Paget's Disease of Bone in Indian Patients: Two Case Reports

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ABSTRACT

Paget's disease of bone is rare in India but getting reported more often. Is a disease of defective remodeling of bone of unknown etiology, incidentally diagnosed by finding unexplained elevation of alkaline phosphatase or abnormal skiagram as most of the sufferers are asymptomatic. It is disease of elderly and of European ancestry. Alkaline phosphatase is a simple investigation of choice to diagnose, monitor and screen the patients. Availability of bone scans made it easy to diagnose polyostotic or early disease. Single dose of intravenous zoledronic acid is the drug of choice with high response rates. It is presumed that the incidence of Paget's disease may increase in India as many Indians are living up to 80 years, the age of Paget's disease.

Keywords: Paget's disease, alkaline phosphatase, abnormal skiagram, bone scans, zoledronic acid

Paget's disease (osteitis deformans) is a localized disorder of bone remodeling that typically begins with excessive bone resorption followed by an increase in bone formation. This osteoclastic overactivity followed by compensatory osteoblastic activity leads to a structurally disorganized mosaic of bone (woven bone), which is mechanically weaker, larger, less compact, more vascular and more susceptible to fracture than normal adult lamellar bone. It is also called British disease, highest prevalence being in Europe. Due to significant population with European ancestry and British immigrants USA, Australia and New Zealand also have higher prevalence.

It is rare in Asian countries. It is a very ancient disease, archeologists discovered the disease in the bones of people from Roman era 20 BC, though first described by Sir James Paget in 1876. This is a disease of elderly, rare before age of 40, except rare autosomal recessive juvenile form. Prevalence varies between 1% and 3%, and in people aged above 80 years in Europe, 10% were suffering from this disorder. This is the commonest bone disorder in Europe second to osteoporosis. Men and women are equally affected.

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Paget's disease is rare in India. The first case was reported by Dr Vyagreswarudu from Visakhapatnam in 1953, the same city from where we are reporting two cases of Paget's disease. Dr Anjali et al reported a series of 51 patients seen in Vellore over 8 years; they did not differ in clinical presentation from that seen in West. Dr Joshi et al reported 17 cases scattered over Western India.

Dr Bhadada and coworkers reported 21 cases from a multicentric study involving seven centers. Dr Bhatt reported three cases from Mumbai. Dr Mohan from Chennai reported 0.66% prevalence in diabetic patients.[1] Here we present two cases of Paget's disease, one followed up for 8 years and second one recently diagnosed.

CASE PRESENTATION

First Case

A 72-year-old male patient consulted us on 05-04-2007 at our hospital for his regular follow-up of hypertension and coronary artery disease as he shifted his residence close to our hospital. He was asymptomatic at that time. As we were going through his previous reports, we found that alkaline phosphatase was abnormally elevated. One of his ultrasound scan of abdomen was reported to have cholelethiasis. Appearance of his face and skull were abnormal, suspicious of Paget's disease.

We were skeptical as we were seeing a Indian patient (Fig. 1). We did his serum calcium, liver function test

including alkaline phosphatase, contrast-enhanced computed tomography (CECT) abdomen, X-ray of skull anteroposterior and lateral view. Serum calcium was normal, alkaline phosphatase was elevated 1,401 U/L (40-140). CT scan of abdomen did not show any biliary pathology. His skull X-ray showed enlargement with osteolytic and osteoblastic lesions suggestive of Paget's disease (Fig. 2). We started him on ibandronate 150 mg to be taken first in the morning on empty stomach once monthly and not to lie down for

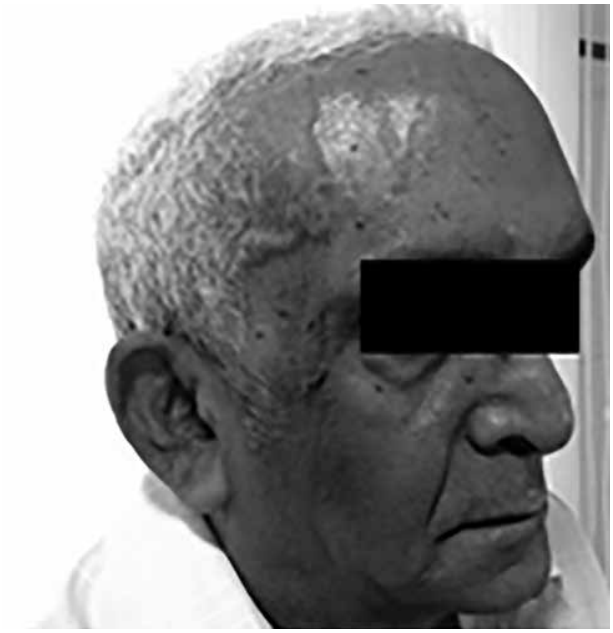

Figure 1. Photo case 1.

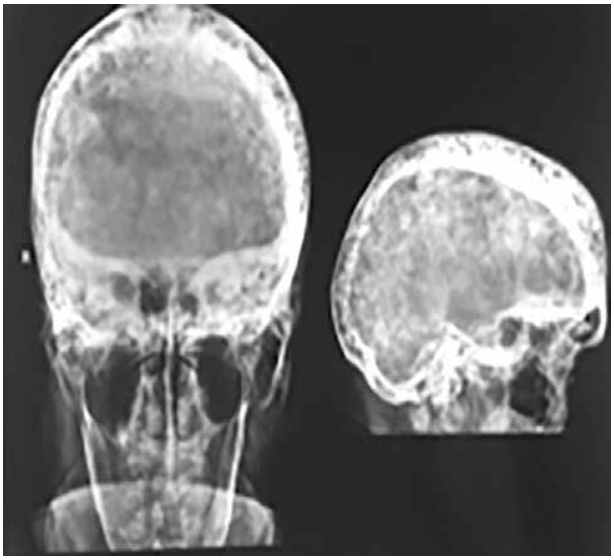

Figure 2. X-ray skull showing cotton wool appearance.

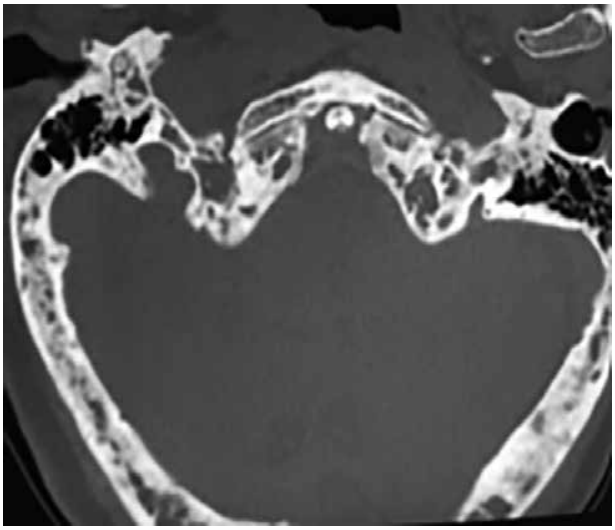

Figure 3. Thickened skull vault with osteolytic and osteoblastic lesions on CT scan.

60 minutes after the tablet. He responded well to the treatment, his alkaline phosphatase came to baseline in 6 months and has remained so until now.

In 2012, he developed hearing problem and he consulted ENT surgeon and his CT scan was showing Paget's disease of cranial vault and base of skull (Fig. 3). He has both conductive and sensorineural deafness. He never lived out of India and none of his family members has similar disease. He is on regular follow-up until now.

Second Case

A 67-year-old female patient was admitted to our hospital for weakness and excessive sleepiness. She is a known hypertensive on telmisartan 40 mg twice-daily. Recently, she was diagnosed to have major depression and is on antidepressant medications for the last 2 months. Her facial appearance was not abnormal except a little prominence of forehead (Fig. 4).

She has no body pains or headache. Her magnetic resonance imaging (MRI) scan brain was done in the view of altered sensorium to exclude organic pathology, which showed diffuse thickening of skull vault suspicious of Paget's disease (Fig. 5).

X-ray skull showed sclerotic and osteolytic lesions confirming Paget's disease (Fig. 6). Her alkaline phosphatase was 476 (60-306). Technetium bone scan revealed hot lesions of skull, right humerus and left sacroiliac joint (Fig. 7). She was given zoledronate 4 mg intravenously over 15 minutes and had no complication.

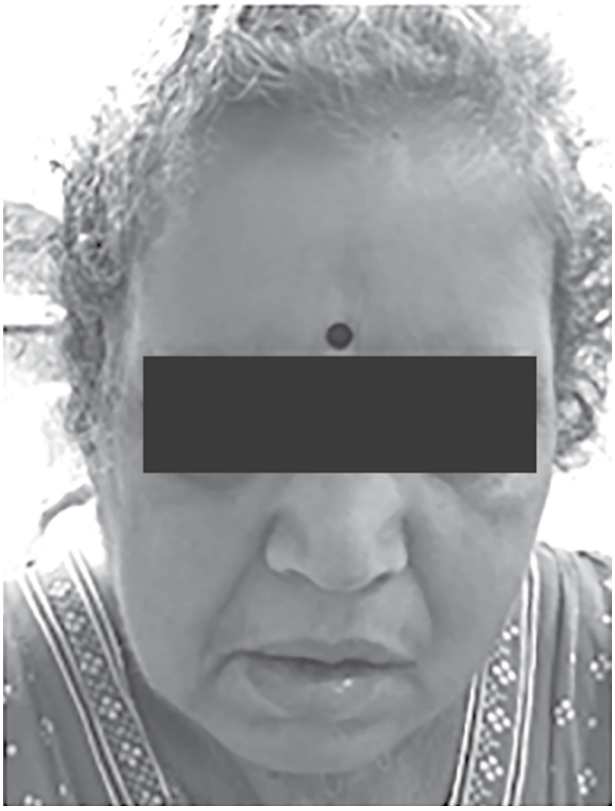

Figure 4. Photo case 2.

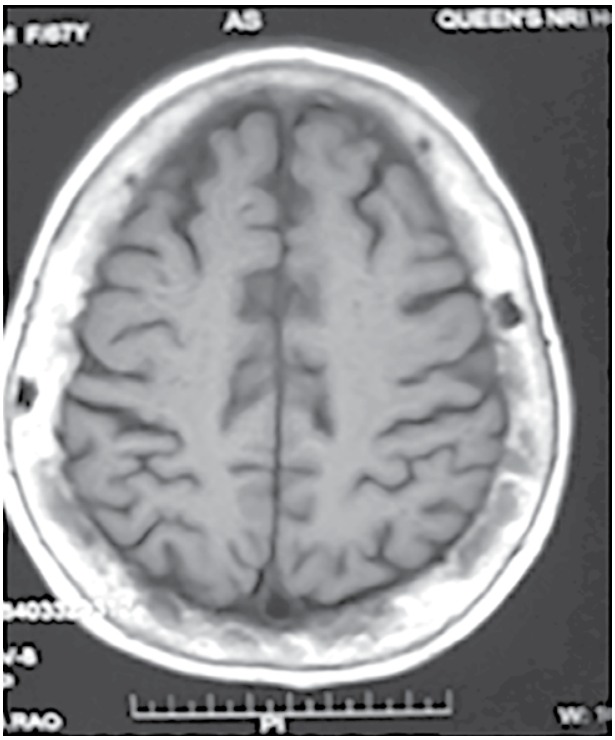

Figure 5. MRI skull showing enlargement, osteolytic and osteoblastic lesions.

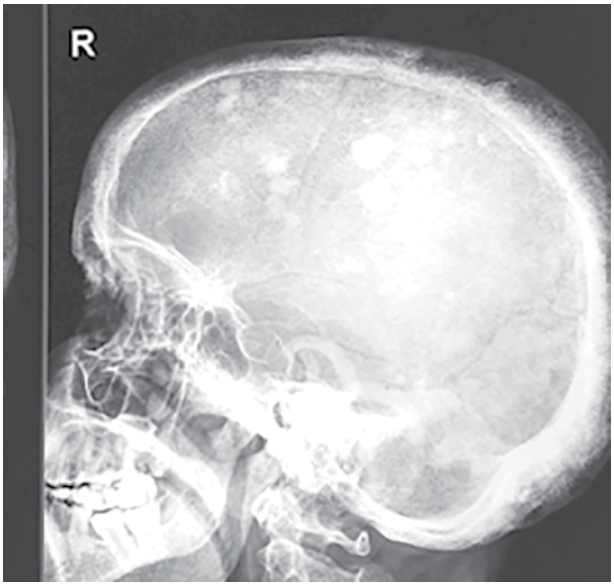

Figure 6. X-ray skull showing lytic and sclerotic lesions.

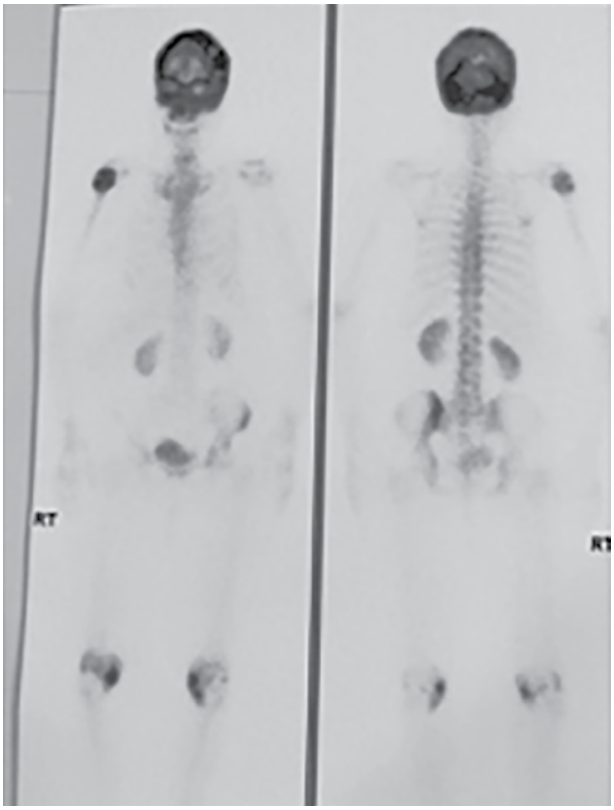

Figure 7. Bone scan showing hot areas in skull, right humerus, left sacroiliac joint.

DISCUSSION

The cause of Paget's disease is not known, it is postulated that genes, environment and virus as

etiological factors. Patients are mostly asymptomatic and accidentally discovered due to elevated alkaline phosphatase as shown in first case or abnormal bone skiagram as in second case. Three stages are described in Paget's disease lytic, mixed and sclerotic. Multiple stages of disease may be demonstrated in different skeletal regions.

Alkaline phosphatase is a marker of osteoblastic activity, it correlates well with disease activity. It declines with successful treatment.[2] Bone-specific alkaline phosphatase is more specific, it is a superior marker if the patient has limited disease or liver disease. Urinary hydroxyproline, N-telopeptide, alpha-C telopeptide are markers of bone resorption but they have limited usage in clinical practice. They are useful to evaluate response to bisphosphonate treatment.

The two cases we presented had abnormal skull X-rays with osteolytic and osteoblastic lesions classical of Paget's disease. Radiographic appearance of pagetic bones are very specific; not only they confirm the diagnosis, they stage the disease and are useful for evaluating therapeutic response. Any bone may be involved but small bones of hand and ribs are rarely affected and fibulae are spared.

Sparing of fibula is an excellent observation made by Dr Paget in his first case. CT scan and MRI are of advantage if brain and spinal cord are involved. Paget's disease has predilection for axial skeleton-spine, pelvis, sacrum, skull and femur are involved in that order of frequency. The disease does not spread from one bone to another and new sites of involvement are rare after initial diagnosis.

Facial bone involvement[3] and autosomal recessive juvenile Paget's disease[4] have also been reported from India. Thirty percent of familial Paget's disease may have genetic mutation in sequestosome SQSTM1/p62 gene. Familial clustering was also reported from India.[5] Bone pain is the commonest symptom which may exacerbate in the night and at times bones are deformed. Subtrochanteric fracture is commonest fracture in this disorder. Fractures may heal with medical management.[6]

When cranium is involved hat size may progressively increase and the patient may have vertigo and deafness and occasionally visual loss. Our first patient had progressive deafness. If platybasia occurs due to softening of bones of the base of skull, the disease may precipitate brainstem and cerebellar compression syndromes. Vertebral fractures or canal stenosis may lead to compression of spinal cord and lead to paraparesis and incontinence of bowel and bladder.

In the second case, patient had abnormal skull bones on MRI and pagetic disease was confirmed by skull X-ray. She also had abnormal technetium scan which was suggestive of involvement of skull, right shoulder and left sacroiliac joint. Periarticular involvement of bone may lead to secondary osteoarthritis.

Though technetium scan detects disease early, evaluates disease extent and activity, at least one site of lesion must be X-rayed to confirm the disease as the test is not specific. Dr Sujata reported 9 cases of Paget's disease in 3,050 cases referred for bone scan over 7-year period.

Bisphosphonates are the drugs of choice; therapeutic response is evaluated by normalization of alkaline phosphatase at 6 months. First case responded well, by normalizing alkaline phosphatase within 6 months and second case has not yet completed the stipulated duration. Introduction of zoledronic acid revolutionized the treatment of Paget's disease; with one single dose 90% patients normalize their alkaline phosphatase within 6 months and most of them remain so even after 5 years and rarely require second dose. The concept of treating patients with symptomatic disease, severe osteolytic lesions, alkaline phosphatase two times of normal and disease close to joint is changing.

Though controversial, people are opting to treat the disease with single dose of zoledronic acid irrespective stage and activity unless contraindicated. Zoledronic acid is drug of choice and rarely it may cause influenza like symptoms in some patients.[2] Contraindicated if glomerular filtration rate is less than 30%, calcitonin can be used in such a situation. Calcium and vitamin D should be supplemented, more so if the patient is on bisphosphonate therapy. If surgery is planned on pagetic bone and if it is elective at least he must on 3 months bisphosphonate therapy to prevent excessive bleeding.

Patients should be followed up for life. Untreated patients should undergo annual check-up with alkaline phosphatase and X-ray. Treated patients should have alkaline phosphatase checked 3-4 months and X-rays done annually. A person having family history of Paget's disease and aged above 40 years should check his alkaline phosphatase every 2-3 years and if alkaline phosphatase is in upper limit, he should undergo bone scan.

CONCLUSION

Paget's disease can be found in India, though rarely. The incidence of disease may go up as good numbers of Indians are living beyond the seventh decade. It is prudent to think of Paget's if no other reason could be found for elevated alkaline phosphatase and if we find both lytic and sclerotic lesions in a bone on skiagram.

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Exercise Impact on the Knee

Different exercises produce different impacts on the knee joints. The best and safest exercises causing minimum impact on the knee after knee replacement or patients with knee arthritis are walking, biking, hiking, riding an exercise bike, riding an elliptical trainer and walking on the treadmill. In sports one can play doubles tennis and not singles. One can also participate in downhill or cross-country skiing. The maximum stress-producing exercises are jogging and golf swings. Impact

- Biking generates the least force, producing impact of about 1.3 times the person's body weight.
- Treadmill walking was next best, producing forces of 2.05 times the body weight.
- Walking on level ground generated forces of 2.6 times the body weight.
- A game of tennis produces forces of 3.1-3.8 times the body weight; serving produces the highest impact.
- Jogging produced forces of 4.3 times body weight.
- Golf swings produces forces of 4.5 times body weight on the forward knee and 3.2 times body weight in the opposite knee.