

Spontaneous rapid osteolysis in Paget's disease after internal fixation of subtrochanteric femoral fracture

Khurjekar K S, Vidyadhara S, Dheenadhayalan J, Rajasekaran S

ABSTRACT

Rapidly-progressive spontaneous progression of the osteolysis following internal fixation of pathological fracture in patients with Paget's disease has not been previously reported. We describe two patients, aged 59 and 65 years, respectively, who had pathological subtrochanteric fractures in Pagetic femora fixed internally using an interlocked intramedullary nail, and who developed spontaneous rapid osteolysis. Both patients responded favourably to long-term treatment with alendronate, with resultant fracture union and resolution of osteolysis.

Keywords: biphosphonates, osteolysis, Paget's disease, pathological fracture, spontaneous rapid osteolysis

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INTRODUCTION

Spontaneous osteolysis of bone, although rare, has been described in many situations like Paget's disease of bone and prolonged immobilisation after fracture⁽¹⁻³⁾. In Paget's disease, a metabolic disease with both osteoblastic and osteolytic activity, patchy sclerosis and lysis are seen, depending upon the phase of the disease. Extensive osteolysis in Paget's disease has been reported after immobilisation following fractures, which may be severe enough to result in hypercalcaemia^(1,4). Early activity and mobilisation have been noted to reverse the osteolysis due to immobilisation. Rapid osteolysis in Paget's disease has also been reported in the proximal femur following total hip arthroplasty⁽⁵⁾. Immobilisation was not the mechanism of osteolysis here as the patient had begun partial weight-bearing with crutches, even on the second postoperative day. We report two patients with Paget's disease who developed rapid osteolysis of femur following internal fixation of subtrochanteric fracture. In both patients, complete reversal of osteolysis was achieved with oral alendronate therapy.

Knowledge of this phenomenon is important as it mimics postoperative infection or malignant transformation, a well-known entity that is also seen in Paget's disease. Daily alendronate appears to be an easy and effective method of permanent reversal of this phenomenon.

CASE REPORTS

Case 1

A 59-year old retired male clerk sustained a subtrochanteric fracture of the femur following a trivial fall at home. Radiographs showed all the classical features of Paget's disease with patchy sclerosis, mild irregularity and varus deformity of the proximal femur (Fig. 1a). The patient had occasional pain in the left hip for three years prior to sustaining the fracture. The skeletal survey confirmed monostotic Paget's disease. Serum alkaline phosphatase (ALP) and calcium levels were normal. The fracture was stabilised with a gamma nail and the reamed material was sent for biopsy. Histopathological examination confirmed the diagnosis of Paget's disease of the bone. Apart from minimal difficulty in reaming due to sclerosed bone, surgery was uneventful. Postoperatively, parenteral tramadol was administered for pain relief, with antibiotic prophylaxis consisting of single dose of intravenous cefuroxime. Mobilisation was started from the second postoperative day using axillary crutches. The wound healed uneventfully by primary intention.

At one month follow-up, the patient was mobilising well, without swelling or tenderness at the surgical site. Radiographs revealed osteolysis of medial cortex on the distal fracture fragment, extending from the calcar to 4 cm below the lesser trochanter (Fig. 1b). The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and ALP levels were normal. There was no leukocytosis. At seven weeks, the osteolysis had significantly increased in size to 12 cm × 4 cm (Fig. 1c). The CRP was 4.8 mg/dL and total leukocyte count was 9,800 per mm³.

Department of
Orthopaedics and
Spine Surgery
Ganga Hospital
Swarnambika Layout
Ramnagar
Coimbatore 641009
Tamil Nadu
India

Khurjekar K S, MS
Trauma Fellow

Vidyadhara S, MS, DNB
Spine Fellow

Dheenadhayalan J, MS
Consultant

Rajasekaran S, MCh,
FRCS, PhD
Director and Head

Correspondence to:
Dr S Rajasekaran
Tel: (91) 422 223 5050
Fax: (91) 422 223 2652
Email: sr@
gangahospital.com



Fig. 1 Case 1. Serial radiographs show: (a) fracture of the right femur at the subtrochanteric level in typical Paget's disease; (b) early osteolysis distal to the fracture at four weeks following surgery; (c) massive osteolysis (12 cm × 4 cm) at seven weeks follow-up; (d) bony union of fracture at 20 weeks with complete reversal of osteolysis.

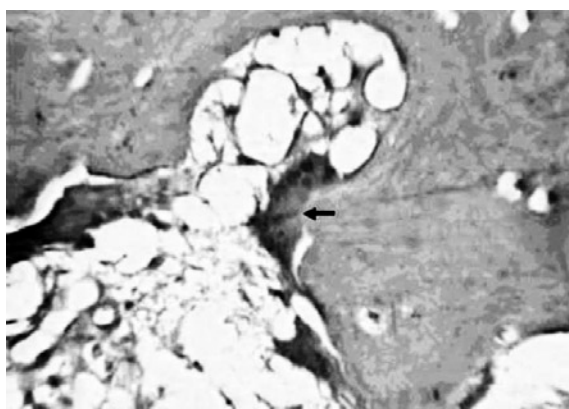


Fig. 2 Case 1. Photomicrograph shows multinucleated osteoclasts suggestive of active resorption and compact bone with mosaic pattern of cement lines confirming an active Pagetic lesion (Haematoxylin & eosin, ×100).

A core biopsy was performed at the site of osteolysis. The tissue sample was negative for aerobic culture and the histopathological examination revealed vascular tissue amidst lamellar bone, with multinucleated osteoclasts indicating active resorption. The compact bone with mosaic pattern of cement lines confirmed active Pagetic lesion (Fig. 2). The patient was started on alendronate (10 mg per day) for six months after the fracture union. Reversal of osteolysis was noticed at four weeks, which completed by 20 weeks (Fig. 1d).

Case 2

A 65-year-old man was brought to the hospital with a history of fall at home, with subsequent pain in the left hip and inability to walk. Radiographs

showed sclerosis, thickening and irregularity of the proximal femur, with a subtrochanteric fracture (Fig. 3a). Blood investigations were apparently normal. The subtrochanteric fracture was internally fixed with a gamma nail and primary bone grafting. Histopathology of the reamed material confirmed Paget's disease. At fourth week follow-up, osteolysis (Fig. 3b) was noticed in the radiographs just distal to the fracture (3 cm × 2 cm). There was no local sign of infection and CRP was negative.

The osteolytic lesion progressed rapidly to a size of 6 cm × 4 cm at 8 weeks postoperatively (Fig. 3c). A core biopsy confirmed Paget's disease with no evidence of malignancy. There was no microbial growth on aerobic culture. The patient was put on alendronate at a daily dose of 10 mg per day. Although the osteolysis progressed for almost eight weeks postoperatively, complete reversal was achieved by six months on alendronate therapy. Bone union was achieved at 22 weeks (Fig. 3d) and alendronate was continued for another six months. At the last follow-up, 26 months after surgery, the patient was symptom free without any radiographical evidence of osteolysis.

DISCUSSION

Spontaneous osteolysis of the bone has been reported with tumorous conditions, sarcomatous transformation of bone lesions, Gorham's disappearing bone disease, Paget's disease, and prolonged immobilisation after fracture⁽¹⁾. Paget's disease of the bone is

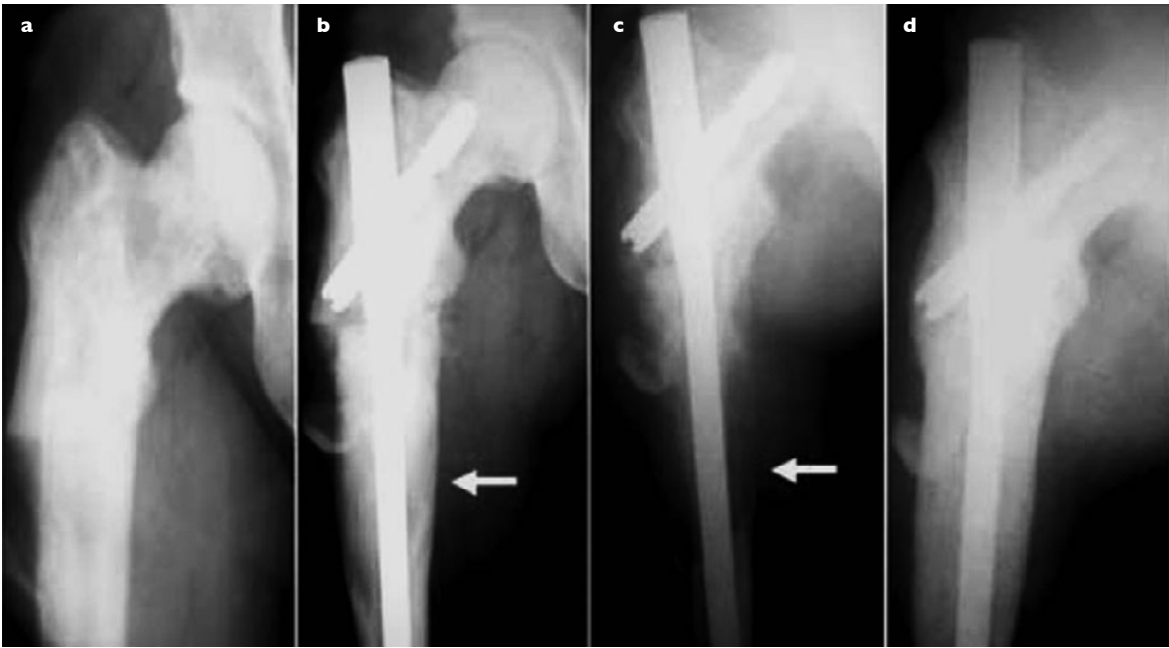


Fig. 3 Case 2. Serial radiographs show: (a) pathological subtrochanteric fracture of the left femur in typical Paget's disease; (b) early osteolysis distal to the fracture (3 cm × 2 cm) at four weeks follow-up; (c) extensive osteolysis at eight weeks follow-up; (d) complete reversal of osteolysis at 22 weeks.

a condition with increased metabolic activity and is associated with both osteogenesis and osteolysis. The amount of lysis and sclerosis depends on the exact phase of the disease and one may override the other⁽⁵⁾. Although focal and patchy areas of lysis are more common, massive osteolysis has also been noted. Rapid but reversible osteolysis following primary total hip arthroplasty and revision arthroplasty have been reported^(5,6). Osteolysis in Paget's disease can also occur with immobilisation, sarcomatous transformation, metastasis, and with other malignancies⁽¹⁾. Osteolysis following conservative treatment of trauma in Paget's disease could possibly be attributed to immobilisation. Immobilisation in Paget's disease can cause massive osteolysis, producing hypercalciuria⁽⁴⁾. However, association of spontaneous rapid extensive osteolysis following internal fixation have not been previously reported. Both of the reported cases were ambulatory with early partial weight-bearing following surgery. The exact cause for the rapid osteolysis is not yet clear in this situation.

The radiological picture was ambiguous by virtue of the absence of periosteal reaction and the presence of focal osteolysis. In addition, as rapid progression of osteolysis was unusual, the possibility of infection or malignancy was considered. But both patients did not have constitutional symptoms or local signs supporting suspicion of infection or malignancy. Blood profiles were also apparently normal with only a mild increase in ESR. Uncertainty of the aetiology

and the rapid of progression of lysis led us to perform a biopsy and aerobic culture. Histopathological examination showed multinucleated osteoclasts indicating active resorption and compact bone with mosaic pattern of cement lines, suggestive of an active Pagetic lesion. Microbial culture examination as well as histopathological report ruled out infective pathology.

Prompt pharmacological intervention appears to be important in reversing the osteolysis in Paget's disease. In the medical management of Paget's disease, alendronate is more potent compared to calcitonin. Alendronate has a longer duration of action and lesser side effects⁽⁷⁾. Biphosphonates have been considered the drug of choice in the medical management of Paget's disease⁽⁷⁾. These drugs are related to pyrophosphate, a naturally-occurring mineralisation inhibitor. They act by inhibition of enzymes of mevalonate pathway that is essential for cell survival, inhibition of osteoclastic activity, and also by apoptosis of osteoclasts⁽⁷⁾. Selby et al have suggested alendronate to be the most preferable biphosphonate in the treatment of osteolytic Paget's disease⁽⁷⁾. Both our patients showed fracture union in 20 weeks and 22 weeks, respectively. The reversal of osteolysis was achieved with a daily dose of alendronate and it was continued for a total period of one year. At the last follow-up, both patients were asymptomatic clinico-radiologically.

Knowledge of this phenomenon appears to be important as it may be confused for malignant

transformation, which is a more common and well-known entity in Paget's disease. Daily alendronate therapy appears to be an easy and effective method of permanent reversal of this phenomenon. Although the report of two patients is an insufficient number to advocate the therapy of alendronate in all patients with pathological fracture in Paget's disease following internal stabilisation, the drug must be started at the earliest upon suspicion of osteolysis.

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