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# A 50-Year-Old Man Presenting With Cough and an Endobronchial Lesion After Initiation of Highly Active Antiretroviral Therapy

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A 50-year-old black man with newly diagnosed HIV/AIDS, genital herpes, and latent syphilis presented with a nonproductive cough. The patient received a diagnosis of HIV and started highly active antiretroviral therapy (HAART) with emtricitabine/tenofovir disoproxil fumarate, darunavir, and ritonavir 2 months prior to presentation. CD4<sup>+</sup> count was 1/ $\mu$ L and viral load was 538,884 copies/mL prior to initiation of HAART. The patient endorsed compliance with all medications since diagnosis. The patient had a persistent, dry cough at time of HIV diagnosis that had acutely worsened during the 2 weeks leading to admission. He denied fevers, chills, hemoptysis, or dyspnea but did endorse drenching night sweats.

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## Physical Examination Findings

The patient was a thin-appearing man in no acute distress. Vital signs were as follows: heart rate, 123/min; BP, 139/92 mm Hg; temperature, 37.4°C; respiratory rate, 24/min; and oxygen saturation 97% while on room air. Significant physical examination findings included decreased breath sounds and faint rhonchi in the posterior left upper lung field. Cardiovascular, oropharyngeal, abdominal, and genitourinary examinations were unremarkable.

## Diagnostic Studies

Laboratory data on presentation were as follows: WBC, 10<sup>3</sup>/ $\mu$ L; lactic acid, 1.0 mM; CD4<sup>+</sup> count, 237/ $\mu$ L; HIV viral load, 646. Liver function tests and basic chemistries were unremarkable. Blood and urine cultures were

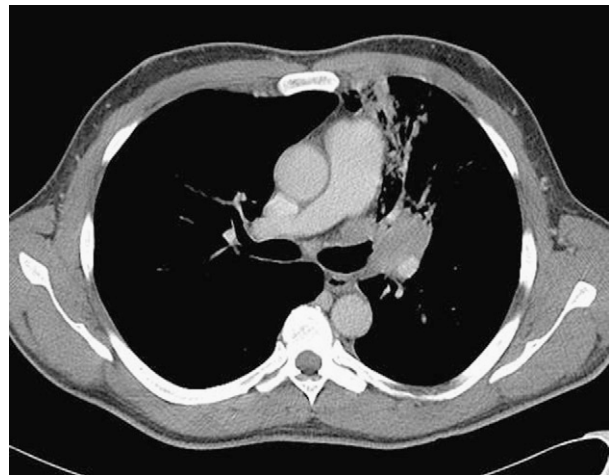


Figure 1 – Contrast-enhanced chest CT scan showing left hilar mass with infiltration into the proximal left upper lobe bronchi and distal mainstem bronchus.

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Figure 2 – Chest CT scan showing postobstructive volume loss with patchy centrilobular micronodular opacities in the left upper lobe.

negative. Contrast-enhanced chest CT scan showed a left hilar mass with infiltration into the proximal left upper lobe bronchi and distal mainstem bronchus (Fig 1). Left-sided mediastinal and hilar lymphadenopathy were also noted. There was also postobstructive volume loss with patchy centrilobular micronodular opacities in the left upper lobe (Fig 2). The patient underwent flexible fiber-optic bronchoscopy, which revealed two friable, polypoid, pearly endobronchial masses causing 80% and 60% obstruction of the left upper and left lower bronchi, respectively (Fig 3). Histopathologic results are shown (Figs 4, 5).

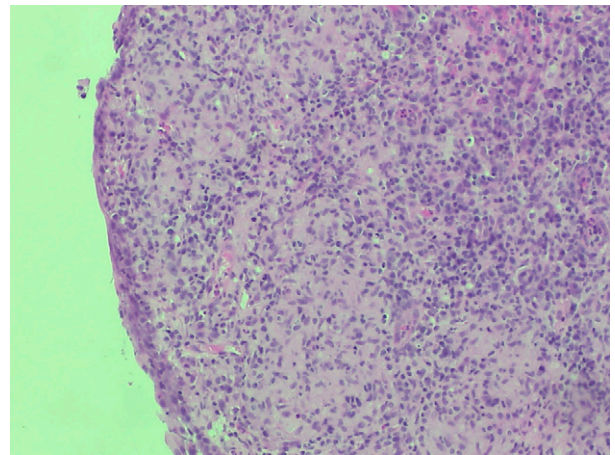


Figure 4 – Endobronchial biopsy demonstrating an ill-defined granuloma with numerous epithelioid histiocytes (hematoxylin and eosin, original magnification  $\times 100$ ).

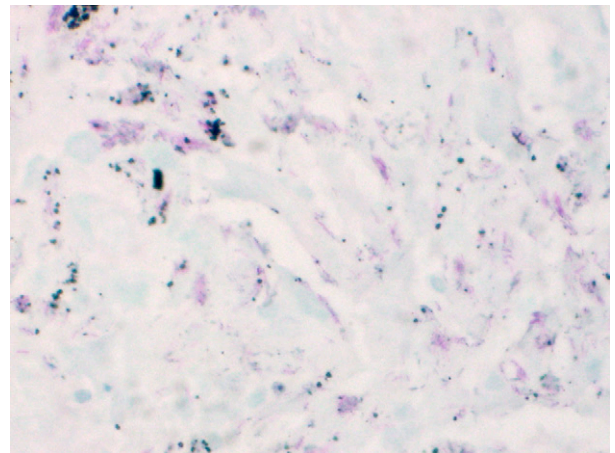


Figure 5 – Numerous acid-fast bacilli (AFB)-positive mycobacteria within epithelioid histiocytes (AFB, original magnification  $\times 400$ ).



Figure 3 – Friable, polypoid, pearly endobronchial lesions causing partial obstruction of the left upper and left lower bronchi.

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*What is the diagnosis?*

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*Diagnosis: Immune reconstitution inflammatory syndrome with *Mycobacterium avium* complex infection causing endobronchial lesions*

## Discussion

Immune reconstitution inflammatory syndrome (IRIS) is a rare but increasingly common disorder among patients with HIV in the era of highly active antiretroviral therapy (HAART). The paradoxical clinical deterioration of patients with IRIS is due to a robust and dysregulated inflammatory response to a previously treated or clinically silent underlying opportunistic infection in the setting of restored T-cell function in response to effective antiretroviral therapy. Nontuberculous mycobacteria (NTM) commonly serve as this antigenic reservoir, with *M avium* complex (MAC) being the most frequently encountered. Of all patients receiving HAART therapy, the incidence of IRIS is estimated at 17% to 32% and the incidence of MAC-associated IRIS is roughly 3.5%. The extent of immunosuppression prior to therapy, degree of viral suppression after therapy, and a marked recovery of CD4 memory T cells following initiation of HAART place patients at a higher risk of developing IRIS. In observational studies of MAC-associated IRIS, the median decline of HIV RNA load is 2.5 log<sub>10</sub> and median increase of T-cell lymphocytes is from 20 cells/μL to 120 cells/μL after initiation of HAART.

The precise pathophysiology of IRIS is not completely understood, but it is likely related to the dramatic reduction in HIV viral load that leads to a biphasic recovery of CD4 cells. Because the half-life of the HIV virus is only 1 to 4 days, it is possible to observe a 90% to 95% decline in viral load and subsequent increase of T lymphocytes in the first 1 to 2 weeks of antiretroviral therapy. A decline in cytokines also leads to a short-term increase in circulating CD4 cells via redistribution of cells previously aggregated in peripheral lymphatic tissues. Long-term rise of the CD4 lymphocyte population is achieved through clonal expansion of naive lymphocytes in the thymus occurring 4 to 6 weeks after initiation of HAART. This rapidly increased number of CD4 memory T lymphocytes mounts an exuberant local and systemic inflammatory response to a previously encountered antigen leading to clinical deterioration.

The clinical manifestations of NTM-IRIS vary widely but most commonly include peripheral lymphadenopathy, intraabdominal disease including abdominal pain, peritonitis or ascites, and/or pulmonary-thoracic disease. The most common symptoms of pulmonary involvement

include cough or wheezing (93% of patients), fever (80%), night sweats (73%), and dyspnea (47%). The severity of symptoms may range from mild respiratory symptoms to ARDS and respiratory failure. Symptoms may occur as early as 2 weeks after initiation of HAART, however, the median interval from therapy to diagnostic procedure is 10 weeks.

Diagnosis of IRIS is particularly difficult because there is not a universally accepted set of criteria for its definition. Generally the accepted features that should be present to make a diagnosis include the presence of AIDS with low pretreatment CD4 count, a response to HAART as seen by decreasing viral loads, a clinically significant inflammatory event, a temporal relationship with the initiation of HAART therapy, and the absence of an alternative cause for the clinical presentation. The diagnosis of pulmonary NTM-IRIS often requires bronchoscopy with BAL or tissue biopsy. Tissue will show granulomatous inflammation and mycobacteria on acid-fast staining.

Radiographic findings of NTM-IRIS most commonly consist of mediastinal or hilar lymphadenopathy, parenchymal infiltrates, cavitory lesions, and/or lung nodules. In this patient, CT scan findings included centrilobular micronodular opacities with a tree-in-bud morphology. This is most consistent with a primary bronchiolar infectious process, however, postobstructive pneumonia due to malignancy cannot be ruled out until tissue is collected. Endobronchial lesions may be a characteristic finding of MAC-associated IRIS and frequently result in partial or complete bronchial obstruction. In the proper clinical setting, newly discovered endobronchial lesions should raise suspicion for MAC-associated IRIS.

Treatment of IRIS has not been extensively evaluated, but appropriate antimicrobial treatment alone is often adequate in non-life-threatening presentations. HAART should typically be continued except in severe cases. Interruption of HAART and administration of corticosteroids may be required in patients with ARDS or tracheal compression from extensive lymphadenopathy. Although primary and/or secondary prophylaxis has not been shown to confer protection from MAC-associated IRIS, treatment of a diagnosed or suspected opportunistic infection is recommended 2 weeks prior to initiation of HAART to decrease the antigenic substrate for a pathologic inflammatory response.

Despite short-term morbidity associated with IRIS, long-term outcomes are typically favorable. Patients with IRIS are more likely to have successful viral

suppression and immune reconstitution at 24 months of HAART, particularly in patients who adhere to medication regimens.

### Clinical Course

Biopsy of this patient's endobronchial lesions showed granulomatous inflammation and numerous acid-fast bacilli (AFB)-positive mycobacteria within epithelioid lymphocytes. BAL showed 1+ AFB; nucleic acid amplification was negative for *Mycobacterium tuberculosis*. The patient was started on antimicrobial treatment of MAC with rifabutin, ethambutol, and clarithromycin, and sputum culture subsequently grew *M avium-intracellulare scrofulaceum*. The patient continued on HAART and MAC therapy upon discharge. He had rapid improvement of his symptoms, and a 6-month follow-up chest CT scan showed complete resolution of the endobronchial disease as well as the lymphadenopathy and micronodular opacities.

### Clinical Pearls

1. *IRIS should be considered when inflammatory signs or symptoms occur with a temporal relation to initiation, reinitiation, or change to a more effective combination HAART causing an increase in CD4 cell count, a decrease in HIV viral load or both.*
2. *MAC-associated IRIS typically presents clinically as localized lymphadenitis, abdominal pain, cough, fever, and/or night sweats, features that may be indistinguishable from active MAC.*
3. *MAC is the most commonly encountered NTM causing IRIS. Obstructive endobronchial lesions are a*

*characteristic finding of MAC-associated IRIS, however, tissue biopsy sample is often required for diagnosis.*

4. *Treatment requires appropriate antimicrobial therapy, however, interruption of HAART and corticosteroid therapy may be required in severe cases. Treatment of opportunistic infections prior to initiating HAART is generally recommended.*

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### Suggested Readings

French MA, Lenzo N, John M, et al. Immune restoration disease after the treatment of immunodeficient HIV-infected patients with highly active antiretroviral therapy. *HIV Med.* 2000;1(2):107-115.

Salama C, Policar M, Venkataraman M. Isolated pulmonary *Mycobacterium avium* complex infection in patients with human immunodeficiency virus infection: case reports and literature review. *Clin Infect Dis.* 2003;37(3):e35-e40.

Shelburne SA III, Hamill RJ. The immune reconstitution inflammatory syndrome. *AIDS Rev.* 2003;5(2):67-79.

Phillips P, Bonner S, Gataric N, et al. Nontuberculous mycobacterial immune reconstitution syndrome in HIV-infected patients: spectrum of disease and long-term follow-up. *Clin Infect Dis.* 2005;41(10):1483-1497.

Shelburne SA, Visnegarwala F, Darcourt J, et al. Incidence and risk factors for immune reconstitution inflammatory syndrome during highly active antiretroviral therapy. *AIDS.* 2005;19(4):399-406.

Murdoch DM, Venter WD, Van Rie A, Feldman C. Immune reconstitution inflammatory syndrome (IRIS): review of common infectious manifestations and treatment options. *AIDS Res Ther.* 2007;4:9.

Crothers K, Huang L. Pulmonary complications of immune reconstitution inflammatory syndromes in HIV-infected patients. *Respirology.* 2009;14(4):486-494.