Assessment and Pathophysiology of Charcot Arthropathy
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History: Neuropathic arthropathy was first described by the eminent French neurologist Jean-Martin Charcot in cases of tertiary syphilis. Charcot advocated a theory of "neurotrophism," alleging that an unknown substance from bone was required to keep bone healthy. Charcot arthropathy presents in a number of locations in the body, with the location of the lesion dependent upon the neurologic pathology. For instance, it presents in the foot in cases of stocking glove neuropathy as seen in diabetes, but may present in the shoulders in the case of the thoracic cord lesion associated with syringomyelia. In diabetes, most cases occur in patients with a decade-long history of the disease. Notably, neuroarthropathy in this setting was first described in the 1930’s. In that decade diabetics first began to enjoy prolonged survival following the beginning of mass extraction of insulin in 1923.

Phenomenology: Metabolic markers of bone turnover in Charcot arthropathy indicate that excessive type I collagen breakdown products (e.g. n-terminus telopeptide and others) are present in serum and urine, while markers of anabolic bone function (e.g. alkaline phosphatase) are normal. This is felt to indicate a dysregulation of osteoclast function rather than a suppression of osteoblasts. The global bone mineral density appears to be decreased in patients with active Charcot in the foot and ankle, even when measured by remote DEXA scans at the proximal femur. Autonomic dysfunction as a component of the patient’s neuropathy appears to be strongly correlated with neuroarthropathy.

Temporal Staging: Eichenholz described a staging system for neuroarthropathy in a non-peer reviewed monograph in 1966. It is purely descriptive, based both on radiographs and clinical exam, and has not been validated. It is nevertheless encountered in the literature as a common reference point.

Stage 1. Development
Stage 2. Coalescence
Stage 3. Reconstruction

Etiology: Three theories have been advanced as potential mechanisms for the development of the disease:

1. The neurotraumatic hypothesis: Unrecognized microtrauma leads to repetitive injury ultimately outstripping the bone ability to repair small trabecular fractures. Dissolution of bone then proceeds.
2. The neurovascular hypothesis: Excessive bone blood flow developing from autonomic dysregulation of the small arterioles leads to bone resorption.
3. The neurotrophic hypothesis: Originally proposed by Charcot himself. An unknown factor from nerve positively maintains bone health.

Problems exist with all three hypotheses and the absence of a true animal model of Charcot arthropathy hinders progress. The neurotraumatic hypothesis can be challenged by cases of arthropathy occurring in patients at bedrest and the occurrence of neuroarthropathy in non-weightbearing joints such as the shoulder in syringomyelia. The neurovascular hypothesis lacks a clear mechanism to connect increased bone blood flow to bone resorption as well as the contrarian example of routine fracture healing, in which bone mineral is deposited in the presence of up to a ten-fold increase in local blood flow. The neurotrophic hypothesis lacks a specific neurotransmitter known to affect bone clinically, but several small peptide transmitters have been shown to have receptors on osteoclasts.

Potential for biologic treatment: Outlining the pathophysiology may lead to a targeted medical treatment. Bisphosphonates can be used to diminish the markers of osteoclast activity, but any clinical correlate a more rapid healing response has yet to be established.