

Clinical Quiz

Conservative treatment of humeral fracture in a patient with Paget's disease of bone

K. Raptis¹, E.G. Ballas², I.P. Stathopoulos^{3,4}, A. Mari⁵, S. Tournis⁴

¹First Orthopaedic Department, KAT Hospital, Athens, Greece; ²First Orthopaedic Department, University of Athens, Attikon Hospital, Athens, Greece;

³Third Orthopaedic Department, University of Athens, KAT Hospital, Athens, Greece; ⁴Laboratory for the Research of the Musculoskeletal System

“Theodoros Garofalidis”, University of Athens, KAT hospital, Athens, Greece; ⁵5th Department of Medicine, Evagelismos Hospital, Athens, Greece

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Clinical case

A 60-year-old man presented to the emergency department after sustaining a closed injury of his right, dominant arm caused by a fall from a standing height. Upon physical examination, local tenderness and swelling of the affected humerus were evident without signs of neurovascular deficit. Plain radiographs revealed a displaced transverse fracture of the humeral diaphysis (Figure 1A). The whole humerus showed abnormal bone architecture with mixed lytic and sclerotic lesions. Other findings included areas of decreased bone density, cystic lesions and bone enlargement with cortical thickening. No other associated injuries were present and the skin was intact. His past medical history was largely unremarkable with the exception of tobacco use and an ankle fracture operatively managed about 20 years ago. No other deformities or a positive family history for bone disease were present. The patient did not report bone pain or any neurological symptoms prior to the traumatic event.

Additional laboratory studies were ordered to evaluate the above radiographic findings. These revealed a serum calcium level of 9,1 mg/dL (normal range 8,4-10,2 mg/dL), a phosphate level of 3,7 mg/dL (normal range 2,3-4,7 mg/dL), a parathyroid hormone (PTH) level of 48 pg/ml (normal range 10-65 pg/mL), a C-reactive protein (CRP) level of 1.01 ng/l (normal range <10 ng/l), a total alkaline phosphatase (ALP) level of 520 U/L (normal range 56-119 U/L), a bone ALP level of 80.7 ng/ml (normal

range 38-49.3 ng/ml) and a 25(OH)-Vitamin D level of 33.4 ng/ml (normal range >30 ng/ml). Whole body radionuclide bone scan showed increased uptake at the right humerus, left hemipelvis and the right iliac crest (Figure 2). Based on the clinical and imaging findings, the diagnosis of a pathologic humeral fracture secondary to polyostotic Paget's disease was established.

The patient underwent manual closed reduction and a coaptation splint was applied in the emergency setting. Ten days post-injury the coaptation splint was replaced by a functional brace and follow-up visits were arranged. They included weekly radiographic evaluation for four weeks and then routinely once a month for six months. At four months from injury fracture union was evident radiographically (Figure 1B). At the latest follow-up, eight months post-injury the patient was free of pain, had full elbow motion and 90° shoulder abduction. He has returned to his previous level of activity without major restrictions.

Commentary

Paget's disease of bone (PDB) is the second most common bone disease in Europe, after osteoporosis and was first described by Sir James Paget in 1876. PDB is characterized by excessive breakdown and formation of bone tissue and is associated with morphologic and functional abnormalities of the osteoclasts. Its prevalence ranges from 0.5% to 4.6% in adults over 55 years of age, with slight male predominance. There is significant geographic variation in the prevalence of the disease among western nations, with the greatest incidence reported in people of Anglosaxon origin. In other nationalities, including the Greek population, the prevalence of the disorder is lower. Additionally, the epidemiology of PDB seems to be changing, with several groups reporting a reduction in its incidence, as well as in the severity of disease^{1,2}.

PDB involves either a single bone (around 40% of patients) or multiple bones (around 60% of patients). Virtually any bone

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Corresponding author: Konstantinos Raptis, MD, MSc, First Orthopaedic Department, KAT Hospital, 2 Nikis str., Kifissia, 14561, Athens, Greece
E-mail: kraptis1981@hotmail.com

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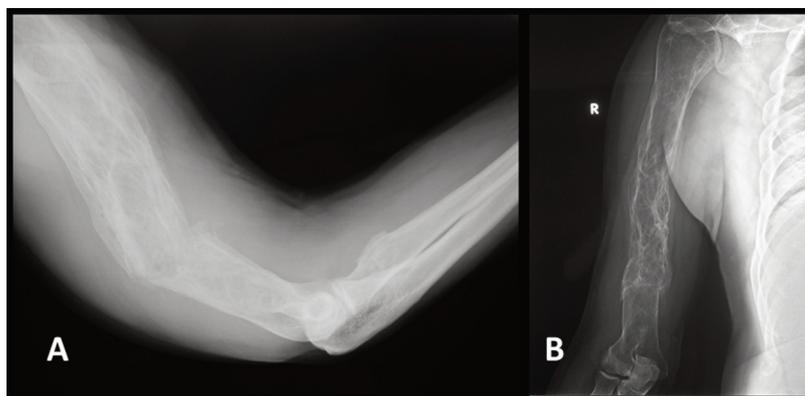


Figure 1. **A.** Lateral radiograph of the right humerus. Transverse diaphyseal fracture with posterior angulation. **B.** Anteroposterior radiograph of the right humerus four months post-injury. Union of the fracture.

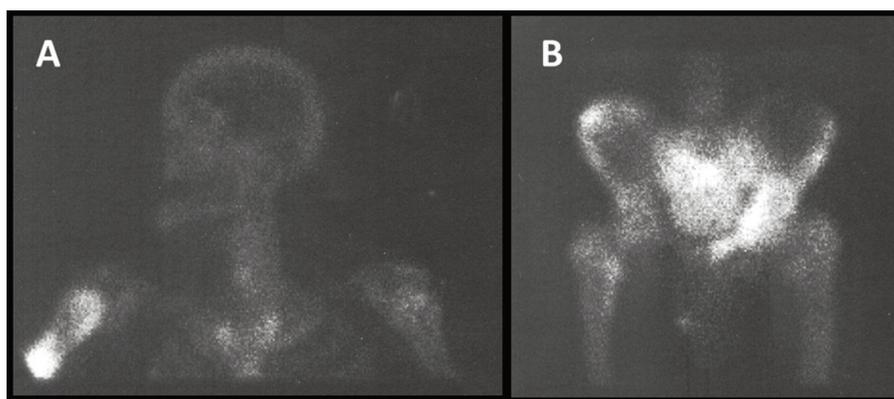


Figure 2. Increased radionuclide uptake at the right humerus, left hemipelvis and right iliac crest.

can be affected but this entity predominates in pelvic bones and sacrum, followed by the spine, skull, femur, tibia, humerus and clavicle. Our patient presented with polyostotic involvement affecting the right humerus, left hemipelvis as well as the right iliac crest. PDB is very often asymptomatic. The most common clinical signs and symptoms are pain, increased skin temperature facing affected superficial bones, compression myelopathy and nerve root injury. Interestingly, in some patients as in ours, bone fracture may be the first evidence of the disease. Complications include diaphyseal fractures most commonly femoral or tibial, joint arthritis, neurological problems and osteosarcoma with an incidence of approximately 0.1%. PDB is associated with increased bone turnover with alkaline phosphatase activity elevated in 85% of patients as in our case. Diagnosis is primarily radiological with sclerosis, lysis, thickened trabeculae and cortices, leading to bone enlargement. All these imaging findings were apparent in our patient. The radionuclide bone scan is the most sensitive tool for detecting PDB and bone biopsy is rarely required to establish the diagnosis^{1,3}.

Pathologic fractures are the most common complication of PDB due to localized disruption of bone architecture. Excessive bone resorption and abnormal bone formation result in biomechanically weakened bone and predispose to fracture³. Epidemiological studies have shown that fractures occur in about 10% of cases involving long bones. Pagetic bone is brittle so most limb fractures are caused by falling from a standing height, as in our patient, while most of the vertebral fractures occur “spontaneously” during the activities of daily living. Usually, they present in areas of high mechanical stress, in the weight-bearing bones of the lower extremities. Severe bowing deformity of weight-bearing bones, especially the femur and tibia, predisposes to transverse fissure lines on the convex side, leading to complete fracture. Chronic fractures may occur along convex surfaces of long bones and are frequently asymptomatic. The commonest bone to suffer a pathological fracture due to PDB is the femur and approximately 20% of these fractures occur in the upper third of femoral shaft. The incidence of a humeral pathological fracture is extremely rare since the

humerus is involved only in 2% of the cases most commonly in the diaphysis^{4,5}. Whether the healing process of such fractures is normal or delayed is controversial, but there are many reports of an increased incidence of non-union. Other major complications are high rate of malunion, particularly in proximal femur, excessive bleeding, compartment syndrome, focal disuse osteopenia, hypercalcaemia, and hypercalciuria^{2,3}.

Fracture management in PDB patients remains a challenge. The ultimate goal of treatment is to relieve patients' symptoms and allow sufficient mobilization of the affected extremity. Thus, when discussing the management of these fractures, bone special biomechanical characteristics, abnormal bone remodeling and mineral disorders should be taken into consideration. Although internal fixation is considered the gold standard for lower extremity fractures, conservative treatment has been advocated most frequently in humeral fractures. In the majority of the reported cases the result of non-surgical treatment was satisfactory⁴. Moreover, operative treatment can be technically challenging due to bone enlargement, deformity, and increased vascularity. Patients with PDB demand a thorough medical evaluation before surgery as the polyostotic involvement and the associated hypervascularity predispose to an increased rate of intraoperative bleeding and high output cardiac failure, especially in the elderly patients³. Intramedullary nailing is the surgical technique of choice compared with plate and screw fixation, as it prevents opening of the fracture site, provides mechanical reinforcement of the humeral diaphysis to its whole length and provides sufficient stabilization allowing immediate postoperative rehabilitation. However, distal locking can be difficult and can complicate the method⁴. On the other hand ORIF with plate fixation predisposes to new fracture due to stress concentration at the edges of the plate⁴.

Although there is indirect evidence that antiresorptive agents reduce the fracture risk in PDB, there are no large trials proving so or providing data about their role in fracture healing in PDB patients². Most studies advocate the use of a potent nitrogen-containing bisphosphonate, including oral alendronate or risedronate or intravenous pamidronate or more recently zoledronic acid. Of note, the latest appears to have an advantage over the rest bisphosphonates in achieving remission of the disease. In addition, there are some encouraging reports about PDB patients treated with denosumab. Primary indication for pharmaceutical intervention is the presence of bone

pain. Other indications include planned surgery at an active pagetic site in patients with asymptomatic active PDB in order to avoid excessive bleeding during the operation, the rare development of hypercalcaemia in association with immobilization in patients with polyostotic disease and the presence of pagetic sites near nerves in skull base disease⁶.

In our case, we decided to proceed with conservative management of the fracture for a number of reasons. The fracture involved a non-weight bearing bone and the displacement was amenable to manipulation and correction with closed reduction. Moreover given the associated hypervascularity of the lesion there was increased risk for intraoperative bleeding. Finally we decided to with-hold bisphosphonates administration given the concern that prior bisphosphonate treatment might impair fracture union and bone repair¹. Our management led to satisfactory results in terms of bony union and function since the patient returned to his previous activities without limitations. Given the low trauma fracture he is scheduled for iv zoledronic acid infusion, although clear evidence that such intervention would lead to prevention of complication is currently lacking¹.

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Questions

1. Pathologic fractures in Paget's disease:

- A. Occur most frequently in the lower extremity and are managed non-surgically
- B. Occur most frequently in the tibia and are managed surgically.
- C. Occur most frequently in the humerus and are managed with internal fixation

D. Occur most frequently in the femur and are managed with intramedullary nailing

Critique

Pathologic fractures in Paget disease is not an uncommon complication. The most common location of appearance of such

fractures is the lower extremity, most frequently the femur, followed by the tibia. In cases of a femoral pathologic fracture intramedullary nailing is the treatment of choice since plate fixation can cause excessive stresses and predisposes to new fracture. In the rare cases of humeral involvement, conservative treatment is preferable offering satisfactory results.

The correct answer is D.

2. Characteristic radiographic findings of Paget's disease include:

- A. Long bone bowing
- B. Hip and knee osteoarthritis
- C. Both lytic and sclerotic lesions

D. Bone enlargement with cortical thickening

E. All of the above

Critique

Paget's disease, though frequently asymptomatic has characteristic imaging findings depending on the phase of the disease. Long bone bowing is typical and osteoarthritis can appear as well. Both increased and decreased bone density can be revealed on plain radiographs due to abnormal bone remodeling leading to excessive bone resorption and abnormal bone formation. The final result is a large bone with obvious cortical thickening.

The correct answer is E.