For a deeper discussion of these topics, please see Chapter 269, "Inflammatory Myopathies," in Goldman-Cecil Medicine, *25th Edition.*

Miscellaneous Conditions

Other rheumatologic syndromes that may be harbingers of neoplasia include eosinophilic fasciitis, palmar fasciitis, reflex sympathetic dystrophy, erythromelalgia, Sweet's syndrome, and osteomalacia. Up to 15% cases of Sweet's syndrome (i.e., acute neutrophilic dermatosis) are associated with malignancy, and it can manifest as an acute, self-limited polyarthritis or vasculitis. Knee pain or shoulder pain with normal physical examination findings can be a referred pain from various neoplasms.

HEMATOLOGIC DISORDERS WITH RHEUMATIC MANIFESTATIONS

Hemophilia

Acute, painful hemophilic arthropathy of the knees, elbows, and ankles is the most common manifestation of hemophilia. Repeated episodes of hemarthrosis result in synovial proliferation and chronic inflammation, causing chronic hemophilic arthropathy.

Chronic hemophilic arthropathy is characterized by joint deformity, fibrous ankylosis, and osteophyte overgrowth. Radiography typically shows degenerative arthritis. Besides prompt administration of factor concentrate replacement, acute hemarthrosis must be treated conservatively with cold applications and joint immobilization followed by a structured physical therapy program. Aspiration (after factor replacement) is needed only if concomitant sepsis is suspected or the joint is very tense.

Sickle Cell Disease

Musculoskeletal complications of sickle cell disease include painful crises, arthropathy, dactylitis, osteonecrosis, and osteomyelitis. Sickle cell crisis is the most common musculoskeletal feature, and it can produce painful arthritis of the large joints and noninflammatory joint effusions adjacent to areas of bony crisis. Osteonecrosis of the femoral head, shoulder, and tibial plateau may result from repeated local bone ischemia or infarct.

Dactylitis manifesting as bilateral, painful, swollen hands or feet (i.e., hand-foot syndrome) may be the first manifestation of the disease in infants and young children. It usually resolves spontaneously in a few weeks. Increased risk of septic arthritis and osteomyelitis, most often due to *Salmonella* species, has been associated with hemoglobinopathies.

Multiple Myeloma

Rheumatologic manifestations of multiple myeloma include bone pain resulting from lytic bone lesions, pathologic fractures, and osteoporosis. Thoracolumbar pain in the setting of hypercalcemia, renal insufficiency, and anemia suggests the possibility of multiple myeloma. Multiple myeloma can manifest atypically and mimic specific autoimmune disorders such as Sjögren's syndrome (SS) and SLE.

Amyloidosis

Amyloidosis is a disorder of protein folding in which insoluble fibrillar proteins are deposited in the extracellular space in one or more organs, disrupting tissue structure and function. The clinical manifestations and prevalence depend on the type of amyloidosis.

Myeloma-associated amyloidosis (i.e., amyloid light-chain [AL] amyloidosis) is one of the most common forms of systemic amyloidosis. Amyloid proteins derived from monoclonal light chains can involve the synovium and the articular cartilage, producing rheumatoid arthritis–like polyarthritis. Joint stiffness is more pronounced in amyloid arthropathy, and deposition of amyloid protein at the glenohumeral joint produces enlargement of the anterior shoulder, called the *shoulder pad sign*. Other rheumatic manifestations of AL amyloidosis include muscle weakness, pseudohypertrophy of muscles, and pathologic fracture from osteolytic lesions, jaw claudication that mimics giant cell arteritis, and sicca syndrome due to exocrine gland infiltration.

The amyloid protein can be identified as apple green birefringence on Congo red staining of an abdominal fat pad aspiration or rectal mucosal biopsy specimen. The other principal systemic forms of amyloidosis are secondary amyloidosis (i.e., deposition of amyloid A [AA] protein), hereditary amyloidosis, and β_2-microglobulin–associated amyloidosis.

Endocrine Disorders

Endocrine diseases usually manifest with diffuse, poorly defined musculoskeletal symptoms and joint pain that is more often periarticular than articular. Clinical suspicion of endocrinopathy is by far the most important diagnostic step. Routine clinical laboratory tests such as ESR, ANA, rheumatoid factor, uric acid level, and an antistreptolysin O (ASO) titer are usually not helpful, and radiographs often first suggest the possibility of endocrinopathy.

Diabetes

One of the most common musculoskeletal complications of diabetes is diabetic cheiroarthropathy (i.e., diabetic hand syndrome). It is characterized by insidious development of waxy thickening of the skin of the fingers and hands and by flexion contractures of the metacarpophalangeal joints and interphalangeal joints. Patients cannot press the palms together completely without a gap with the wrists fully flexed (i.e., prayer sign). Although this syndrome is associated with the duration of diabetes and the control of blood sugar, it may develop before the onset of overt diabetes and mimic sclerodactyly.

Dupuytren contracture and stenosing flexor tenosynovitis (i.e., trigger finger) may be identified. People with diabetes are more prone to develop a carpal tunnel syndrome. Diabetic periarthritis of the shoulders (i.e., adhesive capsulitis or frozen shoulder) is more common in patients with diabetes, especially in women with a long history of diabetes. Capsulitis is characterized by staged progression of pain and restriction of shoulder motion, and bilateral involvement occurs in about one half of patients.

Patients with long-standing, poorly controlled diabetes may develop a painless, swollen, deformed joint known as a Charcot