Atraumatic intracapsular neck of femur fractures after prolonged bisphosphonate treatment: a new atypical variant?

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Summary

We present 2 cases of elderly females presenting with atraumatic, near-vertical (Pauwels grade 3), intracapsular neck of femur fractures. Following diagnosis of osteoporosis on DEXA scans, they had received alendronic acid for 7 and 10 years respectively. Routine blood tests and serum estimations of calcium, vitamin-D and thyroid-stimulating hormone, done at admission, were within the normal ranges. These patients were managed with a hemiarthroplasty and a dynamic hip screw (DHS) respectively, following discontinuation of bisphosphonates. We present these 2 cases in light of emerging evidence that associates long-term bisphosphonate use with atypical low energy femoral fractures. Only subtrochanteric/diaphyseal fractures have been reported to date.

Case Report

Case 1

A 78-year-old lady noticed severe pain in her right hip on waking up one morning and was unable to bear weight through this leg. Radiographs showed a displaced intracapsular fracture in the right proximal femur (Figure 1a). This was a near-vertical fracture through the femoral neck (Pauwels grade 3) (8). The neck-shaft angle on the contra-lateral proximal femur was 125°. Full-length orthogonal views of the right femur did not show further fractures, lytic lesions or diaphyseal stress reactions. She denied any preceding groin or thigh pain or any recent trauma. She had a diagnosis of osteoporosis confirmed with a DEXA scan seven years previously (T score -5.3 at spine and -3.7 in the femur) and had been on alendronic acid (70mg weekly) since then. She had a low-calcium diet and was previously diagnosed with hyperparathyroidism for which she is not on any treatment. She had never received steroids or long-term antibiotics and had never smoked. Haematological investigations revealed normal full blood count, C-reactive protein and liver function tests, with mildly raised creatinine (Table 1). She had normal serum estimations of adjusted serum calcium, vitamin D (25-hydroxycholecalciferol) and thyroid stimulating hormone (TSH).

She received a cemented hemiarthroplasty [45mm Exeter Trauma Stem (ETS), Stryker™ UK Ltd., Newbury, UK]. The resected proximal femur was sent for histopathological examination. The alendronic acid was discontinued post surgery. Further investigations revealed normal serum electrophoresis and light chain quantitation (LCQ) but a mildly elevated parathyroid hormone (PTH) (88; range 15-65 ng/L). Light microscopy of decalcified, HE-stained (haematoxylin and eosin) sections showed disconnected, predominantly thin and partially thick trabecular bone, with necrosis, haemorrhage and acute inflammatory cells, but no features of malignancy or diffuse inflammation (Figure 2). She had routine hip fracture care during her stay on the trauma ward, including ortho-

Introduction

Bisphosphonate-related femoral fractures are increasingly being reported (1, 2). These typically occur with minimal or no trauma in the subtrochanteric or diaphyseal region (3, 4) and are associated with a history of prolonged bisphosphonate therapy and short duration of prodromal thigh pain. The radiological hallmarks include a transverse or short oblique orientation, unicortical break on the lateral (tension) side of the femur, smooth-looking fracture edges and surrounding cortical hypertrophy (1, 3). Available evidence suggests impaired recruitment of osteoblasts and osteoclasts (4), suppressed new bone formation through reduced bone turnover (5), reduced bone remodeling (6, 7), accumulation of microdamage and subsequent crack propagation leading to fracture. To our knowledge, intracapsular fractures have not been previously reported in relation to bisphosphonate therapy. Informed consent was obtained from both patients discussed below.
geriatrician-directed medical care and progressive mobilisation by physiotherapists. She was able to ambulate with a frame when discharged to her own home on the 8th post-operative day. She was pain-free and ambulating with a stick when followed up at 6 months.

Case 2
An 84-year-old lady presented to A&E with a three-day history of spontaneously occurring and progressively worsening pain in her left hip. Three hours prior to A&E admission she had felt a ‘crack’ in her thigh and was now unable to bear weight on this leg. Radiographs revealed a minimally displaced intracapsular fracture, which was near-vertical (Figure 1b). The contralateral neck-shaft angle was 125°. She had been diagnosed with osteoporosis on a DEXA scan 15 years earlier and had been on alendronic acid (70mg weekly) for ten years. A repeat DEXA scan 3 years prior to presentation had confirmed continuing osteopenia (T score -2.2 at spine and -1.4 in the left femur). Her other medications included amlodipine and bendroflumethiazide. Routine blood tests at admission (full blood count, urea & electrolytes, etc.) were within normal ranges (Table 1). Her fracture was stabilized with a dynamic hip screw. Histopathological analysis of the reamings from the femoral head showed normal osteonal architecture and lacunar density, with no signs of previous fracture or remodeling (Table 2). The alendronic acid was discontinued and she was discharged home 7 days later. She was ambulating well when reviewed in the fracture clinic 6 weeks later, and radiographs showed callus at the fracture site.

Discussion
We report the first clinical cases and histopathological
analyses of intracapsular fractures in relation to prolonged bisphosphonate therapy. Both patients had received alendronic acid (7 and 10 years respectively) for DEXA-confirmed osteoporosis. One patient had prodromal pain, but both fractures were atraumatic. Radiographs showed near-vertical, smooth-looking fracture lines in the femoral neck, starting on the tension side, i.e. the lateral cortex (9). These radiological appearances share some features with the previously reported subtrochanteric fractures. However, our histopathological findings (normal osteonal architecture and osteocyte lacunar density without any features of previous fractures or attempted healing) differ from those reported in the only histological case study to date (10).

The femoral neck has previously been shown to contain significantly less cellular periosteum (due to far fewer osteoprogenitor cells) and more mineralizing periosteum compared to the diaphyseal region (11). This renders the femoral neck periosteum thinner and at risk of fracture. It is plausible that the angulation on the femoral neck and its relatively smaller cross-sectional area compared to the diaphysis, could then lead to a much more rapid fracture propagation without remodeling, before prodromal thigh pain becomes established. This could possibly explain the particular fracture orientation observed on the two patients’ radiographs, and the absence of previously reported histological features (12). A differential diagnosis would be the stress fractures reported to occur in femurs with coxa vara (13); however in each case, both hips looked symmetric, the contralateral neck-shaft angles measured more than the conventional cut-off for coxa vara, and the fracture lines were smooth and near-vertical.

Although we cannot establish a direct causal relationship, this
case series does suggest a new anatomical variant and adds to the growing body of evidence linking atypical femoral fractures with long-term bisphosphonate therapy. There are no consensus guidelines as yet on the optimal duration of bisphosphonate therapy. We suggest that any patient with prolonged bisphosphonate treatment presenting with thigh pain without a history of trauma, should be promptly investigated radiologically, and the bisphosphonate discontinued until clinical and radiological features of fracture healing are established.

References

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