Articular Involvement in Disseminated Histoplasmosis in a Kidney Transplant Patient Taking Azathioprine

To the Editor:

Histoplasmosis can manifest itself in the joints of immunocompromised patients. It is a potentially fatal opportunistic infection and should be considered when these patients present with unexplained joint swelling, erythema nodosum, or sepsis.

An 81-year-old farmer from Minnesota developed acute-onset painful swelling over the ulnar aspect of the right palm. He denied work-related injury or trauma. Hand radiographs did not show evidence of a foreign body. Cephalexin was started for presumed cellulitis, but 4 days later the hand lesion evolved into a localized area of purple discoloration, 3 × 2.5 cm, with central clearing. He developed generalized weakness, myalgias, large-joint arthralgias, worsening hand erythema, productive cough, fever (101.2°F), and hypotension (88/59 mm Hg), and was hospitalized for presumed sepsis. He was treated empirically with vancomycin and ceftriaxone. Physical examination showed a nontender, nonfluctuant, nonindurated ecchymotic lesion on the ulnar aspect of his right hand distal to the hypothenar eminence, with full active and passive range of motion of wrist and fingers and no tenderness along the digital tendon sheaths. There was no synovitis in the metacarpophalangeal, interphalangeal, or radiocarpal joints. His right knee and ankle were warm and swollen with limited range of motion but no erythema. He had a small palatal ulcer.

His history was pertinent for hypertension, hyperlipidemia, ischemic cardiomyopathy, gout, and degenerative arthritis of the knees. He underwent a cadaveric kidney transplant in 1982 because of endstage renal disease from chronic interstitial nephritis and was maintained on azathioprine 100 mg and prednisone 5 mg daily with excellent allograft function. Surgical history was pertinent for splenectomy in 1981.

Laboratory studies showed hemoglobin 12.1 g/dl and white blood cell count 4.8 × 10^9/L. Serum creatinine was 1.9 mg/dl, up from a baseline of 1.4 mg/dl. C-reactive protein was 79.4 mg/l (normal < 8 mg/l). Human immunodeficiency virus serology and BK virus quantitative polymerase chain reaction (PCR) were negative. Blood cultures for aerobic and anaerobic bacteria and fungi were negative after 5 days. Urine cultures were negative. Ceftriaxone was started for presumed cellulitis, but 4 days later the hand lesion evolved into a localized area of purple discoloration, 3 × 2.5 cm, with central clearing. He developed generalized weakness, myalgias, large-joint arthralgias, worsening hand erythema, productive cough, fever (101.2°F), and hypotension (88/59 mm Hg), and was hospitalized for presumed sepsis. He was treated empirically with vancomycin and ceftriaxone. Physical examination showed a nontender, nonfluctuant, nonindurated ecchymotic lesion on the ulnar aspect of his right hand distal to the hypothenar eminence, with full active and passive range of motion of wrist and fingers and no tenderness along the digital tendon sheaths. There was no synovitis in the metacarpophalangeal, interphalangeal, or radiocarpal joints. His right knee and ankle were warm and swollen with limited range of motion but no erythema. He had a small palatal ulcer.

Histoplasmosis is a potentially fatal opportunistic infection causing articular manifestations that rheumatologists should keep in mind when patients in endemic areas taking immunosuppression present with unexplained joint swelling, erythema nodosum, or sepsis. Urine and serum histoplasma antigen test returned at 6.45 ng/ml and H. capsulatum blood antigen at 116 ng/ml (normal = undetectable). Fungal immunodiffusion studies showed positive H and M bands consistent with disseminated histoplasmosis. H. capsulatum was also identified by DNA probe in the synovial fluid from the right knee. On hospital day 4, results of Histoplasma capsulatum urine antigen test returned at 6.45 ng/ml and H. capsulatum blood antigen at 116 ng/ml (normal = undetectable). Fungal immunodiffusion studies showed positive H and M bands consistent with disseminated histoplasmosis. H. capsulatum was also identified by DNA probe in the synovial fluid from the right knee. On hospital day 4, results of Histoplasma capsulatum urine antigen test returned at 6.45 ng/ml and H. capsulatum blood antigen at 116 ng/ml (normal = undetectable). Fungal immunodiffusion studies showed positive H and M bands consistent with disseminated histoplasmosis. H. capsulatum was also identified by DNA probe in the synovial fluid from the right knee. On hospital day 4, results of Histoplasma capsulatum urine antigen test returned at 6.45 ng/ml and H. capsulatum blood antigen at 116 ng/ml (normal = undetectable). Fungal immunodiffusion studies showed positive H and M bands consistent with disseminated histoplasmosis. H. capsulatum was also identified by DNA probe in the synovial fluid from the right knee.

Histoplasmosis is a potentially fatal opportunistic infection causing articular manifestations that rheumatologists should keep in mind when patients in endemic areas taking immunosuppression present with unexplained joint swelling, erythema nodosum, or sepsis. Urine and serum histoplasma antigen testing should be sought for screening as they allow for a quicker diagnosis than cultures and are more readily available than PCR or in situ hybridization testing. DNA probe for H. capsulatum or fungal culture can help identify the infection in synovial fluid. Success of therapy and identification of relapse can also be monitored over time by antigen testing.

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Figure 1. Right palm skin biopsy: panels A (× 6) and B (× 20), H&E staining, demonstrate dense granulomatous inflammation throughout the dermis with abundant histiocytes. No infectious organisms were identified. Panels C (× 10) and D (× 20), Grocott’s methenamine silver staining, demonstrate numerous yeast-like structures throughout the mid- and deep dermis (arrows). Some had surrounding pseudocapsules and demonstrated narrow-based budding. These deep dermal fungal microorganisms were morphologically consistent with H. capsulatum. Panfungal and histoplasmosis in situ hybridization studies were positive. Gram and Fite stains were negative.