Alendronate Bisphosphonate Therapy and Osteonecrosis of the Jaw: Successful Retreatment

Thomas J. Balshi, DDS, PhD, FACP* / Glenn J. Wolfinger, DMD, FACP* / Vicki C. Petropoulos, DMD, MS** / Stephen F. Balshi, MBE*
*PI Dental Center at the Institute for Facial Esthetics, Fort Washington, PA
**University of Pennsylvania, Philadelphia, PA

INTRODUCTION

Currently, osteoporosis is the most common disease of bone metabolism encountered in dental implant patients.[1] Estimates suggest 10 million individuals are diagnosed, and almost 34 million more have low bone mass, placing them at an increased risk of disease acquisition.[2] Approximately one third of patients over the age of 60 are affected, with women incurring events twice as often as men.[1] This number increases greatly when including those taking medications prophylactically.[1]

Alendronate sodium (Fosamax, Merck and Co., Whitehouse Station, USA) is one of three (Aredia, Novartis Pharmaceuticals, Basel, Switzerland), (Zometa, Novartis Pharmaceuticals, Basel, Switzerland) second-generation nonhormonal bisphosphonates (BPs) used in oral dose tablet form for the treatment of osteopenic conditions. Bisphosphonates possess a high affinity for bone inhibiting osteoclastic function and decrease bone resorption, resulting in a net gain of bone density. [1,3-5]

Patients using bisphosphonates, cannot meet systemic demands requiring repair and remodeling which is critical to maintaining bone function, ultimately presenting painful exposed avascular bone in the mandible (maxillary and simultaneous events have been documented).[6] It is theorized that this unrepaired microdamage presents an ideal environment for osteonecrosis.[6]

Marx et al, were the first who adopted the terminology to describe spontaneous or surgically induced non-healing ulcers in the jaws that occur in patients taking bisphosphonates.[7] This is termed biphosphonate-induced osteonecrosis of the jaw (BONJ).[7] In 2003, BONJ was a condition that was first recognized and reported. BONJ is sometimes termed bisphophonate-related osteonecrosis of the jaw (BRONJ).[7,8-11] According to the AAOMS, the diagnosis of necrosis of the jaws induced by BP is based on: (1) exposed bone greater than eight weeks in duration; (2) it is induced by BP; (3) no history of radiation therapy to the jaws. [12]

Currently, BONJ is considered long term and irreversible, despite attempts to discontinue medication usage.[13]

OBJECTIVE

To accurately portray the management of a patient presenting with mandibular osteonecrosis following alendronate bisphosphonate exposure and immediate loading of dental implant treatment of the mandible.

MATERIALS & METHODS

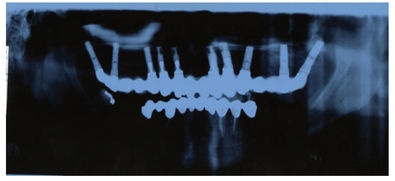
Initial Presentation

54 y.o. African American woman presented for immediate load dental implant reconstruction of her maxillary arch due to a failing fixed tooth-supported reconstruction which was fabricated 3 years previously.

Past medical history: good health with exception of breast cancer (lumpectomy), accompanied by radiation treatment four years prior and evidence of osteopenia which was treated with an oral dosage of 70mg/wk alendronate bisphonate (Fosamax, Merck) for one year.

INITIAL TREATMENT

Abutment teeth #'s 2,3,6,7,9,10,11,12,15 were extracted and ten Brånemark System implants (Nobel Biocare, Yorba Linda, CA) were placed in areas #'s 1,2,5,6,7,10,11,12,15,16, following the Teeth in a Day™ immediate loading protocol.[14-18] The maxillary implant-supported prosthesis was placed without any complications or evidence of osteonecrotic activity.

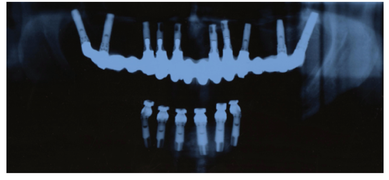


Maxillary Implant-Supported Reconstruction in Place Following TIAD Immediate Loading Protocol

-Approximately 4 years later the patient presented with a failing lower reconstruction with extensive decay and tooth mobility which deemed a poor long-term prognosis for the existing mandibular dentition.

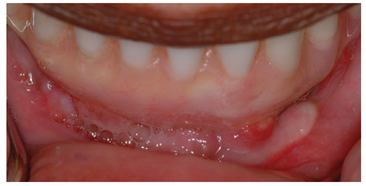
TREATMENT 4 YEARS LATER

-Teeth #s: 22,23,24,25,26,27 were extracted and 6 immediately loaded Brånemark System implants were surgically placed in areas #'s: 20,22,24,25,27,28 following Teeth in a Day™protocol.

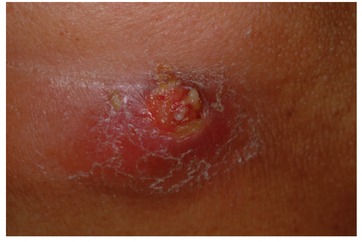


Immediate placement of mandibular implants with screw retained provisional prosthesis

TWO WEEKS POST-OP



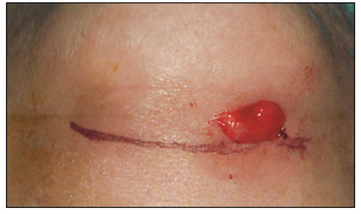
An area of ulceration was noted area #22



Submandibular swelling under her lateral inferior aspect with a hematoma. (Courtesy of Quintessence)

- Patient was presecribed Keflex (Lilly, Switzerland), 500mg for 10 days.

SIX WEEKS POST-OP

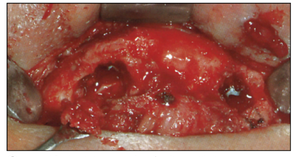


Submental cutaneous incision accessed area (Courtesy of Quintessence)

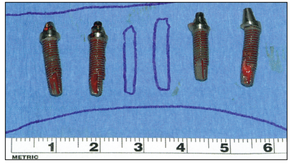
-Purulent discharge exuded from the lesion on left inferior border of the mandible.
-Biopsy obtained for assessment on fungi, anaerobic and aerobic bacterial cultures
-CT scan showed massive loss of the inferior border of the mandible, bilaterally with and island of cortex in the midline.
-Cancellous bone totally devoid around a wide perimeter surrounding the implants on both sides
-Lab tests showed Stenotrophomonas Maltophilia organisms and oral bisphosphonate induced osteonecrosis of the mandible with a secondary osteomyelitis and foreign bodies

MANAGEMENT OF BONJ

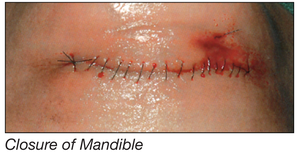
-Piperacillin tazobactum combination administered prior to surgery, 4.5g every 8 hours for five days
-Mandibular prosthesis removed
-Extraoral incision made along the inferior border of the mandible
-Granulation tissue and necrotic bone removed
-Irrigation with chlorhexidine (3M ESPE, St. Paul, MN)
-Removal of last two posterior implants on right and left sides which were encapsulated in granulation tissue
-Closure of mandible



Open Debridement of Mandible (Courtesy of Quintessence)



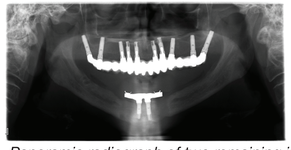
Four Posterior Implants Removed (Courtesy of Quintessence)



Closure of Mandible (Courtesy of Quintessence)

TWO MONTHS AFTER REMOVAL OF FOUR MANDIBULAR IMPLANTS

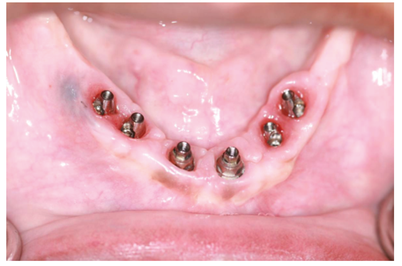
-Implant overdenture made with a gold bar
-Patient advised to discontinue her alendronate bisphosphonate medication indefinitely after consulting physician



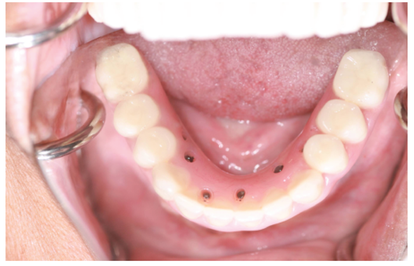
Panoramic radiograph of two remaining implants

2.5 YEARS AFTER INITIAL MANDIBULAR IMPLANT PLACEMENT: RETREATMENT OF MANDIBULAR ARCH

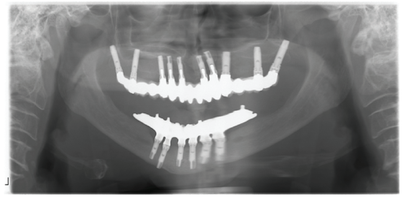
-Patient returned for implant placement in mandibular arch
-CTX tests performed (Quest Diagnostics Lab) which indicated 457pg/ml
-4 Brånemark System Implants placed in areas #'s: 20,22,27,29 and all immediately loaded



Four Mandibular Implants Placed Following 2 Year Drug Holiday



Final Mandibular Prosthesis



Panoramic radiograph showing 8 years post operative of maxillary and 2 years post operative of mandibular implants

DISCUSSION AND CONCLUSION

--The patient had history of taking sodium alendronate for 5 years when she presented for the implant placement in the mandibular jaw. She met the criteria suggested by AAOMS and was diagnosed with BONJ.

--It is of utmost importance to use serum levels of morning fasting CTX as suggested by Marx et al[19] to asses patients'risk of developing BONJ by oral administration of BPs.

CTX Value	Risk of BONJ
300 to 600 pg/ml (normal)	none
150 to 299 pg/ml	none to minimal
101 to 149 pg/ml	moderate
Less than 100 pg/ml	high

--It may be needed to place a patient on a "drug holiday" prior to any surgical intervention and subsequent surgery if the patient's condition allows it.
--As osteoporosis is on the rise, and greater populations taking BP's and therefore further consideration of the long term use of BP's is needed.
--More studies that investigate serum CTX will be helpful as it relates to number of years taking BP's to aid in establishing future guidelines

ACKNOWLEDGEMENTS

We would like to acknowledge Dr. Robert Marx for his contributions to this patient's care as well as Dr. Richard Rasmussen.

REFERENCES

1. Chacon GE, Stone EA, Larsen PE, Beck FM, McGlumphy EA: Effect of alendronate on endosseous implant integration: an in vivo study in rabbits. J of Oral and Maxillofacial Surg 64:1005-9, 2006.

2. National Osteoporosis Foundation Website

3. Migliorati CA, Casiglia J, Epstein J, Jacobsen PL, Siegel MA, Woo SB: Managing the care of patients with bisphosphonate associated osteonecrosis: an American academy of oral medicine position paper. 136(10):1658-68,2005.

4. Licata, AA: Discovery, clinical development, and therapeutic uses of bisphosphonates. Ann Pharmacother 39:668-77,39,2005.

5. Hunter, TS: Prevention and treatment of osteoporosis in managed care settings. Journal Managed Care Pharm 8(1):58-65,2002.

6. Famiglia MC, Summerlin DJ, Krivisik E, et al: Osteonecrosis of the mandible or maxilla associated with the use of new generation bisphosphonates. Laryngoscope 116:115-20, 2006.

7. Marx, RE: Bisphosphonate induced exposed bone (osteonecrosis/petrosis) of the jaws. Risk factors, recognition, prevention and treatment. J Oral Maxillofac Surg 63:1567-75, 2005.

8. Marx, RE: Pamidronate (aredia) and zoledronate (zometa) induced avascular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg 61:115-18,2003.

9. American Association of Oral and Maxillofacial Surgeons Position Paper on Bisphosphonate-Related Osteonecrosis of the Jaws. J of Oral Maxillofac Surg 65:369, 2007.

10. Hellstein JW, and Marek CL: Bisphosphonate osteochemonecrosis (bis-phossy jaw): Is this the phossy jaw of the 21st century? J of Oral Maxillofac Surg 63:682-689, 2005.

11. Mitchel DY, Eusebio RA et al: Risedronate pharmokinetics and intra-and inter-subject variability upon single-dose intravenous and oral administration. Pharmaceutical Research 18:166-70, 2006.

12. Advisory Task Force on Bisphosphonate-Related Osteonecrosis of the Jaws, American Associate of Oral and Maxillofacial Surgeons. AAOMS position paper on bisphosphonate-related osteonecrosis of the jaws. J Oral Maxillofac Surg 65:369-76, 2007.

13. Kurtzman, GM, Silverstein LH, Peden J, Shatz PC: Implications of bisphosphonate use for the dentist: An introduction. Dentistry Today 25(8):80-5,2006.

14. Balshi TJ, Wolfinger GJ: Immediate placement and implant loading for expedited patient care: a patient report. Int J Oral Maxillofac Implants17(4):587-92, 2002.

15. Balshi TJ, Wolfinger GJ: Teeth in a day. Implant Dent 2001;10(4):231-3.

16.Balshi TJ, Wolfinger GJ: A new protocol for immediate functional loading of dental implants. Dent Today 20(9):60-5, 2001.

17. Petropoulos VC, Balshi TJ, Balshi SF, Wolfinger GJ: Extractions, implant placement, and immediate loading of mandibular implants: a case report of a functional fixed prosthesis in 5 hours. Implant Dent. 2003;12(4):283-90.

18. Balshi, TJ, Wolfinger, GJ: Single tooth incisionless-sutureless surgery: Teeth in a Day. Prosthodontic Insight 16(1):1-5, 2003.

19. Marx RE, Chiloi JE, Ulea JJ: Oral Bisphosphonate induced osteonecrosis: Risk factors, prediction of risk using serum CTX testing, prevention, and treatment . J of Oral and Maxillofac Surg 65:2397, 2007.

20. Marx RE, Oral and Intravenous Bisphosphonate Induced Osteonecrosis of Jaws.History, Prevention and Treatment. Quintessence Publishing Co. Inc. Hanover Park, IL 2007, p. 84.