Spontaneous femoral shaft fracture after long-term alendronate

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Abstract

Alendronate is used as first-line treatment for osteoporosis in postmenopausal women worldwide. The evidence supporting its benefit in reducing the risk of fragility fracture among this high-risk group is well established. Due to its mechanism of action, there were concerns about potential reduction in bone turnover, repair of microdamage and hence reduced bone toughness and increased risk of fractures with long-term use. A number of cases have been reported from other countries describing a pattern of atraumatic mid-femoral fractures in women on long-term alendronate therapy. We present a case of an atraumatic femoral shaft fracture in an elderly woman on long-term alendronate therapy admitted to a UK Hospital.

Keywords: alendronate, femur, fracture, spontaneous, elderly

Introduction

Bisphosphonates have become the mainstay of osteoporosis treatment [1, 2]. Initial concerns about potential over-suppression of bone turnover and delayed bone healing and repair seem to have been allayed by evidence of long-term benefit [2].

We present a case of an atraumatic femoral shaft fracture in an elderly woman on long-term alendronate therapy.

Case report

An 82-year-old women felt pain in her right thigh and her leg gave way while walking downstairs in a shop. Her x-ray showed a transverse fracture of her femoral shaft with marked cortical thickening (Figure 1). Eight years previously she had suffered vertebral crush fractures and was started on alendronate 70 mg weekly.

Her fracture was internally stabilised, and she was investigated for possible causes of pathological fracture. Routine blood investigations including bone biochemistry were within normal range. Myeloma was excluded by a negative serum and urine electrophoresis. Parathyroid hormone and vitamin D levels were normal. Bone densitometry was normal (femoral neck T-Score +0.8). C-terminal telopeptide crosslinks (CTX, a biochemical marker of bone resorption) were elevated at 1.02 µg/l (normal range 0.1–0.5 µg/l).

Isotope bone scanning showed increased uptake at the site of the known fracture, the right sixth rib and the left lateral malleolus. A plain x-ray showed a longitudinal fracture of the left distal fibula which was treated conservatively. The patient again denied any preceding trauma. CT scan of thorax, abdomen and pelvis revealed no evidence of cancer.

In view of a report linking this pattern of femoral shaft fractures to long-term alendronate therapy [3], her alendronate was stopped. At 13-week follow-up, callus formation was demonstrated radiologically.

Discussion

Alendronate inhibits the production of important membrane anchoring molecules required by osteoclasts to adhere to the osteoid surface, also inducing apoptosis of osteoclasts. Some osteoclast activity is needed for repair of microdamage, and concerns have been raised that over-suppression of osteoclasts may result in stress fractures [4, 5]. In experimental animals, alendronate was shown to cause inhibition in repair of microdamage, resulting in increased fragility [5].

Odvina et al. reported on nine patients with unusual atraumatic fractures, most commonly of the femoral shaft, who had taken alendronate for 3–8 years [4]. Bone biochemistry, vitamin-D levels and PTH were within reference ranges. Severe suppression of bone formation was confirmed by a bone biopsy after double tetracycline labelling. Cheung et al.
reported an 82-year-old women who sustained a mid femoral shaft fracture while walking. She was on alendronate for 10 years and her bone biopsy also showed severe suppression of bone turnover [6]. Schneider reported a similar fracture in a 59-year-old women [7]. Two retrospective case series [8, 9] identified 42 patients who presented with unexplained femoral shaft fractures linked to prolonged alendronate therapy.

Our case follows the same pattern with the exception that, in the absence of a bone biopsy, we could not confirm that bone turnover was suppressed. The slightly raised CTX, hotspots on the bone scan and some visible callus at 13 weeks all indicate at least some osteoblast and osteoclast activity which cannot be accurately quantified as normal or suppressed on this evidence.

Although the safety and effectiveness of bisphosphonate therapy is well established [1, 2], these cases point to the fact that indefinite duration of treatment with alendronate is not without complications. The limited number of reports states that alendronate-induced fractures occur after 3–10 years of regular use. The optimum duration of treatment and strategies for detecting patients at risk of this complication remain a matter of conjecture [10].

Key points

- Alendronate is an effective treatment for osteoporosis with a good evidence base for fracture prevention.
- Long-term therapy may, rarely, lead to spontaneous or very low trauma fractures, particularly of the femoral shaft.
- An association with thickened femoral cortices is typical.
- Over-suppression of bone turnover with accumulated micro-damage is a likely mechanism.
- Fracture healing may be delayed.

References


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