Extrapulmonary Sarcoidosis following Immune Reconstitution in HIV Infection

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Introduction:

Sarcoidosis is a multisystem granulomatous disease driven by dysregulated CD4+ T cell activation and proliferation in response to unknown antigens in genetically predisposed individuals. Overactive, proliferative CD4 T cell populations mark this autoinflammatory response. In contrast, in HIV infection, CD4 T lymphocytes are markedly reduced through viral-mediated processes and disruption of TNF-alpha signaling. Because of these opposing physiologies, cases of incident or coincidental sarcoidosis are rarely observed in the setting of HIV infection.

Case:

A 36-year-old African American male presented to the hospital following a syncopal episode in the setting of a 1-week history of night sweats, headaches, decreased appetite and mild dyspnea. Physical exam revealed palpable cervical and axillary lymphadenopathy. Evaluation and imaging revealed the presence of pulmonary emboli without evidence of right heart strain, and the patient was initiated on anticoagulation. Further evaluation revealed undiagnosed HIV-1 infection with 155,000 viral copies/mL and absolute CD4 count of 580. Imaging showed diffuse lymphadenopathy and hepatosplenomegaly, and the patient underwent axillary lymph node biopsy before discharge.

Following discharge, he was initiated on highly active antiretroviral therapy (HAART) with bictegravir/emtricitabine/tenofovir. Five months later, outpatient monitoring revealed new hypercalcemia and worsening renal function. At that time, his CD4 count was 566, with an undetectable viral load. The patient was admitted to the hospital for further evaluation, which revealed serum calcium of 14.5 mg/dL, BUN 25 mg/dL, and Cr 3.68 mg/dL (baseline 1 mg/dL). Serum 1,25 hydroxy vitamin D level and serum ACE were markedly elevated. Parathyroid hormone was appropriately suppressed. Serum and urine protein electrophoresis and immunofixation were negative for monoclonal gammopathies. Lymph node biopsy from prior admission showed noncaseating granulomas without evidence of fungal, mycobacterial, or lymphoproliferative disorder. He had no evidence of pulmonary or cutaneous involvement. After extensive evaluation, a diagnosis of extrapulmonary sarcoidosis was made. The patient was initiated on prednisone and IV fluids, with subsequent normalization of serum calcium levels and resolution of his lymphadenopathy on outpatient follow-up.

Discussion:

The advent and advances of antiretroviral therapy have dramatically altered the care and prognosis of HIV infection. HAART initiation can produce a rapid reduction in viral burden and a more gradual recovery of CD4 T cells, referred to as immune reconstitution, which is typically first seen among memory CD4 T cells as early as 3-6 months following initiation of HAART. Immune reconstitution of CD4 T cell populations with the initiation of HAART may precipitate reactivation of opportunistic infections, such as tuberculosis or more rarely, subclinical autoimmune diseases, such as sarcoidosis, as seen in this patient. This case of extrapulmonary sarcoidosis exemplifies a rarely observed but clinically significant sequelae of immune reconstitution following initiation of HAART. HIV-positive patients should be monitored for signs and symptoms of immune-reconstitution-associated inflammatory syndromes when initiated on HAART.

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