PARANEOPLASTIC RHEUMATOLOGIC SYNDROMES


Take home points:
1. The triad of hypertrophic osteoarthropathy (HOA) is polyarthritis, clubbing, periostitis of the distal ends of long bones.
2. Carcinoma polyarthritis can be differentiated from RA by late age of onset, explosive onset, asymmetric distribution, predominance of lower extremity involvement, absence of erosions on radiography.
3. There is good evidence that dermatomyositis is associated with malignancy whereas the evidence for polymyositis and malignancy is questionable

Rheumatology and malignancy – associations:
- Direct invasion of bones, joint, muscle
- Synovial reaction to bony or soft-tissue tumors
- Hemarthrosis (caused by hemorrhage into joint or peri-articular structures).
- Secondary gout
- Paraneoplastic syndromes (remote non-metastatic) effects of a tumor
- Treatment-related malignancy secondary to immunosuppressive drugs
- Chemotherapeutic drugs causing rheumatologic phenomenon

Hypertrophic osteoarthropathy (HOA):
- Triad of polyarthritis, clubbing, and periostitis of the distal ends of long bones
- Arthritis is symmetric and affects the knees, ankles, elbows, wrists, MCP’s, PIP’s
- Synovial fluid is “non-inflammatory”, WBC < 2000.
- Periostitis of the long bones can cause deep bone pain that can mimic bony mets; can be differentiated by the fact that HOA pain is usually dependent in nature (alleviates by elevation).
- Most frequently associated with NSCLC; can rarely occur with small-cell, mesothelioma, pulmonary mets, lymphoma
- Look for symmetric bilateral periostitis of distal long bones (especially distal tibia).
- Treat with NSAIDs for symptomatic relief; HOA can resolve with treatment of the underlying malignancy

Carcinoma polyarthritis:
- Seronegative inflammatory arthritis that mimics RA
- Differentiated from RA by late age of onset, explosive onset, asymmetric distribution, predominance of lower extremity involvement, absence of erosions on radiography; also no RF, no family history, no deformation of joints and no rheumatic nodules
- Differential diagnosis includes direct tumor invasion into joints and HOA
- Associated most with breast cancer in women and lung cancer in men
- Treat with NSAIDs and intra-articular steroids; treatment of underlying malignancy can lead to resolution.
Amyloid arthritis:
- Most commonly occurs in patients with multiple myeloma
- Synovial fluid is non-inflammatory, WBC<2000, and deposits of AL amyloid (apple-green birefringence) can be seen.
- Symmetric, painless; “shoulder pad sign”
- Other clinical manifestations: peripheral neuropathy, carpal tunnel, peri-articular SQ deposits, macroglossia, nephropathy, cardiomyopathy
- Diagnosis by synovial fluid, BM biopsy, SPEP/UPEP
- Treat the multiple myeloma; NSAIDs if arthritis is painful.

Secondary gout:
- Seen in leukemia, lymphoma, myeloma, and tumor lysis syndrome
- Associated with high levels of uric acid

Dermatomyositis:
- Risk of cancer highest in first 3 years after dx and elderly patients (age>65) are at highest risk
- Malignancies associated are similar to age- and sex-matched general population except for possible higher association with ovarian cancer; malignancy exists in approximately 15% of patients, with RR of approximately 3.
- No clear association between malignancy and polymyositis
- Clinical features: proximal muscle weakness, elevated CK, heliotrope rash, Gottron’s papules (over MCP, PIP joints), “mechanic hands”
- Treatment: cancer-associated dermatomyositis is more resistant to steroids and cytotoxic therapies but radical treatment of underlying malignancy can cause regression.

Lambert-Eaton myasthenic syndrome:
- Reduced release of ACh from nerve terminals caused by antibodies against calcium channels
- Excessive fatigue on exertion, hyporeflexia, proximal muscle weakness, especially in the lower extremities
- Differentiated from myesthenia gravis by initial increase of strength on repetitive movements, followed by decreased strength with continued exercise
- Associated with SCLC in 60% of patients and is usually discovered 1-2 years after the onset of muscle weakness
- Medications that enhance release of ACh are helpful whereas anticholinesterase drugs are not

Paraneoplastic vasculitis:
- Necrotizing vasculitis can occur with myeloproliferative and lymphoproliferative syndromes, MDS, and less frequently malignant melanoma, and lung, prostate, colon, breast, and ovarian cancer
- Cutaneous leukocytoclastic vasculitis can present as palpable purpura, urticaria, maculopapular eruptions and/or arthritis and is the most common form of cancer-associated vasculitis
- Polyarteritis nodosa can occur with hairy cell leukemia
- Treatment: often responds to steroid therapy but frequently recurs