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The Bilateral Insufficiency Fracture of Proximal Femur due to Bisphosphonate Overuse in the Nonosteoporotic Bone

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Abstract

62 year old female underwent closed reduction of subtrochanter fracture by the minor trauma. She was checked quantitative computerized tomography (QCT) for the bone mineral density. It showed highly elevated density above the normal range. She could easily take the bisphosphonate for 3 and half years without regular evaluation of the bone mineral density. The fracture was bilateral and atypical fracture pattern in the subtrochanter area. These kinds of fracture were occurred in the osteoporotic bones in the previous literature, so we hardly conclude the culprit of bisphosphonate related atypical fractures. The prevalence of these kinds of insufficiency fracture among the normal population and bisphosphonate medicated patients has been still debated but we can strongly suggest that our fractures were related to the bisphosphonate medication because she was a nonosteoporotic bone who took a bisphosphonate medication.

Keywords: Bisphosphonate; Atypical fracture; Nonosteoporotic bone; Subtrochanter; Femur

Introduction

Concerns over osteoporosis are increasing with the growth of the elderly population. In response, bisphosphonate therapy is being widely used for the treatment of osteoporosis and prevention of fractures and outstanding results are being reported about the effects of bisphosphonates on fracture prevention [1-3]. It has been found that these drugs are deposited in the mineral component of the bone leading to the reduction in osteoclast formation and to apoptosis that reduce bone resorption, and thereby increase bone density [4]. There drugs are known to be relatively safe but concerns have been raised about the possibility of their negative effects on bone strength from long-term use that inhibits normal bone resorption and regeneration [5-7]. Based on a case of a low-energy femoral proximal fracture that occurred in a normal patient without osteoporosis who had been taking alendronate for a long time, this report explains the causal relation between preventive long-term intake of bisphosphonates and its resulting insufficiency fracture through the clinical and radiographic findings.

Case Report

A 62-year-old female patient was brought in to the hospital through emergency room with main complaints of pain in the right side hip joint area due to a fall from a standing height in her room which occurred on the same day. According to the patient's medical history, she has been orally taking alendronate (70 mg tablet) for about 3 and half years without having gone through an osteoporosis test. The patient stated in her family history that it was easy for her to take the drug without an osteoporosis test because her husband was an internal medicine doctor, her daughter was a gynecologist, and her son-in-law was a neurosurgeon. There was no additional calcium or vitamin analogue drug. She has no specific medical history of medication or operation. Her menopause's age was 55 years and there was no medication for the postmenopausal syndrome. The patient who was diagnosed as osteoporosis with any kinds of osteoporosis test tools such as QCT, DEXA could have medication under government medical insurance support in Korea.

From a bilateral anteroposterior pelvis radiograph, a transverse fracture was observed at the right femoral subtrochanter, while a thickening of the lateral femoral cortex finding was observed at the left femoral subtrochanter (Figure 1). Otherwise, no pathologic finding was seen and bone quality was good in the plain x-ray. This radiographic



Figure 1: A Plain radiograph shows sclerotic change in the distal end of proximal fracture fragment (white blanked arrow) and thickening of the femoral cortex with a localized lateral cortical reaction at the level of fracture on the opposite side (white arrow).

finding indicated an atypical fracture seen in atypical insufficiency factures and not in acute traumatic fractures. According to the QCT bone densitometry performed after hospitalization, the T-score was 0.3 and the Z-score was 3.2, while the bone density finding indicated an increase compared to normal findings (Figure 2). The ALP was normal at 51 IU/L (reference value 31-104), the PTH-intact was normal at 55.96 pg/ml (reference value15-65), 25 (OH) Vitamin D at 10.74 ng/ml (reference value11.4-37) indicated insufficiency, and the N-terminal telopeptide showed a low score of 18 BCE/nM Cr (reference value for menopausal women 26-124). A day after the sustained injury, a closed reduction and an internal fixation were performed on the right subtrochanteric femoral fracture using Gamma 3 (Stryker, Trauma,

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Received December 28, 2015; Accepted February 23, 2016; Published February 27, 2016

Citation: Kim H, Chung K, Bae K, Hwang J (2016) The Bilateral Insufficiency Fracture of Proximal Femur due to Bisphosphonate Overuse in the Nonosteoporotic Bone. J Clin Case Rep 6: 716. doi:10.4172/2165-7920.1000716

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GmbH, Schonkirchen, Germany) intramedullary device for bone fixation (Figure 3). The patient used a wheelchair starting on the third day after the surgery and a walker on the fifth day after the surgery. Free of any complications, the patient was discharged on the ninth day after the surgery. After the surgery, the use of alendronate was discontinued and we started synthetic parathyroid hormone (teriparatide) after 2 months of operation because we couldn't find of any bone callus in this patient and we couldn't expect normal bone healing in this type of insufficiency fracture. So we decided to prescribe hormone even though the bone quality was normal. It was based on the other authors' experiences. We continued this medication for 10 months but we failed to gain of union. We conducted long nail system with static mode and additional augment plating without bone graft on the 13th month of 1st operation. We gained complete union at the 11 month follow up after 2nd operation (Figure 4).

Discussion

Alendronate is the oldest and most widely used drug in the class









Figure 4: We converted long nail system with augmented plating without bone graft because of nonunion on 13th months of first operation. The last follow up x-ray after 11 month of 2nd operation showed complete union (A-femur AP view, B-lateral view).

of bisphosphonate drugs as it is known to reduce the occurrence of fractures by over 50% compared to a control group [8] and is found to be safe and effective in general [9]. It has been reported that the drug's function of inhibiting bone resorption is maintained for 5 additional years even after discontinuing the drug after taking it for five-years [10]. However, recent studies have reported the negative effects resulting from long-term use of the drug, and cause analysis on these effects or their impact on complications is still open to dispute [2,7,9,11,12]. Ott had stated that long-term use of alendronate may have a negative effect on the bone regeneration process [11]. However, in a 2002 report about atypical insufficiency femoral neck fractures associated with etidronate, Iwamoto and Takeda referred to alendronate as a drug that can reduce side effects of atypical insufficiency fracture having less influence on bone regeneration [13]. Since then, reports have been made about atypical insufficiency fractures in femoral subtrochanter, which is normally known to occur in fractures due to high-energy injuries, presenting, in particular, the radiographic features that compose the fractures, such as the thickening and hardening of the cortex, transverse fracture, and anterior cortex spike [7]. In the present case, these radiographic features were likewise found in both sides of the proximal femoral fracture area. In this case, with a history that does not show specific external trauma but a mild injury, the atypical insufficiency fracture occurred in the femoral subtrochanter, which is unlikely to sustain such a fracture from a mild injury. However, unlike the reports related to atypical insufficiency fractures [9,12], the present case revealed above normal range in the T-score and Z-score of QCT results from the bone densitometry. Given the findings from this case and other reports discussed above, it is judged that the atypical insufficiency fracture is caused by the bone structure becoming brittle to trauma with an increase of bone mineralization and decrease of bone elasticity due to long-term use of alendronate for over five years. In the present case,

one thing that needs to be considered after the surgical treatment on the right subtrochanteric femoral fracture is the selection of osteoporosis medication. First of all, alendronate treatment should be discontinued while a switch to anabolic osteoporosis agent can be considered. The second thing that needs to be considered is whether to perform surgery on the opposite side at the level of the atypical insufficiency fracture. The patient has not suffered any weight bearing pain on this side nor has she complained about any current pain when walking. Thus, it was determined that radiographic observation would be planned for later with the consent of the patient. The osteoporosis treatment was switched to teriparatide, a recombinant form of parathyroid hormone. Although it is deemed that medications facilitating bone formation would later have a positive effect on fracture union in the atypical insufficiency fracture at the femoral subtrochanter, continuous research is necessary for patients in this groups.

Conclusion

There are many studies that suggest that the occurrence rate of insufficiency fracture will not be significantly different from that of a control group that did not receive bisphosphonate treatment. However, as seen in the present case, the fact that insufficiency fracture occurred to a patient with normal condition who had been taking bisphosphonate signifies that the drug is a more definite causative agent of insufficiency fractures. We recommend that bisphosphonate should be considered as a 2nd drug line to treat the osteoporosis and the long duration of treatment of at least 3 years should be converted to no bisphosphonate osteoporosis medicine. If the patients who are taking bisphosphonate feel the spontaneous thigh pain, a doctor should check the plain x-ray and bone scan for the evaluation of insufficiency fracture. And the annual follow up examination of DEXA, x-ray and bone scan are helpful for the early detection of insufficiency fractures in the patients who are taking the bisphosphonate.

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Page 3 of 3