Alveolar ridge mass with multifocal intraosseous radiolucent lesions

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THE CHALLENGE

A 56-year-old woman was evaluated in the Department of Oral and Maxillofacial Surgery, College of Dentistry, University of Florida, Gainesville, for a painful swelling of the left mandibular vestibule (Figure 1). She reported having experienced pain in the area, beginning as localized tooth pain, for several years. She then developed a mass in the left mandibular vestibule and a progressive loss of sensation to the left mandibular lip and chin. The swelling and numbness had been present for about 10 months at the time of her clinic visit. She also noted that her partial denture no longer fit secondary to the pain and swelling. Her medical history included type 2 diabetes mellitus, hypertension, hypercholesterolemia, hypothyroidism, and glaucoma and cataracts. Her medications included several antihypertensive medications, insulin and thyroid hormones.

The clinical examination revealed a large left vestibular swelling that had displaced her mandibular left posterior teeth (Figure 1). A panoramic radiograph revealed a multilocular radiolucent lesion of the left mandible (Figure 2). The patient underwent computed tomographic imaging, which revealed a large destructive lesion involving the left mandible (Figure 3). An oral surgeon performed a biopsy. The patient underwent further laboratory blood, serum and urine studies. A skeletal survey revealed radiolucent lesions in the skull (Figure 4), clavicles, pubic bones and right humerus.

Can you make the diagnosis?

A. Metastatic malignancy
B. Langerhans cell histiocytosis
C. Multiple myeloma (plasma cell myeloma)
D. Hyperparathyroidism (multiple brown tumors)
THE DIAGNOSIS

Multiple myeloma (plasma cell myeloma) consists of a monoclonal proliferation of malignant plasma cells. It accounts for about 1 percent of malignancies overall in the United States but nearly 50 percent of all primary bone malignancies in the United States. It affects primarily an older population, and men are affected more often than are women. The etiology of this condition is not totally clear, but in some cases a higher incidence has been seen in those exposed to radiation, pesticides and other chemical carcinogens.

Clinical presentation. The most common clinical presentation is that of bone pain. Anemia or thrombocytopenia also may occur. Renal insufficiency is a complication in later stages of the disease, as can be pathological fractures. Diagnosis is made by means of identification of an increase in plasma cells in the bone marrow (> 30 percent). Also required for diagnosis are a monoclonal increase in a serum M protein other than immunoglobulin (Ig) M (usually IgG in 70 percent or IgA in 20 percent of all cases of multiple myeloma) and an increase in either the κ or the λ light chain. Patients also may have free light chains in the urine (Bence Jones proteins). Multiple lytic lesions of bone are noted on radiographic skeletal surveys, with common sites being vertebrae, the skull, pelvic bones, the ribs, the humeri and the femurs.

About 70 to 96 percent of patients with multiple myeloma in the United States may have lesions of the maxilla or mandible, according to Regezi and colleagues. Oral plasma cell neoplasms may appear in several forms: localized multiple myeloma, solitary plasmacytoma of bone or extramedullary plasmacytoma of soft tissue. Approximately 3 percent of plasma cell neoplasms are solitary plasmacytomas involving bone, according to Knowling and colleagues. Extramedullary plasmacytoma is rarer still overall, but it has been reported in the nasal cavity, larynx, nasopharynx and palatine tonsils and intraorally in the tongue, palate and parotid gland. Multiple myeloma of the oral cavity can manifest as gingival masses, expansion of bone, toothache, tooth mobility or migration, soft-tissue ulceration or gingival bleeding, or radiographically as multiple, “punched-out” radiolucent lesions that may be destructive or move teeth. The patient also may have mandibular paresthesia, sometimes termed “numb-chin syndrome.”

In approximately 10 percent of patients, the systemic deposition of amyloid material in soft tissue is associated with multiple myeloma. Sites may vary throughout the body, but the most common oral site is the tongue, where it manifests as a firm enlargement or macroGLOSSIA. The primary microscopic feature of multiple myeloma is the presence of neoplastic plasma cells (Figure 5) that invade and replace normal tissue. Immunohistochemical staining performed for antibodies against the λ and κ light chain immunoglobulins, which are produced by the plasma cells, mark a mostly monoclonal population of only one antibody type in multiple myeloma, differentiating it from benign or reactive plasmacytic proliferations. In normal B-cell populations, the κ:λ ratio is usually 2:1, and these two proteins are distributed randomly with respect to one another. In the case described in this article, the clinicians performed immunohistochemical staining—including markers for plasma cells and light chain immunoglobulins (Figures 6 and 7)—that revealed strong monoclonal positivity for λ, a light chain immunoglobulin. Blood studies performed for this patient revealed elevated IgA λ monoclonal proteins, and urinalysis demonstrated the presence of free λ light chains.

Treatment. Treatments for multiple myeloma include radiation therapy and chemotherapy. Intravenous bisphosphonate chemotherapy may pose a dental complication in the form of increased incidence of bisphosphonate-related osteonecrosis of bone. In the majority of cases, the disease is aggressive and results in a poor prognosis, with a five-year survival rate of approximately 25 percent. The patient described in this article underwent one round of radiation therapy at our institution before transferring to another facility to continue chemoradiation therapy. Follow-up information for this patient is unavailable.

DIFFERENTIAL DIAGNOSES

Metastatic malignancy. Metastatic cancers to the jaw are most commonly from breast, lung, thyroid, colorectal, prostate and kidney cancers. Most patients are older than 60 years, and sex prevalence depends on the type of primary cancer. The vertebrae, ribs, pelvis and skull are the most common sites of metastasis. The mandible is affected much more often than
is the maxilla. Clinically, the patient usually exhibits a soft-tissue mass, pain, loosening of teeth or paresthesia. Radiographically, the patient usually has an ill-defined radiolucency, sometimes described as “moth-eaten,” that may mimic radiolucencies similar to those seen in periodontal disease; the lesion can result in widening of the periodontal ligament space and may even appear as a mixed radiolucent-radiopaque lesion if it is the result of a bone-producing carcinoma. This patient’s lesions radiographically were more well-defined than would be expected in metastatic malignancy. In addition, the histopathological examination of a metastatic lesion typically would demonstrate features similar to those of its origin.

**Langerhans cell histiocytosis.** Eosinophilic granuloma, the mildest form of Langerhans cell histiocytosis (LCH), may be seen in the jaws and skull, as well as other areas such as the long bones, pelvis and vertebrae. In adults, it has been estimated that the jaws are involved in 30 percent of cases of LCH and the skull in 21 percent. The mandible is the more commonly affected jawbone. Oral manifestations may include a soft-tissue mass, pain, gingivitis and loosening of teeth, and ulcer. Radiographic manifestation in the jaw lesions may vary but may be described as a “teeth floating in air” similar to the appearance of destructive periodontitis or as intraosseous round, oval or irregular radiolucencies that may appear punched out. However, LCH generally is considered a disease of children and young adults; most patients who have it are younger than 20 years. Therefore, this patient did not fall into the likely demographic. The eosinophilic granuloma form of LCH, which would be the most likely of the forms to be seen in this patient’s age group, usually is a solitary lesion, unlike the lesions in this case. In addition, the histopathological features of LCH are characterized by the infiltration of Langerhans cells (histiocytelike cells) and the presence of varying numbers of eosinophils.

**Hyperparathyroidism (multiple brown tumors).** Brown tumors of bone are a signal of the terminal stage of hyperparathyroidism and may be seen in the mandible, ribs, clavicles and most often pelvis. The maxilla is involved less often. Clinically, brown tumors may appear as a mass or a bony expansion. Radiographically, they may appear as well-defined unilocular or multilocular radiolucent bodies. The tumors may resorb roots. The lesions may be solitary or multiple. A ground-glass radiographic appearance of bone and loss of lamina dura also can be seen and will be evident if the disease has advanced to a brown-tumor–production stage.

Primary hyperparathyroidism most often affects women older than 60 years (usually resulting from a parathyroid adenoma) and usually manifests with hypercalcemia and hypophosphatemia. Secondary hyperparathyroidism usually is associated with chronic renal disease; patients with this condition will have hypocalcemia and hyperphosphatemia. The patient described in this article did not have laboratory values consistent with these characteristics, nor was ground-glass bone or a generalized loss of lamina dura present on the panoramic radiograph. Also, this diagnosis is seen rarely now, as hyperparathyroidism most often is diagnosed via serum calcium level testing before it progresses to this end stage. The histopathological features of a brown tumor are similar to those of central giant cell granuloma, in which the presence of numerous giant cells with multiple nuclei is the distinctive feature.

**CONCLUSION**

Multiple myeloma may manifest with a variety of intraoral clinical findings, including bone...
pain and paresthesia, soft-tissue swelling or mass, toothache, tooth mobility or movement, bony expansion, and radiographic findings generally in the form of multiple radiolucencies that may have a punched-out appearance. In cases that appear initially in the oral cavity, it may be difficult to differentiate clinically and radiographically between multiple myeloma or plasmacytoma and a range of other differential diagnoses, including even inflammatory lesions such as osteomyelitis. Clinicians should refer any suspect lesions for biopsy and appropriate follow-up testing to determine the diagnosis. In addition, in patients who have received a diagnosis of multiple myeloma, the dentist should manage dental care vigilantly and be aware of accessory complications related to the disease and treatment such as renal failure, bleeding disorders, amyloidosis and potential development of bisphosphonate-related osteonecrosis. ■

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