Clinical features of atypical femur fracture

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Abstract

Objectives: We aim to elucidate the clinical outcomes of bisphosphonate-associated atypical femoral fracture and the clinical results depending on the bisphosphonate therapy period.

Methods: Twenty cases involving 15 patients who had been diagnosed with atypical femoral fracture between 2004 and 2014 and who had been followed up for at least 12 months were retrospectively analyzed. The control group was composed of 15 typical femoral fracture patients. We used plain radiography and physical examinations to determine the period of time required for fracture healing as well as complication occurrence. We investigated the bisphosphonate administration status and duration and the names of its components, bilateral fracture occurrence status, the period of time required for bone union, and reoperation or bone graft status due to nonunion.

Results: Revision surgery involving a bone graft was performed due to nonunion in 1 out of 15 cases. Except in one revision case, the duration of the union was 11.9 months on average in 14 cases of atypical fracture patients, and 4.3 months on average in the control group. This difference was statistically significant (p < 0.05). The bisphosphonate administration duration was positively correlated with the union period (p < 0.05). In contrast, there was no statistically significant correlation between the bisphosphonate administration duration and the incidence of bilateral atypical fractures (p > 0.05).

Conclusions: Atypical femoral fractures required more time for bone union than typical ones and prolonged bisphosphonate administration led to a longer period of time required for bone union.

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Keywords: Atypical femur fracture; Bisphosphonate

1. Introduction

Typical femoral fractures usually do not occur in the subtrochanteric area and comminuted fracture patterns appear in many cases. Conversely, atypical femoral fractures are relatively more commonly found in the subtrochanteric area with specific features [1]. Atypical femoral fractures are primarily characterized by transverse or exhibit short oblique fracture configurations, non-committed fracture patterns, medial spikes, localized periosteal thickening of the lateral cortex, generalized thickening of the femoral cortices, and confer prodromal symptoms such as pain [2–4] (Fig. 1).

The American Society for Bone and Mineral Research (ASBMR) task force established major and minor features of atypical femoral fractures and classified them into complete and incomplete categories [5]. Although these criteria are of great help in understanding atypical femoral fractures, some features are still controversial.

While bisphosphonate is commonly used to prevent osteoporotic fractures, many researchers have recently reported atypical femoral fractures without trauma or following mild trauma among the patients who have been administered bisphosphonate for extended periods of time [5–7]. However, it is actually difficult to conduct research on the association
between bisphosphonate and an atypical femoral fracture, which occur very infrequently. The direct associations between atypical fractures are still controversial and the definite cause of atypical femoral fractures is unknown.

This study aimed to determine the period of time required for bone union in atypical femoral fractures associated with bisphosphonate, evaluate their prognoses and determine the association between the bisphosphonate administration duration and the prognoses.

2. Subjects and methods

2.1. Study population

Twenty cases involving 15 patients who had been diagnosed with an atypical femoral fracture between 2004 and 2014 and who had been followed for at least 12 months, were retrospectively analyzed (Table 1). The control group was composed of 15 typical femoral fracture patients, taking into account gender, age, injury sites, BMI, fracture patterns, and surgical procedures. The patients with underlying disease, which could possibly affect bone union, were excluded from the control group. In 5 out of 15 cases of atypical femoral fractures, bilateral atypical femoral fractures were found.

A case in which an atypical fracture occurred seven years after a typical fracture on the other side was included in the control group.

2.2. Methods

We used plain radiography and physical examinations to determine the period of time required for fracture healing as
As complication occurrence. When anterior, posterior, and lateral radiographs of the fracture site showed that bone continuity was maintained or that ossification of the callus covered at least three-fourths of the fracture plane and when the fracture site involved no pressure pain or movement, it was defined as a bone union. We investigated the bisphosphonate administration status and duration and the names of its components, bilateral fracture occurrence status, the period of time required for bone union, and reoperation or bone graft status due to nonunion.

2.3. Statistical analysis

An SPSS 22.0 program was used to perform a paired t-test and correlation analysis at the $p < 0.05$ significance level.

3. Results

The mean age of the atypical fracture patients was 77.9 (58–103 years) years. The mean follow up period was 15.3 months (12–34 months). Of the 15 patients, 7 patients showed subtrochanteric fractures, and in 8 patients femoral shafts were involved. Twelve of 15 patients had a history of bisphosphonate administration. Of the 3 patients without bisphosphonate administration, 1 had multiple myeloma, 1 was using methotrexate (MTX) for rheumatoid arthritis, and 1 had no history of specific conditions or medication. As for bisphosphonate, alendronate was used in 10 cases and risedronate in 2 cases. Revision surgery involving a bone graft was performed due to nonunion in 1 out of 15 cases. Except in one revision case, the duration of the union was 11.9 months on average in 14 cases of atypical fracture patients, and 4.3 months on average in the control group. This difference was statistically significant ($p < 0.05$) (Table 2).

In 2 out of 5 cases of bilateral atypical femoral fractures, both an atypical complete fracture on one side and an atypical incomplete fracture on the other side were found at the same time. Of these, one case involved bilateral femoral intramedullary nailing and the other was followed up because no clinical symptom of an incomplete fracture was found. In the other 2 cases, preventive intramedullary nailing was performed for the incomplete fracture on the other side, which was found three months and two years after the surgical treatment for an atypical complete fracture, respectively. In 1 case, surgical treatment was performed for an atypical complete femoral shaft fracture seven years after an atypical fracture had occurred on the other femoral shaft.

Table 2

|                     | Group A (n = 15) | Group B (n = 15) | P-value |
|---------------------|-----------------|-----------------|---------|
| Union periods (months) | 11.93 ± 8.16   | 4.27 ± 1.98     | 0.008   |

Group A: Atypical fracture, Group B: Typical fracture (Values were presented as Mean ± S.D.).

Fig. 2. Correlation of medication period and union period in atypical femoral fracture cases.

The mean bisphosphonate administration duration was 73 months (12–135 months). The bisphosphonate administration duration was positively correlated with the union period ($p < 0.05$) (Fig. 2). In contrast, there was no statistically significant correlation between the bisphosphonate administration duration and the incidence of bilateral atypical fractures ($p > 0.05$).

Fig. 3. Hip AP view shows complete fracture of left subtrochanter and incomplete fracture (white arrow) of right subtrochanter (A). Immediate postoperative radiography (B).
4. Discussion

With an increasingly aging population, the use of antiosteoporotic agents is on a gradual increase and atypical femoral fractures related to bisphosphonate administration are being reported. Now many researchers show that prolonged bisphosphonate administration may lead to a higher incidence of atypical femoral fractures.

The atypical femoral fracture group required statistically significantly more time for bone union than the typical femoral fracture group. While many researchers report the same result, the definite cause of which has not yet been found, impaired osteogenesis related to a severely suppressed bone turnover is seemingly associated with atypical femoral fractures or delayed union, taking into account a lower bone turnover rate and impaired osteogenesis among the patients administered with bisphosphonate [2,8].

The bisphosphonate administration duration was found to be positively correlated with the union period in the cases of atypical fractures. Therefore, since prolonged bisphosphonate administration can lead to a higher incidence of delayed union in atypical femoral fractures, prolonged bisphosphonate administration requires a great deal of care and drug holidays.

The incidence of bilateral fractures in this study was as high as in prior ones: 5 out of 15 cases involved bilateral femoral fractures in this study [5]. In the cases of atypical femoral fractures, therefore, it is necessary to carefully observe the other femur because bisphosphonate administration may increase the incidence of bilateral femoral fractures.
(Fig. 3). Recent research has shown that prolonged anti-osteoporotic agent administration may lead to a higher incidence of bilateral fractures [2,9]. No statistically significant correlation was found between the two factors, probably because of the small sample. Nonetheless, further research should be conducted on this issue.

Since incomplete fractures of the other femur can be healed using conservative treatment in some cases but develop into complete ones in other cases, the need for prophylactic internal fixation is still controversial. Some researchers suggest performing prophylactic internal fixation when the patients feel pain in their lower limb and when periodic x-rays, magnetic resonance imaging (MRI) scans, and bone scans show that a fracture is imminent [10]. Das De et al. recommended prophylactic internal fixation when an atypical incomplete femoral fracture is found along with its clinical symptoms among the patients administered with bisphosphonate for a long time [11]. In this study, a unilateral atypical fracture was followed by an atypical incomplete fracture on the other side in four out of five cases of bilateral atypical femoral fractures and prophylactic internal fixation was performed in three of the four cases because of the prodromal pain in the other lower limb and impending fracture patterns on x-ray findings. All cases were successfully treated using preventive intramedullary nailing. It is probably desirable to perform prophylactic internal fixation when an atypical incomplete fracture is identified along with its clinical symptoms.

Delayed union or nonunion in femoral fractures can remarkably increase the treatment duration and medical expenses, lower the quality of life, and lead to poor prognoses. A bone graft can be effective against nonunion, which occurred in one out of fifteen cases in this study and was treated through revision surgery with bone grafting (Fig. 4).

In addition to a bone graft, synthetic parathyroid hormone agents could reportedly increase the rate of bone unions among fracture patients and stimulate bone unions among the patients with nonunions [12–14]. It is believed that parathyroid hormone agents can also help shorten the period of time required for bone union in atypical femoral fractures and further research should be conducted on this issue.

Atypical femoral fractures are hard to treat and require a great deal of care. It is necessary to use bisphosphonate both because it is known that the incidence of atypical femoral fractures is not high and because bisphosphonate administration is very effective in preventing osteoporotic fractures. However, it is necessary to protect against complications in using bisphosphonate. Further, atypical femoral fractures need to be treated, taking clinical features into account.

5. Conclusion

Atypical femoral fractures required more time for bone union than typical ones and prolonged bisphosphonate administration led to a longer period of time required for bone union. Because atypical femoral fractures are bilateral ones in many cases, a unilateral atypical fracture may require continuous radiographic observation of the other femur.

Consent for publication

We have obtained consent to publish from the participants.

Competing interests

The authors have no competing interests to declare.

Ethics approval and consent to participate

The protocol of this study was approved by Inha university hospital Institutional Review Board (Approval number: INHAUH 2016-06-016).

Authors’ contributions

All authors listed made substantial contributions to this study. KHM contributed to the design of the study. NCK and JSS wrote the article and collecting data. All authors have read and approved the final manuscript.

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