Microscopic Evidence for Paget’s Disease in Two Osteoarchaeological Samples from Early Northern France

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ABSTRACT Paget’s disease is a chronic condition of unknown cause localized to one or more bones of the human skeleton. It is basically an abnormal and excessive remodelling of bone, alternating phases of active bone resorption and formation and quiescent phases of diminished bone turnover. This combination produces a diagnostic pathologic appearance characterized by irregular bony fragments with a thickened and disorganized trabecular pattern (mosaic). To date, only two histological confirmations, although disputable, have been reported in medieval and 16th century samples from England (Aaron et al., 1992, Bell & Jones, 1991). This paper presents evidence of the disease from two sites in Normandy. The first one, Lisieux 413, dates from 300–350 AD and the second one, Saint Pierre-sur-Dives 16, dates from 1000–1100 AD. The remains were examined macroscopically, radiologically and microscopically.† Paget’s disease was suspected in Lisieux based on gross morphology of the calvarium. In the case of Saint Pierre-sur-Dives 16 Paget’s was suspected based on the pelvis, the left femur proximal thickening and a fragmented vertebra. Radiographs showed in both cases osteolytic and osteosclerotic stages of the disease. Thick sections (70 µ) from both skeletal lesions (calvarium of Lisieux 413 and femur of Saint Pierre-sur-Dives 16) demonstrated the earliest observations of the mosaic pattern of cement lines joining areas of lamellar bone in thickened trabeculae. Paget’s evidence in palaeopathology ought to be based on the association of macroscopic, radiographic and microscopic features. Copyright © 2002 John Wiley & Sons, Ltd.

Introduction

In 1877, Sir James Paget reported, under the title of osteitis deformans, the advanced clinical form of the bone disease which now bears his name. The disease is the most common bone disease after osteoporosis and all the malignant processes affecting the skeletal system. It is more likely to strike males than females (sex ratio of 1.1 to 1.2). It is seldom discovered before 40 years of age; however Régnier & Audran (1997) came to the conclusion that the onset of the disease occurs most probably in young people.

The aetiology of Paget’s disease remains unknown. Heredity, genetic disorders, or environment have been suggested as possible causative factors. Rebel et al. (1980) suspected a viral agent by the discovery of paramyxovirus nucleocapsid-like (measles, SRV = RS Virus Respiratory Syncytial Mucous) inclusions in pagetic osteoclasts. Basle et al. (1996) speculated more recently on the excessive production of Interleukin 6, a chromosome 6 link, or an over expression of C-fos proto-oncogen.

Cases suggestive of Paget’s disease have been reported in the palaeopathological literature and, relying on gross morphological and radiological aspects, its existence may be suspected as early as Neolithic times (Wells & Woodhouse, 1975; Pales, 1929; Hutchinson, 1889). These cases remain as ‘possible cases’, however, since no

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histologic confirmation (mosaic, excessive remodelling, and a resorption front) were produced as an argument for its existence at such early times.

**Material**

The Lisieux-Michelet 413 calvarium came from a skeleton recovered from one of the 1100 burials excavated by Didier Paillard in Lisieux from 1990 to 1992. The site is dated according to two periods: 750 burials are dated from the 4th century AD and 350 burials are dated from the 7th century AD. The skeleton belonged to a mature and gracile female of short stature, interred in a wood coffin. The skeleton is dated from 330–340 AD according to the archaeologist. The cranium was flattened and fragmented at the time of discovery. The remaining post-cranium is poorly preserved due to early grave violation.

The Saint-Pierre-sur-Dives 16 skeleton came from a seigniorial chapel excavated by Jean Desloges in 1997. Twenty graves were dated from the 11th century AD. The skeleton number 16 was confined in a stone jug. The bones belonged to a mature male of 165 cm and are well preserved.

**Methods**

In addition to radiographic (plain x-ray and CT scan) and morphological examination, microscopic slides were prepared. The preparation of the section did not involve decalcification. A calvarium fragment (Lisieux 413) and a transverse section in the midshaft of the left femur were embedded in methyl metacrylate (Technovit 9100 Kulzer). Blocks obtained were sawn in 100 µ slides, then thinned to 50–70 µ by hand with abrasive powders between two plates of glass. Light and circularly polarized-light microscopic observations were used.

**Results**

**Lisieux-Michelet 413**

Only the calvarium presents alterations suggestive of Paget's disease (Figure 1). The periosteal surface of the occipital bone is preserved. By contrast, the parietal and frontal bone surfaces are porous, coarsened and frosted. The whole parietal bones are thickened (left 13 mm, right 12 mm). The frontal bone is preserved anteriorly but posteriorly and supra-orbitally affected by a thickening similar to the parietal bones. On a cross section of the right and fragmented part of the frontal, a bounded and alveolate area is visible. The temporal bones are preserved. Endocranially, the left sphenoid larger wing surface is greyish and porous and the vessels' grooves of both pariets are enlarged and deepened. The vertex is partially destroyed and the areas limiting the affected bone and the preserved one show some destruction that may explain the post mortem fragmentation of the calvarium. Facial bones and fragments of mandible were not affected. A cotton-wool appearance, de-differentiation of outer and inner tables from Figure 1. Lisieux 413. Right profile of the 4th century calvarium with coarsened parietal bone, preserved temporal and occipital bones.

Figure 2. Lisieux 413. CT scan of the 413 4th century calvarium showing the thickened trabecular bone.
the diplot as well as vault thickening are the main aspects on the calvarium radiograph and CT scan (Figure 2). No osteoporosis circumscripta is visible. Cortical bone is thinned but trabeculae are thickened and irregular (Figure 3A).

Microscopically, there are mosaic patterns (disorganized trabeculae) of cement lines joining areas of lamellar bone and portions of woven bone with enlarged osteocytic cavities (Figure 3B). Under the inner and outer cortical bone, trabeculae are enlarged and affected by the numerous resorption fronts, evidenced by osteoclastic lacunae. Post-mortem artefacts, deposits and tunnel of fungal origin, are worth mentioning, although the above osteoclastic and osteoblastic features are not blurred (Figure 3C).

Saint-Pierre-sur-Dives 16

The left femur, pelvis and a single lumbar vertebra are affected. The vertebral plates are coarsened and irregular. The lateral cortical bone is thickened as well as the trabeculae in the vertebral body. However, there is a scarcity of trabecular bone compared to the other vertebrae. The posterior arch is absent.

The left femur weights 420 g compared to 355 g for the right one. The frontal cervico-diaphyseal angles are similar in both femurs, without coxa vara. The third proximal portion of the diaphysis is enlarged. The diaphyseal diameter is 110 mm in the hypertrophied portion compared to 90 mm in the lower portion of the diaphysis. The femoral head and the femoral neck are less obviously enlarged. The pathological surface is slightly coarsened and porotic. The sagittal curve is slightly increased on the left femur compared to the right femur. The linea aspera is smoothed in front of the altered portion of the diaphysis.

A frontal section of both femurs shows a cortical thickening of the left. Two types of bone tissue are seen:

— The thickened cortex from the head to the trochanter is compact and homogeneous or slightly porotic, and the medulla is obliterated;
— In the lower portion of the lesion, the porous cortical bone is centrally wedge-shaped and

Figure 3. Lisieux 413. A. Macroscopic view of the thin section of the parietal bone sample showing thickening and the specific arrangement of trabeculae and enlarged vascular spaces. B. Microscopic view with circularly polarized light (×100) of the calvarium (4th century) section showing thinned cortical lamellar bond (1) and irregular and thickened trabeculae with bands of immature bone (2). C. Microscopic view with circularly polarized light (×100) of a calvarium section showing mosaics with cement lines (short arrows) and an osteoclastic front (long arrows), post-mortem deposits (white asterisks), and post-mortem tunnel of fungal origin (white squares).

inserted inside the normal cortex around a partially obliterated medulla.

Radiographs of the femur show the cortical thickening, a crotch-medullar de-differentiation and a fibrillar aspect of the medulla on the diaphysis level. Compared to the right femur, the gross hypertrophy of epiphysis and diaphysis is clear. The growth front in the mid portion of the diaphysis appears as a clear limit between pathologic and normal bone with a characteristic V-shaped osteolytic focus (Figure 4).

A midshaft transverse slice of the left femur taken just up to the transition between preserved and affected bone gave similar microscopic aspects to the Lisieux 413 cranial observation. A thick periosteal apposition is visible and a trabecular bone with mosaic patterns, association of multiple resorption fronts and apposition of new bone (Figure 5A and 5B) replace the cortical bone.

Radiographs of normal and affected vertebrae show a dense and thickened cortex with the characteristic ‘picture-frame’ vertebra. Fibrillar and dense aspects of trabeculae are confirmed with a CT scan as having a ‘cotton-wool’ aspect.

The pelvic contour is smooth and the bone surface is coarsened and irregular. The ilia are thicker compared with the normal pelvis. The pelvic inlet is heart-shaped and narrowed.

Radiographic abnormalities of the pelvis are seen on coxal bones and sacrum with trabecular thickening along the inner contour, sclerosis and a lucent central portion (Figure 6).

**Discussion**

The association of macroscopic, radiographic and, especially, microscopic aspects in both skeletal samples give excellent evidence of Paget’s disease. Some rare osteoclastic—osteoblastic forms of bone metastasis (particularly from prostatic carcinoma) called ‘pagetoid’ may be confused histologically with the ‘mosaic pattern’ of Paget’s disease. In addition, fibrous dysplasia, chronic osteoperiostitis as seen in treponematoses and leprosy, fluorosis, myelofibrosis, tuberous sclerosis, axial osteomalacia and rare dysplastic disorders (fibrogenesis imperfecta, familial expansile osteolysis) may sometimes mimic the radiographic features of Paget’s disease. Therefore the evidence for Paget’s in palaeopathology is based on the association of macroscopic, radiographic and microscopic features.

Surprisingly, Paget’s disease is frequent today in the population over 60 years of age but rarely discussed in the palaeopathological literature (Stirland, 1991). Collins-Cook (1980) has collected 18 studies having reference to 27 examples of possible cases. Most descriptions which are solely macroscopic or radiographic do not refer to Paget’s disease. Among the most ancient cases, Bauduin (1914) confused osteoarthritis deformans and common osteoarthritis and Thurner (quoted by Collins-Cook 1980) attributed to Paget’s a probable
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A

Figure 5. Saint Pierre-sur-Dives. A. Microscopic view with circularly polarized light (x 100) of left femur transverse section showing cement lines, immature forms of bone with larger osteocyte lacunae and irregularly defined vascular canals. B. Microscopic view with circularly polarized light (x 100) of the left femur transverse section showing mosaics and a resorption front edging an enlarged vascular space.

Figure 6. Saint Pierre-sur-Dives 16. Radiograph of the 11th century pelvis showing dense contours and a central lucent area of the ilia.

osteomyelitis. After microscopic examination, Denninger’s (1933) and Fisher’s (1935) cases have been re-attributed to other diagnoses due to the absence of mosaic. Pales (1929) and Wells & Woodhouse (1975) described rather convincing cases but no microscopic examinations were performed for evidence of Paget’s characteristic aspects. Bell & Jones’ (1991) description on poorly preserved bone tissue using a scanning electron microscope (SEM) in backscattered electron imaging mode is well studied in reference to mineralization, osteocytic cavities, reversal lines versus diagenetic features, but no cross or circular polarized light imaging was opposed to the SEM structural interpretation. Aaron et al. (1992) studied the thickness of trabeculae and the extension of resorption cavities on undecalcified material but the illustrations of poorly preserved material are not completely convincing. However, the microscopic description of Bell & Jones (1991) and Aaron et al’s (1992) samples do define criteria consistent with a diagnosis of Paget’s disease.

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Conclusions

Mosaic, trabecular thickening, excessive bone resorption and formation are microscopic evidence of Paget’s disease in a 4th century and an 11th century sample from Normandy. They are also associated with macroscopic and radiographic features specific for the disease. These are: bony enlargement, coarsened trabecular patterns, epiphyseal involvement and an advancing wedge of radiolucency. Therefore, the antiquity of Paget’s disease is demonstrated. In addition, we hope to have demonstrated the essential contribution of a simple microscopic technology to palaeopathology without compromising the principle of preservation of valuable osteoarchaeological material.

References