tibia, and radius. The primary form of HOA (i.e., primary pachydermoperiostosis) is usually a self-limited disease of childhood. The secondary form may be generalized or localized and is mainly associated with lung cancer and suppurative lung disease.

HOA is also associated with cardiovascular disease (e.g., cyanotic congenital heart disease, infective endocarditis), hepatobiliary disorders (e.g., liver cirrhosis, primary biliary cirrhosis), and gastrointestinal disease (e.g., inflammatory bowel disease, celiac disease). Periostitis without digital clubbing can be seen in thyroid acropachy, hypervitaminosis A, fluorosis, venous stasis, hyperphosphatemia, and sarcoidosis. Isolated chronic digital clubbing, which is mainly associated with pleuropulmonary disease, does not seem to cause HOA.

The pathogenesis of HOA remains unknown, although several possible mechanisms have been proposed. HOA is usually accompanied by bone and joint pain associated with periarticular periostitis. The pain is usually exacerbated by dependency and relieved with limb elevation. Typical signs of periostitis include periosteal new bone along the distal ends of long bones, which can be seen on plain radiographs. When periostitis is not obvious on plain radiography, a bone scan is useful to demonstrate early evidence of disease. When HOA is clinically suspected, radiologic evaluation of the thorax is important because of the association between HOA and lung neoplasms.

In many cases, symptomatic management with nonsteroidal anti-inflammatory drugs or other analgesics while treating the underlying disorder provides significant relief of symptoms. In refractory cases, bisphosphonates such as pamidronate and zoledronic acid have been reported to be effective.

Rheumatoid Arthritis–Like Syndrome

Inflammatory rheumatoid arthritis–like syndrome has been associated with solid neoplasms and hematologic malignancies. Clinical characteristics associated with this paraneoplastic syndrome include acute onset or late onset, asymmetrical disease frequently involving the lower extremities, nonspecific synovitis in large joints that spares the wrists and hands without bony erosion, negative results for rheumatoid factor and cyclic citrullinated peptide antibody. However, these features are not specific and may be confused with elder-onset rheumatoid arthritis, seronegative rheumatoid arthritis, spondyloarthropathy, remitting seronegative symmetrical synovitis with pitting edema (RS3PE), or polymyalgia rheumatica (PMR).

RS3PE manifests with sudden onset of polyarthritis, pitting edema, and prominent constitutional symptoms. More than one half of RS3PE cases are associated with malignancy. Lymphoproliferative disorders such as leukemia and lymphoma may simulate various rheumatic syndromes from direct invasion of the synovium, articular tissues, or juxta-articular bone, producing synovitis or bone pain.

Lupus-Like Syndrome

Antinuclear antibodies (ANAs) can be seen in patients with solid neoplasms (e.g., gastric, cervical, and breast carcinomas, testicular seminoma), lymphomas, or myelodysplastic disorders, but the significance of these autoantibodies is not well understood. The association between SLE and occult malignancy is uncertain. It is not necessary to search for underlying malignancy in a patient with typical manifestations of SLE. However, lupus-like autoantibodies and unexplained Coombs- positive hemolytic anemia or thrombocytopenia without clinical signs of rheumatic disease warrant further investigation for an occult neoplasm.

Raynaud's Phenomenon and Scleroderma-Like Syndrome

The sudden onset of Raynaud's phenomenon and scleroderma-like syndrome can herald an underlying tumor such as hematologic malignancies and carcinomas of the liver, ovary, testis, bladder, breast, or stomach. Scleroderma-like skin changes may also occur in patients with osteosclerotic myeloma with *p*olyneuropathy, *o*rganomegaly, *e*ndocrinopathy, *m*onoclonal gammopathy, and *s*kin abnormalities (i.e., POEMS syndrome) and in those with carcinoid tumors.

Characteristics that suggest secondary Raynaud's phenomenon include age at onset older than 50 years, symptom asymmetry, symptoms that persist year round, and rapid digital ulceration and necrosis. Secondary Raynaud's is also suggested by scleroderma-like syndromes in patients older than 50 years, rapid progression of skin sclerosis, or a poor response to therapy. The lack of Raynaud's phenomenon can be another distinguishing characteristic of paraneoplastic scleroderma-like syndrome because Raynaud's phenomenon occurs in approximately 95% of cases of systemic sclerosis.

Polymyalgia Rheumatica

Clinical symptoms and signs of PMR include shoulder and pelvic girdle pain and morning stiffness, a high erythrocyte sedimentation rate (ESR), and anemia of chronic disease. Although the association between PMR and cancer is controversial, several features are atypical for PMR and may suggest an occult malignancy: disease onset before the age of 50 years, asymmetrical or localized involvement of typical sites, an ESR less than 40 or higher than 100 mm/hr, and a poor response to low doses of glucocorticoids.

Myelodysplastic syndromes and myeloproliferative syndromes are frequently associated with PMR. Myelodysplastic syndromes also are associated with a variety of musculoskeletal symptoms and signs, including cutaneous vasculitis, monoarticular or polyarticular arthritis, lupus-like conditions, Raynaud's phenomenon, polychondritis, and pyoderma gangrenosum.

Vasculitides

Vasculitis is rarely associated with malignancy and is most commonly seen in patients with lymphoproliferative disorders and myelodysplastic syndrome. Cutaneous leukocytoclastic vasculitis is the most common manifestation of vasculitic paraneoplastic. Although clinical presentations of paraneoplastic vasculitides are indistinguishable from those of the idiopathic condition, a chronic, relapsing disease with cytopenias and poor response to conventional treatment suggest a hidden malignancy.

Inflammatory Myopathies

The association between inflammatory myopathies and malignancies has been well established.