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Ewing's tumor of the jaws

Douglas D. Damm, DDS Dean K. White, DDS, MSD
James F. Drummond, DDS, MSD, PhD Gerald A. Ferretti, DDS, M Dent Sc

Abstract

Ewing's tumor is a disease of children and adolescents with rare occurrence after the third decade of life. Involvement of the jaws is uncommon. The clinical and radiographic presentations are highly variable and may mimic an inflammatory lesion. An example of metastatic Ewing's tumor to the maxilla in a 13-year-old female is presented. A review of Ewing's tumor of the jaws is presented with emphasis on the clinical findings, treatment, and prognosis.

James Ewing[1] initially described the primary malignant tumor of bone bearing his name in 1921. He described the disorder as a diffuse endothelioma of bone because the form of the neoplastic cells suggested an endothelial nature and because these cells rarely were found lining fine spaces which contained red blood cells. He stressed that this lesion is distinctly different from osteogenic sarcoma, since it presents different clinical and histological features and because it is sensitive to radiation.

The origin of the neoplastic cells of Ewing's tumor has been elusive. A number of sophisticated studies utilizing light microscopy, electron microscopy, cytochemistry, and cell culture techniques have failed to provide an explanation which is agreeable to all. Immature reticulum cells,[2,3] primitive myeloid cells,[4] hemangiogenic cells,[5] immature mesenchymal cells,[6,7] and histiocytic cells[7] all have been presented as the possible cell type represented by Ewing's tumor. A hypothesis presented by Llombart-Bosch et al.,[7] if true, would help explain the variety of theories on the origin of Ewing's tumor. They suggest that the tumor is not a unique neoplasm but a heterogeneous collection of small round cell sarcomas of bone. They describe the pluripotential marrow mesenchymal cell with its ability to differentiate along fibroblastic, histiocytic, and angioblastic cell lines as the cell of origin responsible for the difficulty in deciding on a single cell of origin.

The typical histologic pattern of Ewing's tumor consists of dense collections of uniform cells which exhibit basophilic round to oval nuclei with an associated slightly granular cytoplasm and indistinct cell outlines.[8] These cells tend to aggregate into packets which are surrounded by thin strands of fibrous tissue. Reticulin staining demonstrates fibers normally present only within the fibrous septa or around blood vessels. The cellular packets are typically devoid of reticulin fibers. Periodic acid-Schiff (PAS) stain reveals the presence of glycogen in the cytoplasm of the tumor cells in more than 90% of the cases.[9]

Ewing's tumor is a disease of children and adolescents, rarely occurring after the third decade of life.[9] The disease exhibits a male predilection.[8] The tumor may occur in any bone, but it is seen predominantly in the lower extremities and pelvic girdle.[8,9] Involvement of the jaws is uncommon. In one of the larger series of Ewing's tumor Dahlin[8] reported only 1% of 299 cases occurred in the jaws. Clinical reports of Ewing's tumor metastatic to the jaws also are few in number.[10]

The following case describes a patient with primary Ewing's tumor of the right pelvis with a secondary involvement of the maxilla.

Clinical Report

A 13-year-old Caucasoid female presented to the Orthopedic Clinic of the University of Kentucky Medical Center with the chief complaint of intermittent pain in the right hip for the previous year. During the previous month, the pain had increased in

intensity and was associated with exercise and direct pressure to the area.

The physical examination was within normal limits except for a right flank fullness which extended laterally to the buttocks. Liver enzymes were normal; an intravenous pyelogram displayed deviation of the right ureter medially; bone scan disclosed increased uptake in the right iliac wing; and CAT scan revealed an expansile lytic lesion of the right ileum with a marked soft tissue involvement. An incisional biopsy was performed and a diagnosis of Ewing's tumor was made.

The patient received 6420 (4500 large field and 1920 reduced field) rads of radiation treatment to the right hip mass. In addition, a four-drug chemotherapeutic regimen which included adriamycin, Cytoxan®, vincristine, and actinomycin D was administered. The Cytoxan produced bladder toxicity and the adriamycin was associated with cardiac changes; therefore, both eventually were discontinued. All chemotherapy ceased approximately two years after initial presentation.

Chest radiographs taken four months after completion of the chemotherapy revealed several lung lesions. Bone marrow biopsy and bone and liver scans were negative for tumor. The patient again was placed on Cytoxan, vincristine, 5-fluorouracil and BiCNU, but this therapy was discontinued because the lesions progressed during chemotherapy.

Because of lack of response to the chemotherapy, the patient was administered 4000 (1500 whole lung and 2500 reduced field) rads of radiation therapy. Following this therapy, a nodularity of the left mid-lung still was present even though it was considerably smaller. A 1000 rad boost to this area was scheduled, but after receiving 400 rads, the patient did not return.

Approximately one month later, the patient returned complaining of mild chest pain on the left side. Chest radiographs revealed both fluid and the nodularity of the left lung. There was question whether the nodularity represented a persistent tumor or fibrotic changes. Without any other known sites of active disease further irradiation was declined and the patient was told to return in one month for a new chest radiograph.

Within six weeks, the patient was referred by her local dentist to the University of Kentucky Department of Pediatric Dentistry for evaluation of acute pain and swelling of her right mid-face. Upon presentation, the patient was receiving penicillin as prescribed by her dentist. Extraoral observation revealed extensive right facial swelling with inflammation of the overlaying skin. Intraoral examination disclosed a large distal carious lesion of the right maxillary first molar and overeruption of the second molar which exhibited a Class IV mobility. The radiographs disclosed a large distal carious lesion of the first molar, overeruption of the second molar, and extensive loss of bone support of both the first and second molars (Fig 1). The differential diagnoses included metastatic Ewing's tumor versus an inflammatory lesion orginating from the first molar.

Excavation of the carious lesion in the first molar revealed deep involvement but no pulpal exposure. Because of the mobility and the pain associated with the second molar — in addition to the lack of an inflammatory cause for the changes — extraction of the second molar with curettage of the socket was performed. When removed, the molar was found to have a 3 x 1cm mass of friable, tan, soft tissue attached to its radicular surface. The specimen was submitted to the University of Kentucky Department of Oral Pathology for histologic examination.

The microscopic sections of the soft tissue exhibited a dense sheet of round to oval, lightly basophilic nuclei which presented a sparse speckled chromatin pattern. The nuclei were surrounded by a finely granular eosinophilic cytoplasm which exhibited poorly defined cell outlines. Rare mitotic figures were seen. Thin fibrous supporting septa were noted coursing through the sheets of neoplastic cells (Fig 2). Reticulin staining revealed no fibers present within the cellular proliferations. Widely scattered tumor cells demonstrated a positive cytoplasmic reaction with the PAS stain and this staining was not present in the PAS stain with diastase. Large areas of necrosis were present; scattered islands of viable tumor cells were seen encircling blood vessels within the necrotic zones (Fig 3). An overlaying acute inflammatory infiltrate was present predominantly in the areas of necrosis. A diagnosis of metastatic Ewing's tumor was made.

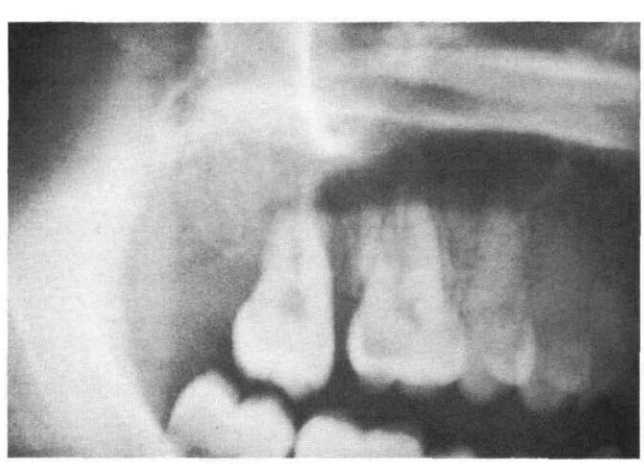


FIG 1. Panoramic view of the right maxilla which depicts overeruption of the second molar and significant bone loss.

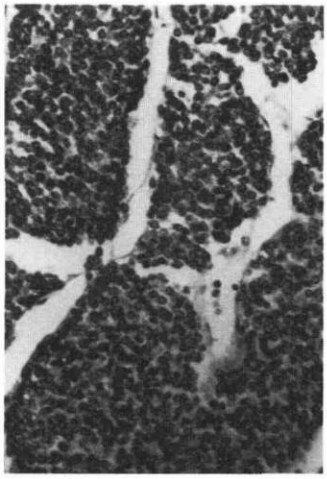
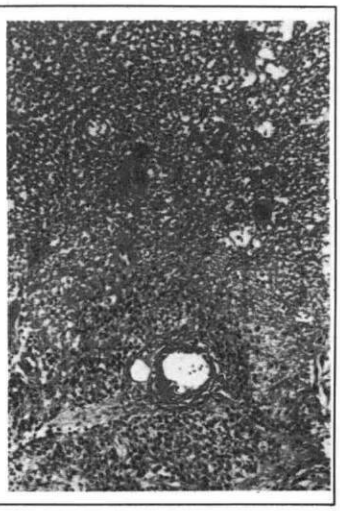


FIG 2. (*left*) Sheets of neoplastic cells supported by thin fibrous septa. The tumor cells are seen as lightly basophilic nuclei with finely granular ill-defined cytoplasms. (H&E stain; original magnification 100x)

FIG 3. (*right*) Scattered islands of viable tumor cells encircling blood vessels within the necrotic zones. (H&E stain; original magnification 40x)



Secondary to the discovery of active disease in the right maxilla, the patient was placed on a chemotherapeutic regimen which included Cytoxan, vincristine, and 5-fluorouracil. Over the next seven months, she presented with worsening respiratory distress and severe pain which required large doses of analgesics. The patient developed a progressive dyspnea over a five-day period and died of cardiopulmonary arrest secondary to pulmonary complications of metastatic Ewing's tumor approximately three and a half years after her initial presentation.

Discussion

A search for clinical reports of Ewing's tumor of the jaws published in English from 1921 to 1983 revealed 111 cases. With this case, 112 examples are included in this review.

In 26 of the cases, no location was stated. Of the remaining 86 examples, 77 were primary in the jaws and 9 were secondary lesions. In primary jaw involvement, the mandible (52 cases) was involved twice as often as the maxilla (25 cases). Of the nine secondary lesions, three originated from the femur, two from the radius, and one each from the tibia, fibula, rib, and pelvis. The secondary lesions in the jaws exhibited the same mandibular predominance with twice as many occurring in that location. The current example is the first known clinical report of a secondary jaw lesion in Ewing's tumor which originated from the pelvis.

The age and sex of the patients were reported in 77 of the 112 cases. The age range was from 2 to 44 years of age, with the mean occurrence at 16. Twenty-six per cent occurred in the first decade, 48% in the second decade, and only 26% after the age of 19. In the current review, 43 males and 34 females were reported; this produced a 1.26:1 male predominance.

An extensive radiographic description was not present in many of the cases reviewed. No radiographic finding has been found to be diagnostic of Ewing's tumor,[11] and it may appear similar to many entities both inflammatory and neoplastic.[11,12] Radiographic features which were seen in the review included: cortical expansion and thickening; ragged, ill-defined radiolucencies; opacification of the maxillary sinus; adjacent soft tissue masses; and variable amounts of a periosteal reaction. An "onion peel" or "sun ray" periosteal reaction has been described in Ewing's tumor in long bones,[11] but several authors[13-15] have mentioned that this is a rare finding in the jaws. Fifteen examples of periosteal reactions of the jaws in Ewing's tumor were found.

An initial oral symptom was reported in 71 instances. In several of these cases, more than one symptom was noted. The list of symptoms in decreasing prevalence were swelling (56 cases), pain (26), epistaxis (4), tooth mobility (3), paresthesia (3), trismus (1), numbness (1), chronic sinusitis (1), and nasal stenosis (1). Tooth mobility and displacement has been mentioned by deSantos and Jing[16] as a helpful guide in the clinical separation between neoplastic and inflammatory disorders. They remarked that inflammatory lesions produced resorption of teeth with little or no displacement while rapidly growing neoplasms like Ewing's tumor produced marked displacement of the teeth without significant resorption. This case exhibited overeruption of the right second maxillary molar without significant root resorption.

Bones involved with Ewing's tumor often present with hemorrhage, necrosis, and an overlaying soft tissue mass[17] which mimics an inflammatory process.

The current case supports the similarity because the patient presented with signs and symptoms of an inflammatory process and the referring clinician had prescribed penicillin in response to that presentation.

Sixty-three of the previous reports described the method of treatment. Surgery, radiation, chemotherapy, and various combinations all were utilized. The most appropriate method of therapy is controversial because of the low percentage of cures. Bhansali and Desai[18] found radiation was the most frequent treatment for Ewing's tumor because the tumor was very radiosensitive, but Dahlin[8] preferred surgery with adjunctive chemotherapy. Recently, in a study of 303 cases, Kissane et al.[19] demonstrated that in localized cases, radiation therapy in combination with multiagent chemotherapy produced a prolonged survival rate of 40%.

Follow ups were presented in 57 of the oral cases. Thirty-nine patients (68.4%) were dead of their disease at the time of publication and only four (7%) patients had survived longer than five years. Five-year survival of all Ewing's tumors was approximately 15%[20] and has been related to the presence or absence of metastatic lesions at diagnosis, the site of the initial lesion, the age of diagnosis, and the presence of systemic symptoms — especially fever.[21] Peripheral lesions like those of the mandible and those distal to the knee and elbow were associated with improved survival.[21]

Conclusion

The current case and the literature review present several important points for the pediatric dentist.

1. Ewing's tumor in the jaws is a relatively rare entity.
2. The disease is most frequent in the second decade of life.
3. The clinical and radiographic presentations are highly variable and may mimic an inflammatory lesion.
4. Displacement of teeth without significant resorption appears to be correlated more to a neoplastic process rather than an inflammatory one.
5. Appropriate therapy is difficult to define, although recent limited success has been achieved with radiation and multi-agent chemotherapy.
6. Long-term survival is approximately 15%, with a better prognosis associated with distally located primary sites.

Dr. Damm is an associate professor, oral pathology; Dr. White is an associate professor, oral pathology; Dr. Ferretti is an associate professor, pediatric dentistry; and Dr. Drummond is a professor, oral pathology, College of Dentistry, University of Kentucky, Lexington, KY 40506. Reprint requests should be sent to Dr. Damm.

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