Imaging of Paget Disease of Bone and Its Musculoskeletal Complications: Review

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Objective

Paget disease is the second most common bone disease after osteoporosis that affects elderly persons in the United States. We revisit Paget disease of bone and present the gamut of imaging findings associated with this skeletal disorder, both uncomplicated and complicated.

Conclusion

Paget disease of bone shows a plethora of imaging patterns and variable appearances that are related to the pathologic stage of the disease. Because patients with Paget disease may develop various musculoskeletal complications, recognition of the key imaging features of the condition may allow prospective diagnosis of the disease and its associated musculoskeletal complications and can preclude biopsy.

Introduction

Paget disease (osteitis deformans) is a chronic skeletal disorder characterized by abnormal and excessive remodeling of bone. The disease was named after Sir James Paget who described the condition in 1877 [1] in a detailed essay recognized in the medical literature as “a lesson in accurate and lucid writing” [2]. Paget disease is estimated to affect approximately 3–4% of individuals older than 40 years [2–4] and is the second most common bone disease after osteoporosis that affects the growing population of older persons in the United States [5].

Abnormal osseous resorption and apposition in Paget disease produce variable clinical and imaging manifestations. Although the disease may be asymptomatic, it can be painful or deforming and associated with various and debilitating musculoskeletal complications [3, 6–8]. Radiologists play a central role in the imaging diagnosis of the process and its multifaceted manifestations. Radiography remains the most inexpensive method to evaluate patients with Paget disease of bone. CT, bone scintigraphy, and MRI have complementary roles in achieving the correct diagnosis of Paget disease and its complications.

This article reviews the demographics, basic pathophysiology, natural history, and clinical presentation of Paget disease; describes the imaging appearances of the condition and of its complications; and illustrates many cases of Paget disease of bone, both uncomplicated and complicated.

Demographic Profile

Descriptive epidemiologic studies have shown that the prevalence (4.6%) of Paget disease is considerably higher in the United Kingdom than in other countries. The disease is also common in Australia, New Zealand, Western Europe, and the United States, although it is rare in Scandinavia, Asia, the Middle East, and Africa [9, 10].

Studies, however, indicate a substantial reduction in the prevalence of Paget disease around the world of approximately 50% [9, 11–15]. For example, in Britain the overall prevalence rate documented in 1994 was 2%, indicating a significant decline in prevalence of 40% over a 20-year period [12]. Another large study in England and Wales estimated that the prevalence of the disorder was 0.3% in subjects over 55 years old [13]. Similarly, data indicate a remarkable 50% decline in the prevalence of the disease in New Zealand over the past two decades [14]. Also, a decline in the prevalence of Paget disease has been realized in some European countries over a 20-year period, reaching an overall rate of 0.3% [15]. Epidemiologic studies show that there is a slight male predilection in the condition in a proportion of 3:2, with the frequency of Paget disease increasing remarkably in both sexes with advancing age [9, 11–13, 16, 17].

Cause and Pathogenesis

The cause of Paget disease remains largely unknown even more than one century after its original description. The discovery of characteristic intranuclear and intracytoplasmic inclusion bodies resembling nucleocapsids of the paramyxovirus family of RNA viruses in the osteoclasts of pagetic bone triggered the theory of a slow virus infection [11, 18–20]. Indeed, nuclear inclusions are considered a striking feature of pagetic osteoclasts because they are not present in other bone marrow cells and are consistently found in patients with Paget disease [20]. In addition, osteoclasts in pagetic lesions are increased in both number and size and are
grossly abnormal, containing multiple nuclei [18, 20]. Both the nuclear inclusions similar to those of paramyxoviruses and giant osteoclasts are found in viral infections, so a viral cause of the disorder has been proposed. Furthermore, infection by paramyxoviruses has been shown to increase the release of interleukin 6, an osteotropic factor that induces osteoclast formation [18, 20]. Researchers have found osteoclast overactivity within the marrow microenvironment in abnormal pagetic bone compared with normal bone [10, 18]. Measles virus antigens, respiratory syncytial virus antigens, and the canine distemper virus antigen also have been detected in pagetic osteoclasts [18–20]. Other data refute the viral hypothesis [16, 21]; hence, included among other purported etiologic conditions of Paget disease are vascular diseases, genetic diseases, an immunologic or metabolic disorder, or a true neoplastic process [3, 10, 11, 18, 20, 22, 23].

Natural History and Skeletal Distribution

The primary event in Paget disease is intense focal resorption followed by disorderly bone formation that results in overall abnormal bone remodeling [2, 3]. Paget disease generally is considered a relentlessly progressive disorder that evolves through various stages or phases of activity followed by an inactive or quiescent stage. There is notable variability in the rate of disease progression from one patient to another or in a single individual [2]. Three major phases are recognized: the lytic phase (incipient active), in which osteoclastic resorption predominates; the mixed phase (active), in which there is both osteoclastic and osteoblastic hyperplasia with predominant osteoblastic activity (Fig. 1); and finally, the blastic phase (late inactive), in which osteoblastic activity gradually declines [7]. These three phases of the pagetic process—coupling abnormal osseous resorption and apposition within the periosteal and endosteal cortical envelopes—account for the variable radiographic appearances of the disease. As a result of this anarchic bone behavior that produces disorganized new bone (mosaic), an increased or decreased external bone contour and a narrowed or enlarged marrow cavity are seen, as opposed to bone expansion that was long regarded as a universal feature of the disease [2].

The anatomic distribution of Paget disease usually is asymmetric and most commonly affects the lumbar spine (30–75%), pelvis (30–75% of cases), sacrum (30–60%), femur (25–35%), and cranium (25–65%) [24]. Less frequently, however, cervical and thoracic involvement can be observed [3]. There is a preference for the lower extremities and a tendency for right-sided alterations [2, 3]. The shoulder girdle, particularly the proximal humerus (31%) and scapula (24%), are less commonly affected sites [25]. Pagetic involvement of the ribs, fibula, and small bones in the hands and feet is infrequent [3]. Polyostotic disease (65–90%) is more frequent than monostotic disease [3, 17]. In some patients, however, the disease is initially or totally monostotic, a pattern that is evident in 10–35% of cases [3]. Monostotic Paget disease appears to predominate in the axial skeleton.
although every bone in the skeleton can be the sole site of involvement [2, 3, 7, 8].

**Clinical Presentation**

In Paget disease, almost one fifth of persons with skeletal involvement detectable on radiographs are entirely asymptomatic, so an osseous abnormality is diagnosed first as an incidental finding on radiographs obtained for unrelated purposes [3]. However, the disease is a painful and deforming process manifested occasionally with severe symptoms and signs that may include various skeletal, neuromuscular, and cardiovascular complications [16, 17, 26]. Clinical symptoms vary with the distribution of the disease. Bowing deformities of the long bones of the extremities—usually lateral curvature of the femur and anterior curvature of the tibia, which is perceived as progressing prominence of the shins—are common. Lateral bowing of the humerus also is common.

When present, pathologic fracture, reflecting the structural weakness of the altered bone, with resulting pain and angulation or reduced mobility of joints and secondary osteoarthritis can be crippling [25, 27, 28]. Involvement of the facial bones can produce the characteristic facial deformity known as “leontiasis ossea,” and involvement of the jawbones—seen in almost all cases of Paget disease involving the skull—can cause problems of the teeth related to hypercementosis of the root apices [7, 29–31]. When the skull is involved, increasing size of the head may be noted as a constant change in hat size and hearing loss and entrapment of cranial nerves in their foramina can be present [26, 31, 32]. Involvement of the base of the skull, in particular, may cause platybasia, basilar invagination, and hydrocephalus, whereas vertebral involvement may be associated with compression fractures, nerve root compression, muscle weakness, spinal stenosis, cauda equina syndrome, and kyphosis [8, 19, 33–35]. Other manifestations of the disease include various cardiovascular, endocrine, genitourinary, and psychologic complications [26].

Biochemical studies of Paget disease have revealed that affected patients have a characteristic elevation of serum alkaline phosphatase level secondary to intense osteoblastic activity. Alkaline phosphatase level is considered an important parameter, reflecting overall disease activity, in the assessment and follow-up of patients with Paget disease [20, 23, 36]. The serum osteocalcin level may be elevated as well.
but is a less reliable index of disease activity [36]. Other useful indexes of bone resorption are the urinary excretion of total hydroxyproline and, more recently, of pyridinium cross links [18, 20, 36]. Serum calcium level is usually normal unless fracture or secondary hyperparathyroidism develops because of intense bone turnover [16].

**Imaging Findings**

Imaging is considered to be essential in establishing the diagnosis of Paget disease, evaluating the type and extent of complications, and monitoring the effects of therapy.

The major techniques available for imaging patients with Paget disease are radiography, bone scintigraphy, CT, and MRI.

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**Fig. 6**—Lateral skull radiograph of 64-year-old woman with Paget disease reveals several areas of focal sclerosis (arrowheads) that produce cotton-wool appearance. There is diffuse calvarial thickening.

**Fig. 7**—Anterior bone scan of 67-year-old woman with Paget disease (same patient as Fig. 3) shows intense, increased radionuclide uptake in right hemipelvis.

**Imaging of Paget Disease**

**Fig. 8**—Paget disease of spine in different patients.

**A**, Axial CT scan of T11 vertebra in 57-year-old man shows mixed lytic and sclerotic changes involving vertebral body and arch.

**B**, Axial CT scan of 60-year-old man shows predominant osseous sclerosis of L5 vertebral body, ivory vertebra, that is extending into posterior osseous elements.
Radiography

Radiography is traditionally considered the initial imaging examination for diagnosing Paget disease of bone. The lytic, or incipient active, phase of the disease is characterized by intense osteoclastic activity that is exhibited on radiographs as osteolysis. In the long bones, osteolysis is manifested as a characteristic metaphyseal to diaphyseal wedge-shaped area of radiolucency that assumes the configuration of a flame or blade of grass [7] (Fig. 2). This advancing wedge of osteolysis, which begins almost invariably in the subchondral bone of the epiphysis and extends peripherally into the metaphysis and diaphysis, spreads about 1 cm per year and shows no marginal sclerosis [7]. Subperiosteal cortical thickening and accentuation and coarsening of the trabecular pattern with enlargement of bone contours can be seen in the later stages of the lytic phase. Conversely, on occasion within the area of radiolucency, trabeculae can be obliterated and a hazy ground-glass or “washed-out” pattern is observed. Other skeletal sites including the pelvis, the spine, and the small bones of the hands and feet can be offended as well [3, 4, 7, 8, 37, 38]. In the skull, advancing osteolysis is noted as large areas of radiolucency usually in the frontal and occipital bones and is designated “osteoporosis circumscripta” [3, 7, 8] (Fig. 3). Skull lesions are most prominent in the inner calvarial tables and usually cross the suture lines [7].

Fig. 3—Images obtained of 73-year-old woman with Paget disease at femur. A, Frontal radiograph of distal femur reveals coarsened trabeculae, cross-hatched pattern (arrowheads), and cortical thickening (arrow). B, Axial T1-weighted MR image (TR/TE, 450/16) shows thickened trabeculae (arrowheads) within maintained yellow marrow (asterisk). Cortical thickening (arrows) is appreciated. Preservation of medullary fat in femur excludes superimposed sarcoma. C, Axial T2-weighted MR image (3700/80) shows trabecular thickening (arrowheads) with pagetic bone marrow (asterisk) displaying high signal intensity similar to that of fat. Fat-saturated MR image would have allowed better characterization of process.
Imaging of Paget Disease

The mixed (middle) phase of Paget disease bears characteristics of both the lytic (initial) and the blastic (late) phases. Most patients present in the mixed phase when decreased osteoclastic activity and increased osteoblastic activity are encountered [7]. The mixed phase is notable for all four cardinal features of the disease comprising advancing osteolysis, coarsening and thickening of bone trabeculae along the lines of stress, cortical thickening, and osseous widening [7]. Changes in the long bones are usually pathognomonic and are manifested both as advancing osteolysis that extends toward the diaphysis and as focal bone sclerosis in the epiphysis and metaphysis. Involvement of the pelvis manifests with sclerosis of the iliopectineal and ischiopubic lines and enlargement of the pubic rami and ischium [3, 8] (Fig. 4). Paraacetabular changes can produce acetabular protrusion [3, 8]. In the spine, the mixed phase of Paget disease manifests with cortical thickening along all four margins of the vertebral body cortices, producing the characteristic picture-frame appearance [3, 8, 24, 39, 40] (Fig. 5). Additional changes may include coarsening of the vertical trabeculae or a meshed disorganized trabecular (mosaic) pattern. Flattening or squaring of the anterior margin of the affected vertebral body can be seen. Although involvement of short tubular bones of the hands and feet is unusual, accentuated trabecular pattern and bone enlargement may be visualized in the mixed phase of the disease. In the skull, abnormal bone deposition assumes a characteristic cotton-wool appearance with globular to fluffy foci of variable density [3, 7, 8].

The blastic, or late inactive, phase of Paget disease is characterized by diminished osteoblastic activity and manifests as osteosclerosis. In the long bones and pelvis, coarsening of the trabeculae and cortical thickening, with marked widening and enlargement of bones, are seen. Because of excessive deposition of abnormal bone, the bones are weak and transverse fatigue fractures, which are referred to as “banana fractures,” may occur [7, 8]. Multiple fractures and abnormal bone repair are associated with the development of progressive bowing deformities. In the skull, marked thickening of the inner calvarial table produces marked enlargement of the diploic space known as a “tam-o’-shanter” skull (a tam-o’-shanter is a Scottish cap that is
broad and flattened) [8]. This irregular bone apposition on the inner margins of the cranial vault may produce areas of nerve and brain compression causing neurologic symptoms [31, 35, 41, 42]. Focal osteosclerosis in the skull manifests as a cotton-wool appearance on radiographs (Fig. 6). In the spine, changes of osteosclerosis create an ivory vertebra and enlarged vertebral body with or without sclerosis and enlargement of the posterior elements [8, 24, 39].

Bone Scintigraphy

Although radiography usually is sufficient for enabling the diagnosis of Paget disease, it may underestimate the extent and activity of the disease because conversion of normal bone to pagetic bone may be slow and may manifest with subtle changes [2]. Bone scintigraphy is regarded as a sensitive examination for the detection of the increased blood flow and osteoblastic activity that accompany the os-
meclastic activity seen in Paget disease [16]. Bone scans display markedly increased radionuclide uptake in the entire region of abnormal bone in all three phases of Paget disease and particularly in active disease [43–45] (Fig. 7). In osteoporosis circumscripta, however, intense radionuclide uptake is confined to the margins of the lesion [44].

A disparity in diagnostic sensitivity for Paget disease of bone between bone scintigraphy and radiography, especially noticeable in sites where there are overlapping structures, has been reported, however [7, 46]. Furthermore, nonspecific tracer uptake has rendered scintigraphy a useful technique in revealing the presence and distribution of polyostotic disease rather than in providing a specific diagnosis or delineating the extent of a pagetic lesion.

CT

CT facilitates the diagnosis of pagetic abnormalities in bone like those detected by radiography. Because CT images generally provide superior cortical and trabecular detail in a cross-sectional display, CT conspicuously exhibits the classic findings of Paget disease that include osteolysis, trabecular coarsening, cortical thickening, and osseous expansion [32, 47] (Fig. 8). In addition, CT commonly is helpful in the workup of suspected complications including fractures, spinal stenosis, and secondary neoplasms [25, 33].

MRI

The MRI signal intensity characteristics in Paget disease are variable, reflecting the natural course of the disease process in different phases. Because Paget disease can be confined to one bone or to a portion of one bone, diagnosis may be challenging. Three major patterns of involvement are recognized [4, 24]. The most common pattern is dominant signal intensity in pagetic bone similar to that of fat; this pattern of involvement presumably corresponds to long-standing disease and is noted in most patients [43, 48] (Fig. 9). The second most common pattern probably corresponds to the early mixed active phase when involved bone shows heterogeneous, relatively low T1 signal intensity and high T2 signal intensity [49] (Fig. 10). This pattern of signal intensity alteration, also referred to as the “speckled” appearance, probably corresponds to the presence of granulation tissue, hypervascularity, and edema seen in active disease when abnormal, disorderly bone mineralization is present [4, 32]. The least common pattern of signal intensity changes is seen in the late blastic inactive phase when pagetic bone shows low signal intensity on both T1- and T2-weighted images, suggesting the presence of compact bone or fibrous tissue (Fig. 11). The preservation of fatty marrow signal in pagetic bone generally excludes diagnosis of superimposed sarcoma [48]. In previous studies [4, 41, 43, 50], investigators have reported increased enhancement in pagetic bone after the IV administration of contrast material, which is indicative of hyperemia in active disease or a complication by secondary disease processes.

Complications of Paget Disease

Common complications of Paget disease include osseous deformities, fractures, osteoarthrosis, basilar impression, spinal stenosis, and neurologic abnormalities [33]. Other less commonly encountered complications are bone tumor, soft-tissue mass, osteomyelitis, extramedullary hematopoiesis, rheumatoid arthritis and its variants, and crystal deposition disease [2, 8, 26, 28, 51].

Arthropathy

Osteoarthrosis is a common complication in Paget disease. This complication results from altered biomechanics across grossly abnormal bones and joints, producing cartilaginous
and osseous degeneration. The hip and the knee are the articulations most frequently affected. The pattern of narrowing of the articular space in Paget disease differs in appearance from that in primary degenerative joint disease. With acetabular involvement, either medial or axial joint space narrowing is seen; with involvement of both the acetabulum and the femoral head, axial joint space loss can occur; and with isolated femoral head involvement, superior joint space loss is noted [3] (Fig. 12). Acetabular protrusion may complicate pagetic involvement of the acetabulum. Notably, the formation of osteophytes is not a prominent feature of the disease. Rheumatoid arthritis and its variants, as well as crystal deposition arthropathy, also have been associated with Paget disease [28].

**Deformity and Fracture**

In Paget disease, overall abnormal bone formation results in osseous weakening, with deformity and fractures being common manifestations of the disease [28, 52]. Anterior or lateral bowing of the tibia or femurs is typical (Fig. 13). In the spine, bowing results in kyphosis; in the hip, deformity may manifest as protrusio acetabuli [28] (Fig. 12).

Fracture is the most common complication of Paget disease, which can be crippling because of the high frequency of nonunion in diseased bone. Insufficiency fractures appear as single or multiple linear cortical radiolucent areas on the convex surface of the long bones and are designated “banana fractures” [7, 8] (Fig. 13). These pathologic fractures usually occur in the femur, tibia, humerus, pelvis, and spine [4, 25]. In the femur, which is the most common site of fracture, fractures are usually subtrochanteric in location, followed in decreasing frequency by the upper third of the femoral shaft and the femoral neck [3].

**Neurologic Entrapment**

Neurologic deficits in Paget disease may relate to abnormalities at the base of the skull or the spine. Calvarial enlargement can cause cranial nerve compression with neurosensory disturbances, deafness, blindness, muscle palsies, and trigeminal neuralgia [26, 31, 32]. Basilar impression, hydrocephalus, and verteobasilar insufficiency are additional complications of Paget disease affecting the craniocervical junction [16] (Fig. 14). Spinal stenosis, compression of the spinal cord, and cauda equina can be caused by enlargement of the pagetic vertebral bodies or posterior elements, spinal deformity and fracture, vertebral collapse with hemorrhage, vascular compromise, or secondary neoplasm [24, 33, 34, 39, 51, 53]. Entrapment of the sciatic nerve may present between an enlarged ischium and lesser trochanter or between the abnormal ilium and piriformis muscle [3].

**Neoplasms**

Neoplastic involvement complicating Paget disease is unusual and includes sarcomatous transformation; giant cell tumor; and superimposed tumorous conditions, such as metastatic disease, plasma cell myeloma, and lymphoma [3, 51, 54–56]. The reported frequency of sarcomatous degeneration varies according to the extent of the pagetic process. In patients with widespread skeletal involvement, sarcomatous degeneration may occur in 5–10% of cases, whereas in patients with less extensive skeletal disease, neoplasm may occur in fewer than 1% of cases [20, 55–57]. Patients usually are between 55 and 80 years old, with men affected more commonly than women (2:1 ratio). Clinical findings include focal pain, swelling, or pathologic fracture [17]. Although virtually any bone can be involved, the bones most commonly affected are the femur, the pelvic bones, and the humerus and occasionally the skull and vertebral column [56]. Osteosarcoma predominates (50–60% of cases) followed by malignant fibrous histiocytoma or fibrosarcoma (20–25%); chondrosarcoma (10%); and, less commonly, lymphoma and angiosarcoma (1–3%) [3, 4, 8, 54].

The radiographic findings of malignant transformation comprise osteolysis, cortical destruction, bony spiculation, nonhealing fracture, and a soft-tissue mass [3]. Osteosclerosis or periostitis is infrequent [55]. On bone scans, sarcomatous degeneration may appear as a “cold” area of absent uptake, representing decreased accumulation of the tracer at the site of neoplasm and necrosis. On CT images, neoplastic involvement in pagetic bone appears as osseous destruction and an extraosseous mass (Fig. 15). MRI shows nonspecific signal intensity characteristics of low to intermediate signal intensity on T1-weighted images and inhomogeneous low to high signal intensity on T2-weighted images in affected bone [24]. Prominent inhomogeneous enhancement in pagetic bone complicated by neoplastic disease is evident after the IV administration of contrast material [4, 24, 50].

Giant cell tumor is another type of neoplasm associated with Paget disease, although this association is very rare [3] and has been considered by some authorities a giant cell reparative granuloma [8, 58, 59]. The tumor almost always occurs in the skull or the facial bones, but giant cell tumor can involve the pagetic pelvis, the clavicle, the spine, and the tubular bones. Patients with giant cell tumor complicating Paget disease in general are elderly persons and have polyostotic involvement. Notably, the tumor more frequently is benign than malignant and may show dramatic response to the use of steroids alone. On radiographs, the tumor appears as a lytic expansile lesion with or without an associated soft-tissue mass [8]. MR images display an osseous segment with the variable signal characteristics of pagetic bone and a soft-tissue component of intermediate signal intensity on T1-weighted images and of focal increased signal on T2-weighted images [3]. Cystic and hemorrhagic regions may be present in the tumor.

Although reportedly rare, metastatic disease involving either the nonpagetic bones or the pagetic bones may be as-
associated with Paget disease [3, 8, 60–62]. A lytic lesion within sclerotic bone and a soft-tissue mass may be seen in patients with metastases superimposed on Paget disease [3, 50]. Other neoplastic conditions complicating Paget disease include plasma cell myeloma, lymphomas, and leukemias, although these associations may be random [3, 4].

**Differential Diagnosis**

A constellation of characteristic radiographic features in Paget disease of bone comprising epiphyseal involvement, sharply demarcated osteolysis, and an advancing wedge of radiolucency usually allows institution of the correct diagnosis. Widespread osteosclerosis, bony enlargement, and a coarsened trabecular pattern are imaging features of chronic disease that can be distinguished from findings associated with other diseases. For example, diffuse osteosclerosis may be present in bony metastasis (particularly from prostatic carcinoma), myelofibrosis, fluorosis, mastocytosis, renal osteodystrophy, fibrous dysplasia, and tuberous sclerosis. Additional findings in these other diseases validate the correct diagnosis. In this regard, hepatosplenomegaly (myelofibrosis, mastocytosis), ligamentous ossification (fluorosis), focal radiodensity (mastocytosis and tuberous sclerosis), bowing deformities and ground-glass appearance (fibrous dysplasia), and subperiosteal and subchondral bone resorption (renal osteodystrophy) are changes associated with these other disorders.

Axial osteomalacia is a rare condition associated with a coarsened trabecular pattern on radiographs simulating Paget disease; however, spongy-appearing trabeculae in the cervical spine are characteristic of axial osteomalacia.

Fibrogenesis imperfecta ossium is another rare disease associated with coarse trabeculation, spontaneous fractures, and deformity. Diagnosis relies on the detection of abnormal pathologic characteristics in collagen.

Familial idiopathic hyperphosphatasia (“juvenile” Paget disease) is a rare, autosomal-recessive disorder of bone observed in children that is associated with progressing skeletal deformities; fragile, coarsely trabeculated, and enlarged bones; visual and auditory impairment; premature loss of teeth; and dwarfism. Although the condition that is characterized by very rapid bone turnover may resemble adult Paget disease, onset of familial idiopathic hyperphosphatasia is noted early in life between the 3rd and 18th month, skeletal involvement is universal and symmetric, and epiphyses may be spared [3, 63].

Familial expansile osteolysis is a rare autosomal-dominant bone dysplasia that in its early stage may resemble Paget disease. Patients present in the second through fourth decades of life. Progressive osteoclastic resorption is accompanied by medullary expansion of bone, producing both generalized and local bony changes that unlike Paget disease are rare in the axial skeleton. Pain, pathologic fracture of disintegrated bone, skeletal deformity, loss of dentition, and deafness are features of the disease [3, 64].

Calvarial hyperostosis seen in Paget disease of the skull can simulate other disorders such as hyperostosis frontalis interna, fibrous dysplasia, and skeletal metastasis. Hyperostosis frontalis interna predominates in women and produces thickening of the inner table of the frontal squama. Fibrous dysplasia may cause enlargement of the skull, although facial involvement is characteristic. Osteoblastic metastasis can simulate the cotton-wool appearance of osteosclerotic lesions of Paget disease.

Vertebral sclerosis in the form of the picture-frame vertebra is diagnostic of Paget disease. This particular configuration differs from the accentuated vertical trabeculae of hemangiomas and the rugger jersey spine of renal osteodystrophy. Images of patients with Paget disease may occasionally reveal diffuse sclerosis of an entire vertebral body, the ivory vertebra that can simulate skeletal metastasis and lymphoma or a vertebral pattern similar to that of a hemangioma. However, the relatively common involvement of the posterior spinal elements in Paget disease usually is not seen in hemangiomas.

In the pelvis, osteosclerosis in Paget disease can mimic osteoblastic metastasis. The presence of asymmetric or unilateral distribution, accentuated trabecular pattern, and enlargement of the involved bone are typical features of Paget disease [3].

**Treatment and Prognosis**

Many medications have been used in the effort to treat patients with Paget disease. Most investigators have concluded that medications are a modest help in the control of the disease but are not a definitive therapy with return to normal bone [17, 19]. Calcitonin generally inhibits bone resorption and provides timely pain relief. Although radiographic improvement of osteolysis has been reported during treatment, flares in bone resorption may occur with cessation of therapy, necessitating retreatment with calcitonin. Unpleasant side effects of calcitonin therapy are frequent and include flushing, nausea, and vomiting [15].

The current mainstay of treatment in Paget disease, however, is the second-generation bisphosphonates (i.e., disodium pamidronate, alendronate, risedronate), which are potent inhibitors of bone resorption [23]. A first-generation bisphosphonate (disodium etidronate) produced mineralization defects and complications such as osteomalacia and fractures and is not widely used [35]. The greatest advantage of second-generation bisphosphonates over calcitonin is prolonged remission of the disease in addition to a more dramatic decrease in the parameters of bone turnover compared with calcitonin [10, 18, 20]. Another therapeutic agent that has been used to treat Paget disease is mithramycin, a cytotoxic antibiotic. Mithramycin is best reserved for those cases resistant to other forms of medical treatment.

With respect to surgical treatment, total joint replacement, especially total hip and knee replacement, has result-
ed in marked relief of pain and improved locomotion [27]. Certain intraoperative difficulties may be encountered, however, owing to marked bone deformity (i.e., femoral bowing, acetabular protrusion) and the poor quality of the pagetic bone. Early postoperative complications and loosening of the prostheses are frequent [26]. In patients with Paget disease, open reduction and internal fixation of fractures has been recommended because delayed union often complicates fracture healing [27, 65].

The prognosis for patients with Paget disease varies but has generally improved since the advent of second-generation bisphosphonates. Active disease tends to recur relentlessly, often requiring retreatment with a second course of therapy. Patients in the fifth decade of life need to be treated rigorously, whereas patients in their eighth decade are treated only if symptomatic [16]. Whether this therapeutic approach can avoid the development of sarcoma, the most dreaded complication of the disease, remains unclear.

**Conclusion**

Paget disease is a common skeletal disorder of middle-aged and elderly persons characterized by excessive and abnormal remodeling of bone. The disease varies considerably in severity and evolves through various phases of activity, followed by an inactive phase. The radiographic features of Paget disease are virtually diagnostic, including an initial osteolytic phase and a subsequent osteosclerotic phase. Bone enlargement with increased radiodensity, accentuated trabecular pattern, and deformity is typical. Complications associated with Paget disease are pathologic fractures, neurologic symptoms, skeletal deformities, articular derangements, and secondary neoplasms. CT and MRI help delineate pagetic bone changes and have proved extremely useful in the diagnosis of sarcomatous transformation, which constitutes the most dreaded complication of the disease.

**References**


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