CLINICAL VIGNETTE

A Case of Ankylosing Spondylitis and Chronic Nonbacterial Osteomyelitis

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A 22-year-old man with anxiety and depression presented to the Emergency Department for five months of progressive neck pain, right clavicle pain, and lower back pain. He noted stiffness in his lower back lasting for two to three hours in the morning. His morning stiffness improved with activity such as walking and stretching. He also reported severe fatigue, anorexia resulting in a 20-pound unintentional weight loss, and intermittent night sweats at home.

His vitals included temperature of 36.9°C, blood pressure 135/80, heart rate 110 beats/min. His physical examination was notable for a young male in moderate distress lying uncomfortably in his hospital bed. There was tenderness to palpation along his cervical and thoracic spine. His right clavicle was warm, swollen, and tender to palpation. There was also tenderness at his right sacroiliac joint. Pain at the right sacroiliac joint was elicited with flexion, abduction, and external rotation of his right leg.

Laboratory examination was notable for positive HLA B27, sedimentation rate of 90 mm/hr, and c-reactive protein of 5.4 mg/dL. He had negative testing for ANA, DsDNA, Scl-70, Centromere, Smith, RNP, SSA, SSB, and ANCA. Protein electrophoresis showed polyclonal gammopathy with a negative immunofixation and normal kappa/lambda light chain ratio. Additional infectious testing was negative for QuantiFERON, HIV, coccidiosis, hepatitis B, hepatitis C, Q-fever, brucella, bartonella, gonorrhea, and chlamydia.

Imaging studies included a bone scan showing increased uptake in the right clavicle, cervical vertebras, and thoracic vertebras. Computerized tomography scan of the chest demonstrated a lytic lesion adjacent to the sternoclavicular joint within the medial head of the right clavicle. Magnetic resonance imaging of the sacroiliac joint demonstrated bilateral bone marrow edema of the sacroiliac joints and an erosion on the right sacroiliac joint.

A bone biopsy and resection of the right clavicle was performed. The pathology showed normal hematopoietic bone marrow with mild polyclonal plasmacytosis, fragments of fibromuscular tissue, and focal mild nonspecific inflammation. Additionally, a core biopsy of the T6 vertebra showed only scant fibroadipose tissue with mild inflammation. The biopsy showed no evidence of malignancy or granulomas. Bone cultures were negative for bacteria and acid-fast bacilli.

Rheumatology was consulted to provide input on this complex case and diagnosed the patient with ankylosing spondylarthritis (AS) and chronic nonbacterial osteomyelitis (CNO) based of his clinical symptoms and findings. Patient was started on Naproxen 500mg twice per day for one month. The patient reported improvement in the inflammatory arthritis involving his neck, clavicle and lower back with naproxen treatment. However, his joint pains did not fully resolve and his inflammatory markers remained mildly elevated. Rheumatology subsequently initiated weekly subcutaneous etanercept 50mg injections in addition to treatment with oral naproxen. After 3 months of therapy, the patient had complete resolution of his inflammatory joint pain and his inflammatory markers were no longer detectable.

Discussion

CNO is a non-infection lytic autoinflammatory bone disorder that leads to bone destruction if left untreated. CNO typically involves asymmetric long bones metaphysis of the lower extremities, clavicle, vertebra, and mandible.[1] The pathophysiology of CNO is thought to be due in part to the dysregulation of proinflammatory cytokines including, interleukin-1, interleukin-6, interleukin-20, interleukin-10, interleukin-19, and tumor necrosis factor.[2] CNO is not associated with a single gene mutation as seen in other autoinflammatory disorders, and is likely of polygenetic inheritance.[1]

CNO is associated with a number of autoimmune disorders such as spondylarthritis, psoriasis, palmoplantar pustulosis, inflammatory bowel disease, granulomatosis with polyangiitis, Takayasu, and pyoderma gangrenosum.[3] One retrospective study reported AS is a spondylarthritis disorders commonly associated with CNO, with a prevalence of 25%.[4] Another prospective study of children and adolescents with CNO showed that a large percentage of cases developed sacroiliitis and later meet criteria for AS.[5]

In terms of imaging modalities used in the diagnosis of CNO, magnetic resonance imaging and positron emission tomography imaging can identify active bone lesions as regions with bone marrow edema and increased fluorodeoxyglucose radiotracer

uptake. Computerized tomography cannot differentiate between active or chronic bone lesions in CNO. X-rays are the least sensitive imaging modality for detecting bone lesions in CNO.[1,6,7]

The primary purpose of a bone biopsy in the diagnosis of CNO is to exclude other diagnoses that can mimic the clinical and radiologic findings of CNO such as, infection and malignancy. The pathology findings reported in CNO bone biopsies are typically nonspecific and include destruction of normal bone structure, presence of mixed immune cells (neutrophils, monocytes, lymphocytes, and plasma cells) during early phase of bone disease, and the presence of fibrosis and sparse immune cells in the later phases on bone disease.[1,8]

The initial treatment of CNO includes a four to eight-week trial of non-steroidal anti-inflammatory drugs (NSAIDs). One study reported approximately 43 percent of patients with CNO achieved clinical remission within the first year of starting NSAIDs.[9] Methotrexate is a disease-modifying antirheumatic drug that has shown benefits in CNO.[8] Tumor necrosis factor inhibitors like etanercept, adalimumab, and infliximab have been the mainstay biologic immunosuppressive therapy used in CNO.[2,8] Intravenous pamidronate infusion is a non-immunosuppressive agent used in the treatment of CNO. However, arrythmias due to hypocalcemia can be a life-threatening side effect of pamidronate infusions. Patients undergoing pamidronate infusions typically benefit from initial hospitalization for frequent laboratory monitoring of ionized calcium levels and telemetry observation for arrythmias.[10,11]

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