Paget's disease of the bone


ABSTRACT

Paget's disease of bone is rare in Asia. Association of calcific aortic valve disease with Paget's disease of bone is well documented. We report a patient from north India who also had calcific aortic valve disease.

Keywords: Calcific aortic valve disease, Paget's disease of bone.


As early as 1877 Sir James Paget - an eminent 19th century surgeon described his detailed observations on 5 middle-aged individuals with chronic deforming bone disease. He then believed that these patients suffered from a rare chronic inflammatory disorder and named the condition as osteitis deformans. Subsequently the disorder was designated as Paget's disease of bone after his great contribution. Paget's disease is a focal disorder of bone turnover characterized by increased bone resorption coupled with bone formation with the result that bone becomes architecturally abnormal and mechanically weak. Disease may be monostotic or polyostotic with predilection for axial skeleton. Disorder is mostly confined to Western Europe. Prevalence in UK is around 9% in patients over 55 years old and 10% in persons over their 90s. In India, Japan, Middle East and Scandinavia, the disease is exceedingly rare. This report describes a patient of Paget's disease of bone belonging to North India who also had calcific aortic valve disease.

Case report. A 50 year old middle aged male was referred to endocrine unit of Sher-i-Kashmir Institute of Medical Sciences, Srinagar with complaints of generalized weakness, low backache and exophthalmos. On enquiry he also complained of mild intermittent headache. Examination revealed a middle aged male with strikingly large head (Figure 1). His pulse was 94 beats per minute, collapsing type. BP was 170/60 mmHg. He had peripheral signs of high cardiac output. His height was 158 cm and head circumference was 67 cm (>3SD). He had a gibbus around T12-L2 area (Figure 2). Examination of chest, abdomen and central nervous system was unremarkable. Cardiovascular system revealed a heaving apex in 5th intercostal space just outside mid clavicular line with a systolic thrill over aortic area. First heart sound was muffled and a systolic murmur, grade 4/6, was heard over A2 area radiating along parastral area. A bruit was heard over scalp. Optic fundi were normal and per rectal examination revealed a mild prostatic enlargement.

Investigations revealed a normal hemogram and urine examination. Fasting blood glucose was 83 mg/dl, serum calcium was 8.47 and 9.13 mg/dl, and serum albumin was 3.9 g/dl. Serum alkaline phosphatase was markedly increased 3245 and 2866 U/L (Normal value 72-279). Serum acid phosphatase was 11.8U/L (normal value 0-12). 24 hour urinary calcium was 92 mg. Electrocardiogram revealed biventricular hypertrophy. X-ray chest revealed a cardiothoracic ratio of 0.65 with left ventricular type enlargement. X-ray skull revealed thickened cortex with diffuse osteosclerotic and osteoclastic areas (Figure 3A). X-ray lumbosacral spine revealed a compression fracture of T12 L1 regions (Figure 3B). Technetium scan of whole body revealed increased uptake in skull, pelvic bones and spine (T12-L1 region) (Figure 4A and 4B).

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Echocardiography revealed evidence of aortic valve disease with moderate aortic stenosis and aortic regurgitation with normal left ventricular function. Family screening of other 3 siblings did not reveal any evidence of Paget's disease of bone. They had a normal skull x-ray and serum alkaline phosphatase. A final diagnosis of Paget's disease of bone with calcific aortic valve disease was made.

**Discussion.** The study of ancient skeletons revealed that Paget's disease of bone existed as early as Neolithic period. The oldest, well preserved skeleton thought to represent Paget's disease was unearthed from an Anglo-Saxon burial ground in Durham, England, and was dated to about 950 A.D. Paget's disease can affect any bone but has a predilection for the axial skeleton (the spine, pelvis, femur, sacrum and skull being involved in decreasing order of frequency). Disease can be unifocal or multifocal. The lesions may be predominantly osteolytic or osteoblastic, in most cases a mixture of two changes is seen. The affected bones are often expanded in their dimensions. The bones are weak and can manifest as compression of vertebrae, and bowing and fractures of long bones. Our patient had an enlargement of head and a gibbus at T12-L1, and pain was the dominant symptom at both the sites. Patients with Paget's disease can develop gradually progressive paraparesis and or radiculopathy when spine is affected. Deafness can occur either due to entrapment of auditory nerve or destruction of the ossicles of cochlea, or because of alteration of acoustical properties of bones. Other neurological complications include cranial nerve compression, hydrocephalus due to platybasia, spinal stenosis and vascular steal syndrome affecting cord and brain. Osteoarthritis of major joints is extremely common.

Cardiac output may be increased in extensive Paget's disease but the consequent high-out cardiac failure is extremely rare. Disease is associated with increased incidence of calcific aortic valve disease, the severity of which is proportional to the extent of Paget's disease. Interventricular septal calcification and cardiac conduction abnormalities have also been reported. Our patient had clinical and echocardiographic evidence of calcific aortic valve disease with moderately severe aortic stenosis and aortic regurgitation with normal left ventricular function. He had no symptoms of either left or right heart failure.

The radiological characteristics of the disease are usually the basis of diagnosis. Changes depend upon the stage of disease. Lytic lesions are especially likely to affect cortical bones and may produce advancing osteolytic wedge in long bones. Extensive lytic areas of skull are referred to as osteoporosis circumscripta. The sclerotic changes produced by osteoblastic repair are striking in appearance, bone is thickened and in some areas there may be uniform increase in density (Ivory vertebrae). Patchy mixture of sclerotic and lytic changes is quite common. Bone scintiscanning is useful in assessing the distribution of pegetic lesions. In 9% of patients plain radiographs may appear normal despite scintigraphic evidence of pagetic activity.

A number of biochemical markers reflecting either osteoclast or osteoblastic activity are a reflection of intensity, size, and number of lesions. In most hospital outpatient clinics, total alkaline phosphatase remains the simplest and sensitive marker of disease activity. The most feared complication in Paget's disease of bone is development of sarcoma, this complication occurs in less than 1% of patients. Common sites are pelvis, humerus, femur and skull. Increasing bone pain un-relieved by treatment with rising levels of alkaline phosphatase are pointers towards a possible sarcomatous change.

Paget's disease of bone is believed to be a late complication of a viral infection. Evidence has been presented for the role of measles, respiratory syncytial, and canine distemper viruses. Current hypothesis is that a paramyxoviral infection of bone leads to overproduction of cytokines, resulting in the clinical syndrome of Paget's disease: inherited abnormalities in immune response or in genes regulating bone activity would increase the susceptibility of the individual to develop the disease.

A number of asymptomatic patients probably do not need treatment other than a regular review at 6 monthly or yearly intervals with total serum alkaline phosphatase and urinary pyridinolines as biochemical markers. Simple analgesia and nonsteroidal anti-inflammatory drugs are useful for relief of pain. Bone pains with or without neurological defects, hypercalcemia, treatment of high output congestive heart failure, prevention of hearing loss and skeletal deformities in young patients form the main indications of drug treatment. A number of compounds have been used for the treatment of Paget's disease viz bisphosphonates, plicamycin, gallium nitrate and a combination of these. Etidronate was first used in United States in 1978. It inhibits osteoclast mediated bone resorption (usual recommended dose is 5 mg/kg body weight daily, for a period of 6 months). Multiple courses can be given and 75% of cases continue to be responsive. Pamidronate can be given in short courses to induce a yearly remission (30 mg can be given over two hours on three consecutive days). Clodronate, risedronate, alendronate, tiludronate are other Bisphosphonates effective in oral usage. Clodronate has an excellent side effect profile 10% of subjects complain of gastro-intestinal disturbance with oral clodronate. Oral alendronate, now available in India, is also effective but can cause significant gastro-intestinal discomfort. Our patient in view of his backache and a compression fracture is on oral alendronate, response needs to be seen.
References