Bone 57 (2013) 517–521

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Original Full Length Article

# Monostotic Paget's disease of the femur: A diagnostic challenge and an overlooked risk

J. Bachiller-Corral [a], C. Díaz-Miguel [a], A. Morales-Piga [b,*]

[a] Department of Rheumatology, Ramón y Cajal Hospital, Madrid, Spain
[b] Rare Disease Research Institute (Instituto de Investigación de Enfermedades Raras — IIER), Carlos III Institute of Health (Instituto de Salud Carlos III — ISCIII), Madrid, Spain

ARTICLE INFO

*Article history:*
Received 29 June 2013
Revised 22 August 2013
Accepted 23 August 2013
Available online 1 September 2013

Edited by: Peter Ebeling

*Keywords:*
Paget's disease
Osteitis deformans
Monostotic
Femoral involvement
Radiological diagnosis

ABSTRACT

*Background:* Although radiological diagnosis of Paget's disease of bone (PD) is usually straightforward, monostotic cases may potentially raise specific problems which lead to performing invasive procedures. Therefore, the purpose of this study is to ascertain whether or not monostotic femoral Paget's disease (MFPD) presentation poses particular diagnostic difficulties which prompt excessive use of excisional biopsies.
*Methods:* We retrospectively reviewed the medical records of 24 MFPD patients identified from a series of 412 patients; their clinical features were compared with those of the remaining 164 monostotic cases and the radiological images were systematically assessed.
*Results:* When compared with the remaining monostotic cases, MFPD patients were more prone to having normal alkaline phosphatase levels (31.8% vs. 16.4%; 0.08) and a significantly higher percentage of patients have PD symptoms (75% vs. 51%; 0.02) and complain of bone pain (73.9% vs. 40.8%; 0.003). Six (25%) MFPD patients evidenced a fracture over the pagetic lesion. This incidence is higher than that of the monostotic cases of other locations (8.4%; $p = 0.02$). The existence of PD lesion was not recognised initially in 10 cases and an excisional bone biopsy was performed in 7 (29%). One patient subsequently experienced a fracture through the biopsy site and another two experienced worsening of their previous bone pain.
*Conclusion:* The femur is a relatively common monostotic PD location which often causes diagnostic confusion, prompting a bone biopsy in many cases. Careful assessment of this lesion by X-ray examination may help attain an early appropriate diagnosis and avoidance of unnecessary surgical morbidity.


## Introduction

Paget's disease of bone (PD) is a fairly common medical condition in many European countries, the United States, and other populations of British ancestry [1,2]. For instance, the estimated prevalence in a radiological study undertaken in the United Kingdom in the 1970s in people over 55 ranged between 2% and 5% [3]. Although more recent studies conducted with similar methods in the same geographical area [4] and in other countries [5–7] suggest that the prevalence could be decreasing, PD is still considered to be an important cause of morbidity in this fast-growing age group, despite the fact that a high proportion of patients remain asymptomatic throughout their evolution [8].

One of the consequences of this high prevalence is the frequent finding of a PD bone lesion in current clinical practise. Taking into account the large variety of radiological appearances [2,9–12] – sometimes mimicking those of other significant morbid disorders (i.e.: bone tumours and metastasis) – , PD should always be considered in differential diagnosis of osteoesclerotic as well as osteolytic skeletal lesions [2]. Nevertheless, the most common radiologic appearance of the disease, usually present in its "mixed" and "blastic" phases, is distinctive [12]. In fact, the combination of patchy areas of bone sclerosis or lysis with coarsening of the trabecular pattern, together with local enlargement, mostly at the expense of cortical subperiosteal thickening, is virtually diagnostic of PD [2,9–11]. Therefore, in cases with more than one lesion ("polyostotic PD"), the diagnosis is almost always straightforward because at least one of the locations will show the aforementioned typical features. On the contrary, in monostotic cases, whose frequency has been reported as ranging from 10–20% [2] to close to 50% [13], the diagnosis may be far more difficult and confusion with other conditions may arise [12,14–16]. The issue could be greater in certain skeletal areas where PD's radiological features tend to be less characteristic and, particularly, when the early osteolytic form of the disease is present [17]. In these instances, the need to rule out life-threatening conditions, such as primary bone tumours or skeletal metastasis, prompts the performance of some invasive techniques which are associated with a certain degree of morbidity.

The main goal of this study is to address whether monostotic femoral Paget's disease presentation raises specific diagnostic problems and subsequently causes an excessive number of excisional bone biopsies. In addition, we seek to identify any eventual clinical or radiological feature that may help avoid unnecessary harmful procedures.

* Corresponding author.
*E-mail addresses:* fbachiller.hrc@salud.madrid.org (J. Bachiller-Corral), chelodmp@gmail.com (C. Díaz-Miguel), amorales@isciii.es (A. Morales-Piga).

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http://dx.doi.org/10.1016/j.bone.2013.08.023

**Table 1**
Comparison of numerical (mean ± SD) and categorical (%) characteristics between cases with monostotic PD of the femur and monostotic PD cases of other locations.

| | Monostotic femur involvement [n = 24] | Other monostotic cases [n = 164] | p |
|---|---|---|---|
| Age at diagnosis | 64.6 ± 11.5 | 64.8 ± 11.4 | 0.92 |
| Sex | | | |
| Female | 13 (54.1) | 83 (50.6) | 0.74 |
| Male | 11 (45.8) | 81 (49.3) | |
| Extent of skeletal lesions[a] | 3.2 ± 0.9 | 4.1 ± 1.6 | 0.008 |
| Alkaline phosphatase[b] (U/L) | 199.3 ± 109.3 | 290.0 ± 205.3 | 0.04 |
| Alkaline phosphatase/ extent of bone lesions | 61.6 ± 26.5 | 86.9 ± 106.3 | 0.27 |
| Normal alkaline phosphatase | 7 (31.8) | 26 (16.4) | 0.08 |
| Urinary hydroxyproline[c] (mg/24 h) | 42.2 ± 18.7 | 50.8 ± 30.2 | 0.25 |
| Urinary hydroxyproline/ extent of bone lesions | 13.4 ± 5.6 | 6.8 ± 25.5 | 0.58 |
| Asymptomatic case | 6 (25.0) | 78 (49.0) | 0.02 |
| Bone pain | 17 (73.9) | 58 (35.3) | 0.003 |
| Bone deformity | 11 (45.8%) | 28 (19.4) | 0.03 |
| Fracture | 6 (25.0) | 13 (8.4) | 0.011 |
| Diagnostic biopsy | 7 (29.1) | 10 (6.6) | 0.001 |
| Antiresorptive therapy | 17 (70.8) | 100 (61.7) | 0.15 |

[a] Evaluated by using Coutris' index [20].
[b] Normal range 40–128 U/l.
[c] Normal range 18–40 mg/24 h.

## Patients and methods

From a series of 412 PD patients reviewed in our Unit from 1992 to the present, we retrospectively reviewed the medical records of the 24 (5.8%) in whom the disease was only present as a lesion in the femur. Characteristics of these monostotic femoral Paget disease (MFPD) patients were then compared with those of the 164 monostotic cases from other locations seen during the same period of time. All patients were recorded at diagnosis, and clinical, radiological, and biochemical evaluations were at baseline. Throughout the period of the study, the diagnosis was based on the same roentgenographic criteria [18].

### *Clinical evaluation*

Clinical evaluation included primary bone pain assessment as differentiated from non-specific musculoskeletal pain. Other features, such as typical bone deformity, (anterior and lateral bowing), localised skin hyperthermia, secondary neighbourhood (hip or knee) osteoarthritis, fractures (either complete or cortical fissures), and sarcomatous degeneration were recorded using a computerised purpose-designed codified questionnaire. According to the presence or absence of any of these PD symptoms, patients were classified as symptomatic or asymptomatic.

### *Image evaluation*

Plain radiograph images of PD femoral lesions were available in medical charts in all cases. In addition, "ad hoc" frontal and lateral views of the whole femur were made for this study. Radiological evaluation was made following a structured protocol including the most relevant common PD features: trabecular pattern, cortical thickening and local bone enlargement. According to previous reports, the evolutionary phases of PD lesions were defined as: "lytic", "mixed" or "blastic" [9]. In addition, several radiological traits associated with femoral involvement like coxa vara (neck shaft angle ≤ 115°), anterior and lateral bowing, protrusio acetabuli, and secondary arthropathy (from either hip or knee) were evaluated. The presence or absence of Monckeberg-type vascular calcifications [19] was also recorded. Radiographs were jointly assessed by two expert rheumatologists (A. M-P. and J. B-C.) and consensus was achieved in all cases. Bone scans performed with $^{99m}$Tc-EHDP was available for all patients. The skeletal extent of the disease, based on bone scan uptake, was determined by using the index proposed by Coutris [20]. This index represents the sum of the coefficients conventionally assigned to each lesion according to the amount of bone affected.

### *Biochemical assessment*

Serum and urine samples were obtained after an overnight fasting. Serum total alkaline phosphatase activity (normal range: 40–128 U/l) was assayed by an automated method using a p-nitrophenyl phosphate substrate following the International Federation of Clinical Chemistry

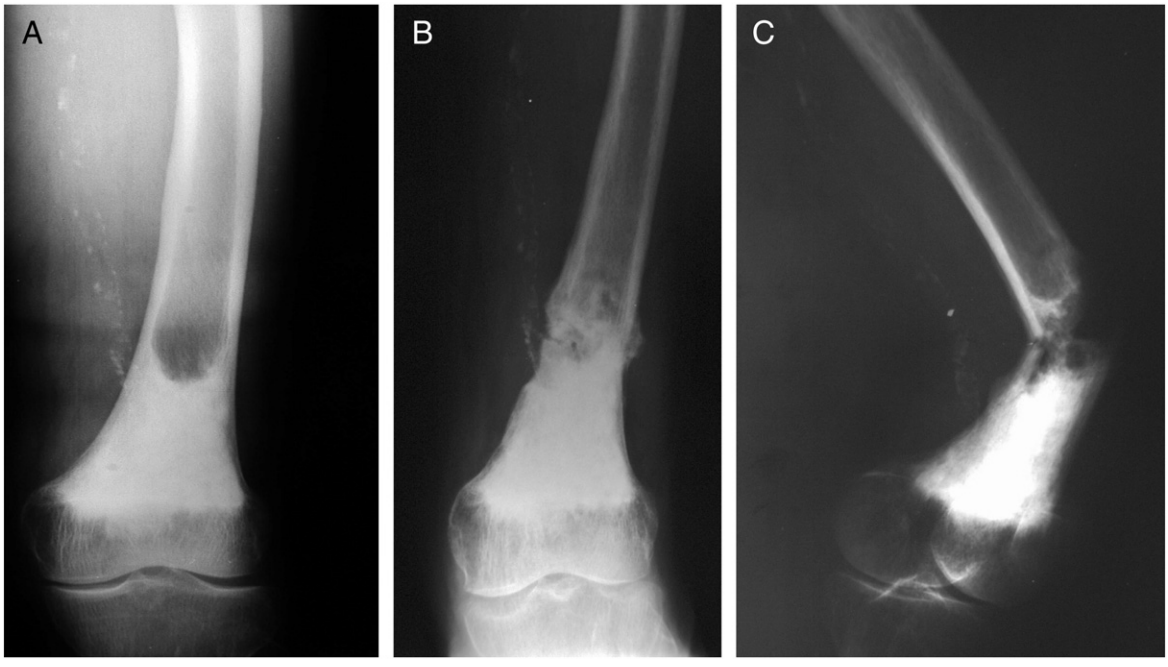


**Fig. 1.** Complete fracture of Paget's disease femoral lesion after biopsy. A. Pagetic lesion in distal femur. B. Lesion after bone biopsy. C. Fracture over the intervened area.