**Chronic Nonbacterial Osteomyelitis in a Child with Previous Juvenile Dermatomyositis**

To the Editor:

Chronic nonbacterial osteomyelitis (CNO) is a sterile osteitis of unknown etiology. The diagnosis is based on characteristic clinical, laboratory, and imaging features. Currently, CNO is considered an autoinflammatory disorder. However, the association of CNO with inflammatory bowel diseases, psoriasis, and vasculitis suggests that both innate and adaptive immunity may contribute to pathogenesis.

A 3-year-old girl presented with proximal muscle weakness, Gottron papules, and periorbital heliotrope rash. Erythrocyte sedimentation rate (ESR) was 30 mm/h (normal 0–12 mm/h); creatine kinase, aspartate aminotransferase, and lactate dehydrogenase were normal. Antinuclear autoantibody (ANA) titers were 1:320; antibodies against Jo-1, ribonuclear proteins, Smith, Ro, La, Scl-70, and double-stranded DNA were not detected. Muscle biopsy result was consistent with dermatomyositis. She was started on oral corticosteroids 1.5 mg/kg/day and methotrexate 0.5 mg/kg weekly. After 9 months, muscle strength normalized and treatment was discontinued. Family history revealed that her brother and maternal grandmother had psoriasis and a paternal uncle was diagnosed with Crohn disease.

When she was 10 years old, she developed right distal femoral pain, swelling, and warmth and had elevated ESR (17 mm/h). Cultures from blood and from the affected bone were normal. A radiograph of the right femur revealed a mottled lucency (Figure 2A). Despite 2 months of intravenous antibiotics, the bone pain persisted. Magnetic resonance imaging (MRI) of the right leg showed a small sequestrum; bone biopsy was in keeping with nonbacterial osteomyelitis. The persistence of bone symptoms for another year, together with the results of a second bone biopsy, confirmed CNO. In addition, recurrent attacks of Raynaud syndrome for another year, together with the results of a second bone biopsy, confirmed CNO. A link between these 2 diseases could be represented by IL-1ß, which can activate and amplify the intracellular T cell response.

What do these diseases have in common? Both CNO and JDM are systemic immune-mediated inflammatory diseases, characterized by cytokine dysregulation. Tumor necrosis factor-α, interleukin 10 (IL-10), and IL-18 play a role in pathogenesis of CNO, whereas type I interferon has been implicated in JDM. Moreover, activation of UPR may trigger the innate immune pathways. What is the role of the innate immune system in the pathogenesis of both JDM and CNO?

We describe a unique case of CNO following JDM in a child with persistently positive ANA titers. From dysregulated adaptive immunity, characteristic for JDM, to prominent innate immune dysfunction, as is suspected in CNO, the child’s immune system responded in distinctive ways to as-yet unknown stimuli. Specific stimuli could have driven the signaling through either immune pathway at different times during childhood. We speculate that the treatment of JDM could have partially reset the innate immune system in this patient. On a subclinical tolerogenic background, a second hit could have stimulated the rapid-acting, non-specific innate immune system, leading to sterile bone inflammation. The sequential immune-mediated manifestations suggest there is crosstalk between the adaptive and innate immune arms, likely through common downstream signaling pathways and/or transcriptional targets.

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REFERENCES


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Figure 2. Images of chronic nonbacterial osteomyelitis of the femur in a child with previous juvenile dermatomyositis. Radiographs at (A) 10 and (B) 17 years of age showed posterior femoral lucencies and periosteal new bone formation. Coronal image of both femurs from total body magnetic resonance imaging (C) performed with inversion recovery sequences at 17 years of age. There is diffuse high signal of the distal right femur with associated low signal cortical thickening (courtesy of Dr. M. Ranson). White arrows show the affected bone area.