Abstract:

Paget’s disease of bone (PDB) is a progressive monostotic or polyostotic metabolic bone disease characterized by focal abnormal bone remodelling, with increased bone resorption and excessive, disorganized, new bone formation. PDB rarely occurs before middle age, and it is the second most frequent metabolic bone disorder after osteoporosis, affecting up to 3 percent of adults over 55 years of age, globally. But, only a handful of cases have been reported from India. This report describes a case of Paget’s disease of bone in a 45-year-old female, emphasizing on the clinical presentation and treatment options.

INTRODUCTION:

Paget’s disease is a focal disorder of accelerated skeletal remodelling that can involve either a single bone (monostotic) or multiple bones (polyostotic). There is excessive bone resorption, followed by excessive bone formation, leading to a highly vascularised bone that is structurally disorganised. This results in bone pain, deformity, skeletal fragility and pathological fractures (1). Paramyxoviruses and genetic susceptibility are postulated to play a role in the aetiology (1). The prevalence of Paget’s disease in the western countries is about 1%–2% and is reported to be rare in the Asian countries (1). Only a few case series from India have been recently reported (2,3).

CASE REPORT:

A 45-year-old lady presented to the OPD with the chief complaints of: Pain in the knee, low backache, pain in the thigh for the past 1 year and Breathlessness on & off for 6 months. Patient was apparently alright 1 year ago. Then she developed pain in those areas, insidious in onset, gradually progressive. Pain was dull aching without any diurnal variations. No specific aggravating / relieving factors. Patient had breathlessness for the past 6 months, while doing her household activity which increases more during exertion & relieved by rest. No history of orthopnea or PND. No history of Chest pain, palpitation, syncope, presyncope, abdominal pain, nausea, vomiting/ diarrhea / constipation/ bleeding from orifices. No history of diplopia, dysphagia, dysarthria, motor deficits, sensory deficits, unconsciousness/ altered sensorium or involuntary movements.
Other than the above chief complaints, the patient’s daughter observed that her mother had a significant loss of height of about 10-15 cms over the past 2-3 years. She was not a known case of diabetes/systemic hypertension/Tuberculosis/Asthma. She attained menopause 2 years ago, cycles were regular during premenstrual period. Post-menopausal period was uneventful. She was a vegetarian by diet.

EXAMINATION:
Conscious, oriented, Comfortable at rest, afebrile. No pallor/ icterus/ cyanosis/ clubbing/ lymphadenopathy/ edema. Extremities were warm. Pulse: 110/min, bounding; BP: 120/60 mm of hg, right arm, supine position, BP :130/60 mm of Hg in lower limb. JVP not elevated. RR : 16/min. CVS/RS/CNS: clinically normal. Musculoskeletal system examination: Patient had short stature (figure 1a). Height was 138 cms. Spine examination showed kyphosis, no tenderness of spine. Hip examination revealed a fixed flexion deformity of hips. Hip movements were painful and terminally restricted. Knee examination showed Genu varum / tibia vara (figure 1b) and extension lag of 20°.

INVESTIGATIONS:
CBC: Hb: 12.2 gm/dL, TC: 7,200 cells/ cu mm, D : P60 L 40, ESR : 6/12 mm/hr, PCV : 36%, Platelets:1.5 cells/mm³, MCV: 32, MCH: 29 pg. Peripheral smear: normocytic normochromic blood picture, adequate RBCs, WBCs & platelets. RBS: 84mg/dL, RFT: Urea: 23mg/dL, Creatinine: 0.6mg/dL,

Serum electrolytes: Na⁺:136mEq/L, K⁺: 4.5mEq/L, Cl⁻: 96mEq/L, HCO₃⁻: 24mEq/L. LFT: Totalbilirubin: 1.0 mg/dl, direct bilirubin: 0.2 mg/dl, SGOT: 22 U/L, SGPT:14 U/L, Total protein: 5.8 gm/dl,albumin: 4 gm/dl. URINE R/E: 1-2 epithelial cells., no albumin,sugar or pus cells. ECG: sinus tachycardia. Chest X-ray (figure 2) was normal.

Figure 1a - Clinical Photograph of Patient Showing short stature Figure 1b - Clinical Photograph of Patient Showing Genu Varum Figure 2 - Xray Chest
Ultrasonogram abdomen: Normal. ECHO: EF 66%, No RWMA, Normal LV Systolic function, Calcific aortic sclerosis and Blood gas analysis showed: mixed venous oxygen saturation (SvO2) of 78% suggesting high output heart failure. Pulmonary Function Test: normal.

High output failure is considered when patient comes with symptoms of heart failure along with warm peripheries, preserved left ventricular function, mixed venous oxygen saturation (SvO2) >70-75% and etiology consistent with high cardiac output state. Thyroid function test was done and RBC transketolase levels estimated to rule out thyrotoxicosis and beri-beri respectively, which can also cause high output cardiac failure. Thyroid Function Test: T3 :196 (N: 75 - 220 ng/dL), T4 : 7.2 (N: 4 - 11 g/dL), TSH : 3.8 (N: 0.5-5.0 ml/U/L). RBC transketolase: 500 (N:440± 120g/ml/hr ). Serum calcium : 8.8 mg/dl ( total & corrected); Serum Phosphate : 4mg/dl (N:2.4-4.1mg/dl); Alkaline phosphatase : 880 (N: 40-140 U/L). PTH : 55 pg/ml (N:10-60 pg/ml); Vitamin D3: 45 (N: 30-100 ng/ml). PTH level- 25 (N: 15.0 - 65.0 pg/ml)

X-ray lumbosacral spine (AP) showing extensive lesions typical of paget's disease. Extensive patchy sclerosis of pelvis and femur with deformation reflecting high turnover and abnormal bone structure. X-ray skull (lateral). There is sclerosis and loss of cortico-medullary differentiation of the vertebral bodies and the neural arches.


FINAL DIAGNOSIS: PAGET'S DISEASE- a polyostotic disease with significant bone involvement and high output cardiac
failure with typical x-ray and bone biopsy findings.

TREATMENT & FOLLOW UP:
1) Symptomatic Management
2) Zoledronic acid 5mg iv infusion, single dose was given. 3) Once a week iv injection of Vit D3 6lakh IU for 2 months given. 4) Oral calcium equivalent to elemental calcium 200mg per day regularly. 6 months follow up of the patient showed symptomatic improvement. Bone pain has reduced and breathlessness improved.

DISCUSSION:
Paget disease of the bone (PDB), also known as osteitis deformans, was first described in a small group of patients in 1877 by Sir James Paget. It is a focal skeletal disorder characterized by an accelerated bone turnover. The skeletal sites most commonly involved are pelvis, vertebral bodies, skull, femur and tibia. The etiology of Paget disease remains unknown, but evidence supports both genetic and viral etiologies. The principal abnormality in PDB is increased number and activity of osteoclasts which are increased by about 10-100 fold. The osteoclastic precursors are hypersensitive to 1,25 (OH)2D3, hyperresponsive to RANK ligand (RANKL) and marrow stromal cells from pagetic lesions have increased RANKL expression. The characteristic feature of PDB is increased bone resorption accompanied by accelerated bone formation. The woven bone which is formed as a result is structurally inferior and can fracture more readily. Pain is the most common presenting symptom. Bowing of the femur or tibia causes gait abnormalities. Secondary osteoarthritis may occur. Spinal cord compression can occur either due to bony enlargement or due to vascular steal syndrome. Skull enlargement causes headache and frontal bossing. Cranial nerve palsies and brainstem compression occur as a result of cranial expansion. Cardiovascular complications in the form of high output cardiac failure may occur due to marked increase in blood flow through the vascular pagetic bone. Venous blood gas analysis is useful in identifying high output state. Our patient had a high output cardiac failure which improved after addressing the underlying cause. Diagnosis: PDB is usually diagnosed from radiological and biochemical abnormalities. It may be suggested on clinical examination by the presence of an enlarged skull with frontal bossing, bowing of long bones or short stature. Typical radiological findings are: bony enlargement and typical lytic and sclerotic changes. Skull radiographs may reveal thickening of diploic areas or enlargement of skull bones or cotton wool appearance. Vertebrae give the appearance of “picture frame” vertebrae. Pelvic X-rays demonstrate disruption of fusion of sacroiliac joints. Radionuclide 99mTc bone scans are more sensitive for identifying sites of active lesions. Our patient had genu varum and patchy sclerosis of central skeleton and thickening of the skull bones. Biochemical evaluation shows normal serum calcium and phosphate levels. There is marked elevation of serum alkaline phosphatase, which is also the most common biochemical abnormality in PDB. There is also an elevation in urinary hydroxyproline levels. The majority of patients with Paget disease of bone remain asymptomatic and do not need treatment. Treatment can be given to asymptomatic patients when the disease is quite active as indicated by the levels of alkaline phosphatase or other markers of bone turnover. Patients with significant symptoms should also be treated.
Second-generation bisphosphonates are the treatment of choice for this disease. In patients with high bone turnover, Vitamin D3 and calcium are supplemented to prevent hypocalcemia and secondary hyperparathyroidism. As per the literature report\(^1\), our patient also showed significant improvement after receiving bisphosphonates, Zoledronic acid.

REFERENCES:


