Autoamputation in a Patient with Cryoglobulinemia

SEAN D. OVERTON, BS, Senior Medical Student; JOHN J. HONG, MD, Assistant Professor of Surgery, Department of Surgery; TERRY L. MOORE, MD, Professor of Internal Medicine, Pediatrics and Molecular Microbiology and Immunology, Director, Division of Rheumatology, Department of Internal Medicine (Division of Rheumatology); FRANK E. JOHNSON, MD, Professor of Surgery, Department of Surgery, Saint Louis University Health Sciences Center, St. Louis, Missouri, USA. Address reprint requests to Dr. F.E. Johnson, Department of Surgery, Saint Louis University, 3635 Vista Avenue at Grand Blvd., St. Louis, MO 63110.

A 54-year-old man presented with a 4-week history of pain and weakness in his hands, and a 2-week history of nausea, vomiting, weight loss, and decreased sensation in his extremities. He had been relatively healthy except for psoriasis and carpal tunnel syndrome. Evaluation of his hands revealed edema, cyanosis, mottling, and Raynaud phenomenon. He was hospitalized for investigations and promptly developed abdominal pain and diarrhea. Computerized tomography revealed free intraperitoneal air; at surgery, necrotic bowel was found and resected. Microscopic examination of the resected tissue showed extensive ulcerations due to intravascular thrombosis. The antinuclear antibody (ANA) concentration was abnormal (titer 1:10,240; normal < 1:80) with antibodies to RNP (233 units; normal 0–19). Interestingly, the remainder of the ANA profile including dsDNA, Sm, Scl-70, SSA, and SSB was negative. Tests for serum antineutrophil cytoplasmic antibody, serum proteinase 3, and serum myeloperoxidase were also negative. The only other abnormal serum immunologic studies were the levels of aldolase (10.2 units/l; normal 1.5–8.1), IgM rheumatoid factor (388 IU/ml; normal < 30), and C4 (< 10 mg/dl; normal 15–50). Analysis of the serum by immunofixation electrophoresis revealed monoclonal IgM kappa and polyclonal IgA and IgM. Quantitation of serum cryoprecipitate by immunonephelometry revealed a level of 16 mg/dl (normal 0). Hepatitis A, B, and C studies were negative, as was a bone marrow biopsy for hematologic malignancy.

Proposed diagnostic criteria for mixed cryoglobulinemia have been published by the Italian Group for Study of Cryoglobulinemias[1]. They are based on clinical, serological, and pathologic findings. Because our patient had mixed serum cryoglobins with a positive rheumatoid factor level, low C4 level, peripheral neuropathy, vasculitis, and necrotic ulcers, he fulfilled these criteria. The diagnosis of mixed cryoglobulinemia is unusual in this patient because he had a negative polymerase chain reaction study for hepatitis C. Studies have shown that greater than 90% of patients with mixed cryoglubulinemia have an associated hepatitis C infection[1]. Because he had Raynaud phenomenon, marked hypergammaglobulinemia, and sclerodactyly as well as an abnormal ANA and abnormal levels of antibodies to RNP, he fulfilled criteria for the diagnosis of mixed connective tissue disease.

He was anticoagulated and treated with hydroxychloroquine, plasmapheresis, and steroids. As his cryoglobulin levels decreased, he improved clinically. Within the first week the swelling in his hands subsided and several of his fingers became necrotic. These areas of extremity necrosis were allowed to autoamputate over time. The photographs show his hands at presentation (Figure 1), one month (Figure 2), and 3 years (Figure 3). Note the initial mottling, cyanosis, and edema, which all resolved in the first month.

REFERENCE

1. Ferri C, Zignego A, Pileri S. Cryoglobins — review. J Clin Pathol 2002;55:4-13.

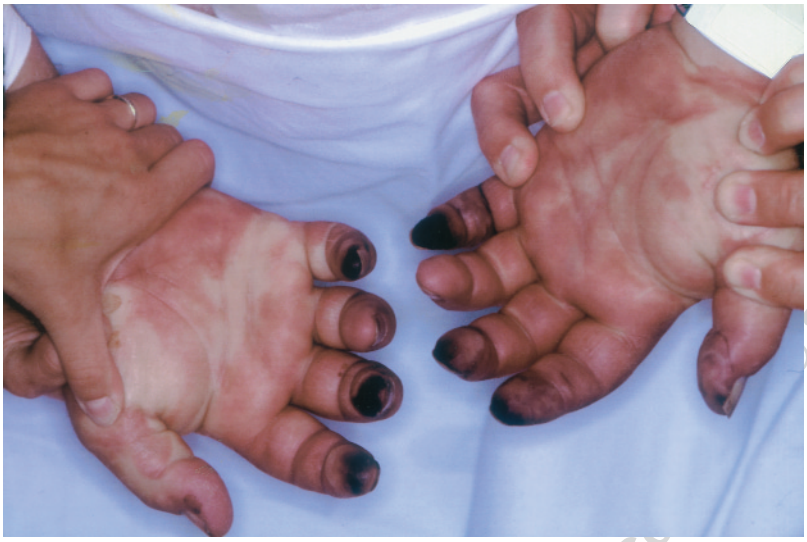

Figure 1. The patient's hands at presentation.

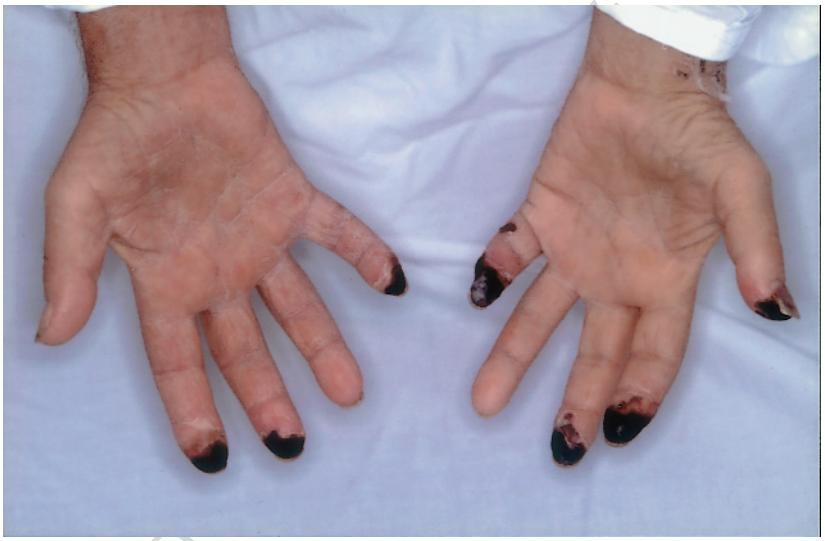

Figure 2. One month after diagnosis.

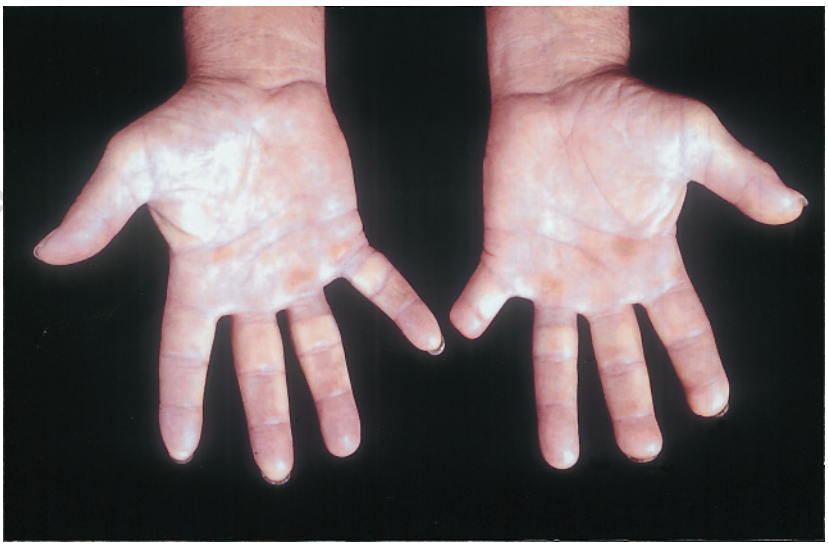

Figure 3. Three years after diagnosis.