A 72-year-old woman presented with acute pain and deformity of the right hip and thigh after a trivial twisting movement with a subsequent gentle fall to the floor. She had been suffering from diffuse pain in both her hips and thighs for 18 months. For the 3 months prior to the fall, her walking ability had declined and she had been sitting in a chair when out of bed. Radiographs revealed a transverse subtrochanteric femoral fracture with a 180-degree displacement of the proximal femur. There was thickening of the lateral femoral cortex and medial spiking at the site of the fracture. The contralateral hip showed thickening of the femoral cortex with a localized lateral cortical reaction at the level of fracture on the opposite side (Figure 1). No osteolytic lesions were found.

The patient had been on alendronate (Fosamax) and calcium supplement therapy for the previous 7 years, after she was diagnosed with osteoporosis. The alendronate dose had been 10 mg once a day for the first 6 years and 70 mg once a week for the following year. She had a low BMI of 16 (underweight is < 18.5), weighed 38 kg, and was 154 cm in height.
The patient was operated with a long gamma nail and was discharged after 3 days. 3 months after the operation, she experienced improvement of the pain in her right hip and thigh while the pain in her left hip continued. The radiographs showed no signs of fracture healing (Figure 2). At 6 months, however, there was further clinical improvement and radiographic signs of healing (Figure 3).

Discussion

Insufficiency subtrochanteric femoral fractures in patients on long-term alendronate therapy have been described as an unusual complication by Kwek et al. (2008) and Goh et al. (2007). These authors reported 17 females on long-term alendronate therapy (mean 5 years) who sustained low-energy subtrochanteric fractures with a fracture configuration similar to the fracture in our patient, i.e. transverse fracture with thickening of the lateral cortex and medial spiking. 9 patients showed contralateral fracture or cortical reaction similar to the reaction seen in our patient. 13 patients experienced prodromal pain preceding the fracture, as in our patient. The pretreatment bone mineral density studies in these patients showed osteopenia in 6 patients and osteoporosis in the remaining patients. The type of osteoporosis was not defined.

Alendronate is a potent inhibitor of bone resorption, and it is prescribed as a first-line therapy for postmenopausal osteoporosis. The skeletal half-life of alendronate is long (Fleisch 1998) and it may last for more than 10 years, as the drug molecules attach to the bone and are not metabolized (Ott 2005). Although the safety and effectiveness of alendronate are well documented (Black et al 1996, 2004, Tonio et al. 2000), the long-term consequences of treatment remain unknown (Ott 2005). Odvina et al. (2005) discussed in detail the possible adverse effects of long-term alendronate therapy with the possible risk of severe suppression of bone turnover. This could possibly impair some of the mechanical properties of bone by increasing the rate of secondary mineralization, leading to brittleness. This is in accordance with the finding of Currey (1984), who stated that increasing bone mineralization gave a high Young modulus of bone elasticity but low work-to-fracture values (a measure of fracture toughness). Mashiba et al. (2001, 2005) found that severe suppression of bone turnover in experimental animals resulted in accu-
mulation of micro-damage. This might explain the occurrence of insufficiency fractures in the subtrochanteric region of the hip where bone is subjected to maximal bending movement (Pauwels 1948). The bilaterality and delayed union of the type of fracture found by Kwek et al. (2008), Goh et al. (2007), and Odvina et al. (2005)—as well as in our case—indicate that the pathology is not a localized one. Histomorphometric analysis by Odvina et al. (2005) showed suppressed bone formation, reduced or absent osteoblastic/osteoclastic surface, and diminished bone matrix.

We believe that the fracture in our patient was related to long-term alendronate therapy at high dose (70 mg weekly in a 38-kg woman). This may support the observations made by others emphasizing the need for increased awareness during long-term alendronate therapy. Hip/thigh pain justifies early radiographs to diagnose early signs of cortical thickening and/or lateral cortical reaction. In such a case, stopping alendronate therapy and further follow-up should be considered.

Contributions of authors
ASN: case study, research, and writing of the manuscript. GOS: supervision and review of the manuscript.

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