

Previously successful dental implants can fail when patients commence anti-resorptive therapy—a case series

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Abstract. This article reports a type of localized osteonecrosis that can occur in patients who have had successful osseointegrated implants for many years and then commence anti-resorptive therapy. Eleven female patients were identified who had successful implant insertion, but who were placed on anti-resorptive therapy (bisphosphonates or denosumab) several years later and developed osteonecrosis around the implants. In each case, the osteonecrosis occurred only around the implants and not around the patient's remaining teeth. The implants of eight patients were removed with a sequestrum of bone tightly adherent to the implant. This is different from the normal pattern of implant failure. Implant failure can occur when patients with successfully integrated implants are later placed on anti-resorptive therapy, and the osteonecrosis takes a particular form where a sequestrum forms that remains adherent to the implant. Why the adjacent remaining teeth are not affected is unclear.

Key words: dental implants; osteonecrosis; anti-resorptive agents; bisphosphonates; denosumab.

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The issues of placing dental implants in patients who are taking bisphosphonates, denosumab, or other medications known to predispose to medication-related osteonecrosis of the jaws (MRONJ) are fairly well known, and protocols are in place to reduce the risk, including discontinuation of the medication, drug holidays, and the

use of testing such as C-terminal telopeptide (CTX) for bone turnover¹. Although it is still somewhat controversial, many authorities recognize that the success rates for implants placed in patients already taking these medications are lower than the normally quoted success rates for implants²⁻⁸.

What has not been as fully realized is the issue of patients who have successfully undergone implant reconstruction and are subsequently placed on bisphosphonates or similar medications, often years later. This article reports some of the issues seen in these patients and the types of problem that can arise.

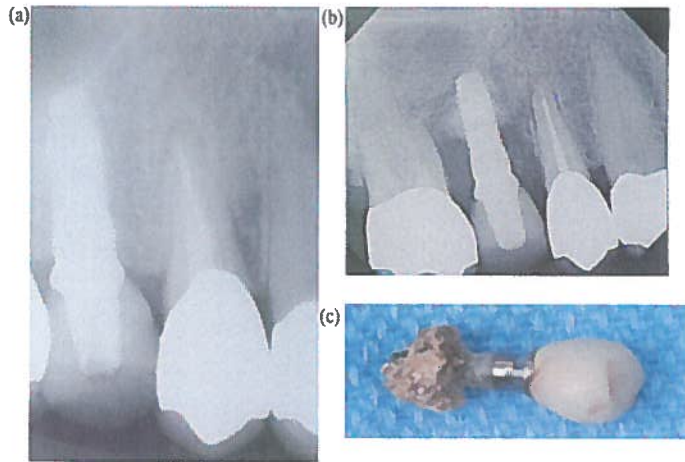


Fig. 1. (a) A successful implant replacing the maxillary second premolar. (b) The same implant 5 years after the patient commenced alendronate therapy; note the possible appearance of a sequestrum near the tip of the implant. (c) Photograph of the implant after removal showing the sequestrum firmly adherent to the implant.

Materials and methods

This study involved 11 patients (all female), seen by the present authors over the past 2 years, in whom implant failure occurred several years after successful insertion. In each case, the failure occurred after the patient had been placed on an anti-resorptive agent for longer than 2 years (mean 4.8 years, range 2.0–13 years). The agents were alendronate (Fosamax) in eight cases, zoledronate in one case, and denosumab (Xgeva) in two cases. In all cases, the implant restorations had been successful and functional

for a number of years prior to commencing the administration of the anti-resorptive agent. No patient was taking steroids, and although many were taking other medications, there were none that should affect implant success.

Results

The mechanism of failure is unusual, in that bone becomes exposed around the implants and the implants are gradually exteriorized with a sequestrum (Figs 1 and 2). In each case, radiographs showed that

the process was localized to the implants. The surrounding teeth were not affected in any of the cases (Fig. 3).

To date, the implants have been removed in eight cases. In the other three cases, the implants will eventually require removal. For the implants that were removed, the bone still appeared to be integrated onto them: the implant was removed firmly attached to a sequestrum of necrotic bone. None of the patients on bisphosphonate therapy had an active infection, although both patients on denosumab did have an active infection. Perioperative antibiotics were prescribed in all cases, and there was satisfactory healing following implant removal and debridement. Nine cases involved the mandible and two involved the maxilla.

Discussion

Late implant failure is extremely unusual and sporadic. In most cases, if implants are going to fail, they do so within a few months of insertion. When failure occurs, the implant normally becomes mobile and is easily removed without any surrounding tissue. Following curettage, the area heals normally.

The type of implant failure described in this article appears to be different, in that the patients had been successfully restored for a number of years and failure only occurred when they were subsequently placed on anti-resorptive agents by a phy-

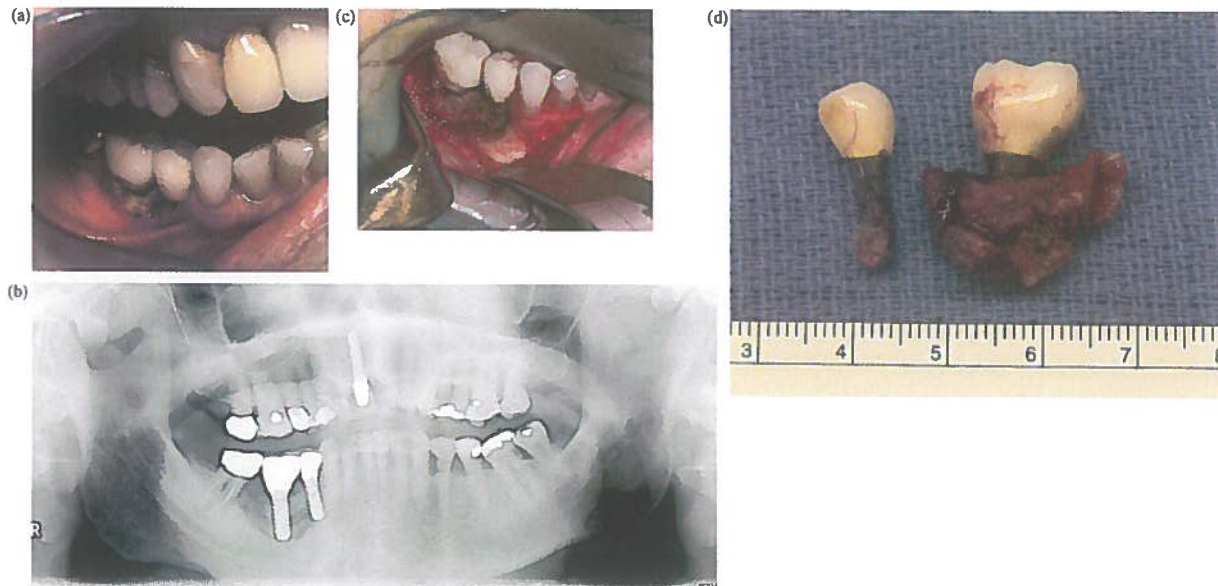


Fig. 2. (a) Appearance of exposed bone around implants in the area of the mandibular second premolar and first molar. (b) Radiographic appearance showing that the osteonecrosis is confined to the area of the implants in the right mandible; the rest of the bone and periodontal condition are within normal limits. (c) Clinical appearance showing a clearly defined area of osteonecrosis around the implants. (d) Appearance following removal of the implants, showing osteonecrotic sequestra firmly adherent to the implants.

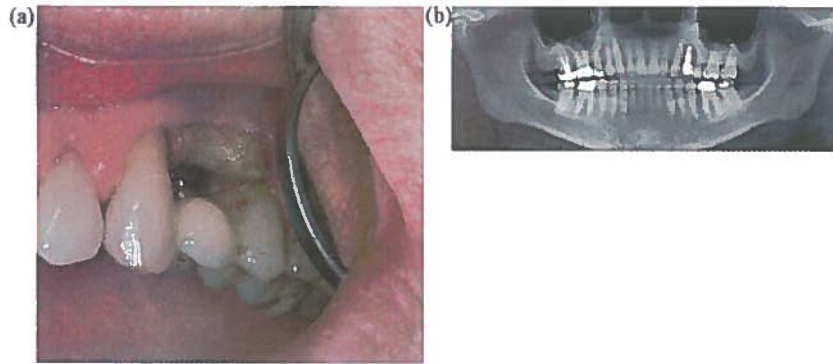


Fig. 3. (a) Exposed bone and osteonecrosis on the buccal aspect of the implant replacing the maxillary first premolar. (b) Radiographic appearance showing that the condition around all of the other teeth is perfectly normal and that only the implant is affected by this osteonecrotic process.

sician (for osteoporosis or metastatic bone disease) and they had been on the medication for at least 2 years. Additionally, the type of failure appears to be different from other types of implant failure, as the implants were still integrated with the bone and came away firmly attached to some surrounding bone. This does not occur with normal implant failure, where the implant is removed on its own.

Also remarkable is the fact that this problem only seems to affect the implants and not the rest of the teeth or any edentulous areas. Conceptually, one might imagine the teeth themselves to be more at risk because they have a periodontal ligament as a source of possible bacterial ingress and failure, and they also have the nutritional needs of the pulp, which are obviously greater than those of an implant. However, it is also possible that because of the lack of a periodontal ligament, the stresses placed on the bone with mastication become high enough to cause localized bone necrosis in this implant patient group. This phenomenon could also occur if the bone surrounding the implants has a higher rate of bone turnover, making it more susceptible to the actions of anti-resorptive medications⁹. It does not appear to be a localized form of peri-implantitis. This phenomenon has not been specifically described previously, but has been alluded to in other reports^{5,10–12}.

There appear to be several features of this late implant failure in patients subsequently placed on anti-resorptive agents that require further study, and patients should be warned of this possibility if they

have successful dental implants and are subsequently placed on these medications.

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None.

Competing interests

None.

Ethical approval

UCSF Human Research Protection Program, number 17-22030.

Patient consent

Written consent has been obtained.

References

1. Flichy-Fernández AJ, González-Lemonnier S, Balaguer-Martínez J, Peñarrocha-Oltra D, Peñarrocha-Diago MA, Bagán-Sebastián JV. Bone necrosis around dental implants: a patient treated with oral bisphosphonates, drug holiday and no risk factors according to CTX. *J Clin Exp Dent* 2012;4:e82–5.
2. Giovannacci I, Meleti M, Manfredi M, Mortellaro C, Lucchina AG, Bonanini M, Vescovi P. Medication-related osteonecrosis of the jaw around dental implants: Implant surgery-triggered or implant presence-triggered osteonecrosis? *J Craniofac Surg* 2016;26:697–701.
3. Tam Y, Kar K, Nowzari H, Cha HS, Ahn KM. Osteonecrosis of the jaw after implant surgery in patients treated with bisphosphonates—a presentation of six consecutive

- cases. *Clin Implant Dent Relat Res* 2014;167:751–61.
4. Jacobsen C, Metzler P, Rossle M, Obwegeser JU, Zemann W, Gratz KW. Osteopathology induced by bisphosphonates and dental implants: clinical observations. *Clin Oral Investig* 2013;17:167–75.
5. Lopez-Cedrun JL, Sanroman JF, Garcia A, Penarrocha MK, Feijoo JF, Limeres J, Diz P. Oral bisphosphonate-related osteonecrosis of the jaws in dental implant patients: a case series. *Br J Oral Maxillofac Surg* 2013;51:874–9.
6. Yip JK, Borrell LN, Cho SC, Francisco H, Tarnow DP. Association between oral bisphosphonate use and dental implant failure among middle-aged women. *J Clin Periodontol* 2012;39:408–14.
7. Gupta R. Early implant failure in patient associated with oral bisphosphonates. *Indian J Dent Res* 2012;23:298.
8. Kasai T, Pogrel MA, Hossaini M. The prognosis for dental implants placed in patients taking oral bisphosphonates. *J Calif Dent Assoc* 2009;37:39–42.
9. Garetto LP, Chen J, Parr JA, Roberts WE. Remodeling dynamics of bone supporting rigidly fixed titanium implants: a histomorphometric comparison in four species including humans. *Implant Dent* 1995;4:235–43.
10. Kwon TG, Lee CO, Park JW, Choi SY, Rijal G, Shin HI. Osteonecrosis associated with dental implants in patients undergoing bisphosphonate treatment. *Clin Oral Implants Res* 2014;25:632–40.
11. Holzinger D, Seemann R, Matoni N, Ewers R, Millesi W, Wutzl A. Effect of dental implants on bisphosphonate-related osteonecrosis of the jaws. *J Oral Maxillofac Surg* 2014;72:1937. <http://dx.doi.org/10.1016/j.oms.2014.04.037.e1-8>.
12. Starck W, Epker B. Failure of osseointegrated dental implants after diphosphonate therapy for osteoporosis: a case report. *Int J Oral Maxillofac Implants* 1995;10:74–8.

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