Bilateral Typical Femoral Fractures in a Patient with Metastatic Breast Cancer on Long-Term Bisphosphonate Therapy: A Case Report

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Abstract

An atypical femoral fracture may be one of the devastating side effects of bisphosphonate. We present a patient who obliged to multiple surgeries for atypical femoral fracture of the femur after bisphosphonate therapy. A 63-year-old woman had been on anti-estrogen therapy for skeletal metastasis of the breast cancer. She received 90 mg of pamidronate disodium for 2 years and 4 mg of zoledronic acid for 4 years. Four month after she developed spontaneous left thigh pain, she fell from a standing height. X-ray films showed a subtrochanteric fracture of the left femur. The patient underwent surgery with an intramedullary nail, and radiation therapy was delivered to the fracture site because the possibility of a pathological fracture was unable to be excluded. Radiographs showed some evidence of callus formation, but the fracture line persisted. Two years later, the intramedullary nail broke at a screw hole in radiographs. Bipolar hip arthroplasty was performed and bone chips were grafted at the fracture site. Ten weeks after the operation, callus formation was satisfactory and she was able to walk without pain. One year after the first operation on the left femur, she complained of spontaneous pain in the right thigh and radiographs showed a lateral cortical beak sign with no evident fracture line. The patient underwent intramedullary nailing to prevent subsequent fracture. The radiological fracture sign were improved one year after the operation. The prophylactic intramedullary nailing is effective for the patients with lateral cortical thickening and/or a medial spike on X-ray.

Keywords: A Typical Femoral Fracture (AFF); Breast cancer; Bisphosphonate; Zoledronic acid; Operation; Prophylactic intramedullary nailing; Bipolar hip arthroplasty

Introduction

Zoledronic acid is a potent bisphosphonate (BP) that has been used to reduce skeletal-related events in breast cancer patients with bone metastasis [1]. Side effects associated with BP therapy include oesophagitis, renal dysfunction, osteonecrosis of the jaw, and infusion-related reactions [2,3]. Recently, some reviews have raised concern that prolonged BP therapy may also be associated with atypical femoral fractures (AFFs). The radiographic features of AFFs include a transverse fracture line at the point of origin in the lateral cortex and a prominent medial "spike", cortical “beaking” or “flaring” adjacent to a discrete transverse lucent fracture line, or focal thickening of the lateral cortex [4]. We report a case of bilateral AFFs in a patient with metastatic breast cancer who had been given high-dose treatment with zoledronic acid.

Case Report

A 63-year-old Asian woman had received a diagnosis of breast cancer with skeletal metastasis in 2004 and had been on anti-estrogen therapy since then. She was advised to commence BP therapy to prevent skeletal complications, and received 90 mg of pamidronate disodium intravenously once a month for two years. The cumulative dose of pamidronate disodium was 1980 mg. In 2006, she was switched to treatment with 4 mg of zoledronic acid intravenously once a month. The cumulative dose of zoledronic acid was 208 mg. After 6 years of BP therapy, she developed spontaneous left thigh pain. Four month later, she fell from a standing height. An X-ray film of the left femur (Figure 1) showed a transverse fracture in the subtrochanteric region associated with lateral cortical thickening and a medial spike. The patient underwent insertion of an intramedullary nail (9.3 mm in diameter) into the left femur (Figures 2a). At 16 days after the operation, radiation therapy (30 Gy) was delivered to the fracture site because the possibility of a pathological fracture was unable to be excluded. Serial radiographs showed some evidence of callus formation, but the fracture line persisted after 2 years. She then developed severe pain at the left mid-thigh and radiographs showed that the intramedullary nail had broken.

Figure 1: A transverse fracture in the subtrochanteric region associated with lateral cortical thickening and a medial spike on the left femur.

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were measured 2 weeks before bipolar hip arthroplasty (serum tartrate-

Bone metabolism markers were within normal limits when they

left femur, the beak sign and fracture line were both improved (Figure

complete fracture did not occur. At 10 weeks after the operation on the

after the operation (Figure 3d), the patient did not develop pain and

visible at the site of the lateral cortical beak sign about four weeks

occurred. Therefore, she underwent intramedullary nailing of the right

the patient requested treatment of her right femur before a fracture

sign with no evident fracture line (Figures 3a and b). The blood test

fracture union. At 10 weeks after the operation, callus formation

in spite of delayed union of the fracture site. An after bipolar hip

administration of zoledronic acid was stopped focusing

arthroplasty, administration of zoledronic acid was stopped focusing

in patients with osteoporosis. There have been several reports about

AFFs in breast cancer patients with bone metastasis who were on

zoledronic acid therapy [9-13]. Puhaindran et al. reported that all of

their patients who developed AFFs had prodromal ipsilateral thigh pain

for at least two months, and suggested that it was useful to ask patients

receiving long-term intravenous BP therapy about such symptoms

[13]. Physicians who manage patients with skeletal metastases should

be aware of the emerging association between BP therapy and AFFs,

wince heightened awareness will lead to early detection of incomplete

fragments. In the report of the task force on AFFs, Shane et al. stated that

healing of complete fractures was not assessed in 196 of 310 reported

cases, but healing was delayed in 26% of the other 112 cases [14].

Therefore, if there is no symptomatic and radiographic improvement

of an incomplete fracture after conservative therapy, prophylactic

intramedullary nailing should be strongly considered because these

patients may progress to complete fracture. In our patient, the right

femur underwent intramedullary nailing before complete fracture

occurred and the fracture line was first detected at four weeks after

the operation. Therefore, there seems to be little possibility that an

incomplete fracture will heal with observation alone. In this case, the

AFF on the left side was misdiagnosed and treated with radiation

therapy. AFFs should be differentiated from bone metastatic lesion on

the basis of characteristic radiological findings before the treatment

because radiation therapy would not have inhibited bone remodeling.

Moreover teriparatide therapy that could accelerate healing of the

fracture is contraindicated for a patient who received radiation therapy
to the bone metastasis.

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