

LATE-SCLEROTIC PHASE DIAGNOSIS OF PAGET'S DISEASE OF BONE: A CASE REPORT

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Abstract:

Background: Paget's disease of bone (PDB), is a chronic skeletal disorder marked by abnormal bone remodeling due to increased osteoclastic activity followed by disorganized osteoblastic bone formation. It commonly affects older adults and present with pain, deformities, or fractures.

Methods: A 64-year-old male with Parkinsonism and hypertension, who reported chronic low back and groin pain. Laboratory evaluation revealed markedly elevated serum alkaline phosphatase (422.2 U/L), and MRI imaging showed suggestive of PDB in the late sclerotic phase.

Results: A single intravenous dose of zoledronic acid (5 mg) was administered, resulting in symptom relief and planned biochemical follow-up. Calcium and vitamin D supplementation were initiated to prevent treatment-related complications.

Conclusion: A multidisciplinary team involving physicians, clinical pharmacists, and nurses was critical in ensuring optimal care, preventing complications, and improving patient outcomes and quality of life.

Keywords: Bone resorption, MRI imaging, Paget's disease of bone, Serum alkaline phosphatase, Zoledronic acid.

Introduction:

Paget disease of bone, also known as “*Osteitis deformans*”, is a chronic skeletal disorder marked by localized regions of abnormal and disorganized bone remodeling. The pathological process is characterized by excessive activity of osteoclasts, leading to increased bone resorption, then followed by a compensatory but unregulated osteoblastic bone formation.⁽¹⁾PDB is the second most common metabolic bone disorder, with its etiology remains unclear, however it is thought to be influenced by various genetic and environmental factors.⁽²⁾ Viral agents such as paramyxovirus, canine distemper virus, and respiratory syncytial virus have also been implicated as potential causative factors.⁽³⁾ Paget's disease may be influenced by distinct genetic factors, as around 5–40% of patients report a family history; however, the majority of cases occur in individuals without any known familial background.⁽⁴⁾ It mainly affects 1-2% of the population, most typically those over the age of 55 years and men are more prone as compared to women.⁽⁵⁾The primary risk factors for paget's disease of bone include advancing age, male gender, and ethnic background.⁽⁶⁾Many patients with paget's disease of bone are asymptomatic, and the condition is often detected incidentally through elevated serum alkaline phosphatase levels or characteristic findings on radiographic imaging. When symptoms are present, common clinical manifestations include bone pain, bowing of long bones, skull enlargement and hearing loss. The degree of serum alkaline phosphatase elevation typically reflects the level of disease activity.⁽⁷⁾ Complications include bone fractures, skeletal deformities, secondary osteoarthritis, and neurological problems like nerve compression. In rare conditions, the disease may progress to malignant transformation, such as the development of osteosarcoma.⁽⁸⁾ This case highlights the importance of biochemical markers and imaging in diagnosing PDB and emphasizes the role of bisphosphonates in management.

Case Presentation:

A 64-year-old male patient was referred from the Orthopedic Department to the Orthogeriatric Rheumatology Department at a Multispecialty Hospital with a clinical suspicion of either Diffuse Idiopathic Skeletal Hyperostosis (DISH) or osteoporosis. The referral was made in view of his complaints of low back pain and bilateral groin pain persisting for the past one year. The patient reported a history of a slip and fall one year ago, following which he was managed with NSAIDs and vitamin supplements at a nearby hospital. However, his symptoms progressively worsened, and over the past six months, he has been unable to bear weight or walk. There is no history of hearing loss, joint pain, or joint deformities, and had normal bowel and bladder control. He was a smoker and alcoholic for past 20 years and had stopped before 4 years. He has known co-morbidities, including Parkinsonism and hypertension, and is on regular medication—Tablet Syndopa 110 mg once daily and Tablet Amlong 10 mg once daily. General physical examination was unremarkable, and local examination revealed normal posture. Laboratory investigations are summarized in Table 1. Notably, serum alkaline phosphatase was markedly elevated at 422.2 U/L, while all other investigations were within normal limits. To rule out lumbar disc disease, the magnetic resonance imaging (MRI) scan study of lumbosacral spine with whole spine and hip joint screening was performed. The imaging revealed diffuse sclerosis with mild bony expansion, central lytic lesions with coarse trabecular pattern in the entire vertebrae, pelvic bones, and bilateral proximal femur—findings suggestive of Paget's disease in the late sclerotic stage (figure-1). At the L2-L3, L3-L4, and L4-L5 levels, there was a mild diffuse annular disc bulge with central and bilateral paracentral disc protrusions causing indentation of the anterior thecal sac, along with moderate bilateral lateral recess narrowing, compressing the traversing nerve roots (figure-2). The diagnosis of Paget's Disease of Bone (PDB) was confirmed based on the clinical presentation, radiographic and MRI findings, as well as supportive biochemical results.

TEST	RESULT	UNITS	REFERENCE RANGE
HBA1C	5.4	%	<6% is normal
Serum Folate	2.47	ng/mL	0.6 – 20
Serum Vitamin B12	262.3	pg/mL	188 - 908
THYROID PROFILE			
Free T3	4.76	Pmol/L	3.1 - 6.8
Free T4	1.01	ng/dL	0.92 – 1.67
TSH	1.50	uIU/mL	0.270 – 4.20
OSTEOPOROSIS PROFILE			
Serum Creatinine	0.87	mg/dL	0.5 – 1.2
Serum Calcium	8.15	mg/dL	8.1 – 10.4
Serum phosphorus	4.25	mg/dL	2.7 – 4.5
Serum albumin	4.32	gm/dL	3.5 – 5.0
Serum alkaline phosphatase	422.2	U/L	30- 120
Serum vitamin D	34.2	ng/mL	>30 is normal

Table – 1: Patient's laboratory investigation results

The patient was administered with a single dose of intravenous infusion of zoledronic acid 5 mg in 100 ml normal saline solution over a period of 15 minutes. A follow-up appointment was scheduled after three months to assess the treatment response and monitor serum alkaline phosphatase levels. If a reduction in alkaline phosphatase level is observed, yearly zoledronic acid infusions will be continued to the patient. If the alkaline phosphatase level rise, the zoledronic acid regimen will be initiated to every three months. For pain management, the patient was prescribed Tablet Celebrex 200 mg twice

daily (1-0-1) along with Tablet Pan 40 mg twice daily for 5 days. Additionally, calcium and vitamin D supplementation was advised to continue until the next visit to support bone health and strength.

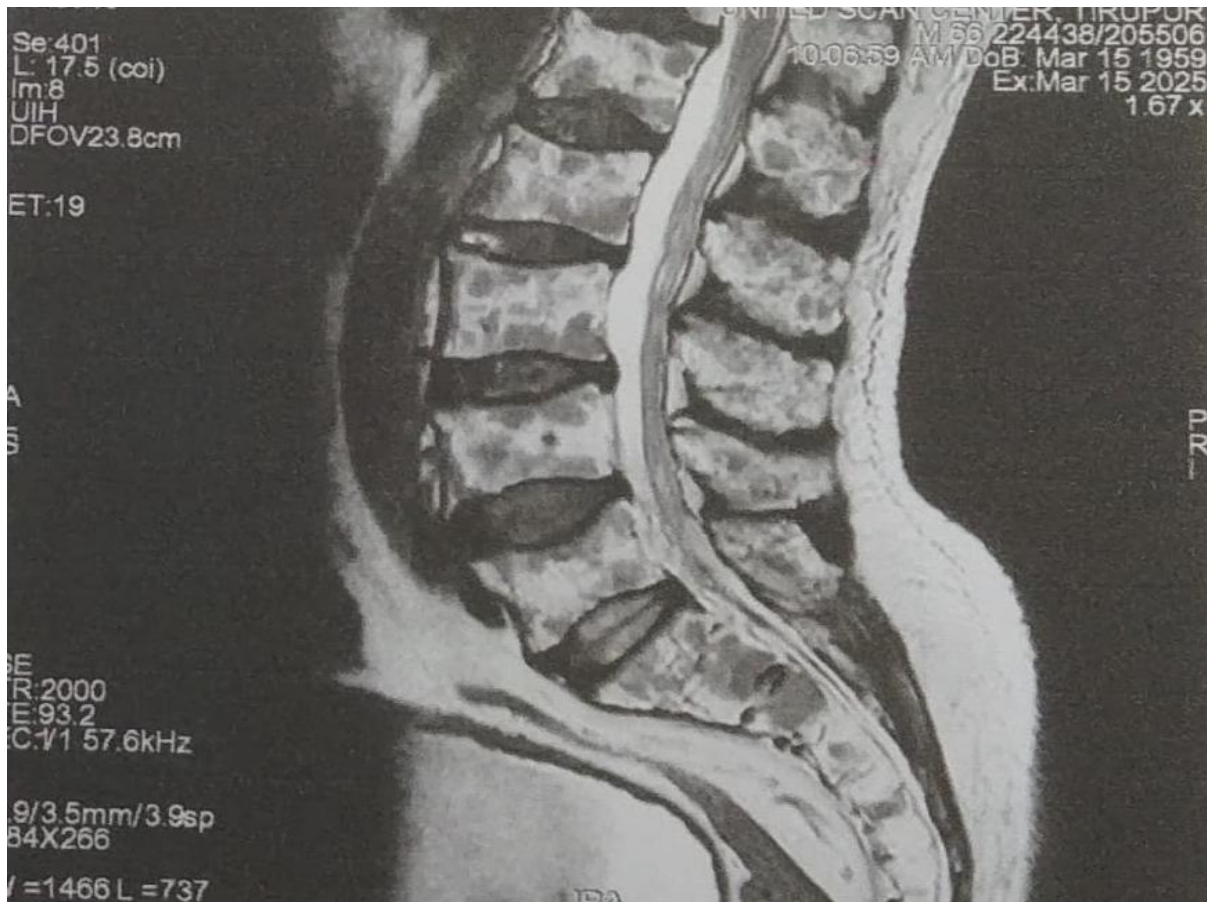


Figure-1: MRI spine showing diffuse sclerosis with mild bony expansion, central lytic lesions with coarse trabecular pattern in the entire vertebrae, pelvic bones, and bilateral proximal femur.

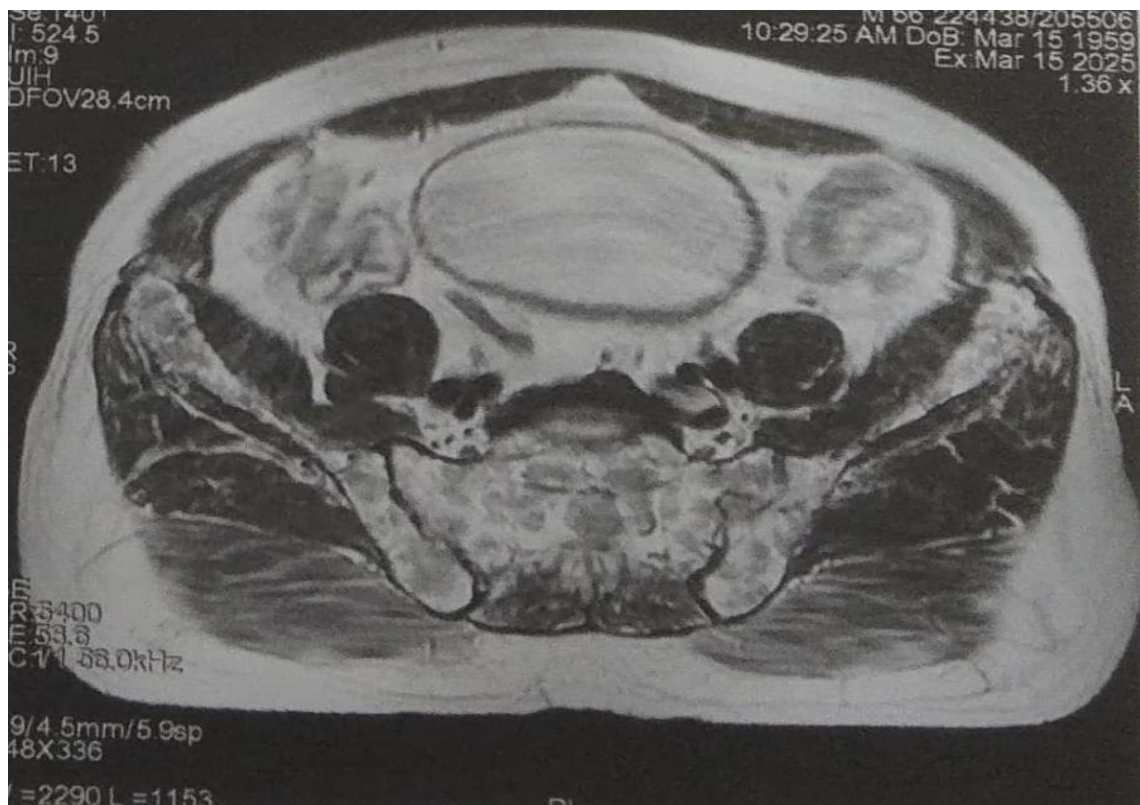


Figure-2: MRI spine showing diffuse annular disc bulge with central and bilateral paracentral disc protrusions causing indentation of the anterior thecal sac.

Discussion:

Paget's disease of bone is a chronic, progressive skeletal disorder characterized by focal regions of increased osteoclastic bone resorption, subsequently leading to a compensatory and disorganized increase in osteoblastic bone formation.⁽⁹⁾ The risk of developing Paget's disease of bone increases with advancing age, with its incidence approximately doubling with each subsequent decade after the age of 50.⁽¹⁰⁾

Multiple genes have been associated with Paget's disease, including pathogenic mutations in the *SQSTM1* gene, which result in the activation of RANKL-induced NF- κ B signaling pathways and subsequent upregulation of osteoclast activity.⁽¹¹⁾ Additional susceptibility-related genetic mutations are predominantly identified in genes that play a key role in osteoclast function.⁽¹²⁾ Paget's disease is characterized by lesions containing numerous large, hyperactive osteoclasts with heightened RANKL sensitivity and elevated cytokine secretion, such as interleukin-6. The disease progresses through distinct phases, beginning with an osteolytic phase marked by increased osteoclast activity and elevated bone turnover markers. This is followed by excessive osteoblastic activity, resulting in disorganized, woven bone with abnormal architecture and sclerotic features. Despite increased bone mass, the structural integrity is compromised due to poor microarchitecture. Pagetic lesions can affect both trabecular and cortical bone at various skeletal sites, though the reason for this distribution remains unclear.⁽¹³⁾

The diagnosis was ultimately confirmed through MRI imaging and laboratory findings. Serum alkaline phosphatase (ALP) is commonly used as both a diagnostic and prognostic marker for this disease. This hydrolase enzyme, linked to osteoblastic activity, functions as an orthophosphoric monoester phosphohydrolase and is primarily derived from the liver and bones. It plays a crucial role in promoting bone formation and mineralization.⁽¹⁴⁾ For patients with elevated bone turnover, biochemical follow-up is advised as a more reliable and objective indicator of relapse than symptom-based assessment.⁽¹⁵⁾ Imaging studies help determine the stage of disease severity and identify the specific parts of bone that are affected.

Bisphosphonates are the primary treatment for Paget's disease, acting as potent inhibitors of osteoclastic bone resorption and regarded as the first-line pharmacological agents. Zoledronic acid, in particular, has proven to be the most effective in promoting sustained biochemical remission and significantly reducing bone turnover.⁽¹⁾

Hypocalcemia and secondary hyperparathyroidism have been observed in patients with Paget's disease of bone (PDB) following treatment with bisphosphonates (BPs), particularly with the more potent intravenous zoledronic acid. It is essential to correct serum calcium levels and address any vitamin D deficiency prior to initiating BP therapy. Continuing calcium and vitamin D supplementation even after achieving normocalcemia may help shorten the duration of secondary hyperparathyroidism.⁽¹⁶⁾

Clinical pharmacist played a vital role in educating patient about Paget's disease, treatment regimens, and potential side effects. They also reinforced the importance of adherence to calcium and vitamin D supplementation and assisted with the administration of intravenous bisphosphonates in outpatient settings. Pharmacists were responsible for verifying and dispensing prescribed medications, educating patients on the proper administration of these drugs, and recommending adjustments or additional supplementation when necessary.

Conclusion:

This case report illustrates the diagnostic and management challenges of Paget's disease of bone in elderly patients with comorbidities. Diagnosis was confirmed through clinical assessment, elevated alkaline phosphatase levels, and MRI. Treatment with Intravenous zoledronic acid effectively reduced bone resorption, leading to biochemical remission and symptom relief. Potential complications, such as hypocalcemia and secondary hyperparathyroidism, were managed with supplementation and regular follow-up. A multidisciplinary team, including physicians, nurses, clinical pharmacists, and pharmacists was essential in providing education, treatment, and ongoing care, highlighting the value of collaborative management in improving patient outcomes and quality of life for patient with Paget's disease of bone.

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Declaration of the patient consent

The authors certify that all appropriate patient consent has been obtained.

Conflicts of interest

There are no conflicts of interest.

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