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An emerging pattern of subtrochanteric stress fractures: A long-term complication of alendronate therapy?☆

Ernest Beng Kee Kwek [a,*], Seo Kiat Goh [a], Joyce Suang Bee Koh [a], Meng Ai Png [b], Tet Sen Howe [a]

[a] *Department of Orthopaedic Surgery, Singapore General Hospital, Outram Road, Singapore 169608, Singapore*
[b] *Department of Diagnostic Radiology, Singapore General Hospital, Outram Road, Singapore 169608, Singapore*

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Summary

Background: Subtrochanteric insufficiency fractures in post-menopausal patients have not been commonly reported in the literature. A recent increase in the incidence of such fractures occurring in patients while on alendronate therapy led us to conduct a retrospective review of these patients in our institution.
Methods: Seventeen patients, with a mean age of 66 years, sustained low energy subtrochanteric fractures within a 20-month period. These patients were incidentally found to be on alendronate therapy for an average of 4.8 years. Clinical data and history were reviewed and roentgenograms were evaluated by a single investigator. All additional imaging and bone mineral density measurements available were analysed.
Results: A characteristic fracture configuration suggestive of an insufficiency stress fracture was identified on plain radiographs. This consisted of (a) cortical thickening in the lateral side of the subtrochanteric region, (b) a transverse fracture, and (c) a medial cortical spike. In addition, 9 (53%) patients had bilateral findings of stress reactions or fractures, and 13 (76%) had symptoms of prodromal pain.
Conclusions: These insufficiency fractures could possibly have developed from the over suppression of bone turnover from prolonged alendronate therapy, in keeping with recently published evidence. This study further highlights the need for heightened awareness of alendronate's potential adverse effects.

☆ The corresponding author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

* Corresponding author. Tel.: +65 81274347; fax: +65 62262684.
E-mail address: kwekasc@pacific.net.sg (E.B.K. Kwek).

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Introduction

Subtrochanteric stress fractures are not widely described in the current literature. In the younger age group, fatigue stress fractures in this region are known to occur in runners and athletes.[4,9] Subtrochanteric insufficiency fractures in the older osteoporotic age group have not been commonly reported, and only isolated cases have been mentioned in relation to patients with hypophosphatemic osteomalacia,[6] pcynodysostosis,[14] or in whom fluoride therapy has been prescribed.[16]

We have noticed a recent increase in incidence of these fractures occurring in older patients in our institution who have been receiving alendronate, a potent inhibitor of bone resorption. Most of these fractures resulted from low energy trauma, and some were preceded by prodromal pain in the affected limb.

A retrospective review of these patients was undertaken to determine if a causal relationship with alendronate usage could be established, and to further define this pattern of fractures. We observed a peculiar but consistent fracture configuration that suggested an insufficiency fracture. Moreover, a number of patients had radiological evidence of stress reactions either before the fracture occurred or on the contralateral femur. These findings were all the more unusual given that they were on anti-resorptive therapy for osteoporosis.

Materials and methods

We retrospectively reviewed all patients admitted to our institution from 1 May 2005 to 31 January 2007 with a low energy subtrochanteric femur fracture whilst on alendronate therapy. Subtrochanteric fracture was defined as a fracture within the region of the femur 5 cm distal to the lesser trochanter. Exclusion criteria included patients with high energy trauma, pathological fractures secondary to underlying malignancies, and subtrochanteric extensions from intertrochanteric fractures. Ethical approval was obtained from the Institutional Review Board prior to commencement of the study.

All clinical data and history were reviewed from case records and via telephone interviews. Roentgenograms were evaluated by a single investigator, and fractures were classified according to the AO comprehensive classification for subtrochanteric fractures (type A: simple transverse or short oblique; type B: comminution with medial or lateral wedge; type C: severe comminution with loss of segmental continuity). Bone mineral density measurements prior to initiation of alendronate therapy were traced where possible.

Senior orthopaedic surgeons from our institution, using their preferred technique for fixation, carried out surgical fixation of these fractures at the earliest feasible date. Intraoperative specimens were sent for histology to exclude a malignant process in patients where an index of suspicion was present. Bone scintigraphy was also performed in selected patients to exclude bony metastases.

Results

Seventeen patients were identified in our study group and their details are tabulated in Table 1. All fractures were sustained in low energy circumstances, commonly a fall after tripping, although seven patients (patients 2, 4, 5, 9, 10, 15 and 17) experienced acute pain before the onset of a fall, for example whilst getting up from a chair. All patients were female of Chinese ethnicity, with an age range of 53–82 years (mean age of 66 years).

All patients were receiving alendronate treatment with oral calcium supplementation at the time of fracture, with the exception of patient 17, who was on risedronate for 6 years after 4 years of alendronate therapy. Duration of treatment ranged between 2 and 8 years (average 4.4 years). None of the patients were receiving any other concurrent anti-resorptive therapy, such as hormone replacement therapy. Treatment for the majority of patients was initiated either by their primary physicians or gynaecologists.

Pre-treatment bone mineral density (BMD) diagnoses were available for 16 patients, and are tabulated in Table 2. A BMD diagnosis of osteopenia was made in six patients (median T-score at hip −1.35; range −0.4 to −1.9) and 10 patients had osteoporosis (median T-score at hip −2.85; range −2.1 to −3.7). T-scores were not available for some patients due to incomplete medical records. It was also noted that several patients were started on anti-resorptive therapy by their primary physicians as they had previously suffered from other fractures, despite BMD results not clearly in the osteoporotic range.

Significant co-morbidities are listed in Table 1. With the exception of three patients with diabetes mellitus, no patients had thyroid, liver or calcium/phosphate metabolic disorders. Other than patient 4 who was on long-term steroids for chronic eczema, no other identifiable causes for secondary osteoporosis could be found in the remaining patients.

The majority of subtrochanteric fractures were classified as AO type A, with the sole exception being patient 4 who had a small medial wedge