Treatment of bisphosphonates-associated osteonecrosis

Cesar A. Migliorati[1]
Wendy S. Hupp[2]
Erica K.J. Migliorati[3]

[1] Professor - Oral Medicine
[2] Associate Professor - Oral Medicine
[3] Assistant Professor – Restorative and Laser Dentistry
NSU College of Dental Medicine

Address for correspondence:
Cesar A. Migliorati DDS, MS, PhD
Professor - Oral Medicine
NSU College of Dental Medicine
3200 S. University Drive
Fort Lauderdale, FL 33328
Ph. +1 954 262-1749
Fax +1 954 262-1782
E-mail: migliora@nova.edu

Summary

This mini-review will focus on the management of a patient with bisphosphonate-associated osteonecrosis (BON). In order to review the subject the authors report a case of a patient with prostate cancer and metastatic bone disease who was treated with zoledronic acid. Prior to cancer the patient was treated with risedronate for osteopenia but had discontinued this treatment when cancer was diagnosed. During the description of each aspect of the case, a discussion of the rationale used for the case management is presented with support of the available literature. Aspects of interest include the diagnosis of BON, the risk factor for BON for this particular patient, the decision making process for the management of acute and long-term oral cavity problems, and the introduction of high intensity laser therapy to help control pain and reduce infection and local bacterial load.

KEY WORDS: bisphosphonates, osteonecrosis, complication, treatment, laser therapy.

Introduction

Medical advancements in the area of cancer and osteoporosis have been saving lives and improving the quality of life for millions of people around the world. This is in part due to the relatively recent development of medications like the bisphosphonates to counter bone and mineral loss resulting from metastatic bone disease, hypercalcemia of malignancy, osteopenia and osteoporosis, and Paget's disease of the bone (1, 2). However, as it is discussed in this issue of the Journal, nothing comes without a price (3). The recent description of bisphosphonates associated osteonecrosis (BON), an oral complication associated with the use of either the intravenous or the oral formulations, raised a number of questions and concerns on determining the best protocol to treat a patient with such disease (4-9). In this mini-review we will report a case of BON in a patient with metastatic prostate cancer who is under current management by our team at Nova Southeastern University (NSU) College of Dental Medicine. In addition to the management procedures used in this particular case we will also discuss how we made the diagnosis of BON, the specific risk factors present in the patient's history and how we are maintaining the patient with a reasonable quality of life. Furthermore, new information will be provided regarding the use of high intensity laser therapy to assist in the control of pain and secondary infection associated with BON.

Case report

SV, 75 years old male, was referred to our clinic in March of 2006 by his periodontist for evaluation of implants on the right maxilla. The chief complaint was pain and discomfort. The patient first experienced severe pain on the upper right maxilla in October of 2005. Not being able to see a dentist at the time because it was in the middle of the hurricane season that affected South Florida, he was given a prescription for aspirin over the phone. Pain did not subside. He finally was seen by an endodontist who diagnosed the problem as being the result of a "bad root canal filling" of tooth # 5. The endodontic retreatment of tooth # 5 (right maxilla) was performed following all standard procedures but did not resolve the pain and chronic infection. A paraendodontic (apicoectomy) surgery with open flap followed with the goal of "cleaning" the periapical area around tooth # 5. This procedure also did not help the control of either the pain or the infection. During and after both procedures the patient was treated with per oral penicillin. The patient was then referred to the periodontist who had originally placed the dental implants for evaluation of the area of teeth #s 3 (implant), # 4 (implant) and #5 (natural tooth). After the consultation with the periodontist the patient was informed that he needed the help of an oral medicine professional, and was referred to NSU oral medicine clinic.

Medical History - The medical history revealed a diagnosis of prostate cancer in 1994. The patient was treated with total prostatectomy and was given only 4 years to live. During periodic follow-ups a PSA elevation was detected. This required treatment with external beam radiation therapy to the pelvic area and back. The patient was also started on chemotherapy and hormone therapy, which he continues to receive in variable cycles of treatment until today. His medications over the years included docetaxel, goserelin, and bicalutamide. Zoledronic acid intravenous infusion monthly was started on 05/26/05 and discontinued on 02/05/2006 (9 months total time), and was administered due to metastatic bone disease. The patient was also diagnosed with osteopenia sometime ago but could not recall precisely. He had used risedronate per oral for years to

There are no conflicts-of-interest or financial relationships between the authors and any of the companies or products cited in this article.

treat the osteopenia but was off the drug for several years. He denied the use of tobacco and alcohol. Other than these two medical problems, prostate cancer and osteopenia, the patient was well, and was proud to say that he exercised regularly, had good nutritional habits, and good attitude towards life and the success of the treatment of his prostate cancer. The only problem he had was the pain and infection in his mouth that could not be controlled and that were changing his quality of life.

Dental History - His oral hygiene habits included brushing and flossing regularly and the use of mouthrinses with peroxide-baking soda mix. The patient had had extensive dental work in the past and was maintaining relatively good oral hygiene.

Physical examination - The extraoral examination revealed no visible face, head, or neck pathology. There was no evidence of swelling or deformity. However, the area lateral to the nose and infra-orbital on the right side of the face was sensitive to palpation. Intraorally, an area of swelling and erythema, buccal and palatal, around teeth/implants #s 3, 4 and 5 could be observed (Fig. 1). The area was tender upon palpation and percussion. In the buccal attached gingival toward the apical area of the referred teeth/implants there were two areas of fistulation from where a collection of purulent secretion were evident. A scar on the mesial-buccal attached gingiva of # 5 was also present, indicating the area of the incision where the previous surgical procedure had been done. Teeth in the affected area where non-depressible and presented no mobility. Tooth # 5 was endodontically treated and #s 3 and 4 were implant-supported crowns. Periodontal pockets in the area were greater than 3 mm deep especially around teeth #s 4 and 5 where pocket depths ranged from 4-8 mm. There was no visible area of exposed necrotic bone observed at this time. The rest of the oral mucosa showed no deviation from normal and no other pathology in the oral cavity could be found. The radiographic examination confirmed the clinical findings of severe bone loss around # 3, #4 and #5 and the presence of periapical pathology on the apex of tooth # 5 (Fig. 1). Less radiolucent areas were also noticed around the dental implant holding tooth # 4 (Fig. 1).

Diagnosis of bisphosphonates-associated osteonecrosis (BON) - Before we can effectively treat any type of pathology, the most important aspect is to have a correct diagnosis. The diagnosis of BON may be difficult and several aspects must be considered. The clinical presentation has to fit the current definition for BON, and the patient must present risk factors so far recognized as being indicative of an oral complication associated with the use of a bisphosphonate (10).

Definition (Cesar Migliorati, personal communication): We have been using the following definition of BON divided in two stages:

– stage I (the less common): The unexpected presence of pain and infection anywhere in the oral cavity without clinically visible exposed necrotic bone, that mimics dental disease, in a patient taking a bisphosphonate and who has not received radiation therapy to the head and neck. The signs and symptoms persist after the delivery of proper standard dental care;
– stage II (the more common): The unexpected presence of exposed necrotic bone anywhere in the oral cavity in a patient taking a bisphosphonate and who has not received radiation therapy to the head and neck. The necrotic bone persists for at least 6 to 8 weeks after the delivery of proper standard dental care.

Patient characteristics and associated risk factors:

– a cancer patient with metastatic bone disease (multiple myeloma, breast, prostate, lung);
– a patient with osteopenia or osteoporosis;
– a patient on bisphosphonate therapy for any reason;
– the use of intravenous bisphosphonate for a minimum of several months to one year or the oral formulations for a minimum of 3 to 4 years (zoledronic acid, pamidronate, clodronate, alendronate, risedronate, ibandronate). The time on therapy may vary from patient to patient (11);
– a patient with a chronic disease that may have been medicated with long-term corticosteroid therapy and who is under oral bisphosphonate therapy for osteopenia or osteoporosis (9);
– it has also been suggested in the literature that patients with diabetes are at higher risks for developing BON (12).

In the present case, the patient had long-term prostate cancer with skeleton metastasis, took an intravenous bisphosphonate (zoledronic acid) for 9 months and had previously used oral risedronate for several years. His examination revealed that there was no clinical evidence of exposed bone (except for the fact that there were two fistulas: a 1 mm diameter mesial of #5

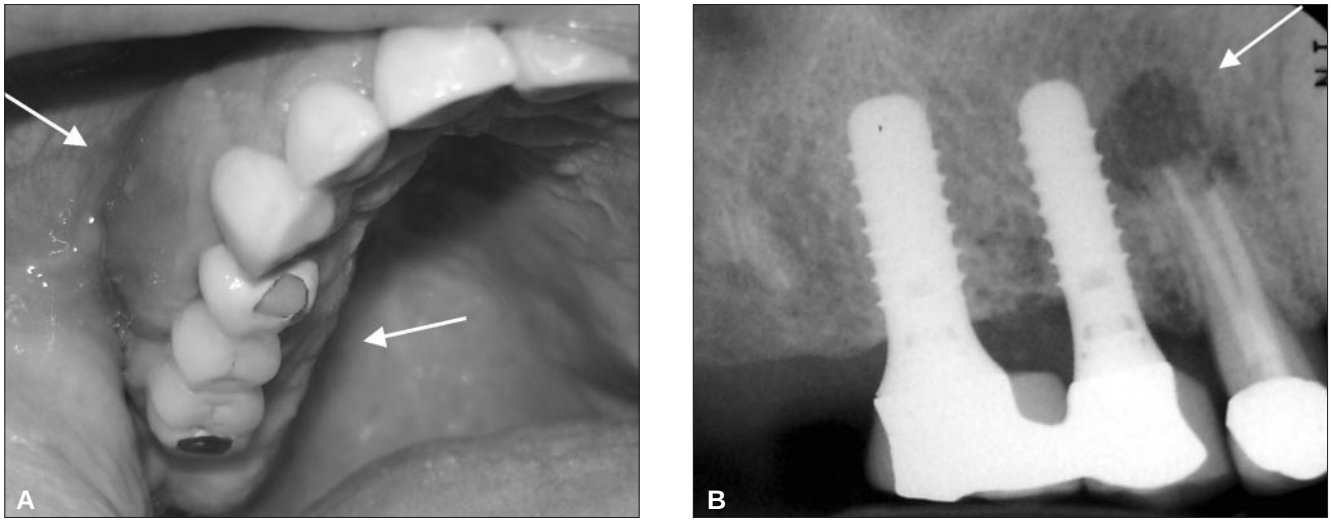

Figure 1 - Initial presentation. **A.** Observe area of swelling on the right maxillary arch on both buccal and palatal aspects (arrows). **B.** Periapical radiograph of the area showing the presence of a radiolucency at the apex of tooth # 5 (arrow).

and a 2mm diameter in the area of # 4, with presence of purulent secretion indicating active infection). In addition, there was presence of persistent pain, severe periodontal and periapical pathology, and poor response to routine standard dental/periodontal procedures. All these aspects considered together lead us to the working diagnosis of stage I BON.

Patient management

When the diagnosis of BON is made, management strategies become a concern for the dental professional as there are not well-established management guidelines that have a scientific basis. The existing guidelines for the management of patients with BON are based on the expert opinion of individuals who have been dealing with this problem since it was first described (4-6, 8, 9). Therefore, in the next step of management of the present case we had to decide how to treat the acute symptoms, since the patient was complaining of severe pain, was concerned about the fact that he had chronic infection and that was changing his quality of life. The patient was informed about the possible nature of this process and its relationship to the bisphosphonates. He was also told that at this time we could not determine what role the use of the two different bisphosphonates might have had in the case. We also told him that because we could not find clinical evidence of exposed necrotic bone, we were basing our diagnosis on his history of bisphosphonate therapy and the fact that he had not responded to standard therapy for dental and periodontal problems used for cases similar to the one he was presenting. We did not want to obtain a bone biopsy for the confirmation of osteonecrosis because of the risk of creating an area of clinically exposed bone and the risk of affecting the stability of the dental implants. Because he had not taken an antibiotic in recent weeks he was given a prescription for clindamycin 150 mg (#60) to take 2 tabs tid (three times/day) for 10 days. The patient was also instructed to continue using the routine oral hygiene procedures and was given a prescription for chlorhexidine 0.12% rinses to be used twice daily.

Two weeks later the patient returned to the clinic for a follow-up consultation. He was feeling better with some improvement of the sensitivity on the right side of the nose and face. The pain went from unbearable and constant to less intense. He completed the course of 10 days on Clindamycin 300 mg tid without complications. In the mean time, between the first and second visits in our clinic, the patient saw a private endodontist who wanted to perform a new endodontic retreatment on tooth # 5 followed by a new flap surgery to assess the bone changes in the area. We then discussed with both the patient and the endodontist why we could not agree with this treatment protocol, once it had already been done without success, and the risk of creating a defect with exposed necrotic bone. Both agreed not to do the procedure. We based this decision on the existing guidelines that recommend conservative, non-invasive care (5, 9). At this visit the patient also informed us that the oncologist was considering using zoledronic acid again due to a possible progress of bone disease. The patient was informed that this was a medical, not a dental decision, and if there was a medical indication for the use of zoledronic acid, he should agree with the suggestion of the oncologist. The clinical examination of the area on the buccal vestibule of teeth #s 3-5 had somehow improved (Fig. 2). The erythema was less intense and there was little suppuration in only one of the two existing fistulas, the more distal one (Fig. 2). The palatal swelling had also improved looking less evident. We could not see any evidence of exposed necrotic bone as yet. During a discussion with the medical oncologist, he was informed of the possibility of BON and decided not to use zoledronic acid at that time. We

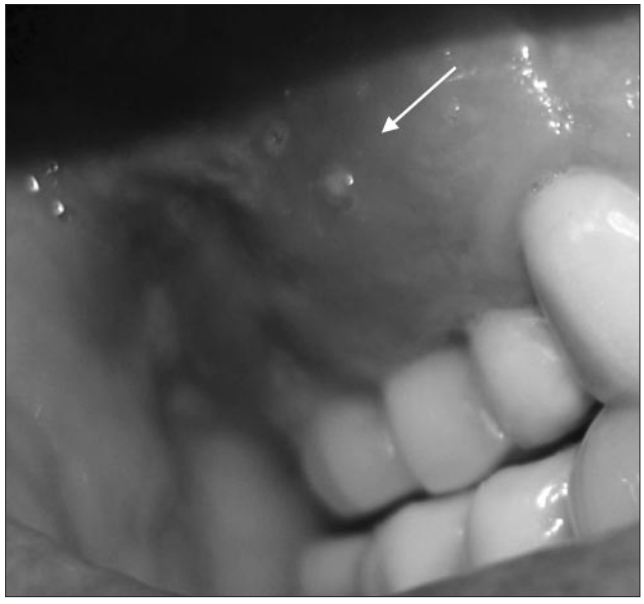

Figure 2 - Two weeks post clindamycin 300 mg three times /day. Observe minor improvement of the swelling but persistent draining fistula (arrow).

decided to place the patient on a follow-up schedule with periodic visits to the clinic. The patient was instructed to inform us immediately in case of any changes in the area. We also considered the occasional use of antibiotic therapy when necessary. The use of chlorhexidine 0.12% mouth rinses bid (two times/d) was maintained. In the following weeks the patient was examined and treated occasionally with clindamycin and twice daily chlorhexidine mouth rinses. This regimen was used when pain returned and the clinical signs worsened. However, there was no considerable improvement of the clinical presentation and pain and chronic infection could not be completely controlled. At this point the patient was referred to a periodontist (EKJM) for evaluation of the periodontal status, the dental implants, and the possibility of using high intensity laser therapy with the objective of associating the antibiotic therapy with the bacterial reduction effect and anti-inflammatory effect of the diode and the CO_2 lasers.

Periodontal/Laser treatment

Clinical and radiographic findings related to the periodontium

The patient was seen by the periodontist on June 29, 2006. At the time the patient presented with spontaneous pain on the right maxilla, around the area of teeth # 3, 4, and 5. The buccal and palatal aspects of the posterior right sextant area were swollen, erythematous, and two fistulas with draining purulent secretion were detected on buccal, apical of tooth #5 and distal-buccal of tooth #4. There was generalized plaque accumulation and the gingival tissues presented bleeding upon probing. On the full mouth periapical radiographs one could observe mild-moderate horizontal bone loss in the area of implant #3, teeth #14 and #15. Around the other teeth there were normal levels of bone crest. Periapical radiolucency was seen in the area of #5 projected toward the distal to join an area of radiolucency superimposed on the implant of #4 where the bone destruction seemed to come to the surface in the bone crest.

Periodontal data collection revealed some pseudopockets due

to overcountouring of porcelain crowns and true periodontal pockets ranging from 5 to 7 mm in the upper left quadrant. In the upper right quadrant pocket depths ranged from 2 mm up to 8 mm (interproximal between #3 and #4).

Periodontal diagnosis, prognosis and treatment plan

The diagnosis was generalized mild gingivitis; mild to moderate periodontitis in the area of #14 and #15 with localized moderate to severe periodontitis/peri-implantitis in the upper right posterior sextant, at the area where BON had been diagnosed.
Prognosis was generally good but guarded to poor for implant #4 and tooth #5. However, because of the diagnosis of BON it was decided that the treatment had to be conservative with the objective of maintaining the dental implants in the mouth and avoiding the creation of a large area of exposed necrotic bone. The periodontal treatment plan was to attempt bacterial reduction and control of inflammation in area of #3 to #5 with scaling and root planning, laser therapy, and a routine periodontal maintenance recall for the rest of the dentition. At this appointment the proposed treatment plan was discussed with the patient. He was reassured that the objective of this procedure was to eliminate local irritants through scaling and root planning. The laser therapy was to be used as an adjunct with the goal of achieving improvement of the general health of the gingiva and periodontium through reduction of inflammation and stimulation of fibroblast proliferation. The laser light was also to be used to reduce the bacterial load and the pain (13-19). Periodontal maintenance recall was also offered to the patient. The patient agreed with the procedure and signed an informed consent.
The periodontal/laser therapy was initiated immediately with debridment of the pockets and cleaning of the fistulas. The patient was given oral hygiene instructions, a Sonicare® powered toothbrush (Philips, Stamford, CT), and Colgate Total® toothpaste (Colgate-Palmolive New York, NY). He was also told to continue to use chlorhexidine mouth rinses twice daily. On every of the following appointments the patient received intrasulcular debridment and laser therapy of the area of teeth # 3-5. On the first three sessions a diode laser of 815 nm (Biolase, Irvine, CA) was used. Treatment was given to the pockets and the fistulas. The laser parameters to treat periodontal pockets were: continuous wave (CW); power 1.0 Watt; laser light delivered through an optic fiber of 400 microns. Pockets 5 mm or deeper were lased for 15 seconds each and pockets up to 4 mm or less for 10 seconds each. The laser delivery tip was introduced in the pockets parallel to the root surfaces toward apical, stopping 1 mm short of the bottom of the pocket, and ”walked” in the pocket as a periodontal probe. (The operator used settings following the recommendations of the laser manufacturer). Profuse irrigation with saline solution was used in the area being treated. Lavage inside the fistulas was also attempted and was done until no more purulent secretion could be seen. The fistulas were penetrated with the laser probe about 2 to 4 mm deep. Laser application consisted of gated wave for 45 seconds (3 × 15 seconds) in each fistula. Profuse saline irrigation continued throughout laser application. Slow but continuous improvement of both the pain and the purulent secretion could be noticed at each presentation. Four weeks into the treatment the patient returned for follow-up. Whereas pain was much improved and present only upon palpation of the area apical of #s 4-5, the fistula more distal to tooth # 4 was increasing in size and still had some purulent secretion. At this visit, treatment with a CO_2 laser of 10,600 nm (Deka Laser, Fort Lauderdale, FL) was started. CO_2 laser was used with the objective of removing the pocket epithelium and promoting reattachment of connective tissue fibers on cementum (20). Bacterial reduction can also be achieved. The laser parameters used were: pulsed wave, power 3.5 Watts, 50 Hz, non contact (NC). The same parameters were used at the entrance of both fistulas, in different directions (teeth #3, #4). According to manufacturers' recommendations, the intrapocket bacterial reduction procedure was done with pulsed wave, power at 2.8 Watts, 50 Hz, contact mode,16 seconds on the buccal and 16 seconds on the palatal aspect of each tooth, probe 1 mm inside the pocket, with profuse saline irrigation throughout the procedure. After two more visits the fistula on tooth # 5 had completely closed (Fig. 3) but the other was still active and enlarging in size seeming that the two processes had merged becoming one only and located more toward the distal of #4 (Fig. 4). CO_2 laser therapy (same parameters) and local debridment continued now in two weeks interval. The reachable implant surfaces were also laser treated with the objective of enhancing cellular adhesion to the irradiated areas (21-23). By the end of November 2006 after four more treatment sessions, the patient presented to the clinic completely asymptomatic and, although now there was clear bone exposure in the area buccal-

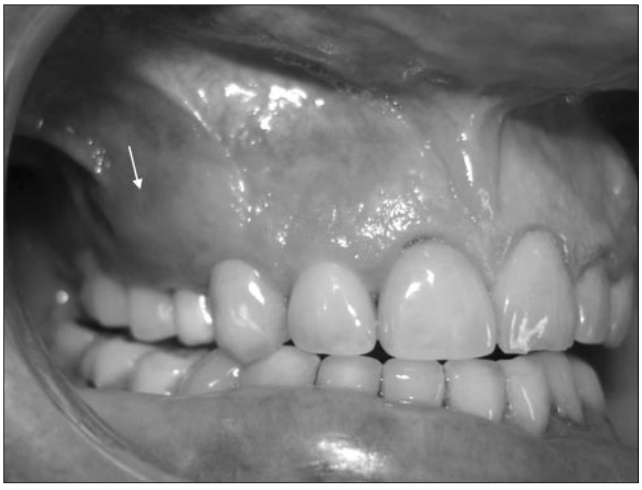

Figure 3 - Four months follow-up when laser therapy and scaling & root planning of the area had started. Observe significant improvement of the area but the presence of a small persistent draining fistula (arrow). Patient has no pain.

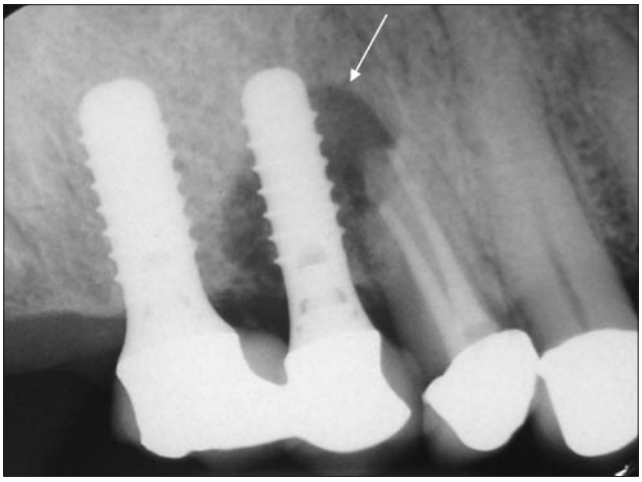

Figure 4 - Radiographic appearance 5 months into maintenance therapy showing persistent and apparently expanding radiolucent lesion (arrow). Pain has not returned.

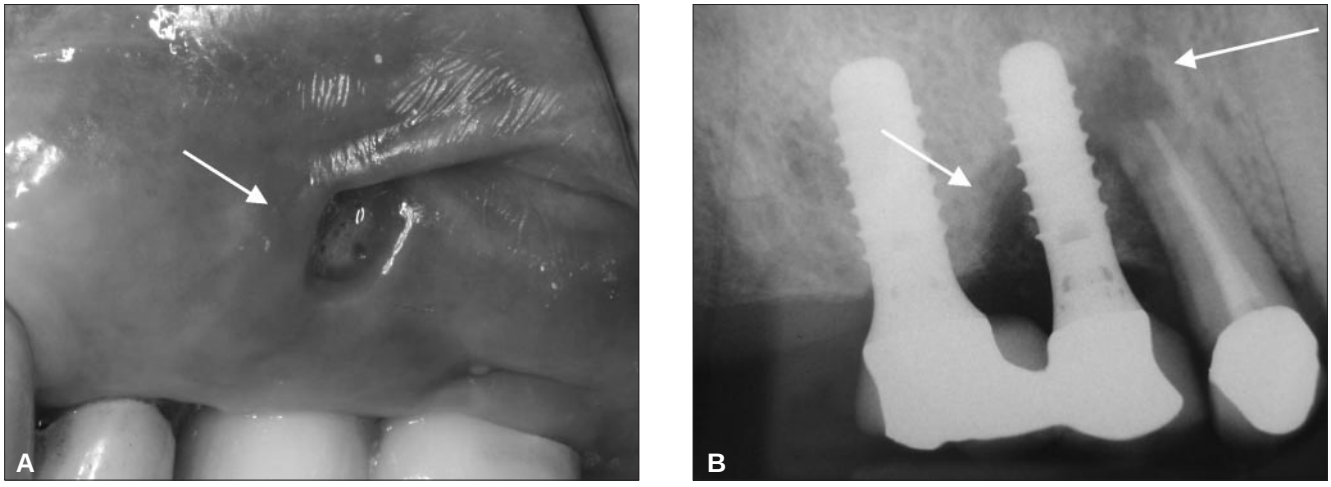

Figure 5 - 8 months into maintenance therapy. Patient remains asymptomatic. **A.** Observe through a mirror the buccal surface of the area being treated with laser therapy and local plaque debridment. Observe that there is now clear evidence of necrotic bone exposure, characterizing stage II BON. However the area is clean and there is no evidence of pus (arrow). **B.** Radiographic appearance of the same area showing signs of improvement, with apparent better calcification in the area (arrows).

distal to tooth # 4 (Fig. 5), there was no more purulent secretion in that opening. The fistula in the area of #5 healed. During the time the patient received periodontal/laser treatment, he had to take only one course of amoxicillin/clavulanate potassium 500 mg three times a day for 10 days and never needed to use analgesics again. Currently, the patient comes to the clinic for follow-up once a month. He is asymptomatic and has no longer used antibiotics. Although the necrotic bone is still exposed, the area is maintained with good home care and mouth rinses with chlorhexidine.

Discussion

The present case illustrates the pitfalls in the management of a patient with BON. The lack of science-based guidelines for the management of patients with this disease makes treatment empiric. Our goal in the present case was to improve quality of life by controlling the progress of the osteonecrotic process, by treating infection, and by eliminating the symptoms. Dental extraction and implants removal would have been another alternative. However, we decided not to extract teeth # 3-5 to avoid the formation of a large area of exposed necrotic bone. The case clearly demonstrates that the pathobiology of the bone osteonecrotic process associated with the use of bisphosphonates still needs elucidation, before we can develop effective management protocols. Our patient, contrary to most of the cases reported in the literature, did not have a tooth extraction as the initiating factor and did not present clinically visible exposed bone (1, 4-6, 8, 9). Therefore, we could not precisely tell when the process started and making the diagnosis of BON was difficult. The process of BON probably started due to the failure of a root canal treatment. However, one can also consider the possibility that the root canal therapy and the paraendodontic surgery failed because the local bone remodeling process was inhibited by the use of a potent bisphosphonate and the osteonecrotic process was already in place when the treatment was done (10). Whether or not the lingering bone remodeling suppression caused by the use of risedronate enhanced the inability of bone healing remains to be investigated. Another concern we had prior to making the diagnosis of BON was to rule out the possibility of metastatic lesion from the prostate cancer. Prostate cancer is the third most common carcinoma to metastasize to the orbit (24). Computerized tomography can be used to evaluate the head and neck in these patients and that was not a concern from the patient's medical oncologist (24).

We tried to illustrate that when the diagnosis of BON is made, before any dental treatment commences, it is important that the dentist or oral surgeon understand the patient's current health status. Discussion of the patient's health history includes a list of medications that have been prescribed. Careful questioning of the patient should address typical lifestyle perspectives: a post-menopausal woman is likely to have been recommended to take over-the counter supplemental calcium and vitamin D to help prevent osteoporosis (5, 9). Often, patients forget to indicate that they are taking a prescription medication such as zoledronic acid or ibandronate that are taken once a month only, or even the once a week doses of alendronate or risedronate. Specific questions may be necessary to be asked during the questionnaire phase. In some cases, the dentist should consult with the physician in order to ascertain the complete list of medications of their common patient.

Patients with multiple myeloma, Paget's disease or cancers that have metastasized to the bones are usually treated with intravenous bisphosphonates (1, 3). Many of these patients have bone pain that is alleviated by the treatment, yet the patient may not always be aware that it is important to let the dentist know of the medication he or she is taking.

When a patient develops oral problems during treatment with bisphosphonates, referral to a dentist who is familiar with treating BON should be made (oral medicine specialist or oral surgeon) (4, 5, 9, 11). The type of bisphosphonate i.e. oral or intravenous, the dosage, the duration, and the condition or disease that is being treated, are all important items to be discussed. The chronology of symptoms is also important to be taken into account.

A common complaint reported, as illustrated by the present case, is dull to severe pain in the orofacial region. The dentist should investigate and suspect an odontogenic etiology at first. The patient may initially have pain that is related to a dental or periodontal problem, temporomandibular joint dysfunction, or malignant metastasis to the orofacial region. Abscess formation may be secondary to a necrotic pulp or infection around the root, and appropriate dental/periodontal treatment should be given. However, in many patients, the pain is attributed to a

"bad tooth" that is treated by surgical extraction, and subsequently an area of BON develops (6). If the patient is taking a bisphosphonate, the possibility that the symptoms are truly from the BON must be considered. Some patients complain about a rough area on the gingival soft tissues that is irritating the tongue, buccal mucosa or labial mucosa as the first symptom (5, 9, 11). This is likely to be the exfoliation of a section of necrotic bone that is coming through the mucosa and traumatizing adjacent tissue. These areas of mucosa are subject to infections due to the oral microflora, becoming quite painful. Spontaneous development of BON without tooth extraction may be due to microfractures in the jaws that are not able to heal because of the bisphosphonate medications (10).

Treatment of BON: The goals of treatment of BON are to eliminate pain and infection and to prevent the loss of additional bone (9, 25). We followed these guidelines to manage the case here reported. Although we may have felt tempted to remove the involved dental implant, the institution of laser therapy as an adjunct to local periodontal debridment, as well as good home maintenance performed by the patient, prevented the process from progression. Therefore, oral function and appearance could be preserved without risking the formation of a larger necrotic bone defect that is easily infected and difficult to maintain. As demonstrated in the present case, while BON appears clinically and radiographically similar to osteomyelitis, the treatment of BON can focus on non-surgical intervention. Systemic antibiotics and chlorhexidine mouthwash should be prescribed. Oral prophylaxis and good home care should be accomplished to reduce the bacterial burden. Where rough areas of bone are irritating other tissue, the bone should be smoothed with a dental handpiece or, if available, removed with a laser light (1, 26), or else covered by a removable appliance that does not put any pressure on the bone or surrounding soft tissue (11). Frequent re-evaluation should be planned until the acute symptoms are resolved. In some cases, atraumatic removal of the necrotic bone should be accomplished. In addition, as it was demonstrated in this case, high intensity laser pocket disinfection can be used effectively. Although we have only a one-year follow-up in this case, one could see that laser therapy was important in achieving pain control and infection control, preventing the patient from constantly taking painkillers and antibiotics. Although this information comes from personal observation, it may present a new alternative for the chronic management of BON. Lasers may be expensive devices but when available to the well-trained dentist, the laser light can assist in improving patient care in dentistry.

It has been recommended that no further elective invasive procedures (surgery that involves the bone) should be performed in patients with BON (5, 6, 9, 11, 25). However, in more advanced cases, aggressive surgical management may become an option. However, long-term controlled studies with larger populations are necessary. Non-surgical endodontic therapy may be substituted for extraction of teeth (27).

Finally, dentists have been tempted to ask their patients to discontinue bisphosphonate therapy. We believe that this practice should never be done. If a patient is taking a bisphosphonate there is a medical reason for it. Most of the patients being seen in the dental offices are those with osteoporosis and osteopenia. It is recommended that the dentist consult with the physician to what is appropriate to consider as alternative treatments (4). The risk involved in the discontinuation of an oral bisphosphonate for a patient with osteoporosis includes hip fracture. It is known that hip fracture is associated with high mortality. The reported range of death 1 year after hip fracture is 20 to 25% (28). One must consider that even when a patient on bisphosphonate therapy develops BON, treatment outcomes are reasonable, as it has been demonstrated in this case report.

References

1. Dunstan CR, Felsenberg D, Seibel MJ. Therapy insight: the risks and benefits of bisphosphonates for the treatment of tumor-induced bone disease. Nature Clin Prac Oncol. 2007;4:42-55.
2. Lambrinoudaki I, Christodoulakos G, Botsis D. Bisphosphonates. Ann N Y Acad Sci. 2006;1092:397-402.
3. Krueger CD, West PM, Sargent M, et al. Bisphosphonate-induced osteonecrosis of the jaw. Ann Pharmacother. 2007;41:276-284.
4. American Dental Association Council on Scientific Affairs. Dental management of patients receiving oral bisphosphonate therapy: expert panel recommendations. JADA. 2006;137:1144-1150.
5. Migliorati CA, Casiglia J, Epstein J, et al. Managing the care of patients with bisphosphonate-associated osteonecrosis: An American Academy of Oral Medicine position paper. JADA. 2005;136: 1658-1668.
6. Woo S-B, Hellstein JW, Kalmar JR. Systematic review: bisphosphonates and osteonecrosis of the jaws. Ann Intern Med. 2006; 144:753-761.
7. Shane E, Goldring S, Christakos S, et al. Editorial - Osteonecrosis of the jaw: more research needed. J Bone Min Res. 2006;21: 1503-1505.
8. Rossi D, D'Orto O, Pagani D, et al. Bisphosphonate-associated osteonecrosis of the jaws: a therapeutic dilemma. Oral Surg Oral Med Oral Pathol. 2007;103:e1-e5.
9. Ruggiero SL, Fantasia J, Carlson E. Bisphosphonate-related osteonecrosis of the jaw: background and guidelines for diagnosis, staging and management. Oral Surg Oral Med Oral Pathol. 2006; 102:433-439.
10. Migliorati CA, Siegel MA, Elting LS. Bisphosphonate associated osteonecrosis: a long-term complication of bisphosphonate treatment. Lancet Oncol. 2006;7:508-514.
11. Migliorati CA, Schubert MM, Peterson DE, et al. Bisphosphonate-associated osteonecrosis of mandibular and maxillary bone: an emerging oral complication of supportive cancer therapy. Cancer. 2005;104:83-93.
12. Khamaisi M, Regev E, Yarom N, et al. Possible association between diabetes and bisphosphonate-Related Jaw Osteonecrosis. J Clin Endocrinol Metab. 2007;92:1172-5.
13. Coffelt DW, Cobb CM, MacNeill S, et al. Determination of energy density threshold for laser ablation of bacteria. An in vitro study. J Clin Periodontol. 1997;24:1-7.
14. Moritz A, Gutknecht N, Doertbudak O, et al. Bacterial reduction in periodontal pockets through irraditaion with a diode laser: a pilot study. J Clin Laser Med Surg. 1997;15:33-37.
15. Moritz A, Schoop U, Goharkhay K, et al. Treatment of periodontal pockets with a diode laser. Lasers Surg Med. 1998;22:302-311.
16. Qadri T, Miranda L, Tuner J, et al. The short-term effects of low-level lasers as adjunct therapy in the treatment of periodontal inflammation. J Clin Periodontol. 2005;32:714-719.
17. Theodoro LH, Haypeck P, Bachmann L, et al. Effect of Er:YAG and diode laser irradiation on the root surface: morphological and thermal analysis. J Periodontol. 2003;74:838-843.
18. Mouhyi J, Sennerby L, Nammour S, et al. Temperature increases during surface decontamination of titanium implants using CO2 laser. Clin Oral Impl Res. 1999;10:54-61.
19. Rossmann JA, Israel M. Laser de-epithelialization for enhanced guided tissue regeneration. Laser Light Amp Dent. 2000;44:793-809.
20. Marques MM, Pereira AN, Fujihara NA, et al. Effect of low-power laser irradiation on protein synthesis and ultrastructure of human gingival fibroblasts. Lasers Surg Med. 2004;34:260-265.
21. Kato T, Kusaraki H, Hoshino E. Bactericidal efficacy of carbon dioxide laser against bacteria-contaminated titanium implant and subsequent cellular adhesion to irradiated area. Lasers Surg Med. 1998;23:299-309.
22. Pereira AN, Eduardo CP, Matson E, et al. Effect of low-power laser irradiation on cell growth and procollagen synthesis of cultured fibroblasts. Lasers Surg Med. 2002;31:263-267.
23. Kreisler M, Haj HA, Gotz H, et al. Effect of simulated CO_2 and

GaAlAs laser surface decontamination on temperature changes in Ti-plasma sprayed dental implants. Lasers Surg Med. 2002;30: 233-239.
24. Harrison LB, Sessions RB, Hong WK. Head and neck cancer: a multidisciplinary approach. 2nd ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2004:844.
25. Marx RE, Sawatari Y, Fortin M, et al. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. J Oral Maxillofac Surg. 2005;63:1567-75.
26. Kimura Y, Fujita A, Yamashita A, et al. Effects of erbium, chromium:YSGG laser irradiation on canine mandibular bone. J Periodontol. 2001;72:1178-1182.
27. AAE position statement: Endodontic implications of bisphosphonates-associated osteonecrosis of the jaws. December 2006. Available at: http://www.aae.org/dentalpro/guidelines.htm. Accessed online March 12, 2007.
28. Robbins JA, Biggs ML, Cauley J. Adjusted mortality after hip fracture: from the cardiovascular health study. J Am Geriatr Soc. 2006;54:1885-1891.