

## The Tip of the Iceberg

**L**ast year, I was asked to write a piece on “anything I wanted” for my component society newsletter. In pondering a topic, I realized I had been seeing a series of patients with a very confusing problem, and I wrote an article about them. After its publication, the state oral and maxillofacial surgery association asked to reprint it for its members, and I have since received a request from another component society to publish it in their newsletter. The Dental Board of California had the issue on the agenda for a recent meeting due to the growing concern for these patients. As a result of this, I would like to offer a modification of the original article to our readers.

This is neither a scientific article, nor is it an absolutely pure editorial. It is not supported with any significant research, laboratory studies, or extensive literature reviews.

There exists a subset of patients that has a very significant problem that needs to be shared with the dentists in our community. There is growing concern about these people that is supported by some articles and observations by other clinicians.<sup>1,2</sup> It is my hope I can share my experiences in what is believed to be an escalating problem.

There are a number of radiographic lesions of the jaws associated with systemic conditions. Within this group are primary bone tumors along with metastatic tumors from distant malignancies as well as osteoporosis. Specifically, multiple myeloma, metastatic breast cancer and metastatic prostate cancer create radiolucent or sometimes mixed lesions that can be seen in the jaws.

Treatment of these diseases is complex with many modalities and therapeutic agents used. Some of the more commonly accepted and increasingly popular agents in these and other tumor management protocols are bisphosphonates, used to inhibit osteoclastic activity and limit the spread of the disease within the bone. These drugs, such as zoledronate (Zomeda) and pamidronate (Aredia) are given intravenously once a month. Alendronate (Fosamax) is an oral form of the drug used in the treatment of osteoporosis, usually in the postmenopausal female.

One of the apparent, but not scientifically well documented, side effects of these drugs is altered bone metabolism resulting in what has been termed bisphosphonate-associated osteonecrosis. This is a condition where the bone in the jaws necroses spontaneously or more frequently as a result of a dental traumatic etiology such as an extraction or an ill-fitting prosthesis.

Patients complain of pain, possible purulent drainage if there is a secondary infection, loose teeth or exposed bone in their jaws. Examination will reveal a variety of findings. In some patients, there may be little that is noted to be abnormal; in others, it will be obvious there are small or impressively large amounts of exposed necrotic bone. These are the extreme presentations with a host of possibilities in between.

Radiographically, and paralleling the clinical findings, there may be no obvious bone pathology to the extremes of radiolucent areas within the jaws. Frequently, there appears to be a mottled, dysplastic bone present in the area of the symptom-



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atic sites. Poorly healing extraction sites in the affected area are common. Rarely is a specific sequestrum identifiable, and on some occasions, spontaneous fracture of the mandible can be noted.

This condition needs to be differentiated from acute or chronic osteomyelitis as well as osteoradionecrosis. Osteomyelitis is a pure infection of the cancellous and cortical portions of the bone that generally is of bacterial origin. It can be acute or chronic, and has limited margins within the bone. Osteoradionecrosis is a condition where the bone in a field that has had significant radiation loses vascularity with ultimate necrosis and possible exposure. Bisphosphonate-associated osteonecrosis has some of the characteristics of each of these conditions but is neither. There is not an obvious infectious cause and the patient has not had radiation.

The tendency in these patients is to perform endodontic procedures on many of the teeth in the area that is symptomatic, usually in the absence of a better diagnosis. This is likely to be unsuccessful since the origin of the pain is not dental, but rather from the necrotic bone. Subsequent to endodontics, apicoectomy or extractions are done. Such surgical procedures results in a potential acceleration of the problem with increasing bone necrosis.

We are left with the question: How do we treat them? Philosophically, as dentists, we are taught to “do” for our patients. It must be recognized, for this group of patients, “doing” may be more deleterious than not doing. While it is sometimes difficult to take a cognitive approach with our patients, it is imperative we establish a good working diagnosis and consider the implications of treatment before we perform invasive procedures. The first rule of medicine is to do no harm.

A good treatment philosophy for bisphosphonate-associated osteonecrosis

is to counsel the patient and advise them of the nature of their problem including the long-term poor prognosis for healing. It is very helpful to put the complication into perspective relative to the control of the malignancy that is offered by bisphosphonates. My interaction with the primary care hematologists and oncologists has, in the past, supported this philosophy of management. Make every attempt not to do any invasive procedures unless absolutely indicated. When a patient is acutely infected with purulent discharge noted, culture, and sensitivities (although likely they will grow oral flora) are indicated, as well as topical antibacterial rinses and irrigation. Systemic antibiotics that are appropriate for the oral flora are often prescribed as well.

For the patient with chronic exposed bone, minimal or no treatment is a good method of preventing further harm. When spicules of bone are loose, certainly, limited debridement is helpful to the patient. Rough edges can be smoothed gently with a bone file without anesthesia since the bone is dead. This is a procedure that may need to be repeated intermittently. Hyperbaric oxygen has not been shown to be of great value in re-establishing vascularity to the area.

Marginal or segmental bone resections have been done by some of our colleagues. In the treatment of osteoradionecrosis or osteomyelitis, surgeons resect back to bleeding bone since there is an end to the radiation field or area of bone infection and the damage that accompanies it. While it has been reported that segmental resections to bleeding bone can be done, in bisphosphonate-associated osteonecrosis patients, it is unclear as to whether or not that trauma will precipitate additional bone necrosis. This puts the clinician in a difficult situation of develop-

ing a successful margin. Bone grafting with cancellous bone or with vascularized grafts are relatively contraindicated since the grafts are unlikely to heal to the necrotic bone edges.

There is no indication as to the number of patients on these drugs who are experiencing this problem, and the epidemiology is unclear. Patients with osteoporosis who take oral bisphosphonates do not appear to be at-risk levels equivalent to the intravenous drug group, though there are a growing number of reported cases in that group as well. It also has been noted that cessation of the drug does little to change the prognosis for these patients since the damage has already been done. In cases where the bisphosphonates are continued for the systemic well-being of the patient, it is unclear whether or not additional damage ensues.

We have a problem that has developed in a subset of patients with very serious diseases. There may be no alternative to the cessation of bisphosphonate therapy in some primary or metastatic bone malignancies. We all will be seeing more patients with this problem — either self-referred or coming from their treating physicians. As dentists, we are reminded that thinking rather than doing is always the best course of action, as it is always in the best interest of the patients. It is being suggested that a pretreatment dental evaluation and care as in radiation patients would be appropriate. However once the patient presents with symptoms, a word to the wise ...

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**Reference:** / 1. Ruggiero SL, et al, Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases. *J Oral Maxillofac Surg* 62(5):527-34, 2004.

2. Marx RE, Pamidronate (Aredia)- and zoledronate (Zometa)-induced avascular necrosis of the jaws: a growing epidemic. *J Oral and Maxillofac Surg* 61(9):1115 (letter to the editor), 2003.

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