Denosumab-associated Periprosthetic Atypical Femur Fracture: A Case Report

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Learning Point of the Article:

Denosumab has the potential of occurring periprosthetic AFFs like bisphosphonate.

Abstract

Introduction: Denosumab is generally used for 5–10 years to treat postmenopausal osteoporosis. Although atypical fractures caused by bisphosphonate use are well known, reports of denosumab-associated femur fractures are rare.

Case Report: Herein, a 75-year-old woman suffered an atypical periprosthetic femoral fracture 31 months after receiving denosumab. The fracture occurred transverse to the stem tip with lateral cortical thickening. The patient underwent revision surgery for conversion to a longer cemented stem. The fracture site healed 10 months after revision surgery.

Conclusion: As far as we know, there have been no reports of a case on periprosthetic atypical femur fracture associated with denosumab. Our study shows the potential of periprosthetic atypical femoral fractures in patients using denosumab for a long time.

Keywords: Atypical fracture, periprosthetic femoral fracture, total hip arthroplasty, denosumab, osteoporosis.

Introduction

Total hip arthroplasty (THA) is widely used in patients with advanced osteoarthritic hips. THA shows excellent results and has been recognized as the surgery of the century [1]. THA has been performed for more than 60 years, and its incidence is increasing worldwide. As patients receiving THA grow older, periprosthetic femur fractures (PFFs) occur.

In recent years, orthopedic surgeons have had to handle atypical femoral fractures (AFF) that the American Society for Bone and Mineral Research Task Force defined in 2010 [2]. Among PFFs, some show radiographic features consistent with AFFs, which are strongly associated to administer bisphosphonate for a long time [3, 4]. Bisphosphonates make osteoporosis patients reduce the fracture risk because of the beneficial effects of the drug. However, since bisphosphonates reduce bone remodeling, they may lead to fatigue fractures. As denosumab is a potent bone antiresorptive agent, there is a possibility of fatigue fracture following denosumab use.

Case Report

A 75-year-old woman received denosumab for the 1st time in October 2018 for severe postmenopausal osteoporosis. She had no history of other medication use for osteoporosis. Osteoporosis was diagnosed both clinically and radiographically (Fig. 1). She had no nutritional deficiencies or family history of osteoporosis. She had undergone a hybrid THA because of

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Author's Photo Gallery


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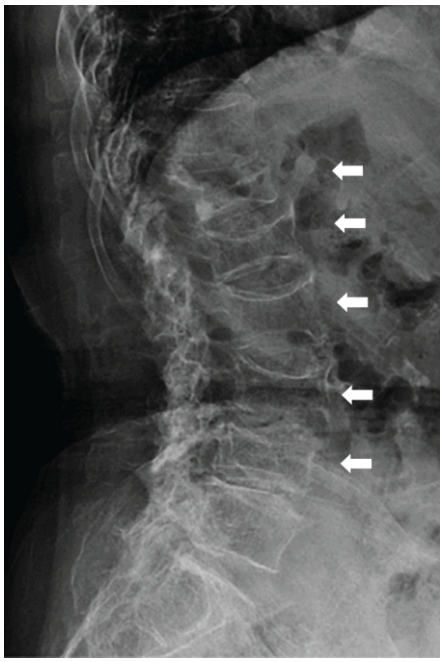

Figure 1: Radiograph of the spine taken in 2018. Severe vertebral compression is highlighted with arrows.

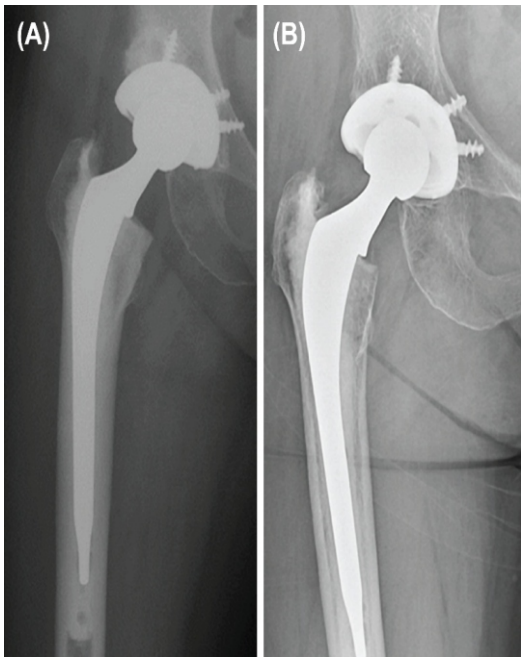

Figure 2: (a) Anteroposterior radiograph of the right hip at the time of the arthroplasty in 2006. (b) Radiograph at the time of denosumab administration for the 1st time in 2018. No pathological changes are observed around the stem.

developmental dysplasia of the right hip in 2006. At our hospital, she received denosumab 60 mg per dose, for a total of six doses. Meanwhile, colon cancer was detected in August 2019, and she underwent endoscopic surgery in September 2019. She also underwent positron emission tomography, which showed no metastasis, after which she underwent regular follow-ups without any anticancer drugs. No regular medications were prescribed for other diseases. She had been generally healthy otherwise. In May 2021, she experienced slight weight-bearing pain in the right hip with no antecedent trauma. Radiographs at the time of THA in 2006 and at the time of denosumab administration for the 1st time in 2018 showed no pathological changes in the femoral shaft around the stem (Fig. 2); however, there was an apparent transverse fracture line with lateral cortical thickening when she felt pain in the right thigh (Fig. 3). Computed tomography revealed femoral cortical reactions more clearly (Fig. 4). She had not received systemic glucocorticoids and proton-pump inhibitors, which had been listed as drugs that affect the bones in a previous study [4]. A diagnosis of denosumab-associated atypical periprosthetic fracture was made. She underwent revision surgery for conversion to a longer cemented stem (Fig. 5a). 10 months later, the fracture site healed (Fig. 5b) and she was possible to walk no cane at the latest visit in August 2022.

Discussion

Due to the good long-term prognosis of THA, the incidence of PFF is rising [5], and currently, PFF is the second most common reason for revision surgery after THA [6]. With aging, it is necessary for some patients to receive medication for osteoporosis. Although antiresorptive agents, like bisphosphonate or denosumab, are the most powerful remedy for decreasing fractures in patients with osteoporosis, they reduce bone remodeling. In addition, they might lead to suppress bone turnover severely and insufficiency femoral fractures over time [7,8].

In 2014, by the American Society for Bone and Mineral

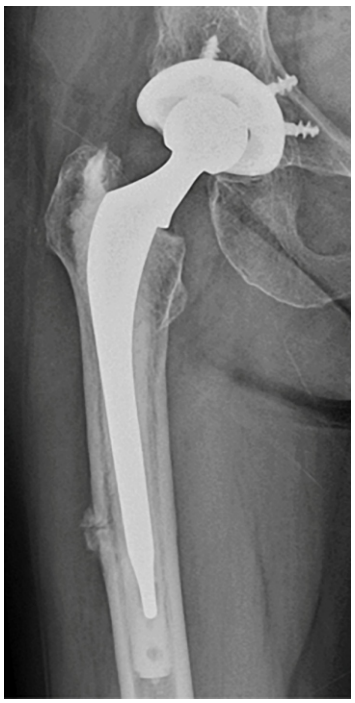

Figure 3: The radiograph taken in 2021 when the patient felt the pain in the right hip shows the transverse fracture line at the lateral cortex with periosteal thickening.

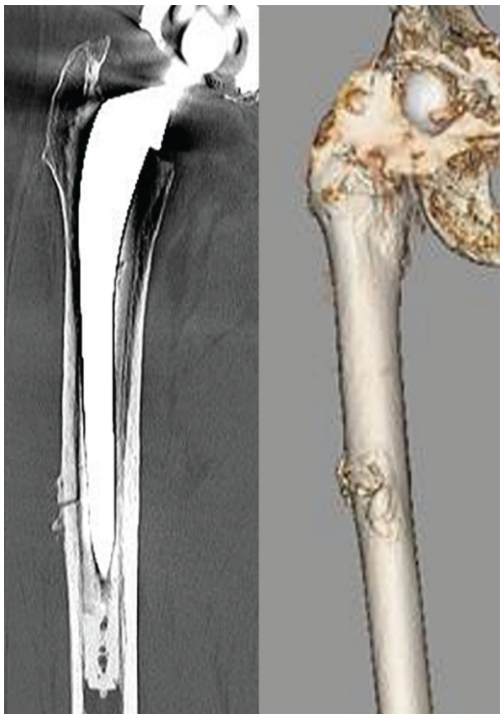

Figure 4: Computed tomography scans of the right hip taken in 2021 depict the periosteal reaction more clearly.

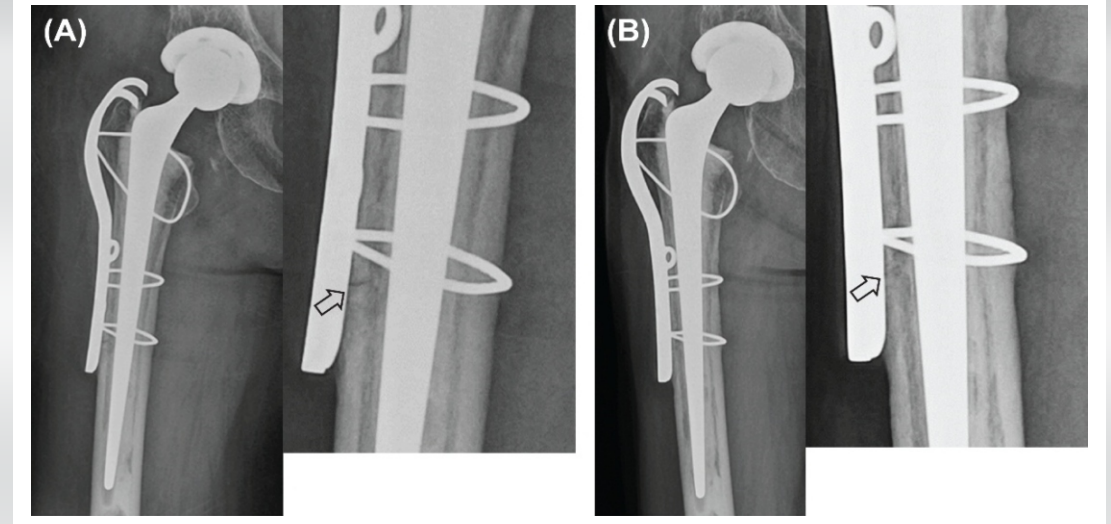

Figure 5: (a) Femoral revision surgery was performed using a long stem. The trochanteric plate was applied in 2021 because of the trochanteric separation during the surgery. (b) After 10 months, in 2022, the fracture has healed.

Research Task Force, the diagnosis criterion of AFF was revised as a minimum of four of the following five major features [9]: (1) Fractures associated with minor or no trauma; (2) minor or no comminuted fractures; (3) transverse fracture line originating from the lateral cortex; (4) complete fractures extending through both cortices and possibly associated with a medial spike, while incomplete fractures involving only the lateral cortex; and (5) regional periosteal or endosteal thickening of the lateral cortex on the fracture site.

The present case demonstrated a Vancouver type-B1 fracture [10] around the cemented stem. The current AFF definition excludes PPFs, however, our case fulfilled the five criteria described above. We support the study by Mondanelli et al. that claims that periprosthetic AFF exists [3]. AFF in patients using denosumab has been reported to be lower than that in patients using bisphosphonate [10, 11, 12]. Dupaix et al. [13] presented the first case of denosumab-associated peri-implant AFF. The patient in that study was treated for a subtrochanteric femur fracture with reamed intramedullary nail placement. After receiving denosumab for more than 5 years, she sustained a fracture around the locking screw placed previously. However, as far as we know, there have been no reports of denosumab-associated periprosthetic AFF. Although denosumab treatment for up to a decade showed a low fracture incidence in patients with osteoporosis and continued increases in bone mineral density with fewer adverse events rate [14], periprosthetic AFFs can occur in patients using denosumab over long periods.

This study is limited by the fact that only one case is described; this is because periprosthetic AFFs do not commonly occur. However, our case demonstrates that periprosthetic AFFs may occur over time in patients undergoing denosumab treatment.

Conclusion

Herein, we describe a case of denosumab-associated periprosthetic AFF. Denosumab decreases fractures in osteoporotic patients by suppressing bone resorption, which reduces bone remodeling and may lead to fatigue fractures. However, it should be borne in mind that denosumab-associated periprosthetic AFFs can occur due to the high survival rate after THA and the need for osteoporotic treatments accompanying aging.

Clinical Message

Denosumab is a good drug that has fewer adverse events and increases bone mass, though, that also has the potential of occurring periprosthetic AFFs like bisphosphonate. We should keep in mind this phenomenon under the high survival rate of THA and gaining need for osteoporotic treatment attendant on aging.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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Consent: The authors confirm that informed consent was obtained from the patient for publication of this case report

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