Parathyroid Disease

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KEYWORDS

• Hypocalcemia • Hypercalcemia • Myopathy • Gout
• Pseudogout • Bone disease

Parathyroid diseases can be associated with important musculoskeletal problems. These problems vary from well-recognized bone diseases to rare complications. This review addresses the joint, bone, and soft-tissue problems that can occur in patients with hyperparathyroidism and hypoparathyroidism. Parathyroid hormone (PTH) works in conjunction with vitamin D to regulate the total body calcium. PTH has dual actions, both anabolic and catabolic, on the skeleton. PTH provides a powerful mechanism for controlling extracellular calcium and phosphate concentrations. Moreover, it exerts a potent influence in the conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol in the proximal tubules of the kidneys.

HYPOPARATHYROIDISM

The absence of PTH or resistance to PTH by the target organs, especially bones and kidneys, results in low serum ionized calcium, high serum phosphate, and decreased 1,25-dihydroxycholecalciferol.[1] Such a low serum calcium level affects the central and peripheral nervous system, skeletal muscles, and myocardium and can be manifested by neuromuscular irritability, depression, neuropsychiatric manifestations, convulsions, paresthesias, muscle cramps, tetany, prolonged QT intervals, and cardiac failure.

Deficient PTH secretion has postsurgical or idiopathic causes. Idiopathic causes are further categorized into congenital or acquired. Congenital hypoparathyroidism is a condition in which the person is born without parathyroid tissue. Patients usually have no family history of the disease. The acquired form of the disease typically arises because the immune system developed antibodies against the parathyroid tissues. In

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response to this, the parathyroid stops synthesizing and secreting PTH. The authors discuss this acquired form of the disease in this article.

Hypoparathyroidism usually starts insidiously, with slowly increasing episodic symptoms dominated by increased musculoskeletal irritability. The main symptoms, such as muscle cramps, stiffness, tetany, and paresthesias, may enter the differential diagnosis of the rheumatic diseases. There may be subcutaneous nodules caused by soft-tissue calcification. Although hypoparathyroidism is not uncommon, the diagnosis is often missed because of its unusual clinical manifestations. The mechanism underlying these skeletal changes in hypoparathyroidism is not well defined. The associated musculoskeletal syndromes are subsequently described.

Ankylosing Spondylitis-like Diseases or Diffuse Idiopathic Skeletal Hyperostosis

The skeletal abnormalities of hypoparathyroidism are caused by calcification, which can simulate ankylosing spondylitis with clinical signs, including morning stiffness, gait, and posture.[2–7] Sacroiliitis is not expected, although it is the earliest manifestation in most patients with ankylosing spondylitis. There may be sacroiliac sclerosis, but not erosions. The patterns of syndesmophytes in patients with hypoparathyroidism can resemble those of ankylosing spondylitis with origin from the vertebral margin and preserved disc space, but more often there is also involvement of the posterior paraspinal ligament.[3,6] The syndesmophytes reported have been predominantly present in the thoracic and upper lumbar region. Bone density is generally increased in hypoparathyroidism.[3] The syndesmophytes observed have been different from osteophytes of degenerative axial arthritis in that the latter osteophytes spread horizontally before curving up and there is reduction in the disc space. In some cases, these spinal changes are associated with bony proliferation about the pelvis, hip, and long bones, and soft-tissue and tendon calcifications.[7] Although sacroiliac joints are generally spared, periarticular ossification has been recorded in this location. The preservation of sacroiliac joints, HLA B-27 negativity, as well as less significant involvement of the anterior intervertebral ligament does not fit with the diagnosis of ankylosing spondylitis. The pain does not disappear despite taking immunosuppressive agents and nonsteroidal antiinflammatory drugs, but many resolve completely with treatment by calcitriol.[8]

Serum calcium may need to be included in the diagnostic work-up of patients with inflammatory back pain, especially if they present with atypical features as previously described. It is important to differentiate hypoparathyroid-related spondylitis from ankylosing spondylitis because the management for the two disorders is different. In fact, some of the drugs used for ankylosing spondylitis, such as bisphosphonates, may worsen hypocalcemia.

The mechanism underlying these skeletal changes in hypoparathyroidism is not well defined. Decreased intestinal calcium absorption caused by a defect in the action of 1,25-dihydroxyvitamin D (1,25[OH] 2D) has been suggested to play a role in a controlled study of paravertebral ligamentous ossification.[9]

Spinal changes in hypoparathyroidism have also been described to be similar to those in diffuse idiopathic skeletal hyperostosis (DISH) (**Fig. 1**), which is characterized by ossification of the anterior longitudinal ligament, of the spine, and various extraspinal ligaments, but is rarely reported before the 50 years of age. Okazaki and colleagues[10] suggested that the ossifying diathesis of paravertebral ligaments, which is the origin of DISH, might be initiated or aggravated by hypoparathyroidism.