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ISSUES RELATED TO DIAGNOSIS AND TREATMENT OF BISPHOSPHONATE-INDUCED OSTEONECROSIS OF THE JAWS

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Abstract
Bisphosphonate medications, used primarily to treat cancer patients and those with osteoporosis, have been linked to osteonecrosis of the jaws. Patients are considered to have bisphosphonate-induced osteonecrosis of the jaws (BIONJ) if they are being or have been treated with a bisphosphonate, have exposed bone in the maxillofacial region that has persisted for more than 8 weeks, and have no history of radiation therapy to the jaws. Patients may present with pain, swelling and discharge, an area of exposed bone, mobile teeth, they may have more subtle complaints, such as a feeling of heaviness in the jaw or numbness. Treatment generally consists of antibiotic and antifungal agents, and oral hygiene must be diligently maintained. However, BIONJ, especially in the advanced stages, may be refractory to treatment, and surgical debridement and resection may be necessary to alleviate pain and eliminate infection. Because of the widespread use of bisphosphonate medications, medical and dental professionals must be able to knowledgably advise their patients concerning the serious potential side effect of treatment, and all treating clinicians must work diligently together to coordinate care. Well-designed studies are needed to establish treatment protocols.

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*(A complimentary copy of this article may be downloaded at **www.thesystemiclink.com.**)*

Key Words: Avascular necrosis, bisphosphonate, jaw, osteonecrosis, osteoporosis, bone cancer

Introduction

With increasing frequency, dentists are making complex diagnostic decisions for their patients who take bisphosphonate medications, which are linked to osteonecrosis of the jaws. The scientific literature presents conflicting information regarding the impact of bisphosphonate-induced osteonecrosis of the jaws (BIONJ) in medicine and dentistry. Articles range from those that express doubt about the role of bisphosphonates as a cause for BIONJ[1] or attempt to prove a lack of impact on surgical procedures,[2] to those suggesting formal treatment protocols.[3–5] At least 1 textbook is devoted entirely to the issue of BIONJ.[6]

Compounding the confusion is the medicolegal environment surrounding BIONJ. A simple Internet search yields a dozen or more solicitations directed toward patients who have been treated with bisphosphonates, especially the oral forms, alendronate and risedronate. One of the authors of this article (MLW) has even received a solicitation from a law office that included a pamphlet for the author to give to patients who might be interested in pursuing litigation.[7]

In this environment of misinformation and litigation anxiety, it is paramount that dental and medical caregivers have a clear understanding of the development, clinical presentation, and treatment of BIONJ. This article will review these issues in an effort to provide clinicians with adequate information on which to base treatment decisions.

Definitions and nomenclature

Several terms have been used to describe osteonecrosis of the jaw, including osteoradionecrosis (ORN), "phossy jaw,"

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avascular necrosis of the jaw, and bisphosphonate-related or -associated osteonecrosis of the jaw. ORN is distinctly different from BIONJ in that ORN patients experience hypoxic tissue changes in a localized area of radiation exposure.[8] In addition, ORN patients typically respond to treatment (e.g., hyperbaric oxygen, surgical debridement or resection and subsequent reconstruction of the necrotic segment), whereas BIONJ patients often do not.[9–11] Similarly, the term "phossy jaw" is more correctly used to describe nonhealing bone found only in the mouth of phosphate miners and match-factory workers in the late 1800s.[10]

Finally, the scientific literature includes such terms as avascular necrosis of the jaw, bisphosphonate-related osteonecrosis of the jaw, and bisphosphonate-associated osteonecrosis of the jaw.[1,3-5,11] The most recent evidence supports a more specific term: BIONJ. Patients are considered to have BIONJ if they fulfill the following 3 criteria:

1. *Current or previous treatment with a bisphosphonate*
2. *Exposed bone in the maxillofacial region that has persisted for more than 8 weeks*
3. *No history of radiation therapy to the jaws*[4]

History

The first description of exposed, nonhealing bone in the mouths of patients receiving intravenous (IV) bisphosphonate medication was in a 2002 textbook by Marx and Stern;[12] however, the relationship between bisphosphonate use and bone exposure was not fully appreciated at that time.

In September 2003, Marx[13] published a series of 36 cases of what was then termed "avascular necrosis" in patients being treated with IV bisphosphonates, zolendronic acid and pamidronate. In the following month, the medication's manufacturer, Novartis,[i] issued a denial of any causal relationship.[1] Then in December 2003, and March 2004, Marx and other colleagues[14] involved in the care of patients receiving bisphosphonates were invited by Novartis to participate in a review of cases in an attempt to further define the problem. The result was development of recommendations for treating BIONJ patients.[15]

In April 2004, Estillo and Van Posnak[16] published a retrospective case study report. This was followed in May by Ruggeirio's report[17] on a series of 63 patients with BIONJ. A precaution was added to the labels of zolendronic acid and pamidronate, and the medical community was informed via a "Dear Doctor" letter[18] regarding the potential for BIONJ. While the vast majority of patients were taking the IV forms of bisphosphonate drugs, a small number of patients were taking an oral form, alendronate or residronate and, in July of 2005, the United States Food and Drug Administration (FDA) required that a cautionary statement[19] be added to the alendronate product literature.

However, perhaps the most noteworthy article in terms of public notification of the problem appeared in the *Wall Street Journal* in December 2004.[20] As print and electronic media began to pick up the story, public awareness grew quickly, and the number of case reports increased.

One question, however, continues to mystify clinicians: Why wasn't BIONJ seen in the studies that preceded FDA approval of the bisphosphonate drugs? In fact, 6 cases of BIONJ were diagnosed during these studies,[21] but it was not recognized that the abnormality might be secondary to the bisphosphonate medication.

To date, more than 2,000 cases of BIONJ have been reported to the FDA,[22] but it is essential for clinicians to maintain perspective on the bisphosphonate problem. In an editorial in the *Journal of Oral and Maxillofacial Surgery*, Assael[22] stated, "While this is an important clinical problem, it should not be allowed to deny patients the important benefits of these drugs or prevent researchers from investigating the potential benefits yet to be gained from bisphosphonates ... Bisphosphonates have done enormous good in fending off hypercalcemia in malignancy, decreasing bone pain and decreasing the risk of often catastrophic pathologic fracture of the femoral neck or spine." Although some successful therapeutic protocols for treating BIONJ patients have been reported,[4,23] to date, no well-controlled prospective studies of treatment outcomes exist.

Bone metabolism

In order to understand the action of bisphosphonates, it is essential to first review normal bone metabolism. The skeleton, along with the coordinated efforts of the kidneys, parathyroid glands, and intestines, plays a significant role in maintaining calcium homeostasis in the body.[24] The skeleton consists of hard cortical bone and trabecular bone. Within trabecular bone is the bone marrow, which is filled with precursor cells capable of differentiating into osteoclasts or osteoblasts. These are the 2 predominant cells responsible for bone remodeling and they secrete substances that either act on other cells or become immobilized in the mineral matrix of bone.[25] Osteoblasts mature into osteocytes which are the most numerous cell type in the mineralized bone matrix. This mineralized matrix becomes a rich source of a number of growth factors, including insulin-like growth factors 1 and 2 (IGF_1 and IGF_2) and bone morphogenic protein (BMP).[26]

[i] East Hanover, NJ

As serum calcium decreases, the parathyroid gland is stimulated to produce parathyroid hormone (PTH). One of the biological actions of PTH is to stimulate osteoclastic bone resorption in an effort to release calcium from the bone into the bloodstream. PTH stimulates the release of the receptor activator of nuclear factor κB ligand (RANK-L) from the membrane of the osteoblast. RANK-L binds to the osteoclast receptor (RANK), causing osteoclastic stimulation and bone resorption. Osteoprotegerin (OPG) is a decoy receptor that competes with the RANK receptor for association with RANK-L. When RANK-L is bound to OPG it is not available to bind to the osteoclast, thereby reducing bone resorption.[24] Therefore, osteoclastic activation or inhibition is regulated by the RANK ligand system (Figure 1).

The stimulated osteoclast secretes acid into the mineral matrix, releasing IGF_1, IGF_2, and BMP. These then bind to the osteoblast precursors, resulting in differentiation, stimulation and maturation into osteoblasts which are responsible for bone formation. Figure 2 provides a slide of a histological section of viable bone.

In cancer patients, this precise hormonal and cellular regulation is significantly, and often lethally, disrupted. Systemically, multiple tumor factors are secreted, including PTH-related protein (PTHrP), resulting in exacerbated PTH-like function. In certain cancers (e.g., lung, breast, and prostate), bone metastases are common[24] most commonly involving the axial skeleton, particularly the long bones, pelvis, and vertebrae.[27] Osteolytic metastases locally produce PTHrP, which stimulates RANK-L production and inhibits OPG secretion from osteoblasts, thereby activating excessive osteoclastic resorption. The results of this osteolysis include hypercalcemia of malignancy, pathologic fractures, including vertebral compression fractures, and compression of neural foramina, including direct compression of the spinal cord.

Osteoporosis also represents an imbalance in bone remodeling, but to a much lesser extent. In healthy individuals, resorbed bone is replaced by an equal amount of new bone; in individuals with osteoporosis, resorption exceeds formation.[28] Increased osteoclastic activity and/or decreased osteoblastic activity are integral components of this imbalance. The various aspects of osteoporosis are discussed elsewhere in this issue of *Grand Rounds in Oral-Systemic Medicine*,[29] but it should be noted that osteoporosis can be a debilitating and sometimes lethal disease. Twenty percent of patients who sustain a hip fracture secondary to osteoporosis die in the ensuing 3 months; 50% never walk again.[30]

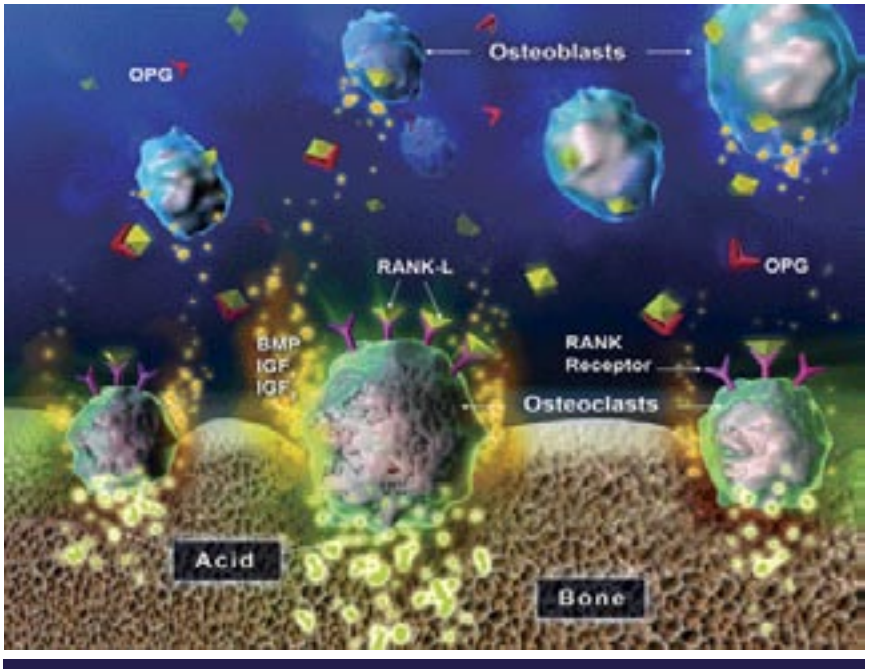

Figure 1: Cellular function in bone metabolism

At the cellular level, bone metabolism is largely mediated by the RANK ligand system. Osteoblasts secrete RANK-L which binds to the RANK receptor on the osteoclast causing bone resorption. As the osteoclast dissolves bone, IGF_1 and IGF_2, along with BMP, are released from the bone and cause osteoblastic growth, producing new bone. OPG competes with the RANK receptor to bind RANK-L, thereby inhibiting osteoclastic bone resorption.

Bisphosphonates

Bisphosphonates were first synthesized by chemists in the late 1950s as a viable substitute for polyphosphate, a compound used in detergent manufacturing that caused scale to form in manufacturing boilers. However, in 1964 the use of these compounds was discontinued by the Environmental Protection Agency because they were not biodegradable.[30]

In 1966 bisphosphonates were first administered to living animals, and an increase in bone mass was noted. In the late 1970s low bone mass was shown to be associated with fracture, and by 1984 the 2 concepts had been linked. Eleven years later, the oral bisphosphonate alendronate was approved by the FDA for the treatment of osteoporosis.[30] Relatively soon thereafter other oral agents, residronate and ibandronate, were approved. The first injectable form of bisphosphonate, pamidronate, was approved for the treatment of bone metastases in 1991, and the more potent zolendronic acid

received approval 10 years later.[17] A third injectable agent, ibandronate, was approved for use in osteoporosis patients in 2006.[31]

Bisphosphonates do not kill osteoblasts as might be assumed. Rather, they interrupt the cycle responsible for osteoclastic structure.[30] Specifically, the nitrogen-containing bisphosphonates inhibit the conversion of dimethylallyl diphosphate into farnesyl diphosphate, which is important for the structural integrity of osteoclasts.[30] Without prenylation of their guanosine triphosphate–binding proteins, the osteoclasts undergo apoptosis. Without osteoclastic function, the bone becomes devoid of its cellular components (Figure 3) and unable to remodel. In addition, bisphosphonates affect osteoblastic activity, resulting in increased production of OPG. OPG has a competitive inhibitory effect on RANK-L, thereby further decreasing osteoclastic stimulation.[32]

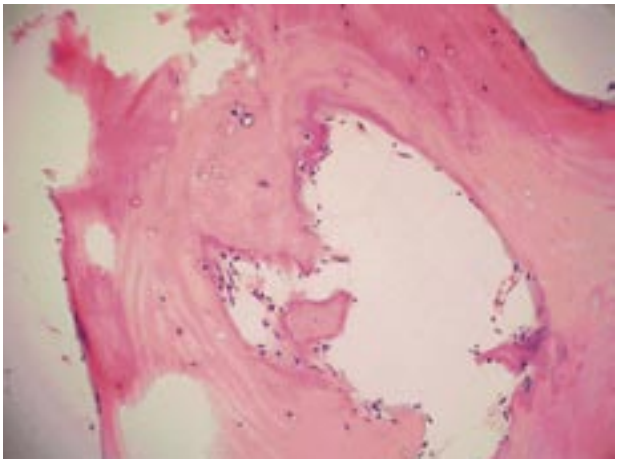

Figure 2: Histological section of viable bone

This slide demonstrates normal bone with osteocytes within the lacunae and the usual complement of osteoblasts and osteoclasts.

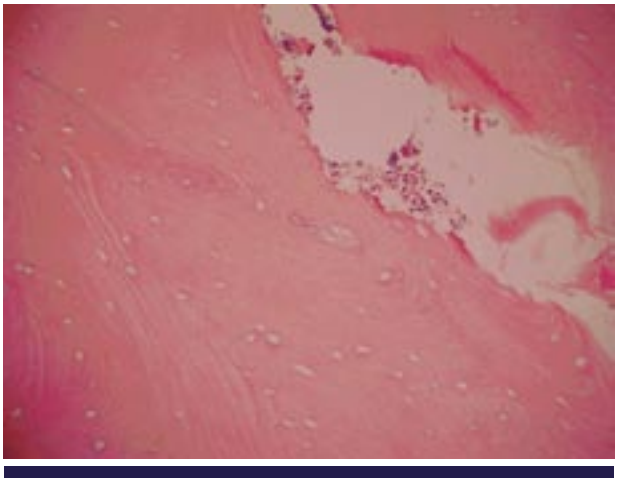

Figure 3: Histological section of necrotic bone tissue

In contrast to the previous slide of viable bone (Figure 2), in this image of bone, the lacunae are devoid of osteocyctes and there is no evidence of osteoclastic or osteoblastic activity. In addition, scattered collections of neutrophils and focal bacterial colonization are seen.

Five different nitrogen-containing bisphosphonate agents are currently available in the U.S.[30,33] (See Table 1 entitled *Bisphosphonate Agents Currently Available in the U.S.*, which may be accessed and downloaded from the *Clinical Decision-Making Tools* section at www.thesystemiclink.com). Two other bisphonsphonates, etidronate and tiludronate, are non-nitrogen-containing agents used primarily in the treatment of patients with Paget's disease and have not been implicated in BIONJ. Their potencies are approximately 1,000 times less than those of the weakest nitrogen-containing bisphosphonates.[33]

In a lecture to the American Association of Oral and Maxillofacial Surgeons, Kimmel[30] proposed the concept of an "anti-resorptive unit" (AR), a unit of measure that could be used to compare the potencies of bisphosphonates in terms of their anti-resorptive action. For example, the injectable bisphosphonates zolendronic acid and pamidronate have a potency of 80 to 100 AR/month, which is 30 to 40 times the potency of the oral bisphosphonates alendronate, residronate, and ibandronate (2 to 6 AR/month). This significant difference accounts for the earlier onset of BIONJ in patients treated with IV agents (6 to 12 months) compared with oral agents (>3 years). Both types of agents have extremely rapid uptake into the skeleton (50% within 30 minutes) and demonstrate a special affinity for areas of rapid bone turnover. Black and colleagues[34] postulated that because the alveolar processes demonstrate a 10-fold increase in bone turnover relative to other parts of the skeleton, this may be the reason that bisphosphonate-induced osteonecrosis to date has been found only in the jaw.

BIONJ incidence

The true incidence of BIONJ is difficult to determine for several reasons. First, because it is a relatively new entity, it has often gone unrecognized in patients treated for exposed bone in the oral cavity.

Second, the incidence of BIONJ is also difficult to determine because not all practitioners have reported known cases to MedWatch,[ii] thereby leading to under-reporting of the disease.

[ii] FDA Safety Information and Adverse Event Reporting Program. Available at: http://www.fda.gov/medwatch/

Third, online surveys of cancer patients that have been conducted are not controlled and may result in only a small population of interested patients answering the survey with a potential for over-reporting.

Perhaps the best estimate of BIONJ incidence in cancer patients comes from a retrospective chart review[35] of 297 multiple myeloma patients, 81 breast cancer patients, and 69 prostate cancer patients who received bisphosphonate therapy between January 1, 2000, and December 31, 2005. The results showed an incidence of 5.39% in multiple myeloma patients, 2.5% in breast cancer patients, and 2.9% in those with prostate cancer.

Determining the incidence of BIONJ in patients taking oral bisphosphonates is made even more difficult by the fact that the actual number of patients receiving these medications is not known and can only be estimated. One estimate, based on numbers of prescriptions written for alendronate, established an incidence of 0.007%, or 0.7/100,000 person-years of exposure.[36] In Australia the estimated incidence of BIONJ in patients treated with alendronate is 0.01% to 0.04%, again based on prescription data.[4] After tooth extraction this rate increased to 0.09% to 0.34%. Although these numbers appear quite small, they must be viewed in the light of Intercontinental Marketing Services Health[iii] data showing that to date, more than 190 million prescriptions for oral bisphosphonates have been dispensed worldwide.[37]

Diagnosis of BIONJ

Signs and symptoms. BIONJ patients may present with various complaints. Marx and Sawatari found that 68.9% of patients presented with an area of exposed bone and pain, 31.1% presented with asymptomatic exposed bone, 23.5% with 1 or more mobile teeth, and 17.6% with a cutaneous fistula, mucosal fistula, or bone exposed through the skin.[23] An expert panel[38] also noted that patients may have more subtle complaints, such as a feeling of heaviness in the jaw or numbness. Eighty-one (68.1%) bone exposures occurred in the mandible alone, 33 (27.7%) in the maxilla, and 5 (4.2%) occurred in both jaws.[23]

Imaging. In the early stages of BIONJ, plain radiography is not especially useful. The most common findings are a hyperostotic lamina dura and widened periodontal ligament.[23,39] However, periapical and panoramic radiographs are helpful in ruling out other causes of dental pain, as well as metastatic lesions.

In more advanced cases, the clinician may diagnose larger areas of osteolysis, sequestra, or osteomyelitis. Computerized axial tomography may assist in identifying the extent of these more severe sequelae and is essential if a resection is planned.

Laboratory examination. Recently, a serum test used to evaluate bone turnover has been successfully applied in BIONJ patients. The C-terminal cross-linked telopetide (CTx) test has been used in metabolic studies as an indicator of the rate of bone renewal.[40,41] Chailurkit stated, "Biochemical markers of bone turnover appear to be of use in assessing early response to therapy. Bone resorption markers, especially serum CTx, are better indicators than bone formation markers for estimating the response to therapy in early postmenopausal women."[42] Marx[39] has established that serum CTx values <100 pg/mL are associated with a high risk of developing BIONJ; values of 100 to 150 pg/mL, a moderate risk; and values >150 pg/mL, minimal to no risk.

The CTx test is performed by Quest Diagnostics[iv] at 1 of 2,000 service centers across the country. Locations may be identified online at http://www.questdiagnostics.com. The test must be ordered by a qualified health professional and the patient must fast for 12 hours beforehand. A small amount of blood is drawn and sent to the Quest Diagnostics facility in California, and results are available in 5-7 working days.[43]

Treatment of BIONJ

Before beginning IV bisphosphonate therapy, patients should be examined by a dentist and an oral and maxillofacial surgeon who are knowledgeable about BIONJ. Appropriate consultations from other dental specialists are advised, especially the input of the periodontist. Appropriate imaging studies should be performed and correlated with the clinical examination. If the patient has existing dental needs, the treating physician and the dentist must decide whether to delay therapy until dental health is achieved.[4] Any such patient must then become a priority for treatment by the dental team. If extractions or other dentoalveolar surgery are necessary, adequate time for bone healing must be allowed prior to initiating IV bisphosphonate treatment. The length of this healing period depends on the type of procedure being performed and on the patient's overall systemic health, but a period of 4 to 8 weeks is ideal. The goal of treatment for this group of patients is to support them in such a manner that they can continue with oncologic treatment.[4] This support would include addressing significant periodontal needs, completing any restorative treatment that might preclude a tooth from becoming abscessed, and adjusting any removable prosthesis to assure there will be no soft tissue breakdown after bisphosphonate treatment has begun. Consideration should be given to removal of large,

[iii] www.imshealth.com

[iv] Corporate Headquarters, Plymouth Meeting, PA

multilobular mandibular tori since they are often sites where BIONJ develops. It is imperative that these decisions be made with the patient's oncologist.[4,36] Guidelines for handling dental needs that arise in patients already receiving bisphosphonate therapy depends on proper staging of their BIONJ.

Staging of BIONJ

Determining the stage of BIONJ is necessary to direct medical therapy and establish the patient's prognosis. A staging system proposed by the American Association of Oral and Maxillofacial Surgeons[4] has been modified by the authors to include CTx testing and is discussed in the text that follows.

Stage 0. Stage 0 patients are typically asymptomatic and are receiving IV bisphosphonates (Stage 0_{IV}) or have been taking oral bisphosphonates for more than 3 years (Stage 0_{Or}). In patients receiving IV bisphosphonates, nonrestorable teeth may be treated by removal of the crown and endodontic treatment of the remaining root.[5] Oral implants or other dentoalveolar surgery should be avoided. Oral hygiene must be diligently maintained.

Stage 0 oral bisphosphonate patients should have treatment deferred, if possible, until a serum CTx level has been obtained. CTx levels >150 pg/mL indicate that dentoalveolar surgery is relatively safe.[33] For those patients with CTx levels <150 pg/mL, the prescribing physician should be contacted to see if the patient can be withdrawn from the bisphosphonate medication for a period of 3 months.[39] If the CTx level remains below 150 pg/mL, the drug holiday is extended for another 3 months. This is repeated until the level is above 150 pg/mL, at which time dental treatment may be rendered. If emergency treatment must be done, a CTx level should be obtained as soon as possible after the procedure and the physician is contacted. Appropriate informed consent must be obtained from the patient prior to initiating the procedure.

In 1 author's (MLW) experience with a small series of patients taking oral bisphosphonates (alendronate or residronate) for more than 3 years, initial CTx levels ranged from 33 to 280 pg/mL. In all cases where the CTx level was low, the treating physician was willing to have the patient suspend bisphosphonate treatment for several months.

Stage I. Stage I_{IV} and Stage I_{Or} patients present with asymptomatic exposed bone. Because the priority for patients receiving IV bisphosphonates is to continue bisphosphonate treatment, a detailed oral examination and noninvasive treatment plan should be undertaken by the dentist, oral and maxillofacial surgeon, and any other involved dental specialists, in close collaboration with the oncology team. The patient should be educated about the exposed bone, instructed in proper oral hygiene of the area, and placed on a maintenance regimen of chlorhexidine oral rinses and frequent follow-up visits.[4] The dentist should watch for any signs of soft or hard tissue infection or additional exposed bone.

Stage I_{Or} patients should initially follow the same regimen. However, a baseline CTx level should be obtained and the treating physician contacted to investigate the possibility of discontinuing bisphosphonate medication. Once again a comprehensive dental examination should be performed and treatment carefully planned. If possible, the patient's dental needs should be temporized or delayed until the CTx level rises above 150 pg/mL.

Stage II. Stage II patients present with exposed bone, pain, and soft tissue or bone infections.[38] Stage II_{IV} patients should have cultures taken to determine appropriate antibiotic therapy. Treatment should be directed toward the results of those cultures; however, not infrequently, oral culture results are read as "normal oral flora." In such cases, the clinician should consider empiric therapy. Appropriate antibiotic and fungal regimens[44] are shown in Tables 2 and 3, respectively. (Table 2 entitled *Antibiotic Regimens for Patients with BIONJ* may be accessed and downloaded from the *Clinical Decision-Making Tools* section at www.thesystemiclink.com. Table 3 entitled *Antifungal Regimens for Patients with BIONJ* may be accessed and downloaded from the *Clinical Decision-Making Tools* section at www.thesystemiclink.com.)

The standard regimen for Stage II_{IV} or Stage II_{Or} BIONJ is penicillin V potassium 500 mg every 6 hours and an oral rinse using chlorhexidine 0.12% twice daily.[20,23] In refractory cases, metronidozole 500 mg every 6 hours is added for 7 to 10 days.[4,23] For patients who are allergic to penicillin, monotherapy with clindamycin may not be sufficient; such therapy has not been efficacious in some cases,[20,23] possibly because of clindamycin's lack of activity against *Actinomyces* spp. and *Eikenella corrodens*.[20,23] Levofloxacin 500 mg daily has proved to be an excellent alternative.[45]

In Stage II_{Or} patients, the only difference in treatment is that the bisphosphonate medication is more likely to be discontinued for several months. A CTx level should be obtained as a baseline measurement, and more extensive treatment may proceed when the level exceeds 150 pg/mL.

Stage III. Stage III patients present with all of the preceding signs and symptoms and at least 1 of the following: pathologic fracture, extraoral fistula, or osteolysis extending to the inferior border.[4] In these patients, more conservative treatment methods may have already failed. Therefore, to alleviate pain and eliminate infection, it may

be necessary to debride or resect large areas of bone;[4] this approach has met with some success.[17,20,23,38,45] Curi and colleagues[44] have described 3 cases in which adjunctive treatment was combined with surgery, but to date no standardized treatment protocols exist. The following case report illustrates 1 private practitioner's (MLW) experience in caring for a cancer patient who was receiving IV bisphosphonate therapy.

Case Report

RD is a 67-year-old white male who initially presented in January 2005 on referral from his dentist for "exposed bone on the lingual mandible" (Figure 4). The patient had completed endodontic treatment on tooth #30 six months previously, but the treatment did not relieve his pain. He complained of increasingly severe pain in the right mandible that radiated anteriorly and of swelling and purulent discharge. He had been diagnosed with renal cell carcinoma and had undergone removal of his right kidney. The cancer had metastasized to his right hip and he had undergone a right total hip replacement. He was being treated with high dose pain medication and zolendronic acid. The dental examination revealed a 2- to 3-mm-diameter area of exposed bone lingual to tooth #30, with anterior swelling, erythema, and 2 draining fistulae over a large multilobulated, lingual torus (Figures 4 and 5, [fistulae not visible on x-ray]). Treatment consisted of clindamycin 300 mg every 6 hours for 10 days, along with a hydrogen peroxide rinse 4 times daily.

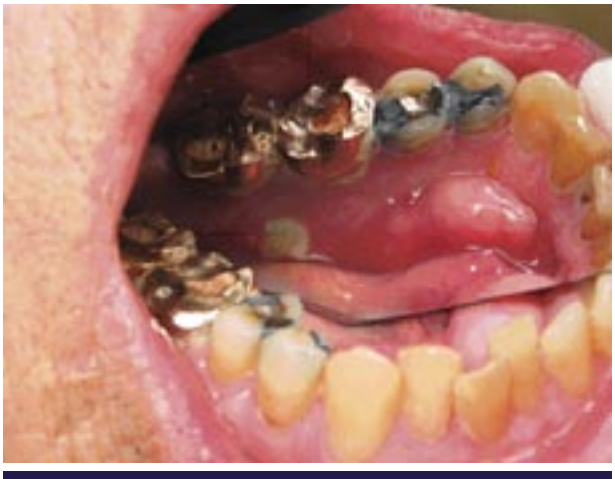

Figure 4

January 2005 *Initial presentation of patient taking zolendronic acid for metastatic renal cell carcinoma. Note small lingual mucosal dehiscence between teeth #30 and 31 and large, multilobulated torus (mirror view).*

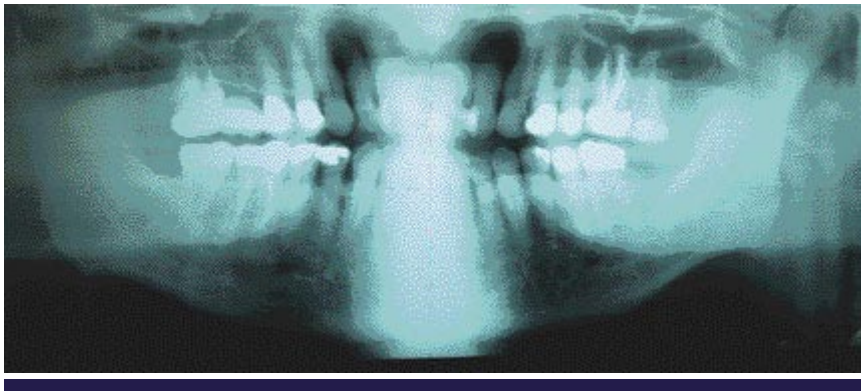

Figure 5

January 2005 *Initial radiograph demonstrating endodontic treatment of tooth #30, hyperostotic lamina dura and extremely dense lingual tori.*

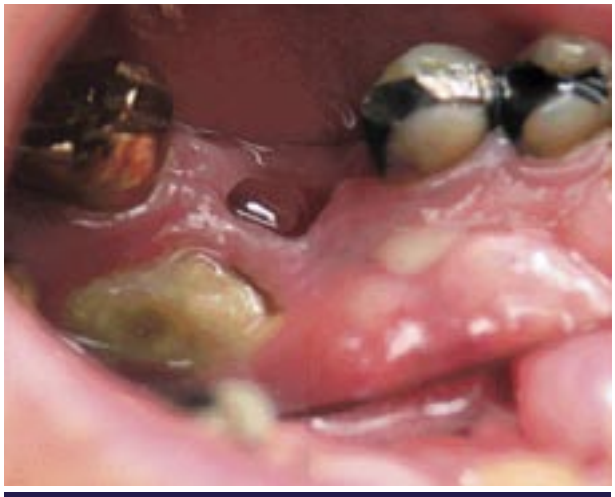

Figure 6

July 2005 *After extraction of #30, patient initially improved but returned with enlarged area of exposed bone and draining fistulae over torus.*

The patient's condition improved but did not resolve. The medication was changed to penicillin V potassium 500 mg every 6 hours, along with metronidazole 500 mg every 6 hours. The patient was then lost to follow-up for several months as a result of a change in health insurance.

In June 2005 the patient returned, complaining of pain, swelling, and discharge. After debridement of a small amount of sequestered bone, the patient was prescribed the same penicillin V potassium–metronidazole regimen as earlier. Because of

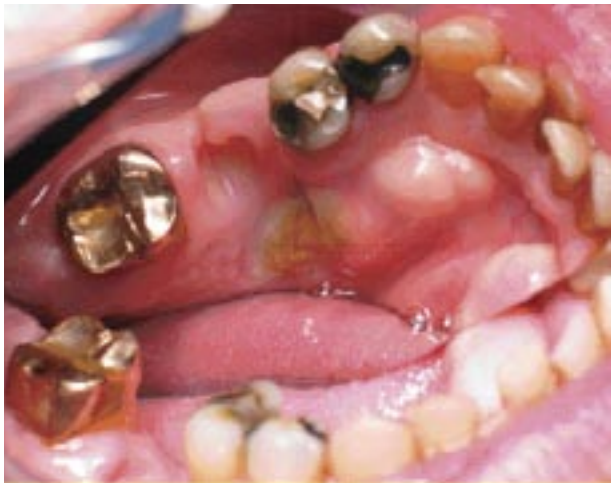

Figure 7

May 2006 *Exposed bone remains but patient is free of infection on maintenance antibiotics.*

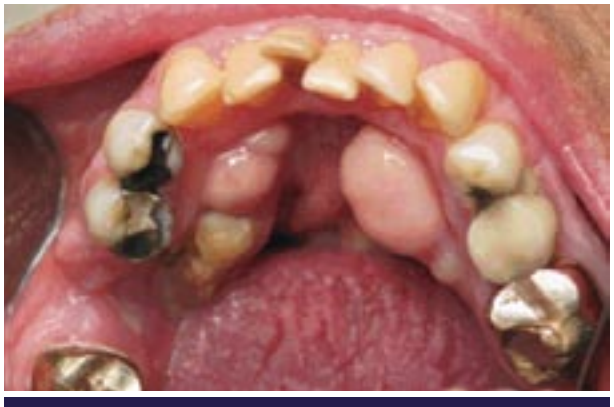

Figure 8

January 2007 *Exposed bone has enlarged with increased involvement of the torus 9 and supparation at the distal aspect of the exposure.*

continued pain and mobility, tooth #30 was extracted. During the procedure, an abscess was noted and infected tissue was debrided; treatment with penicillin and metronidazole was continued and the patient's pain resolved. He continued to struggle with poor oral hygiene on the necrotic segment.

In July 2005, a larger area of exposed bone was found lingual to tooth #30 (Figure 6). One month later, the necrotic bone was surgically debrided, and the antibiotic regimen was continued.

In March 2006, tooth #9 also developed an abcess. To avoid extraction of the tooth and the possibility of additional necrotic bone, the crown of tooth #9 was amputated, endodontic treatment was completed and the root was left in the bone. A small sequestrectomy was completed on the buccal bone of tooth #30 and antibiotic maintenance was continued with Pen VK 500 mg every 6 hours. Figure 7 demonstrates the patient's return to a non-infected status.

In January 2007 the patient presented once more with increasingly severe pain in the right mandible, with swelling and pus (Figure 8). The patient was treated with the PenVK/Metronidazole regimen and the infection resolved. He died of renal cell carcinoma in March 2007. This litany of care is illustrative of the challenges facing clinicians who care for bisphosphonate patients.

Conclusion

Bisphosphonate medications, which are used primarily to treat cancer patients and those with osteoporosis, have been linked to osteonecrosis of the jaw. While the majority of patients who develop BIONJ are cancer patients being given the IV form of the drug, the potential for BIONJ to develop in those taking these medications orally must be considered in patients presenting for dental care. As our understanding of this very complex issue continues to evolve, both dental and medical professionals must stay up to date on the literature and maintain open lines of communication in order to render the best care for their patients.

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