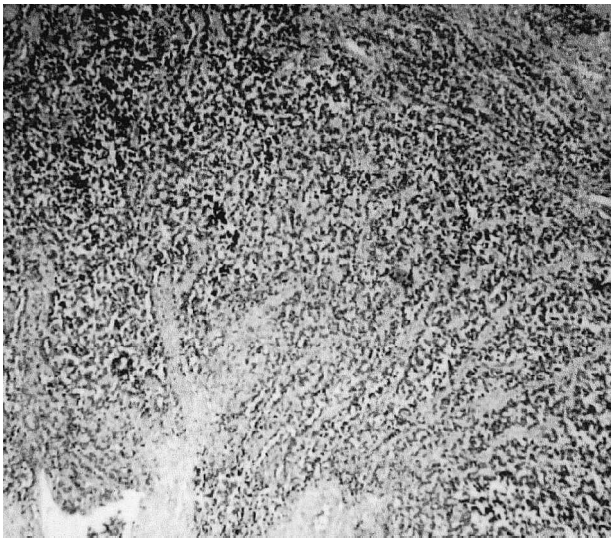

Fig. 1
Photomicrograph of the lesion showing intracellular glycogen (PAS ×40)

From the Departments of Otolaryngology–Head and Neck Surgery, Hospital General Universitario Valle Hebrón, Barcelona, and the University Clinic of Navarra*, Pamplona, Spain.
Accepted for publication: 16 June 2003.

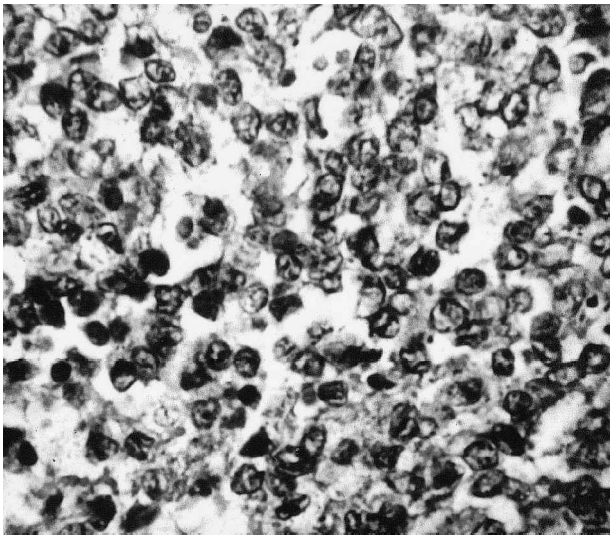

FIG. 2
Photomicrograph showing high membrane immunoreactivity for this marker (013×200)

necrosis. PAS staining demonstrated large amounts of intracellular glycogen (Figure 1). Reactive osseus in peripheral areas and fibroblastic tissue surrounding tumour cells were present. Immunohistochemically, the tumour cells stained for vimentin and CD99 antigen (O13) (Figure 2). Frozen tissue was not available to study the 11–12 chromosomal translocation. The resection margins were free of tumour except at the pterygoid muscles. The definitive diagnosis was of Ewing's sarcoma.

The patient is alive seven years after the last treatment and remains free of disease.

Discussion

Ewing's sarcoma is typically a tumour of infants, it occurs most frequently in the second decade of life. It represents the second most frequent bone malignancy of that period. Males over 13 years are affected more often than females.[3,9]

Swelling and/or pain are the most common presenting symptoms.[2–5,7,9] Others are fever, anaemia, leukocytosis, an elevated sedimentation rate and a pathologic fracture. Patients with systemic findings seems to have a lower survival rate.[4,6]

Radiologically Ewing's sarcoma is usually a poorly-defined osteolytic lesion. The 'onion-skin' periosteal reaction typical of the long bones is unusual in mandibular lesions.[2,4,5] Currently CT scan is used to better define the tumour and evaluate the soft tissue and bone invasion.

Microscopically Ewing's sarcoma shows a mass of small round cells with scant cytoplasm where by means of the periodic acid-Schiff test glycogen granules can be observed. Coagulative necrosis and rich vascularity can be associated with sheets of cells.[3–5,7,9] The tumour usually arises from the medullary or subcortical portion towards the periosteum of the bone. It can destroy the cortex and infiltrate the overlying soft tissues.

The use of immunohistochemistry helps in the diagnosis of Ewing's sarcoma, there is a strong immunoreactivity for O13 (HBA-71, 12E7, RFB-1).[8] Among the neural markers only neuron-specific enolase is positive in ES,[9] although there are studies against this conclusion.[2] The chain $\beta_{[GRA1]}2$ microglobulin from the class I histocompatibility molecules is often positive in Ewing's sarcoma and can help in distinguishing this tumour from neuroblastoma.[9]

- **This is a case report of a patient with Ewing's sarcoma of the mandible**
- **The histology, radiology and immunohistochemistry of such lesions are presented**
- **Ewing's tumours involving the mandible have been previously reported but the facial bone involvement is relatively uncommon**

Ewing's sarcoma is part of a group of undifferentiated round cell tumours and the differential diagnosis includes osteosarcoma, neuroblastoma, reticulosarcoma, rhabdomyosarcoma and lymphoma. There are other conditions that can as an Ewing's sarcoma-like histiocytosis-X, osteomyelitis, multiple myeloma and metastasis.[5,8,9] The intracellular glycogen seen in Ewing's sarcoma is absent in reticulosarcoma and neuroblastoma. Peripheral blood smears can distinguish myeloma and lymphoma.

Nowadays the treatment of Ewing's sarcoma includes chemotherapy, radiotherapy and surgery in some instances. Local control with radiotherapy alone varies between 50 and 77 per cent and long-term survival is less than 25 per cent. When chemotherapy is added, local control reaches 85–90 per cent and survival achieves 60 per cent.[5,9] The principal chemotherapeutic agents used are vincristine, cyclophosphamide, actinomycin-D and doxorubicin.[3,7,9]

The role of surgery in Ewing's sarcoma is debatable. The rationale for surgical intervention could include[7]: (1) reducing the risk for local recurrence; (2) lesion in an expandable bone; (3) eliminating tissue damage by radiotherapy.

At diagnosis, the incidence of metastatic disease varies from 14 to 50 per cent.[3,7] The lung is the most common site of metastasis, and the bone the second one. Initially, to prevent metastatic disease, whole body radiation was recommended. Currently chemotherapeutic agents are preferred as they have less toxicity, better administration and better survival rates. The primary site of Ewing's sarcoma is the most important prognostic factor.[2,7] Lesions of the head and neck have the best survival rates. Survival margins and involvement of neurovascular structures, bone or skin are important for local control of the disease.

Acknowledgement

The authors acknowledge Dr Cervera-Paz for the translation of the article.

References

1 Bessède JP, Monsaint B, Huth J, de Lumley L, Sauvage JP. Ewing's sarcoma of the mandible: a case report. *Br J Oral Maxillofac Surg* 1993;**31**:49–51
2 Siegal GP, Oliver WR, Reinus WR, Gilula LA, Foulkes MA, Kissane JM, *et al.* Primary Ewing's sarcoma involving the bones of the head and neck. *Cancer* 1987;**60**:2829–40
3 de Vita VT. Ewing's sarcoma and peripheral primitive neuroectodermal tumor. In: De Vita VT, Hellman S, Rosenberg SA, eds. *Cancer. Principles and Practice of Oncology*, 5th edn. Philadelphia: Lippincot-Raven, 2113–6
4 Sneige N, Batsakis JG. Ewing's sarcoma of bone and soft tissues. *Ann Otol Rhinol Laryngol* 1988;**98**:400–2
5 Som PM, Krespi YP, Hermann G, Shugar JM. Ewing's sarcoma of the mandible. *Ann Otol Rhinol Laryngol* 1980;**89**:20–3
6 Langman AW, Kaplan MJ, Matthay K. Ewing's sarcoma of the mandible. *Otolaryngol Head Neck Surg* 1989;**100**:74–7

7 Link MP, Grier HE, Donaldson SS. Sarcomas of bone. In: Fernbach DJ, Vietti TJ, eds. *Clinical Pediatric Oncology*. 4th edn. St. Louis, Missouri: Mosby Year Book, 1991; 559–76

8 Rosai J, Soft tissues. In: Rosai J, ed. *Ackerman's Surgical Pathology*, 8th edn. St. Louis, Missouri: Mosby-Year Book, 1996; 2021–133

9 Horowitz ME, Malawer MM, DeLaney TF, Tsokos MG. Ewing's sarcoma family of tumors: Ewing's sarcoma of bone and soft tissue and the peripheral primitive neuroectodermal tumors. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*, 2nd edn. Philadelphia: J.B. Lippincot Company, 1993; 795–816

Address for correspondence:
Dr Juan L. Quesada,
Pº San Gervasio 59,
08022 Barcelona,
Spain.

Fax: +34.932746013
E-mail: jquesada@hg.vhebron.es

Dr Juan Quesada takes responsibility for the integrity of the content of the paper.
Competing interests: None declared