Inflammatory Bone Disorders

Inflammation of bone and marrow is termed osteomyelitis. Although the common use of the term almost always implies inflammation of infectious etiology, special forms of osteomyelitis unrelated to infection do exist. Chronic osteomyelitis is generally a late continuum of the inflammation but can also be seen without proceeding acute phase. Four subtypes of chronic osteomyelitis are reviewed here: infectious chronic osteomyelitis, chronic recurrent multifocal osteomyelitis (CRMO), SAPHO syndrome and Majeed syndrome.

Infectious Chronic Osteomyelitis

Infectious chronic osteomyelitis (ICO) largely results from delay in diagnosis and ineffective antibiotic therapy of its acute predecessor. Bacteria, esp. Staphylococcus aureus, remain to be the leading initial cause. Tuberculous osteomyelitis is most frequently presented as ICO. Typical clinical presentation of ICO includes lower fever, bone pain and lytic change surrounded by a zone of sclerosis on imaging study. But the gold standard of diagnosis is biopsy with tissue culture. Key findings in biopsy include plasma cell infiltrate, necrotic bone fragments with osteoclasts, fibrosis and reactive bone formation. Complication of CIO includes acute flare-ups, pathologic fracture and sepsis. Infectious chronic osteomyelitis is very difficult to eradicate. A 6-week course of intravenous antibiotics is prescribed after surgical débridement of chronic osteomyelitis. ICO accounts for the vast majority cases of chronic osteomyelitis. However, its differential diagnosis should always include the response to stress fracture, reaction to adjacent tumor, and, much less commonly, chronic recurrent multifocal osteomyelitis.

Chronic Recurrent Multifocal Osteomyelitis

Currently, chronic recurrent multifocal osteomyelitis (CRMO) is classified as an inherited auto-immune disease of unknown etiology that symptomatically resembles osteomyelitis, but without the infection. It is a clinical entity distinct from bacterial osteomyelitis, and a rare condition with an incidence of 1:1,000,000. It occurs mainly in children and adolescents and is characterized by a prolonged, fluctuating course over several years with recurrent episodes of pain. CRMO is often multifocal and most often seen in tubular bones, the clavicle, and less frequently the spine and pelvic bones; other locations are rare. The radiographic appearance suggests subacute or chronic osteomyelitis. Histopathological and laboratory findings are nonspecific and bacterial culture is negative. Therefore, CRMO is often diagnosed by exclusion of other bone disorders with similar clinical presentation, especially bacterial infections and neoplasm. A characteristic course, the findings by conventional radiography and magnetic resonance imaging (MRI) can aid diagnosis. The MRI appearance of CRMO lesions in tubular bones and the spine is often rather characteristic and support the diagnosis.

Fortunately, CRMO usually resolves itself. Most (but not all) children do not suffer any major long term disability. Symptoms can be managed. In most cases, the acute outbursts will pass. In the long run, the child can have a normal adult life. It is important to diagnose CRMO to avoid unnecessary diagnostic procedures and initiate an appropriate treatment.

SAPHO syndrome

SAPHO syndrome is a group of chronic disorders that involves the skin, bone, and joints. It is characterized by the constellation of Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis. The first letter of these lesions forms the acronym, SAPHO. Historically, SAPHO was identified after CRMO was discovered and was found associated with a number of dermatologic disorders. Therefore, CRMO is often considered as a manifestation of SAPHO syndrome. Three widely followed diagnostic criteria of SAPHO syndrome were proposed by Kahn and colleague in 1994.
Inflammatory bone disorders in SAPHO syndrome show characteristic anatomic distribution: i.e. anterior chest wall (up to 80% of patients), pelvis and spine. Typically, the changes include chronic inflammation, hyperostosis, osteosclerosis, and paraosteal ossification. Chronic osteomyelitis in long bones usually affects metadiaphysis of the distal femur and proximal tibia. The etiology of SAPHO syndrome remains unknown. Chronic inflammatory bone disorder in the unusual site plus skin lesion should prompt consideration of SAPHO syndrome as a differential diagnosis. Bisphosphonate therapy has been suggested as a first-line therapeutic option in many case reports and series. By a putative link between SAPHO syndrome and spondylarthropathy, a combination of anti-inflammatory and and immunomodulating drugs (Azithromycin and hormonal osteotrophic drugs (calcitonin) are proposed as new treatment of SAPHO syndrome.

**Majeeed syndrome:** is an autoinflammatory disorder consisting of recurrent multifocal chronic osteomyelitis (CRMO), congenital dyserythropoietic anemia (CDA) that presents as hypochromic, microcytic anemia of various severity, and transient inflammatory dermatosis, often manifesting as Sweet syndrome. Majeeed syndrome is inherited in an autosomal recessive manner. Mutations in LPIN2 have been shown to play a role in the etiology of Majeeed syndrome.

**Summary**
In this episode, we reviewed four subtypes of chronic osteomyelitis. Infectious chronic osteolyelitis is the most frequently encountered type. Recurrent multifocal chronic osteomyelitis (or CRMO) is as an inherited auto-immune disease. SAPHO syndrome can be considered as CRMO plus inflammatory dermatosis, whereas Majeeed syndrome also includes congenital dyserythropoietic anemia.

**Infectious Chronic Osteomyelitis (ICO)**
- Bacterial infection is the leading cause
- Low-grade fever, bone pain & lytic change
- Diagnosis by biopsy with tissue culture
- Plasma cell infiltrate, necrotic bone & marrow fibrosis
- DDx. stress fracture, reaction to nearby tumor, CRMO

**Chronic Recurrent Multifocal Osteomyelitis (CRMO)**
- An inherited auto-immune disease
- Mainly in children and adolescents
- Nonspecific histology and lab findings
- Diagnosed by exclusion (esp. infection)
- Spontaneous resolution without squeal in most

**SAPHO Syndrome**
- Auto-immune inflammatory disorders.
- Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis.
- CRMO, hyperostosis, osteosclerosis, paraosteal ossification.
- Anterior chest wall (80%), peripheral arthritis (90%)
- Viewed as CRMO + inflammatory dermatosis

**Majeeed Syndrome**
- An autosomal recessive, autoinflammatory disorder
- CRMO, CDA and inflammatory dermatosis.
KnowledgeBase

- Maybe viewed as SAPHO syndrome + CDA
- Mutation in LPIN2 gene

References / Suggested Readings
Wikipedia: Chronic recurrent multifocal osteomyelitis. (accessed on March 11, 2012)