Periprosthetic Fracture Resembling Atypical Femoral Fracture After Fixation With Retrograde Intramedullary Nail in Elderly Women: A Report of Two Cases

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Abstract. Background/Aim: The number of individuals diagnosed with and requiring medical treatment for osteoporosis continues to increase due to global population aging and the high awareness of osteoporosis. Bone-modifying agents (BMAs) including bisphosphonate and denosumab are widely used for osteoporosis, and atypical femoral fracture (AFF) is also gaining attention as a severe potential side effect of long-term BMA treatment. The definition of AFF excludes periprosthetic femoral fracture; here, we describe two cases of a periprosthetic femoral fracture that resembled AFF. Case Report: The fractures occurred at the proximal tip of the retrograde femoral nail after an internal fixation for a distal femoral shaft fracture in elderly Japanese women. Each woman had been treated with bisphosphonate therapy for >2 years and had continued the bisphosphonate after undergoing surgery for a distal femoral shaft fracture. Each patient had noticed thigh pain before falling down, and plain radiographs showed a short oblique or transverse fracture with medial spike and localized periosteal reaction of the lateral cortex in each case. The fractures were re-fixed with an antegrade intramedullary nail, and bone union was achieved at >1 year after the second operation. Although these two cases were classified as periprosthetic fractures, they fulfilled the characteristics of AFF. Conclusion: Physicians should conduct a thorough interview of patients with a history of BMA treatment in order to correctly diagnose periprosthetic fractures that resemble AFFs, and they should be aware that symptomatic fractures can be prevented by prophylactic fixation. The discontinuance of BMA therapy and the introduction of another drug such as teriparatide may lead to faster healing of surgically treated AFFs.

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The number of individuals diagnosed with and receiving medical treatment for osteoporosis has markedly and rapidly increased as lifespans continue to expand (1). Bone-modifying agents (BMAs) including bisphosphonate and denosumab are the representative drugs for treating osteoporosis and are now used globally. One of the potential adverse effects of long-term BMA treatment is atypical femoral fracture (AFF), which is also gathering attention. Herein, we describe two cases of a femoral subtrochanteric fracture resembling an AFF that occurred at the proximal tip of the retrograde intramedullary nail (IMN) after the internal fixation for a femoral distal shaft fracture in elderly patients.

Case Presentation

Case 1. An 81-year-old Japanese woman presented with right thigh pain after falling to the floor. She had taken 10 mg per day of prednisolone for rheumatoid arthritis and
Bisphosphonate therapy for 8 years to prevent glucocorticoid-induced osteoporosis. The bone mineral density (BMD) values at the lumbar spine and femoral neck were 59% and 66% of the young adult mean (YAM), respectively. Plain radiographs showed a right femoral shaft fracture, non-comminuted and of transverse type (Figure 1A, B). The patient was diagnosed with an AFF based on the 2010 criteria issued by the American Society for Bone and Mineral Research (ASBMR) (Table 1) (2). She underwent open reduction and internal fixation using a retrograde IMN (Figure 1C, D). She stopped taking the bisphosphonate and received teriparatide treatment for the delayed union, and the fracture finally achieved bone union. At approximately 20 months after the operation, the patient fell to the floor; she reported having felt right thigh pain just before falling. Plain radiographs showed a right femoral subtrochanteric fracture at the level of the most proximal transverse screw of the retrograde IMN. It was a non-comminuted and short oblique fracture with a medial spike and a localized periosteal reaction (flaring) of the lateral cortex (Figure 2A, B). Although this fracture resembled an AFF, it was classified as a periprosthetic fracture due to the AFF exclusion criteria. The retrograde IMN was removed, and the fracture was re-fixed with an antegrade IMN. After the second operation, the oral bisphosphonate re-started by the patient's physician after the first operation was stopped again, and teriparatide treatment was re-started.

Table I. The criteria of atypical femoral fracture (AFF).

| Major and minor features<sup>a</sup> | Major features:<sup>b</sup> |
|-------------------------------------|----------------------------|
|                                     | • Located anywhere along the femur from distal to the lesser trochanter to proximal to the supracondylar flare |
|                                     | • Associated with no trauma or minimal trauma, as in a fall from a standing height or less |
|                                     | • Transverse or short oblique configuration |
|                                     | • Noncomminuted |
|                                     | • Complete fractures extend through both cortices and may be associated with a medial spike; incomplete fractures involve only the lateral cortex |

| Minor features: | | |
|-----------------|-----------------|-----------------|
|                 | • Localized periosteal reaction of the lateral cortex<sup>c</sup> |
|                 | • Generalized increase in cortical thickness of the diaphysis |
|                 | • Prodromal symptoms such as dull or aching pain in the groin or thigh |
|                 | • Bilateral fractures and symptoms |
|                 | • Delayed healing |
|                 | • Comorbid conditions (e.g., vitamin D deficiency, rheumatoid arthritis, hypophosphatasia) |
|                 | • Use of pharmaceutical agents (e.g., bisphosphonates, glucocorticoids, proton pump inhibitors) |

<sup>a</sup>Fractures of the femoral neck, intertrochanteric fractures with spiral subtrochanteric extension, pathologic fractures associated with primary or metastatic bone tumors, and periprosthetic fractures are excluded. <sup>b</sup>All major features are required to satisfy the case definition of AFF. None of the minor features are required but sometimes they have been associated with these fractures. <sup>c</sup>Often referred to in the literature as beaking or flaring. Source: 2010 ASBMR (2).
intensity pulsed ultrasound (LIPUS) therapy was used for the prevention of a delayed union. However, 2 months later, the teriparatide treatment was discontinued because of the development of diarrhea and slight fever.

Thereafter, only the oral administration of active vitamin D was continued for the treatment of osteoporosis. Although bone union was delayed at first, it was finally achieved 2 years after the second operation (Figure 2C, D). The patient was able to walk painlessly with a walker, 6 months after the second operation.

Case 2. A 76-year-old Japanese woman who was diagnosed with osteoporosis and had received bisphosphonate therapy for >2 years presented to the prior hospital with right thigh pain after falling backward. The BMD values at the lumbar spine and femoral neck were 82% and 75% of the YAM, respectively. Plain radiographs showed a right femoral distal shaft fracture, of spiral type. This fracture did not fulfil the criteria for an AFF (Figure 3A, B). The patient underwent open reduction and internal fixation using a retrograde IMN at the prior hospital (Figure 3C, D). The patient's bisphosphonate therapy was continued after the operation, and the bone union was achieved 5 months later.

Three years after the operation, the patient fell again. She also reported feeling right thigh pain before the second fall. Plain radiographs showed a right femoral subtrochanteric fracture at the level of the most proximal transverse screw of the retrograde IMN, revealing a non-comminuted and transverse fracture with a medial spike and a localized periosteal reaction (flaring) of the lateral cortex (Figure 4A, B). Although this fracture resembled an AFF, it was also classified as a periprosthetic fracture because of the AFF exclusion criteria. The retrograde IMN was removed and re-fixation with antegrade IMN was performed.
After the second operation, the patient's bisphosphonate therapy was discontinued and both teriparatide and LIPUS therapies were started. Although the bony gap at the lateral cortex remained, bone union was achieved 1 year after the second operation (Figure 4C, D). The patient was able to walk painlessly without a cane or orthosis 3 months after the second operation.
Discussion

Due to the significant increase in the number of individuals with osteoporosis, the use of BMAs (including bisphosphonate and denosumab) has also increased, and AFF as a potential side effect of long-term BMA therapy is observed more frequently. An AFF is a femoral subtrochanteric or shaft fracture associated with long-term BMA treatment. The main factor of AFF is thought to be severely suppressed bone turnover (3). In addition, AFF is reported as a type of stress fracture associated with a bowing deformity of the femoral shaft (4). Although a periprosthetic femoral fracture is excluded by the definition of AFF, the number of reports of a periprosthetic femoral fracture harboring the characteristics of AFF is increasing. Niikura et al. (5) reported a case of bisphosphonate-associated AFF that occurred around the femoral component of a total hip arthroplasty. Tanaka et al. (6) reported a similar case, and they suspected that the fracture was influenced by both stress force related to an implant and lateral bowing concentrating on the fracture site as a mechanical factor (in addition to bisphosphonates as a biological factor).

The present two patients were elderly women who had been treated with an oral BMA for osteoporosis for >5 years. Their second fractures were diagnosed as periprosthetic fractures resembling AFF. These fractures were influenced by a mechanical factor, i.e. stress force concentrated on the femoral sub-trochanter caused by the retrograde femoral nail, in addition to the biological factor of the BMA. To the best of our knowledge, there is no report of such periprosthetic fractures resembling AFF that occurred around an IMN.

The number of femoral distal shaft fractures including femoral supracondylar fractures in the elderly is expected to increase. Although many studies have reported the efficacy of a retrograde IMN for these fractures (7-10), these can now be securely fixed, due to the improved mechanical stability of antegrade IMN with three or four poly-axial distal transverse screws (11). From the experience of our two cases, we recommend that orthopedic surgeons should take the risk of a periprosthetic femoral subtrochanteric fracture in elderly patients into account in the presurgical planning for an antegrade IMN.

It has been reported that some patients with an AFF may have a prodrome such as thigh pain despite the poor radiographic findings (12). In cases of a periprosthetic fracture resembling AFF, the same problem may be expected as in the present two cases. Physicians can correctly diagnose a periprosthetic fracture resembling an AFF by conducting a thorough interview of the patient about his or her BMA history and surgeons can prevent a symptomatic fracture by performing a prophylactic fixation with an antegrade IMN. After the diagnosis, an early discontinuance of the BMA treatment and the introduction of another drug such as teriparatide may lead to faster healing of surgically treated AFFs (13, 14).

Conclusion

We described two cases of a femoral subtrochanteric fracture around the proximal end of the retrograde femoral nail after internal fixation for a femoral distal shaft fracture in elderly women. Although these were classified as periprosthetic fractures and excluded from AFF by the current diagnostic criteria, they were thought to be fractures resembling an AFF based on the patients' history of long-term bisphosphonate treatment and the characteristics of the fractures. We suggest that femoral distal shaft fractures in elderly individuals with a history of BMA therapy should be treated with an antegrade IMN if possible, to avoid the occurrence of a periprosthetic fracture resembling an AFF.

Conflicts of Interest

The Authors state that they have no conflicts of interest to declare in regard to this study.

Authors’ Contributions

YT operated on the patient and wrote the manuscript. SH,YS and MI were involved in patient care, manuscript preparation and review. YK, MH and SK were involved in manuscript preparation and review. All Authors read and approved the final manuscript.

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