Paget’s Disease in India

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Paget’s disease of the bone, first described in 1877 by Sir James Paget, is an extreme example of disordered bone remodeling.1 Disordered bone structure, due to the marked increase in osteoclastic activity and bone resorption, followed by excessive bone formation, is a characteristic of Paget’s disease. This may lead to pain, fracture and deformity. Pagetic bone is highly vascular and contains excess fibrous tissue.2,3

Paget’s disease can be uni- or multifocal and may affect any bone. The most commonly involved bones are the pelvis, vertebrae, skull, femur and tibia. An enlarged skull can lead to headaches or hearing loss. If the spine is involved, enlarged vertebrae may cause compression of the spinal cord or nerve roots. Osteosarcoma or other types of sarcoma occurs in less than 1 percent of patients with Paget’s disease and carries a poor prognosis.2,3

Paget’s disease can be diagnosed in patients by plain X-rays (initial osteolysis, later osteosclerosis), radionuclide bone scanning, or biochemical testing of bone turnover parameters. Although non-specific, a radionuclide bone scan is the most sensitive means of detecting Paget’s disease in the skeleton. As a marker of osteoblast activity, the simple measurement of serum total alkaline phosphatase activity provides a general indication of bone turnover and disease activity in Paget’s disease. For most patients, a decrease in the total serum alkaline phosphatase activity is sufficient to indicate and determine changes in overall disease activity.2,3

The prevalence of Paget’s disease shows wide geographical variation, even within the same country and the same ethnic group. For example, within Britain, there was marked geographic variation, with age- and gender-standardized prevalence rates ranging from 8.3% in parts of northwest England to 4.6% in southern towns and cities.4 About 2 percent of the U.S population older than 60 years of age has Paget’s disease,5 as do up to 6 or 7 percent of the elderly population in Western Europe.4 This contrasts with the rarity of the disorder in some other European regions like Scandinavia, Ireland, and southern Europe.4 Paget’s disease is also common in Australia and New Zealand with prevalence rates of 3-4%.6

In countries with high prevalence of Paget’s disease, bone pain, deformity, fractures, secondary arthritis, neurologic complications, and deafness that may accompany this disease contribute to substantial morbidity in the older population.

An interesting observation is the decline in the prevalence of Paget’s disease in the same population with time. For example, the prevalence of Paget’s seems to have declined in the UK. In a 1994 study, involving 9828 radiographs (4625 men, 5203 women) in 10 towns, the prevalence of Paget’s disease was only 40% of that observed 20 years earlier.7

Paget’s disease has always been regarded as rare in India, China and Malaysia. Isolated cases have been documented in Indians, but no systematic surveys have been undertaken.2 The reports from various Indian centers in this issue of the Journal confirm the existence of Paget’s disease in India, and suggest that it may not be as rare as was previously thought. Although none of the reports is based on a community survey, it seems that the disorder may not be uncommon in southern parts of India. Anjali et al report a series of 51 patients seen in Vellore over 8 years and found that their clinical features and pattern of presentation was quite similar to that reported from the West.8 Joshi SR et al report over eight year, seventeen cases scattered from Western India which has similar demographic of the South Indian cohort. They had a similar low dose response to alendronate like the South Indian cohort which is an interesting observation.9 Bhatt and co workers report 3 cases from Mumbai.10 Bhadada et al report a multicentric study involving 7 centres, with 21 patients.11 The communication from Mohan’s group in Chennai suggest a prevalence of 0.66% in a diabetic population. No clear association has been established between diabetes and Paget’s, and it may be possible that the true prevalence of Paget’s in south India may be close to this figure.12 These reports emphasize the need for population based studies.

The reason for wide variations in Paget’s prevalence is not understood. Some studies have suggested an association with viral infection.13 Inclusion bodies resembling paramyxovirus nucleocapsid particles have been observed in pagetic osteoclasts by electron microscopy,14,15 and canine distemper virus has been localized by in situ hybridization to the bone cells of patients with the disorder.16 There is familial aggregation
of Paget’s disease and it is associated with polymorphisms in DNA coding for centrosome structure.17 Genetics, could therefore also be playing a role in determining prevalence of Paget’s disease, but as is evident from the decline in disease prevalence in Britain, unidentified environmental factors are also major contributors.3

Since the major defect in Paget’s disease is exaggerated bone remodeling, treatment is based on the use of powerful anti resorptive agents. Most experts feel that not all patients require treatment- asymptomatic disease in a non-dangerous site without any major metabolic abnormality can probably be kept under observation, without specific therapy. It is thought that the majority of Paget’s patients are asymptomatic. However, most other patients require treatment. These comprise – symptomatic paget’s disease, patients requiring surgery at a pagetic site, hypercalcemia (rare), or location of lesions at a site which could potentially lead to complications, even if presently asymptomatic.2,3 The failure to treat Paget’s disease has been associated with the further destruction of the bone and the progression of bone deformities.

Bisphosphonates form the mainstay of medical management of Paget’s disease. These agents suppress or reduce bone resorption by osteoclasts. Most bisphosphonates work well in Paget’s disease. Currently, five bisphosphonates are approved by the US Food and Drug Administration for the treatment of Paget’s disease. These include pamidronate, which is given intravenously, and etidronate, tiludronate, alendronate and risedronate, all of which are taken orally.3 A recent study suggests that a single infusion of zoledronic acid produces more rapid, more complete, and more sustained responses in Paget’s disease than does daily treatment with risedronate.18 The case series from Vellore and Mumbai in this issue of the journal both suggest that lower doses of alendronate might work well in Indian patients.8,9 This however, needs to be confirmed in randomized controlled trials. Calcitonin is conventional but now infrequently used therapy. Non-pharmacological measures, pain management and surgery are also used when indicated.

REFERENCES