Bisphosphonate-Induced TRAM Flap Fat Necrosis

Bradley B. Block, M.D. Steven P. Davison, D.D.S., M.D. Washington, D.C.

Paget disease of bone, hypercalcemia, and solid tumors metastatic to bone, particularly breast cancer, by inhibiting osteoclastic absorption of bone. They may have antitumor effects by means of antiangiogenesis; induction of apoptosis; and inhibition of tumor cell growth, adhesion, and invasion. The plastic surgeon should be aware of any side effects that may impact breast reconstruction.

We present the first documented case of bisphosphonate-induced fat necrosis (Fig. 1).

CASE REPORT

A 62-year-old woman underwent a unilateral mastectomy for invasive ductal carcinoma. She underwent reconstruction with an ipsilateral muscle-sparing transverse rectus abdominis musculocutaneous (TRAM) flap (Fig. 2). Modest fat was harvested and was centralized over the medial and lateral perforator rows, replacing 430 g. The patient was a nonsmoker and nondrinker, with a body mass index of 29.2. She had an uneventful recovery, with 100 percent flap survival. The flap was inset horizontally with area II medial to area I under the nipple-areola skin paddle and area III, the least vascularized, placed laterally. Six weeks postoperatively, she was given 4 mg of the bisphosphonate zoledronic acid³ intravenously, for osteoporosis. The next day, the patient called the surgeon with new pain and swelling in the left TRAM flap. Examination revealed areas of induration and firmness suggestive of fat necrosis.

After a 3-month cooling-off period, the area of fat necrosis was removed (Fig. 1). This encompassed 60 percent of the flap, predominantly areas I and II, the best vascularized. The skin paddle and lateral segments were preserved (Fig. 3).

DISCUSSION

No previous report of bisphosphonates/diphosphonates and fat necrosis exists. The most common complication of bisphosphonates is gastrointestinal toxicity. Osteonecrosis of the mandible and maxilla has been documented with no cause for vascular compromise, and has been estimated to

From the Department of Otolaryngology–Head and Neck Surgery, Georgetown University, and DAVinci Plastic Surgery. Received for publication July 5, 2009; accepted August 11, 2009.

Copyright ©2010 by the American Society of Plastic Surgeons

DOI: 10.1097/PRS.0b013e3181c91be2



Fig. 1. Gross specimen of fat necrosis.

occur in 1 to 10 percent of patients.⁴ The pathophysiology of this has yet to be determined but may be related to antiangiogenic effects.

This TRAM flap was well established, with more than adequate time for neovascularization of collateral blood supply.⁵ The areas that necrosed were zones with the greatest perforator flow. Areas of preserved skin centrally and fat laterally were in the most contact with native dermis and neovascularization. This distribution of fat necrosis is inconsistent with normal fat necrosis.

Disclosures: No financial arrangements with either investigator have been made where study outcome could affect compensation. Neither investigator has a proprietary interest in the below-mentioned product, has a significant equity interest in the sponsor of this report, has received payments of other sorts, or has a commercial or financial association to disclose.







Fig. 2. Preoperative views.







Fig. 3. Postoperative views (after fat necrosis was removed).

Bisphosphonates are a widely used class of medications in breast cancer and osteoporotic patients, the side effects of which may impact breast reconstructions, specifically through antiangiogenic effects.² We present this as the first documented case of bisphosphonate-induced fat necrosis and as a caution to plastic surgeons performing breast reconstruction to be vigilant for other presentations.

Steven P. Davison, D.D.S., M.D.

DAVinci Plastic Surgery
3301 New Mexico Avenue, NW 236
Washington, D.C. 20016
davisonplastic@yahoo.com

REFERENCES

- Drake MT, Clarke BL, Khosla S. Bisphosphonates: Mechanism of action and role in clinical practice. *Mayo Clin Proc.* 2008; 83:1032–1045.
- 2. Ottewell PD, Mönkkönen H, Jones M, Lefley DV, Coleman RE, Holen I. Antitumor effects of doxorubicin followed by zoledronic acid in a mouse model of breast cancer. *J Natl Cancer Inst.* 2008;100:1167–1178.
- 3. Novartis Pharmaceuticals Corp. East Hanover, N.J.: Novartis Pharmaceuticals Corp.
- Silverman SL, Landesberg R. Osteonecrosis of the jaw and the role of bisphosphonates: A critical review. Am J Med. 2009;122 (2 Suppl):S33–S45.
- Gatti JE, LaRossa D, Brousseau DA, Silverman DG. Assessment of neovascularization and timing of flap division. *Plast Reconstr* Surg. 1984;73:396–402.