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PERSPECTIVE

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Pathogenesis of Paget's Bone Disease and its Symptoms

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Description

Paget's disease of bone (commonly known as Paget's disease or historically osteitis deformans) is a condition involving cellular remodeling and deformation of one or more bones. Affected bones show signs of dysregulated bone remodeling at the microscopic level, namely excessive bone resorption and subsequent disorganized new bone formation. These structural changes cause the bone to weaken, which can result in deformity, pain, fracture, or arthritis of the associated joints. The exact cause is unknown, although leading theories suggest both genetic and acquired factors. Paget's disease can affect any one or several bones of the body (most commonly the pelvis, tibia, femur, lumbar vertebrae, and skull), but never the entire skeleton and does not spread from bone to bone. Rarely, bone affected by Paget's disease can turn into malignant bone cancer. Because the disease often affects people differently, the treatment for Paget's disease can vary. Although there is no cure for Paget's disease, medications (bisphosphonates and calcitonin) can help control the disorder and relieve pain and other symptoms. Medications are often successful in controlling the disorder, especially when started before complications begin. Paget's disease affects 1.5 to 8.0 percent of the population and is most common in people of British descent. It is primarily diagnosed in older people and is rare in people under the age of 55. Men are affected more often than women (3:2). The disease is named after the English surgeon Sir James Paget, who described it in 1877.

Pathogenesis

The pathogenesis of Paget's disease is described as initially, there is a significant increase in the rate of bone resorption in localized areas, caused by large and numerous osteoclasts. These localized areas of pathological destruction of bone tissue (osteolysis) are seen radiographically as a progressive lytic wedge in the long bones or skull. When this occurs in the skull, it is called osteoporosis circumscripta. Osteolysis is followed by a compensatory increase in bone formation caused by bone-forming cells called osteoblasts that are recruited to the area. This is associated with accelerated deposition of lamellar bone in a disordered manner. This intense cellular activity creates a chaotic pattern of trabecular bone (a "mosaic" pattern), rather than the normal linear lamellar pattern. The resorbed bone is replaced and the marrow spaces are filled with an excess of fibrous connective tissue with a significant increase in blood vessels, causing a hypervascular state of the bone. The hypercellularity of the bone can then shrink, leaving dense "pagetic bone", also known as burned-out Paget's disease. The later stage of the disease is characterized by the replacement of normal bone marrow by highly vascular fibrous tissue. Sir James Paget first proposed that the disease was caused by an inflammatory process. Some evidence suggests that paramyxovirus infection is the underlying cause of Paget's disease, which may support a possible role of inflammation in pathogenesis. However, no infectious virus has yet been isolated as the causative agent, and other evidence suggests that an intrinsic hyperresponsiveness to vitamin D and receptor activator of nuclear factor kappa beta ligand is the cause. Therefore, further research is needed.

Symptoms

Mild or early cases of Paget's disease are asymptomatic, so most people are diagnosed with Paget's disease by accident during a medical examination for another problem. About 35% of Paget's patients have symptoms related to the disease when they are first diagnosed. Overall, the most common symptom is bone pain. When symptoms do appear, they can be

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confused with those of arthritis or other disorders, so diagnosis can be delayed. Paget's may first be noticed as a growing deformity of a person's bones. Paget's disease affecting the skull can cause frontal bossing, increased hat size and headaches. Often, patients may develop hearing loss in one or both ears due to the narrowing of the auditory opening and subsequent compression of the nerves in the inner ear. Rarely, involvement of the skull can result in compression of the nerves that supply the eye, resulting in vision loss.