

A Case Series of Paget's Disease of Bone: Diagnosing a Rather Uncommon Condition in Singapore

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Abstract

Paget's disease of bone is an uncommon condition in the Asian population, with only 2 cases reported in medical literature so far. We discuss 5 cases of Paget's disease who presented over an 8-year period with a wide and interesting variety of clinical features. Though 4 out of the 5 patients were asymptomatic, all of them had characteristic radiological features and elevated serum alkaline phosphatase levels of varying degrees. Diagnosis was based on the clinical features, the elevated serum alkaline phosphatase levels, and most importantly, the distinctive radiographic features, which are almost pathognomonic of the condition.

The incidence of Paget's disease is probably under-reported in Asia and Singapore, as it is rarely encountered and can be easily overlooked due to its usually asymptomatic and benign nature. A high index of suspicion and an active search for its typical features are thus essential for its detection.

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Introduction

Sir James Paget's description in 1877 of "a form of chronic inflammation of bones" which now bears his name was based entirely on clinical and pathological observations in patients with advanced disease.^{1,2} Today, more than a century later, advanced imaging techniques and biochemical tests have allowed us to identify and detect earlier stages of the disease, often in patients without symptoms or signs.

Paget's disease of bone, osteitis deformans, is a localised disorder of bone remodelling. The pathological processes of increased bone resorption and compensatory increase in new bone formation alter the gross structure of the affected bones, which become thickened and structurally inferior.^{1,3} Not surprisingly, bone pain, deformity and fractures are the main presenting features in symptomatic individuals. In addition, the enlarged and deformed bones may compress surrounding structures like nerves and vessels, causing symptoms.

While prevalent in people of Anglo-Saxon origin, this condition is very rarely reported in Asians. A Medline search revealed only 2 previously reported cases among Asians, from Thailand and Hong Kong, respectively.⁴ Here, we highlight 5 cases of Paget's disease of bone seen in the Department of Medicine of a general hospital over an 8-year period.

Case Reports

Case 1

A 78-year-old Chinese lady with a long history of hypertension on diuretic treatment was admitted with a stable head injury following a fall. Plain radiographs of her skull revealed marked thickening of the cortex, as well as multiple islands of sclerosis giving a "cotton-wool" appearance (Fig. 1).

A plain radiograph of her pelvis showed sclerosis and increased trabeculation over the left sacroiliac joint. She had a markedly elevated serum alkaline phosphatase level of 504 U/l (normal range 32 to 103 U/l) with otherwise normal liver enzyme levels. Her serum calcium level was within normal limits. She was diagnosed to have Paget's disease based on the classical radiological features and the elevated serum alkaline phosphatase level.

Case 2

A 72-year-old Indian man was admitted with sudden dysarthria and right-sided weakness. Computed tomographic (CT) scan of the brain revealed a left parietal infarct.

Incidentally, he was noticed to have an enlarged skull, with a prominent forehead, and bilateral genu varum.

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Fig. 1. Lateral skull X-ray of Case 1 showing the thickened bony cortex and focal areas of sclerosis ("cotton-wool" spots) characteristic of Paget's disease.



Fig. 2. Pelvic X-ray of Case 2 showing pelvic bone expansion, areas of sclerosis and lysis, and thickened trabeculae in the pelvis and proximal femur. Note also the presence of a right renal stone.

Further investigations revealed a markedly elevated serum alkaline phosphatase level of 613 U/l and mild hypercalcaemia. His parathyroid hormone (PTH) level was normal. A pelvic radiograph showed expansion of the pelvis as well as marked sclerotic and lytic changes in the pelvis and spine. A right renal calculus was also present (Fig. 2).



Fig. 3. Pelvic CT of Case 3 showing expansion of the right hemipelvis, with marked sclerosis and loss of the marrow cavity. The left hemipelvis is normal.

Case 3

A 61-year-old Chinese man was admitted with pain and swelling of his left leg. He had a right hemicolectomy 2 years previously for adenocarcinoma of the colon. Physical examination revealed a warm, tense, swollen and tender left calf with dilated superficial veins. There were no abdominal or pelvic masses. Per rectal examination was normal. Doppler studies of his left leg confirmed the clinical diagnosis of deep vein thrombosis.

A CT scan of his abdomen and pelvis did not reveal any pelvic masses. However, it showed significant expansion and marked sclerosis of the right hemipelvis, with loss of the normal marrow cavity (Fig. 3). A plain pelvic radiograph showed sclerosis and expansion of the right hemipelvis. Biochemical tests revealed a mildly elevated serum alkaline phosphatase level of 164 U/l. The carcinoembryonic antigen (CEA) level was within normal range.

Case 4

A 53-year-old Chinese lady was referred from a polyclinic complaining of intermittent discomfort in her right upper abdomen. Physical examination was unre-

markable. She had no jaundice or pallor, and there was no hepatomegaly. Routine blood investigations revealed a marginally elevated serum alkaline phosphatase level of 110 U/l, with otherwise normal liver function. An ultrasound of the hepatobiliary system was normal.

She was incidentally noticed to have a *sabre-deformity* of her right tibia at the same presentation (Fig. 4). She had been aware of this deformity for many years but was otherwise well. A plain radiograph revealed anterior bowing of the tibia together with coarse trabeculae, marked cortical expansion and sclerosis (Fig. 5). These changes were typical of Paget's disease involving the tibia.

Case 5

An 80-year-old Chinese man presented with intermittent pain in the left lumbar and lower back region. He had a past history of lithotripsy 5 years previously for a left renal calculus. Physical examination revealed bony tenderness over the left iliac crest, as well as bilateral genu varum. He also had left sensorineural deafness. Abdominal examination was unremarkable, and a per rectal examination did not reveal any prostatic enlargement or nodules. Spinal movement was not significantly reduced, and there was no spinal deformity or tenderness.

A plain radiograph of his abdomen and pelvis revealed marked bony expansion of the pelvic bone with

multiple areas of lysis and sclerosis in the pelvis, sacrum, left hip and T11, T12, L4 and L5 vertebral bodies (Fig. 6). Biochemical investigations showed a markedly elevated serum alkaline phosphatase level of 546 U/l. Calcium and prostatic specific antigen levels were normal. A bone scan showed increased tracer uptake in multiple areas of the skeleton (Fig. 7). The changes were characteristic of polyostotic Paget's disease.

Discussion

These patients were diagnosed to have Paget's disease based on a combination of clinical, radiological and biochemical features. While there is as yet no single diagnostic test, most cases can be confidently diagnosed based on these features.^{5,6}

Clinical Features and Complications of Paget's Disease

Though bone pain and deformity are well-known presenting features, it is important to note that Paget's disease of bone is usually asymptomatic, and the disorder is often first discovered while investigating an unrelated complaint.⁷ This trend is also seen in our patients, as 3 out of the 5 patients did not have any symptoms related to Paget's disease. Only Case 4 had a painless



Fig. 4. Right leg of Case 4 illustrating anterior bowing of the tibia, with increased length and width.



Fig. 5. Lateral X-ray of right tibia

showing anterior bowing with thickened cortex and sclerosis.

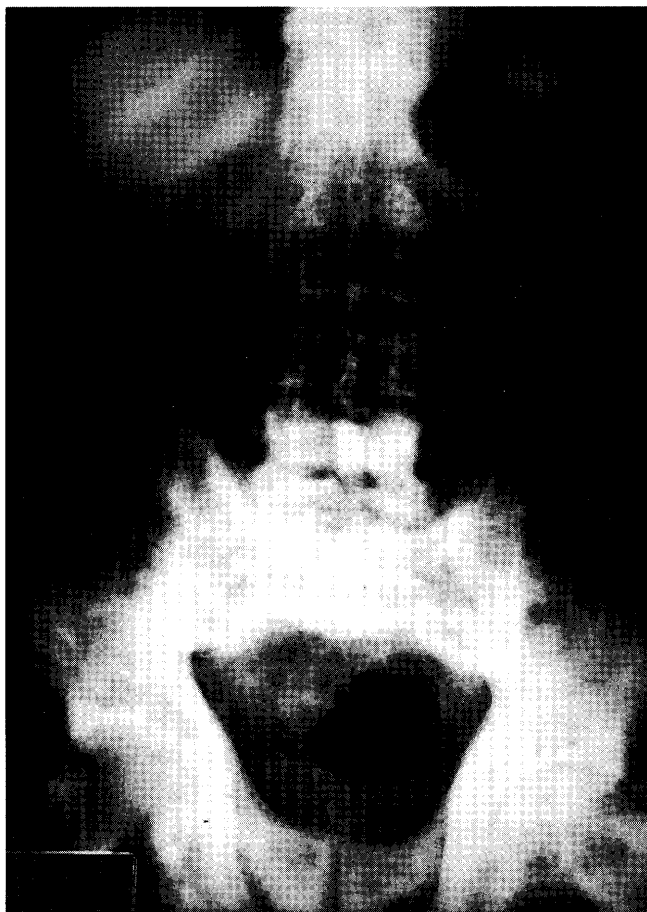


Fig. 6. Pelvic X-ray of Case 5 illustrating the marked bony expansion of the pelvis, with multiple areas of sclerosis in the pelvis, sacrum, left hip, lower lumbar and lower thoracic vertebral bodies.

tibia1 deformity and Case 5 had bone pain.

Fractures are the commonest complications of Paget's disease, and are difficult management problems as they often heal with difficulty and blood loss may be significant due to the increased bone vascularity.⁷ Degenerative arthritis is common in weight-bearing joints whose adjoining bones are affected.⁸ Neurological complications are not uncommon and reflect the involvement of the axial skeleton. Enlargement and deformity of the skull may cause compression of the cranial nerves as they emerge from their foramina, especially the ocular and auditory nerves.⁵ This is seen in Case 5, who had severe left sensorineural deafness. Platybasia, in which the weakened base of the skull becomes invaginated by the cervical vertebrae, may also occur. This can result in involvement of the lower cranial nerves and long tracts, as well as hydrocephalus.^{3,5} Spinal involvement may result in progressive paraparesis or radiculopathy.

Malignant transformation is a rare but serious complication, affecting less than 1% of patients. Most tumours are osteosarcomas, though fibrosarcomas and chondrosarcomas have been found.^{3,7,8} Benign giant cell tumours have also been described.^{3,8} The incidence of high output cardiac failure complicating Paget's disease is probably



Fig. 7. Bone scan of Case 5, showing bowing of the left femur and multiple areas of increased tracer uptake, involving the skull, humerus, vertebrae, pelvis and femur.

overemphasised, as it has been found to be very rare.^{7,8} Increased frequencies of extra-osseous calcification and renal stones have been reported,^{3,7} as was present in 2 of our patients.

Radiology of Paget's Disease

Paget's disease may be monostotic or polyostotic. Although any bone in the body can be affected, there is a predilection for the axial skeleton and lower limbs. In a scintigraphic study of 170 patients, Meunier et al⁹ found that the major sites of involvement were the pelvis (72%), lumbar spine (58%), femur (55%), thoracic spine (45%), sacrum (43%), skull (42%), tibia (34%) and humerus (31%). This trend was generally seen in our patients as well.

Plain radiographs of affected bones are the most useful radiological investigation, as the features are characteristic to the point of being pathognomonic.^{3,6} These include bone expansion or enlargement, cortical thickening, coarse trabecular markings and lytic and sclerotic changes,^{2,10} and are amply illustrated in the radiographs of our 5 patients. Plain radiographs are also useful in detecting complications such as deformities, fractures and malignant transformation.

Radiographic changes resembling Paget's disease, especially those with increased skeletal radiodensity, may also be seen in a number of other conditions. These include metastatic tumour, classically from prostatic or breast cancer, fibrous dysplasia, renal osteodystrophy, and haemangiomas.^{2,3,5,8} Additional features characteristic of these disorders, however, assist in their recognition. For example, fibrous dysplasia presents at a younger age and the affected area often has a homogenous "ground-glass" appearance, while other signs of chronic renal failure, as well as the characteristic "rugger-jersey spine" may be present in a patient with renal osteodystrophy. A vertebral haemangioma may be mistaken for Paget's disease, but it rarely affects the end plates and

neural arches, unlike the latter. Although a metastatic tumour may cause diagnostic difficulty, the bone enlargement, coarse trabeculae and thickened cortex will point to the diagnosis of Paget's disease.^{5,6,10}

Bone scans are the most sensitive means of identifying pagetic sites, and are extremely useful for assessing the extent of the disease.^{6,10} In active disease, dense uptake of radionuclide is a prominent feature, even in lesions not detected by plain radiographs.^{9,10} However, they are not as specific as plain radiographs, as uptake is also increased in areas of degenerative or metastatic disease.³ Conversely, there can also be little or no uptake of tracer in the inactive or sclerotic phase of Paget's disease.⁶

Biochemical Tests in Paget's Disease

The serum alkaline phosphatase level is usually elevated, except in localised or monostotic disease, and in the inactive or sclerotic phase, when it may be normal.⁹ This may explain the minimally elevated alkaline phosphatase level in Case 3, where the lesions were mainly sclerotic, and Case 4, where possibly only the tibia was involved. Bone-specific alkaline phosphatase is a more sensitive parameter than the total alkaline phosphatase level. Measurement of its level is especially useful in cases of monostotic or localised disease, where the total alkaline phosphatase level may be normal, and in cases where liver function tests are abnormal and the hepatic contribution to total alkaline phosphatase concentration is uncertain.^{5,11} In our patients, this problem did not arise as they had normal liver function. Unfortunately, assays for other biochemical markers like urinary hydroxyproline and pyridinoline excretion, are not available for routine use as yet.

Serum calcium levels are usually normal, but may be elevated in patients who are immobilised from any cause, and when there is coexistent primary hyperparathyroidism.³ Thus the mild hypercalcaemia found in Case 2 could be due to immobilisation as a result of the stroke, as his parathyroid hormone level was normal. This was transient, and his calcium levels were normal on follow-up.

Epidemiology of Paget's Disease

Paget's disease is typically a disorder of the elderly, and is generally discovered in patients over 50 years of age, with a slight male preponderance. It is uncommon under the age of 40 years.¹⁻³ Not surprisingly, all our patients were more than 50 years old, and there were 3 males to 2 females.

The disorder is common in the populations of Europe, North America, Australia and New Zealand, particularly in people of Anglo-Saxon origin. It appears to be distinctly rare in Asians, and particularly those from China, India and Malaysia.^{1,3,4} The reason behind this intriguing racial and geographical variation is still unknown.

Importance of Diagnosing Paget's Disease

Though Paget's disease is a benign condition in most patients, it is important for the physician to diagnose it and review the patient regularly. The patient should be monitored for the development of symptoms and complications, such as bone pain and deformity, fractures, neurological complications and malignant transformation. The appearance of any of these is an indication for treatment.^{1,3}

Of our patients, there were 2 who had definite indications for treatment. These were Case 4, who had a deformed tibia, and Case 5, who had bone pain and deafness. However, the former declined treatment while the latter defaulted further follow-up.

Conclusion

As in countries where the condition is more common, our patients with Paget's disease were largely asymptomatic, but had typical clinical, biochemical and radiological features. This enabled a confident diagnosis to be made in each case.

We believe that Paget's disease of bone, though rare, is also probably under-reported in Asia and Singapore.⁴ It can be easily missed because most cases are asymptomatic, as this paper illustrates, and the diagnosis, though important, is often an incidental one. It may thus be worthwhile to adopt a high index of suspicion for this disorder when confronted incidentally with suggestive clinical and radiological features, or an unexplained elevated serum alkaline phosphatase level.

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