Vol. 96 No. 3 September 2003

ORAL SURGERY
ORAL MEDICINE
ORAL PATHOLOGY

CLINICOPATHOLOGIC CONFERENCE

Editor: John R. Kalmar

Huge cystic mandibular mass

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(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96:253-7)

CLINICAL PRESENTATION

A 19-year-old woman presented with a dramatic but painless mass of the mandibular symphysis region (Fig 1). She had first noticed the lesion more than 4 years earlier and reported that it had undergone gradual progressive enlargement since that time. She denied undergoing trauma to the area and said that she had no pain or other symptoms associated with the swelling. Despite her cosmetic disfigurement, the patient had not previously sought treatment because of socioeconomic reasons. Her medical and dental history was otherwise unremarkable. During a clinical examination, the mass was found to be bony, firm, and nontender and seemed confluent with the anterior and inferior borders of the mandible. In the midline area immediately below the residual inferior border of the mandible, the mass was slightly depressible when gentle digital pressure was applied. The anterior mandibular teeth were immobile and vital.

A modified posteroanterior projection radiograph revealed a large, unilocular radiolucency of the mandibular symphysis with internal septations and prominent cortical sclerosis (Fig 2). Magnetic resonance imaging revealed a hypointense cystlike lesion measuring 18 × 12 cm with a high fluid level (Fig 3). Focal areas of cortical discontinuity were seen at the anterosuperior margin. These findings were considered most suggestive of either a cystic process or a well-circumscribed, intraosseous, homogenous soft tissue mass with cystic change.

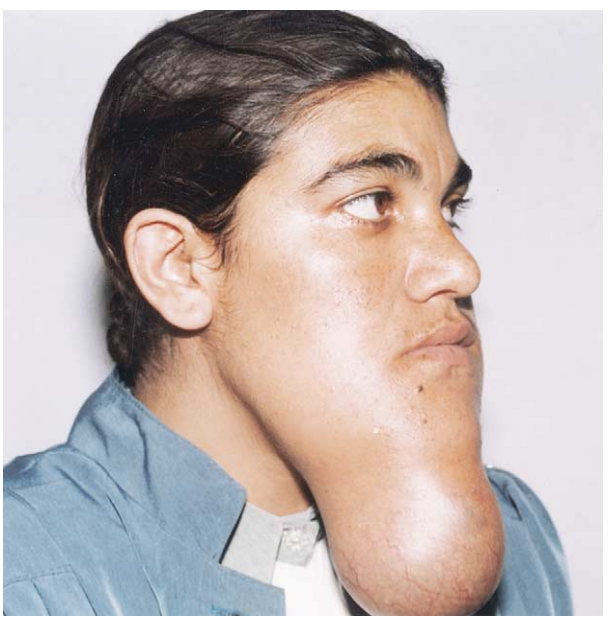


Fig 1. A clinical photograph of our patient shows a prominent mass of the mandibular symphysis.

DIFFERENTIAL DIAGNOSIS

A substantial number of conditions affecting the jaws may present with a cystic radiographic appearance.[1] Several odontogenic cysts and cystic tumors have the potential to reach considerable sizes. Unicystic amelo-

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Received for publication Mar 26, 2002; returned for revision Dec 27, 2002; accepted for publication May 9, 2003.
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1079-2104/2003/$30.00 + 0
doi:10.1016/S1079-2104(03)00354-8



Fig 2. A radiograph of the patient reveals an ellipsoid, well-corticated, expansile radiolucent lesion with fine internal septa extending from the symphysis to the left mandibular ramus. Focal thinning and cortical erosion of the inferior border can be seen.

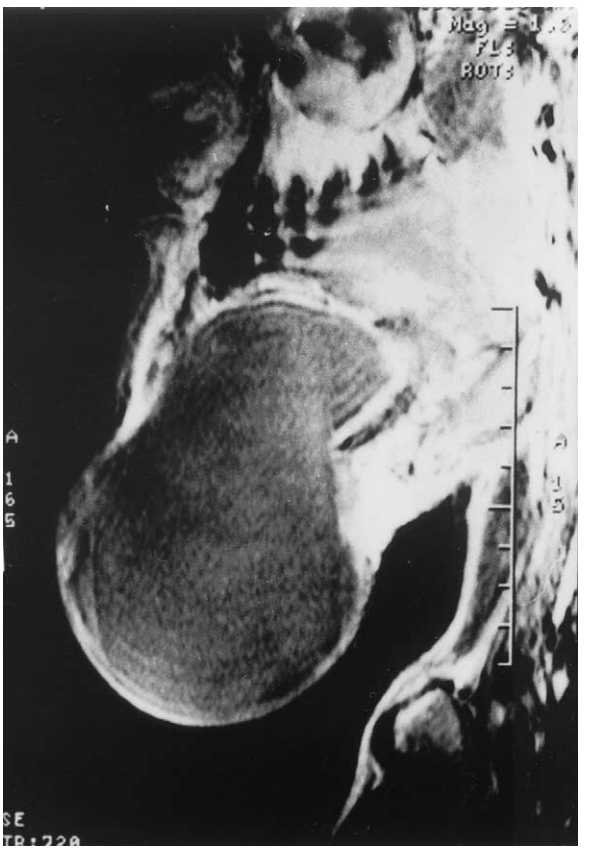


Fig 3. A T1-weighted sagittal magnetic resonance image of the lesion reveals both a uniform hypointense signal with a high fluid level and evidence of focal cortical destruction at the superior margin.

blastoma often presents as a large unilocular radiolucency in young individuals; however, this lesion usually occurs in the posterior mandible, is typically associated with an impacted tooth, and exhibits minimal peripheral sclerosis. An odontogenic keratocyst can initially present as a unilocular radiolucency, but significant cortical expansion is unusual and large lesions typically exhibit a multilocular radiographic appearance. An expansile radiolucent lesion of the anterior mandible crossing the midline in a young person warrants consideration of central giant cell granuloma and the brown tumor of hyperparathyroidism. However, as with odontogenic keratocysts, long-standing lesions of central giant cell granuloma usually present as multilocular radiolucencies. With respect to brown tumor, blood tests ordered during patient workup revealed normal levels of serum parathormone and calcium. These findings essentially excluded the possibility of hyperparathyroidism.

Among benign fibro-osseous conditions, central ossifying fibroma can appear as a well-corticated, expansile radiolucent lesion. More commonly, however, long-standing lesions often present with a mixed radiopaque/radiolucent appearance, exhibiting variable amounts of apparent calcified material. Aneurysmal bone cyst (ABC) affects young patients and may present as marked cortical expansion in the jaw. The radiographic appearance of ABC is predominantly radiolucent with fine internal septations, but these lesions rarely exhibit prominent peripheral sclerosis. ABC may also occur in association with a variety of anatomically contiguous pre-existing lesions, including central giant cell granuloma and benign fibro-osseous lesions. Arteriovenous malformations can cause significant bony expansion and may present as either a unilocular or multilocular radiolucency. In addition, associated peripheral sclerosis suggestive of reactive new bone formation may be seen. Traumatic (simple) bone cyst typically affects children and young adults and can have radiographic similarities to the lesion in our pa-

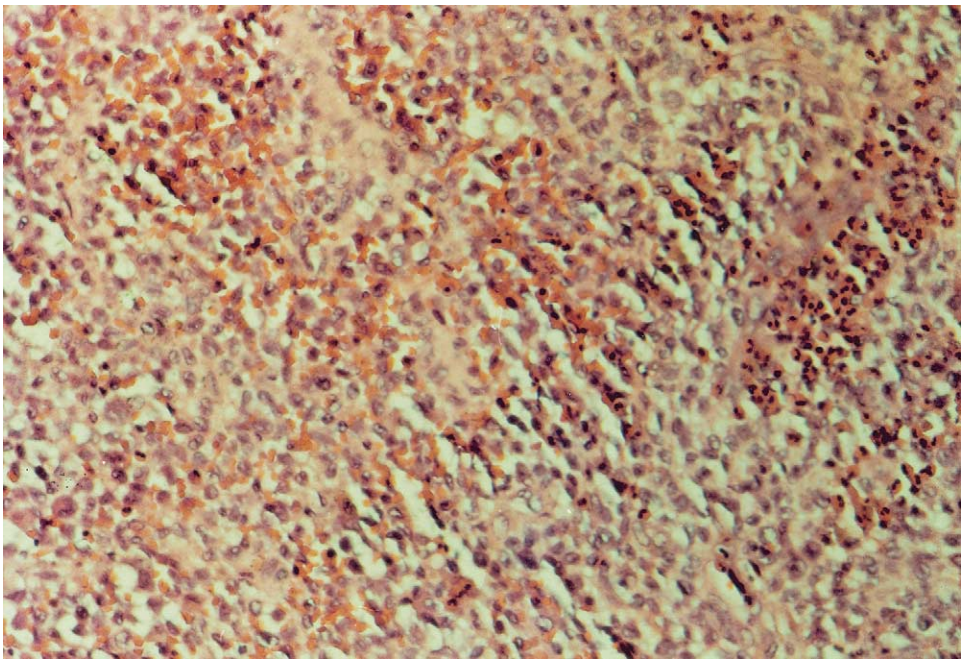


Fig 4. Dense infiltrate of large mononuclear cells with irregular nuclei admixed with clusters of eosinophils (hematoxylin-eosin, original magnification ×200).

tient, but dramatic cortical expansion is unusual. Traumatic bone cyst can also occur in association with other conditions such as benign fibro-osseous lesions.

Mucoepidermoid carcinoma may on occasion arise centrally within the jaws and affect young individuals. Central mucoepidermoid carcinoma is a radiolucent process, with margins that can vary from well defined and corticated to ragged and infiltrative. Chronic osteomyelitis can simulate a malignant bone tumor both radiographically and clinically, but it is usually associated with irregular bone destruction and local symptoms such as pain and tenderness.[2] Langerhans cell histiocytosis, including eosinophilic granuloma (EG), may present in young patients as a painless, well-defined radiolucency with sclerotic margins, but prominent cortical expansion is not typically observed.[1,3-5]

Ida et al[6] examined a variety of disease categories of the jaws, including osteomyelitis, trauma (hematoma), cysts, and benign and malignant tumors, with respect to the occurrence of peripheral sclerosis and periosteal reactions. They suggested that an irregular periosteal reaction and cortical destruction were typically associated with trauma, infection, or malignancy. Given the uniform, sclerotic periosteal reaction seen in our patient, we felt that the findings of diagnostic imaging were most supportive of either a cystic process or a benign neoplasm with cystic change.

DIAGNOSIS

With the patient under general anesthesia, the lesion was extraorally approached, then aspirated, and yellowish, serous fluid was recovered. Soft tissue access was achieved, and a bony window was created, which revealed a cystlike, fluid-filled cavity. No cyst lining could be readily identified, significant hemorrhage was not observed, and there was no evidence of solid tumor. The wall of the cavity was curetted, and fragments of soft tissue resembling granulation tissue were submitted for a histopathologic examination. The histopathologic examination disclosed extensive aggregates of large mononuclear cells resembling macrophages, together with clusters of eosinophils. The histiocytic cells had irregular nuclear outlines, including indentations and grooves; a vesicular chromatin pattern; and abundant, faintly eosinophilic cytoplasm (Fig 4). Scattered multinucleated giant cells were noted, as were infiltrates of plasma cells and lymphocytes. Immunohistochemical staining with an antibody probe for S-100 protein revealed positive expression within the mononuclear histiocytic cells (Fig 5). Neither an aneurysmal bone cyst nor a solitary bone cyst was histopathologically identified within the submitted specimen.

The final diagnosis was Langerhans cell histiocytosis (EG) with extensive cystic degeneration.

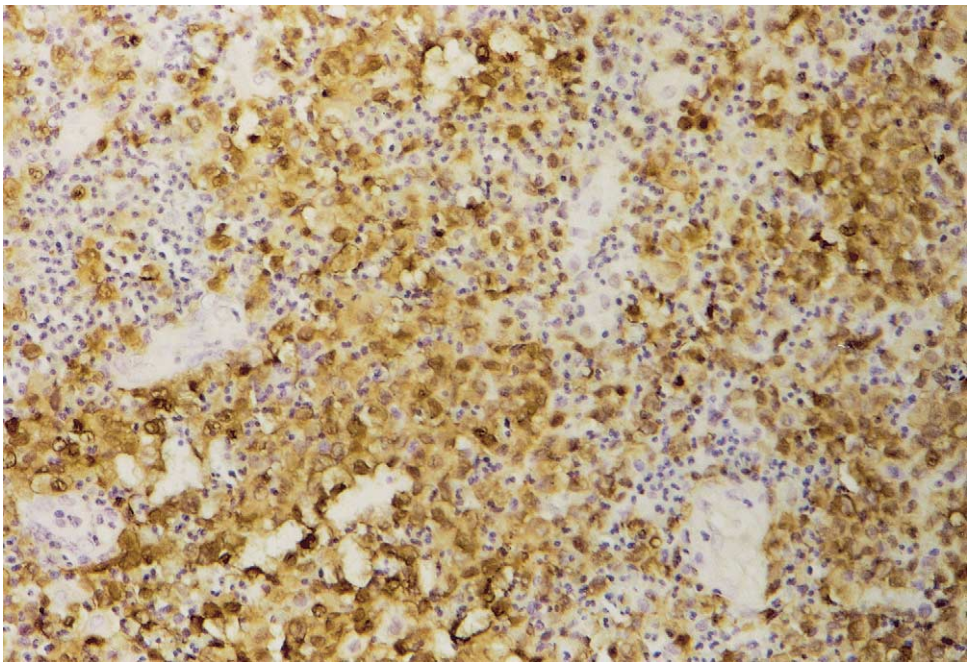


Fig 5. Langerhans' cells of the jaw lesion express S-100 protein, as indicated by brown staining (immunoperoxidase stain with a probe for S-100 protein; hematoxylin counterstain, original magnification ×200).

MANAGEMENT

In consultation with the patient and her family, a treatment plan consisting of thorough surgical curettage followed by low-dose radiation was developed. With the patient under general anesthesia, the lesion was accessed through a submandibular approach and 450 mL of serous fluid was evacuated from the central cystic cavity. Peripheral curettage was performed to remove the rim of lesional tissue. Care was taken to preserve the mandibular cortex in areas that were thin and fragile. After surgical curettage, a relatively unremarkable level of bleeding from the bony walls of the cavity was observed. No grafting material was placed in the defect, and the periosteal and soft tissues were closed primarily. The surgical site healed without complication. The histopathologic appearance of the curetted material was consistent with Langerhans cell histiocytosis, with no persuasive evidence of either concurrent ABC or traumatic bone cyst. After the removal of the cutaneous sutures, the patient was referred to the oncology service for radiotherapy. The patient received 2 Gy weekly for 6 weeks through 4 mV of photon radiation delivered to a depth of 3 cm. Several months after radiotherapy, the area appeared to be healing normally and mandibular augmentation was scheduled to re-establish the normal contours of the mandible. This was accomplished without complication by using an iliac bone autograft. During the second procedure, a biopsy specimen from the symphysis area was obtained, revealing dense fibrous connective tissue with no evidence of recurrent or residual EG. The patient recovered without complications from her reconstructive surgery and has been without symptoms or findings indicating pathosis for more than a year.

DISCUSSION

Langerhans cell histiocytosis, previously known as *histiocytosis X*, is a condition characterized by the proliferation of a histiocyte-like, dendritic mononuclear cell (Langerhans' cell). A variety of clinical presentations have been described, including (1) isolated or multiple lesions arising in bone (monostotic or polyostotic EG); (2) chronic disseminated histiocytosis (Hand-Schüller-Christian disease) often with skin, bone, and visceral involvement; and (3) acute disseminated histiocytosis (Letterer-Siwe disease) characterized by a predilection for occurrence in infants and often presenting with extensive cutaneous, visceral, and bone marrow involvement. Classically described as distinct clinicopathologic conditions, these forms of Langerhans cell histiocytosis are now recognized as having considerable clinical overlap. The prognosis is related to the number of sites and organs involved at the time of diagnosis and to patient age. The prognosis for older patients with Langerhans cell histiocytosis is more fa-

vorable than for young children or infants with this disorder.[7]

Approximately 10% to 20% of all isolated and polyostotic cases of skeletal Langerhans cell histiocytosis (EG) arise in the jaws. The posterior mandible is the most frequently affected site. Associated swelling and pain may be minimal or absent, and the first manifestation of disease can be spontaneous bony fracture. The striking clinical finding of a large mandibular mass in our patient was thought to be highly unusual for EG. A review of the literature failed to yield a previously reported, well-documented example of this disease presenting as a huge cystic mass in the mandible.[4,8,9]

Radiographically, EG often appears as a sharply demarcated radiolucent lesion with a corticated border, but early and aggressive lesions may have poorly defined margins. In the jaws, involvement of the alveolar bone may produce a focal radiolucent defect that can mimic severe periodontitis.

Microscopically, lesions of EG are characterized by infiltrating mononuclear cells that resemble histiocytes. The cells usually possess a lightly staining, eosinophilic cytoplasm with indistinct borders and nuclei that often have prominent grooves and indentations. Characteristically present in Langerhans cell disease, eosinophils can be widely variable in number—not only within the spectrum of this disorder, but also in different portions of a single surgical specimen. Other inflammatory cells, including lymphocytes, plasma cells, macrophages, and multinucleated giant cells, can be seen. Focal hemorrhage and necrosis may also be observed. Immunohistochemistry has facilitated the identification of the lesional cells, because Langerhans' cells strongly express S-100 protein and CD1a, a pattern not seen in normal macrophages. EG is recognized as 1 of several lesions able to secondarily give rise to aneurysmal bone cyst.[10] The diagnostic imaging results from and the clinical and surgical features of the current patient were suggestive of ABC developing within the lesional tissue, but a careful histopathologic evaluation of both the biopsy and curettage specimens failed to provide evidence of ABC. However, given the unusual clinical presentation, we felt that the possibility of EG-induced ABC could not be completely excluded.

The most common treatment for isolated cases of EG is surgical enucleation and curettage. Other modalities that have been used include local radiation therapy, systemic corticosteroids, intralesional corticosteroids, and systemic chemotherapy. In the series presented by Ardekian et al,[11] all the patients were treated with enucleation, with or without peripheral ostectomy, and with radiotherapy. The authors recommended the use of a combination of surgery and low-dose radiotherapy for EG of the jaws, but they noted that additional studies are needed to establish the optimal protocol for this disease.[4,9,11]

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