Immune Restoration Syndrome Manifested by Pulmonary Sarcoidosis

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A 45-year-old women presented with a 4-month history of intermittent chest pain and increasing dyspnea with effort. She had no accompanying history of fever, chills, cough, sputum production, or other symptoms. She had been previously diagnosed, during an admission for cryptococcal meningitis, as having HIV infection and had been treated with highly active antiretroviral therapy for 16 months. The most recent serum values before onset of the dyspnea and chest pain were a viral load of less than 50 copies/mL and a CD4 cell count of 550 cells/mm^3.

Her examination was remarkable only for a few rales from both lung bases. Pulmonary function tests showed a mild decrease in the diffusing capacity of carbon monoxide. The oxygen saturation on room air was 99% at rest, 95–97% with walking, and 92–93% climbing stairs; the latter activity was associated with dyspnea.

Chest radiography revealed normal mediastinal outlines and a diffuse small nodular interstitial abnormality. Unenhanced helical CT of the thorax showed a normal mediastinum with no lymphadenopathy or evidence of pleural or skeletal disease. High-resolution CT revealed nodules having peribronchovascular and fissural distributions (Fig. 1A). Open lung biopsy of the right upper and middle lobes was performed; pathologic examination of the two 4 × 1 × 1 cm lung-tissue samples revealed numerous noncaseating granulomas and associated multinucleated giant cells. Parenchymal fibrosis and thickened septa were also seen. Histopathologic findings on stains for acid-fast bacilli and fungi were negative (Fig. 1B). The final clinicopathologic diagnosis was sarcoidosis. The patient showed marked clinical improvement with prednisone.

Highly active antiretroviral therapy has profoundly affected the treatment of HIV infection. The sustained suppression of viral replication has been shown to reduce mortality and to prolong life in patients with HIV infection [1]. Peripheral blood studies reveal a quantitative and qualitative immune restoration, an indicator of which is an increase in the CD4 cell blood count. Sarcoidosis affecting the lungs after the initiation of highly active antiretroviral therapy has been previously reported [2, 3]. In the cited reports, diagnosis was made after transbronchial biopsy; our pathologist had two large samples of lung tissue, allowing a more confident diagnosis of this disease.

Sarcoidosis is a disease of unknown cause resulting in the formation of distinctive granulomas. In a person with HIV infection, it is hypothesized that highly active antiretroviral therapy leads to a rapid increase in T lymphocytes and restoration of pathogen-specific immunity. In some patients, sarcoidosis is a manifestation of this immune restoration. Our patient showed the characteristic features of sarcoidosis, which is the presence of noncaseating granulomas in a perilymphatic distribution [4]. The high-resolution CT findings in our patient revealed small nodules in a peribronchovascular distribution, along the fissures and interlobular septal thickening. Our patient did not have mediastinal lymphadenopathy, and three of the four previous case reports of sarcoidosis in immune restoration syndrome also did not have this manifestation of sarcoidosis [2, 3]. The lung changes of small nodules in a perilymphatic distribution associated with a lack of mediastinal lymphadenopathy may be a pattern of pulmonary sarcoidosis after immune restoration with highly active antiretroviral therapy. Whether this becomes a characteristic set of imaging criteria remains to be seen from a large series in this group of patients.

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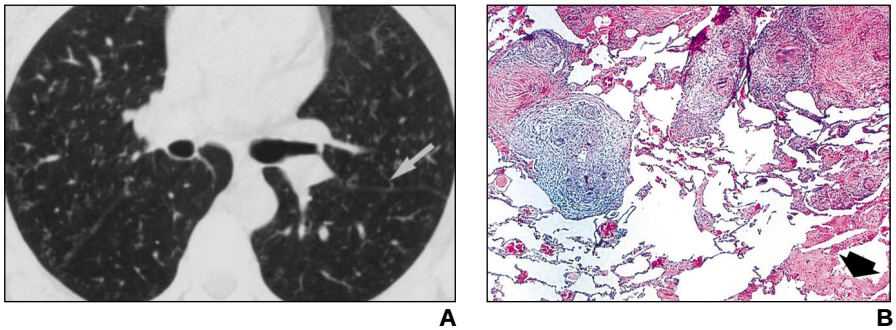

Fig. 1.—45-year-old woman with pulmonary sarcoidosis as manifestation of immune restoration syndrome.
A, High-resolution CT scan of lungs at level of bronchus intermedius reveals ill-defined small nodular opacities in peribronchovascular and fissural distribution. Small amount of interlobular septal thickening (*arrow*) is seen.
B, Photomicrograph of histopathologic specimen shows noncaseating tightly formed granulomas and epithelioid histiocytes and lymphocytes. Perilymphatic distribution of granulomas is evident. Normal lung parenchyma and small region of fibrotic interlobular septal thickening (*arrow*) are seen. (H and E, ×125)

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