

A polyostotic Paget's Disease of bone: a case report of a 50s Chinese male with mini review

Hong Zhao

Zhonghsan hospital of Fudan University

Juan Yu

Zhonghsan hospital of Fudan University

Yuan Ji

Zhonghsan hospital of Fudan University

Zuoqin Yan

`yan.zuoqin@zs-hospital.sh.cn`

Zhonghsan hospital of Fudan University

Case Report

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Abstract

Paget's disease of bone (PDB) is a chronic skeletal disorder characterized by accelerated bone remodeling, commonly seen in European and American populations, but uncommon in Asia. We report a case of polyostotic PDB in a 50s Chinese male with a 5 years left hip pain. His alkaline phosphatase level was 184 U/L and γ -GT was 85 U/L, both increased slightly. A 3-phase bone scan showed heterogeneous nuclear uptake in the skull, thoracic and lumbar vertebra, bilateral pelvis and hips. The left hip pain was misdiagnosed as osteonecrosis for about one year. A bone biopsy was performed to confirm the diagnosis of PDB. The left hip pain resolved completely and ALP decreased to normal level one month after the treatment with IV zoledronate. A mini-review of PDB is also summarized in addition to the case presentation.

1. Introduction

Paget's disease of bone (PDB) is a chronic focal skeletal disorder characterized by accelerated bone remodeling. Its core pathophysiological process is initiated by abnormally active osteoclast-mediated bone resorption, followed by disorganized bone formation, ultimately resulting in structurally abnormal bone with compromised mechanical properties. Clinically, PDB may present in osteolytic, sclerotic, or mixed phases [1]. The disease exhibits significant geographical variation, being common in Europe, the United States, Australia, and other regions [2], but rarely reported in Asia, particularly in China. This low reported prevalence may reflect a genuinely low incidence, but could also be attributable to limited clinical awareness and under-screening. With population aging and the increasing availability of imaging modalities, the actual disease burden in China remains to be clarified. Herein, we report a case of polyostotic PDB in a middle-aged Chinese male and provide a concise review of the epidemiology, pathogenesis, clinical manifestations, imaging, laboratory and pathological features, diagnostic strategy, treatment, and follow-up, with the aim of improving recognition of this rare disease and offering a reference for the identification and management of similar cases.

2. Case Presentation

2.1 Medical History

A 53 male patient was admitted with a 5-year history of pain and discomfort in the left hip region. The pain, which had no obvious precipitating cause, worsened with physical activity and gradually interfered with daily activities over time. His past medical history was unremarkable, with no significant family history or other relevant medical conditions. According to the X ray and MRI, the patient was misdiagnosed and treated as the osteonecrosis of the left femoral head for about one year in other hospitals, but the left hip pain still persisted when the NSAIDs was stopped.

2.2 Laboratory Findings

Laboratory tests revealed that the red blood cell, Hb, ESR, metabolic panels for renal, lipid, and thyroid function were normal. Hepatic function testing was normal except ALP and γ -GT, which were slightly elevated to 184 U/L (N 45–125 U/L) and 85 U/L (N 10–60 U/L), respectively. Parathyroid hormone, vitamin D, calcium and phosphorus levels were normal.

2.3 Imaging Studies

Radiographs showed increased bone density, coarse trabeculation, cortical thickening, and osseous remodeling of the pelvis, bilateral proximal femora, and multiple vertebrae, with more prominent changes in the left femoral head and proximal femur (Fig. 1, A–C). Coronal and axial MRI demonstrated heterogeneous abnormal marrow signal in the left femoral head and proximal femora (Fig. 1, D–E). Collectively, the combination of multifocal osteosclerosis mixed with osteolytic lesion, cortical thickening, coarse trabeculation, and abnormal bone remodeling strongly supported the diagnosis of multifocal PDB. The left hip pain was initially misdiagnosed as osteonecrosis due to making the diagnosis merely according to the X ray and MRI changes of the left femoral head.. Further whole-body planar bone scintigraphy combined with local SPECT/CT was performed (Fig. 2). Fusion images reveal that the multi-focal osteosclerotic lesions have abnormal high radiotracer uptake in the skull, right sixth rib, T4, T7, L1 and L5 vertebra, bilateral acetabula and ischia, femoral heads, and the left proximal femur, indicating multifocal skeletal metabolic abnormalities. These findings were suspected of bone metastasis.

2.4 Pathological Examination

To further clarify the final diagnosis and exclude the bone metastasis, a biopsy of the L5 vertebral body was performed on June 12, 2025. Microscopic examination showed markedly thickened and disorganized trabeculae with numerous irregular cement lines, forming a classic "mosaic pattern" of lamellar bone. Distinct osteoid seams were observed around the trabeculae, and numerous multinucleated giant osteoclasts were seen on the bone surfaces, some eroding into trabeculae to form resorption lacunae. Some marrow spaces were replaced by fibrous connective tissue, interspersed with occasional reactive fibroblasts, small blood vessels, and chronic inflammatory cell infiltration (Fig. 3).

These histological changes were characteristics of Paget's disease of bone, indicating an active mixed-phase lesion. In conjunction with the clinical presentation, laboratory findings, and imaging results, a final diagnosis of polyostotic Paget's disease of bone was established.

2.5 Treatment and Follow-up

After diagnosis, the patient received zoledronic acid for anti-resorptive therapy. Following treatment, his left hip pain improved markedly, and repeated serum ALP decreased at one month and returned to normal level half year after the treatment, indicating effective suppression of bone metabolic activity and favorable clinical responses.

3. Discussion

3.1 Epidemiology and Risk Factors of PDB

PDB shows marked geographical variation, with higher prevalence reported in the United Kingdom, Europe, Australia, New Zealand, and North America, while cases in Asia, particularly China, remain relatively rare [2]. This disparity may reflect genetic and environmental differences, as well as underdiagnosis due to nonspecific symptoms and limited disease awareness. PDB mainly affects middle-aged and older adults, with increasing prevalence with age and a slight male predominance [3]. Our middle-aged male patient was relatively young and presented with multifocal skeletal involvement and active pathological changes. Genetic susceptibility, particularly involving SQSTM1 and osteoclast-regulatory genes, is important, while proposed environmental factors such as measles virus remain inconclusive [4, 5].

3.2 Pathogenesis

The hallmark of PDB is an accelerated and disorganized bone remodeling, primarily driven by excessive osteoclast activity [6]. Abnormalities in the SQSTM1/p62 pathway, together with dysregulation of the RANK/RANKL and NF- κ B signaling pathways, may promote osteoclast differentiation and enhance bone resorption [7–11], followed by compensatory osteoblast activation, but this markedly accelerated bone turnover is poorly coordinated [12]. Because newly formed bone lacks normal structural organization, irregular woven and lamellar bone accumulates, producing the characteristic mosaic pattern. Although affected bones may become enlarged and sclerotic, their mechanical integrity can be compromised by this disorganized architecture. These pathological changes may clinically manifest as bone pain, deformity, pathological fracture, secondary osteoarthritis, and neurological complications.

3.3 Clinical Manifestations and Complications

The clinical presentation of PDB is heterogeneous, ranging from asymptomatic disease to bone pain, deformity, and skeletal complications [13]. Commonly affected sites include the pelvis, spine, skull, and long bones, particularly the hip, the hip involvement often is associated with secondary osteoarthritis [14, 15]. Bone pain is typically deep and persistent and may worsen with weight-bearing. Our patient had a 5-year history of left hip pain with progressive degeneration, while initial radiographic and MRI findings suggested femoral head pathology, which is easily misdiagnosed as osteonecrosis, highlighting the diagnostic challenge. Skeletal expansion and deformity can alter biomechanics, increasing the risk of secondary osteoarthritis and pathological or insufficiency fractures [16, 17]. Skull and spinal involvement may cause hearing loss, nerve compression, or spinal stenosis [18]. Multifocal osteolytic or sclerotic lesions may mimic metastatic bone disease, necessitating careful differential diagnosis. Malignant transformation to sarcoma is rare but should be suspected with rapidly progressive pain or destructive lesions with soft-tissue extension [19].

3.4 Imaging Features

Imaging is central to the diagnosis and assessment of PDB [20]. Plain radiography is the first-line examination, demonstrating stage-dependent changes from osteolysis and cortical lucency to cortical

thickening, coarsened trabeculae, bone expansion, and osteosclerosis. In our patient, radiographs revealed multifocal mixed osteolytic and sclerotic lesions involving the left femoral head and proximal femur, pelvis, and vertebrae. Bone scintigraphy is highly sensitive for detecting metabolically active lesions and determining disease extent, revealing abnormal uptake in the spine, pelvis, and bilateral femoral heads in our case [21]. SPECT/CT further combines metabolic and anatomical information to accurately localize active lesions and characterize associated structural abnormalities [22]. CT is useful for detailed assessment of cortical and trabecular architecture, whereas MRI is mainly reserved for suspected neurological, marrow, or soft-tissue complications [23]. Multimodal imaging is essential for confirming multifocal PDB and differentiating it from metastatic bone disease.

3.5 Biochemical Evaluation

Serum total ALP is the most widely used biochemical marker for assessing disease activity in PDB [24]. Increased osteoblast activity and accelerated bone turnover typically result in elevated ALP, which is also useful for monitoring treatment response. Because ALP may be elevated by hepatobiliary disorders, liver-associated markers such as GGT should be considered when interpreting results. In our patient, ALP was 184 U/L, and its interpretation together with GGT and imaging findings supported active bone remodeling.

Bone-specific ALP (BALP) provides a more specific assessment of bone-derived osteoblast activity and may be particularly useful when total ALP is confounded by hepatic disease [25]. PINP, CTX, and NTX provide complementary information on bone formation and resorption, respectively, but currently serve mainly as adjunctive markers rather than replacements for ALP [26]. Serum calcium and phosphorus are generally normal in PDB and are primarily useful for evaluating overall mineral metabolism and excluding other metabolic bone disorders [27].

3.6. Histopathological Features (Fig. 3)

Histopathological examination provides important evidence for confirming PDB, particularly in atypical or diagnostically challenging cases. The most characteristic finding is the mosaic bone architecture, resulting from repeated cycles of accelerated bone remodeling and disorganized deposition of newly formed bone. Numerous irregularly oriented cement lines separating bone of different generations produce the characteristic mosaic pattern, reflecting both increased bone turnover and disrupted tissue organization. Active lesions typically show numerous enlarged multinucleated osteoclasts with prominent resorption lacunae (Howship's lacunae), together with increased osteoblastic rimming and formation of woven bone, demonstrating the abnormal coupling of bone resorption and formation. Fibrovascular replacement of marrow spaces, characterized by reactive fibroblasts and increased small vessels, may also be observed in metabolically active lesions. PDB is traditionally classified into osteolytic, mixed, and sclerotic phases according to the predominant remodeling pattern. In our patient, the coexistence of abundant osteoclasts, prominent osteoblastic activity, and a typical mosaic pattern was consistent with active mixed-phase PDB.

3.7 Diagnostic Strategy

The diagnosis of PDB requires integration of clinical, biochemical, and imaging findings. Serum ALP and plain radiography are appropriate initial investigations in patients with chronic bone pain or incidental skeletal abnormalities. Bone scintigraphy with SPECT/CT can further assess disease activity and define the extent of skeletal involvement. CT or MRI may be indicated for atypical or complex lesions, particularly when neurological or soft-tissue complications are suspected. Bone biopsy is not routinely required, but is valuable when imaging findings are inconclusive or metastatic disease or malignancy must be excluded. A characteristic mosaic pattern with multinucleated osteoclasts and increased osteoblastic activity provides strong pathological evidence of PDB.

3.8 Current Treatment Strategies

Treatment of PDB is indicated mainly for symptomatic or metabolically active disease, particularly involving weight-bearing bones, the skull, or spine, or associated with deformity, fracture, neurological complications, or planned orthopedic surgery. The goals are to suppress excessive bone turnover, relieve symptoms, and prevent skeletal complications.

Bisphosphonates are the cornerstone of pharmacological therapy [28]. Zoledronic acid is highly potent and provides sustained suppression of bone turnover, reducing ALP levels and bone pain [29]. In our patient, zoledronic acid substantially improved left hip pain and reduced ALP at one month follow-up, indicating effective disease control. Alendronate, risedronate, and pamidronate are alternative options, although zoledronic acid generally provides a more potent and durable response [30]. Calcitonin is less effective and is no longer considered first-line therapy [31].

Surgery does not correct the underlying metabolic disorder but may be required for structural complications, including pathological fractures, severe secondary osteoarthritis, deformity, or neurological compression. Thus, management combines anti-resorptive therapy with individualized orthopedic intervention when indicated.

3.9 Follow-up and Prognosis

PDB is a chronic skeletal disorder; although treatment may achieve biochemical remission, established bone deformities and structural abnormalities are often irreversible. Long-term follow-up is therefore essential.

Serum ALP is the most practical marker for monitoring disease activity and should be assessed before and periodically after treatment. In our patient, ALP decreased from 184 U/L following zoledronic acid therapy, accompanied by improvement in bone pain. BALP or other bone turnover markers may be considered when total ALP is confounded by hepatobiliary disease.

Clinical follow-up should assess recurrent bone pain, functional and weight-bearing capacity, fractures, joint dysfunction, secondary osteoarthritis, neurological symptoms, and new atypical pain. Importantly, biochemical remission does not imply reversal of established skeletal deformity or joint degeneration.

Routine repeated imaging is unnecessary in clinically stable patients with sustained biochemical improvement. Radiography, CT, SPECT/CT, or MRI should be guided by new or progressive pain, fracture, neurological symptoms, rising ALP, or suspected structural complications. Because PDB may reactivate after treatment, continued biochemical and clinical surveillance is recommended to maintain disease control and prevent complications.

3.10 Future Perspectives

Future research on PDB should focus on genetic mechanisms, therapeutic targets, biomarkers, and epidemiology in Asian populations. Further investigation of SQSTM1/p62 and other susceptibility genes may clarify inter-population differences in disease prevalence and phenotype. Osteoclast-related pathways, including RANK/RANKL/NF- κ B, represent potential therapeutic targets, although bisphosphonates, particularly zoledronic acid, remain the clinical standard. More sensitive and specific biomarkers are needed to improve assessment of disease activity and treatment response. Importantly, PDB remains underrecognized in China and other Asian populations. Multicenter cohorts, standardized imaging databases, and genetic studies are needed to define its true prevalence, clinical spectrum, and population-specific risk factors.

4. Conclusion

Paget's disease of bone (PDB) is a chronic skeletal disorder characterized by accelerated and disorganized bone remodeling. In Chinese patients, recognition requires integration of clinical, biochemical, imaging, and pathological findings. Zoledronic acid effectively controls disease activity. This case highlights the importance of considering multifocal PDB in atypical skeletal lesions.

Declarations

Acknowledgements

Not applicable.

Clinical trial number

Not applicable.

Authors' contributions

The study was conceived and designed by Zuoqin Yan and Hong Zhao. The manuscript was drafted by Hong Zhao, and Zuoqin Yan critically revised the manuscript. Data collection was conducted by Hong Zhao, Juan Yu, and Yuan Ji. Zuoqin Yan will be responsible for correspondence during the peer-review, publication, and post-publication processes.

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Data availability

The data utilized and/or analyzed in this study can be obtained from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The patient’s informed consent has been obtained, and our hospital’s ethics committee has confirmed it.

Consent for publication

The patient has provided written informed consent, including consent for the use of personal information, clinical data, and imaging images included in this study.

Competing interests

The authors declare no competing interests.

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Figures

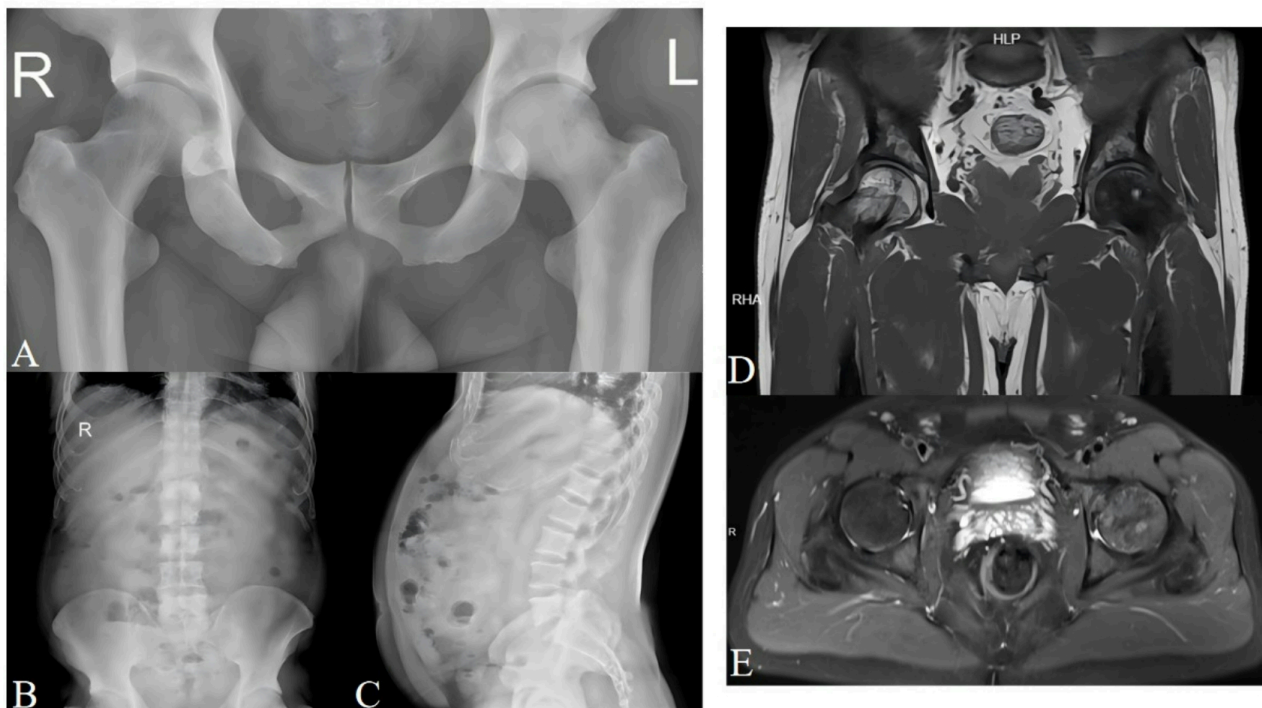


Figure 1

Multimodal imaging findings of multifocal Paget's disease of bone. (A) Anteroposterior radiograph of the pelvis showing increased bone density, coarse trabeculation, cortical thickening, and osseous remodeling involving the bilateral pelvis and left proximal femora (B, C) Anteroposterior and lateral radiographs of the spine demonstrating increased vertebral density, coarse trabeculae, cortical thickening, and multilevel osseous remodeling in L5,L1. (D, E) Coronal and axial MRI of the hips showing heterogeneous abnormal marrow signal mainly involving the left femoral head and proximal femora, corresponding to the structural abnormalities seen on radiographs

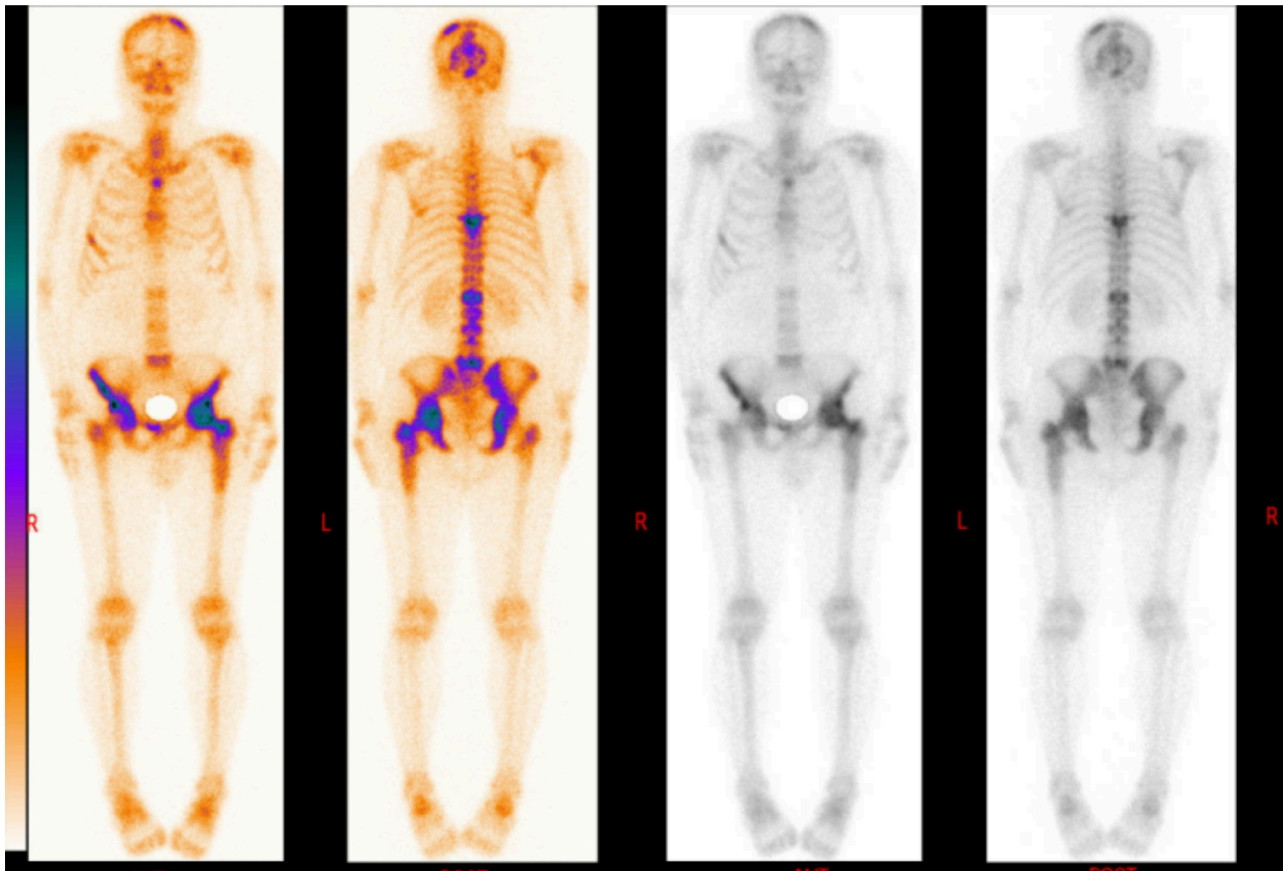


Figure 2

SPECT/CT fusion images demonstrate multiple osteoblastic lesions involving the lumbar spine, bilateral iliac bones, bilateral femoral heads, and pelvis, with heterogeneous radiotracer uptake.

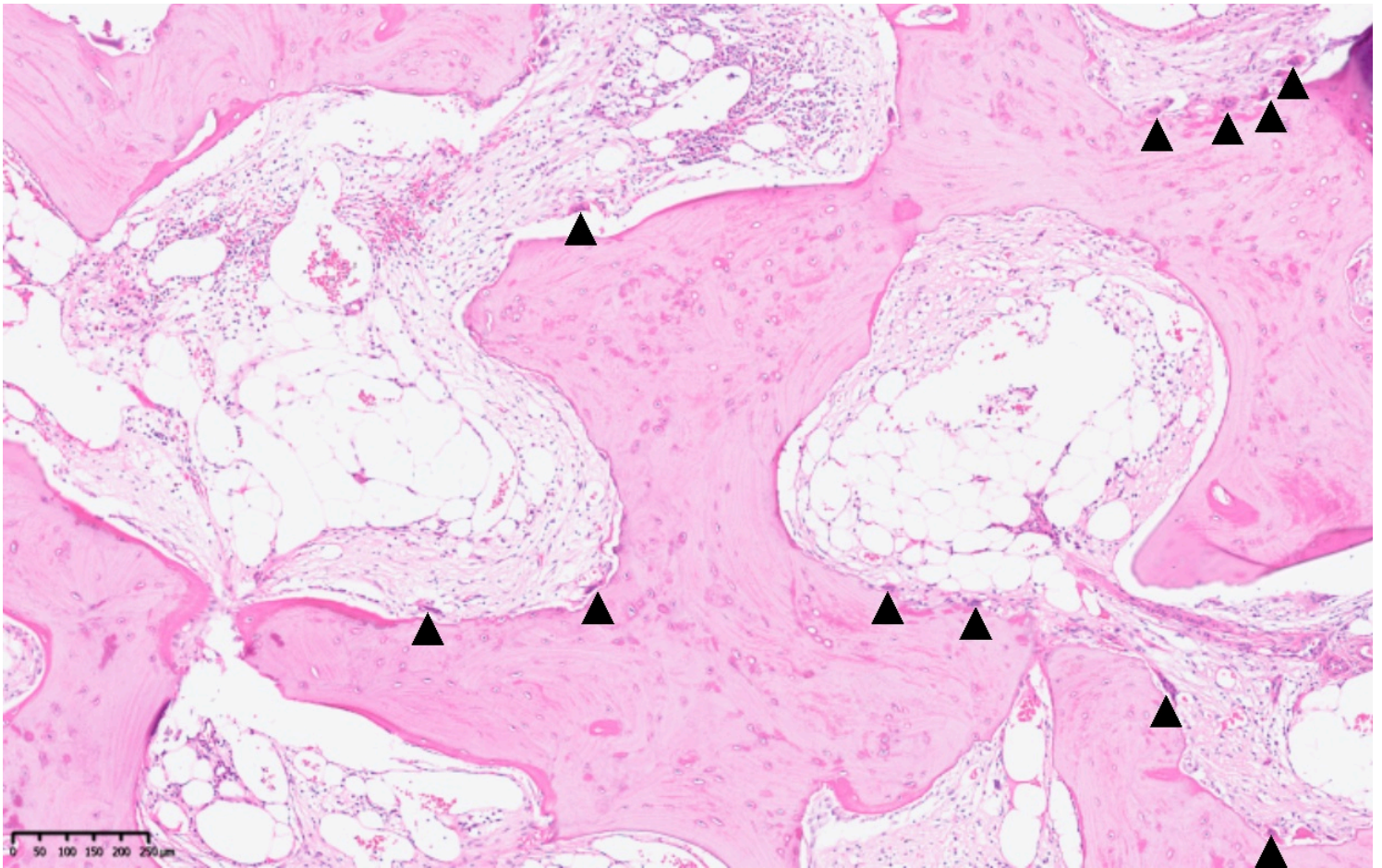


Figure 3

Microscopic examination of the bone biopsy specimen revealed markedly thickened and structurally disorganized trabecular bone with irregular cement lines, consistent with a mosaic pattern of lamellar bone. Numerous reversal lines were present, and the bony trabeculae were surrounded by prominent osteoid seams.

Increased numbers of large, multinucleated osteoclasts (arrow heads) were observed at the bone surfaces, often deeply resorbing into the trabeculae. Osteoblasts were variably increased and lined the newly formed bone. The marrow spaces were partially replaced by fibrous connective tissue, with scattered foci of reactive fibroblasts, small blood vessels, and chronic inflammatory cells.

These findings are characteristic of Paget's disease of bone , reflecting the active mixed lytic and sclerotic phase.