Mycobacterium avium-Intracellulare Complex (MAC) Producing a Periportal Pseudotumor in a Patient With HIV and a Normal CD4 Count

Jessica Johnson, MD¹, Meghan Driscoll, MD², Michael Cohen, MD², and Douglas G. Adler, MD, FACP¹

¹Department of Gastroenterology and Hepatology, University of Utah School of Medicine, Salt Lake City, UT
²Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT

ABSTRACT

Mycobacterium avium-intracellulare complex (MAC) is an opportunistic infection typically associated with profound immunosuppression, such as AIDS. The presentation of disseminated MAC can be subtle and mimic systemic symptoms associated with lymphoma; abdominal pseudotumor is an exceptionally rare presentation. In the era of highly active anti-retroviral therapy (HAART), opportunistic infections are increasingly rare, and secondary prophylaxis for MAC may be discontinued after adequate therapy and immune reconstitution. Recurrence of disseminated MAC after adequate therapy may be due to macrolide resistance, but with an adequate CD4 T-cell count and undetectable HIV viral load, recurrence raises questions of more subtle immune dysregulation.

INTRODUCTION

Mycobacterial pseudotumor is an uncommon presentation of nontuberculous mycobacterial infection, and only a very small number of cases have been described in the literature.¹² The typical clinical presentation of disseminated Mycobacterium avium-intracellulare complex (MAC) is nonspecific and includes fever, weight loss, night sweats, fatigue, diarrhea, lymphadenopathy, and hepatosplenomegaly—features also seen in lymphoma. Anemia and elevated liver function tests, particularly isolated elevated alkaline phosphatase, may be diagnostic clues suggestive of disseminated MAC.²⁻⁴ However, because lymphoma continues to be a significant issue in HIV disease, even in the era of HAART, EUS with core FNA is essential to rule out lymphoma and establish a correct diagnosis.⁵

CASE REPORT

A 55-year-old man with a history of HIV/AIDS was admitted to our institution with malaise, unintentional weight loss, abdominal distension, nausea, and decreased urine output for several weeks. He was diagnosed with disseminated MAC in 2013 when his CD4 count was 53 cells/mm³. He was started on HAART, with good follow-up and adherence to therapy. He was treated with clarithromycin, ethambutol, and moxifloxacin for 1.5 years for his MAC with full resolution of disease. Antibiotics had been discontinued 6 months prior to admission in the setting of adequate response to HAART and negative MAC testing.

Physical exam was notable for cachexia and abdominal distension with a fluid wave. Admission labs showed CD4 count of 520 cells/mm³ and undetectable HIV viral load. AST was 38 U/L, ALT was 29 U/L, and bilirubin was 1.1 mg/dL; alkaline phosphatase was 491 U/L, and platelets and INR were normal. Serum ascites-albumin gradient on diagnostic paracentesis was 1.6 (serum albumin 2.6 g/dL, ascites albumin 1 g/dL).
Abdominal/pelvic computed tomography (CT) with and without intravenous (IV) contrast showed a markedly attenuated portal vein with cavernous transformation. An 4 x 2.9-cm infiltrating mass strongly suggestive of lymphoma was noted in the periportal/portacaval region along the posterior margin of the attenuated portal vein, causing occlusion of the main portal vein (Figure 1). Esophagogastroduodenoscopy (EGD) showed extrinsic compression in the duodenal bulb with mucosal edema and superficial erosions. Endoscopic ultrasound (EUS) revealed extensive celiac, peripancreatic, and periportal adenopathy, with many nodes being greater than 1 cm in diameter (Figure 2). The nodes were round to oval, well-demarcated, and hypoechoic. The portahepatis contained a hypoechoic, heterogeneous, calcified, irregularly shaped, approximately 4 x 3-cm solid mass lesion that strongly appeared malignant and was thought to be the cause of the duodenal compression. The mass was abutting but not arising from the pancreatic head. Tissue samples obtained by EUS-guided fine-needle aspiration (FNA) with a 22-gauge core needle revealed epithelioid histiocytes with abundant acid-fast bacilli and background of necrosis, consistent with MAC infection (Figure 3). Acid-fast culture results also confirmed MAC infection.

The patient was started on treatment for MAC with rifabutin, ethambutol, and moxifloxacin due to clarithromycin resistance, which may occur through a variety of mutations with extended therapy.6,7 A peritoneal drain was placed to allow the patient to drain ascites at home. He has since shown some clinical improvement, but the recurrence of systemic MAC despite 18 months of macrolide-based antibiotic therapy and immune reconstitution points to a poor prognosis. Second-line treatment will only be successful if his persistent focus of infection is removed or if an additional underlying immune deficiency is identified and addressed. Surgical consultation is pending as is insurance approval for interferon gamma injection.

DISCUSSION
Our patient’s presentation of portal hypertension caused by a mycobacterial mass or pseudotumor is extremely rare in
disseminated MAC. Overall incidence of disseminated MAC has fallen more than 10-fold since the introduction of effective HAART. As such, MAC may not initially be considered in the differential for a patient on HAART with immune recovery. MAC is an opportunistic pathogen, typically arising late in HIV progression in people with CD4 counts <50-100 cells/mm³, at which point primary prophylaxis is indicated. Disseminated MAC should be treated with 2 or more antimycobacterial drugs to prevent or delay the emergence of resistance, and this is generally initiated 2 weeks prior to initiation of HAART in order to decrease medication burden, reduce the risk of drug interactions, and reduce the risk of immune reconstitution inflammatory syndrome (IRIS). Secondary prophylaxis is continued until immune reconstitution is achieved with HAART.

Prior to effective HIV and MAC treatment, patients with disseminated MAC survived only a median 107–134 days, and secondary prophylaxis for MAC was life-long. With effective HIV treatment, secondary prophylaxis can now be discontinued in patients adherent to HAART with undetectable viral load an adequate increase in CD4 T-cell counts. Secondary prophylaxis guidelines suggest that risk of recurrence is low after 12 months of successful MAC treatment and a CD4 count of 100 cells/mm³ for at least 6 months after initiating HAART therapy. Studies have shown a low 11% relapse rate after discontinuation of secondary prophylaxis.

Our patient’s MAC recurrence in the setting of a normal CD4 count is still difficult to explain. Perhaps his course represents treatment failure due to acquired clarithromycin resistance, though an intact immune system should be protective in this situation. Alternatively, recurrence may be related to more subtle immune dysregulation independent of CD4 count and viral load. In non-HIV populations, immune dysfunction due to anti-gamma interferon antibodies has been associated with recurrent disseminated MAC infection. This has not been studied in the HIV-positive population, and our patient was not evaluated for anti-gamma interferon antibodies. However, we postulate that he has cell-mediated immune deficiency resulting in of interferon gamma deficiency, which persisted despite T-cell increase. In such cases, administration of interferon gamma has been successful in stimulating a protective immune response.

DISCLOSURES
Author contributions: J. Johnson and D. Adler generated the data and wrote the manuscript. M. Driscoll and M. Cohen generated data. All authors approved the document, and D. Adler is the article guarantor.

Received January 13, 2016; Accepted February 10, 2016

REFERENCES
1. Androulaki A, Papathomas TG, Liapis G, et al. Inflammatory pseudotumor associated with Mycobacterium tuberculosis infection. Int J Infect Dis. 2008;12(6):607–10.
2. Corti M, Palmero D. Mycobacterium avium complex infection in HIV/AIDS patients. Expert Rev Anti Infect Ther. 2008;6(3):551–63.
3. Lange CG, Woolley IJ, Brodt RH. Disseminated Mycobacterium avium-intracellulare complex (MAC) infection in the era of effective antiretroviral therapy: Is prophylaxis still indicated? Drugs. 2006;64(7):679–92.
4. Karakousis PC, Moore RD, Chaisson RE. Mycobacterium avium complex in patients with HIV infection in the era of highly active antiretroviral therapy. Lancet Infect Dis. 2004;4(9):557–65.
5. Rios A. HIV-related hematological malignancies: A concise review. Clin Lymphoma Myeloma Leuk. 2014;14(suppl 1):S96–103.
6. Brown-Elliott B, Nash K, Wallace RJ. Antimicrobial susceptibility testing, drug resistance mechanisms, and therapy of infections with nontuberculous mycobacteria. Clin Microbiol Rev. 2012;25(3):545–82.
7. Siberry GK, Abzug MJ, Nachman S, et al. Guidelines for the prevention and treatment of opportunistic infections in HIV-exposed and HIV-infected children: Recommendations from the national institutes of health, centers for disease control and prevention, the HIV medicine association of the infectious diseases society of america, the pediatric infectious diseases society, and the American Academy of Pediatrics. Pediatr Infect Dis J. 2013;32(suppl 2):i–KK4.
8. Horsburgh CR. Mycobacterium avium complex infection in the acquired immunodeficiency syndrome. N Engl J Med. 1991;324(19):1332–38.
9. Zeller V, Truffot G, Agher R, et al. Discontinuation of secondary prophylaxis against disseminated Mycobacterium avium complex infection and toxoplasmic encephalitis. Clin Infect Dis. 2002;34(5):662–67.
10. Dockrell DH, Edwards S, Fisher E. evolving controversies and challenges in the management of opportunistic infections in HIV-infected individuals. J Infect. 2011;63(3):177–86.
11. Wu U-I, Holland SM. Host susceptibility to non-tuberculous mycobacterial infections. Lancet Infect Dis. 2015;15(15):968–80.
12. O’Connell E, Rosen LB, LaRue RW, et al. The first US domestic report of disseminated mycobacterium avium complex and anti-interferon-γ autoantibodies. J Clin Immunol. 2014;34(8):928–32.
13. Nishimura T, Fujita-Suzuki Y, Yonemaru M, et al. Recurrence of disseminated Mycobacterium avium complex disease in a patient with anti-gamma interferon autoantibodies by reinfection. J Clin Microbiol. 2015;53(4):1436–38.
14. Vinh DC, Masannat F, Dzioba RB. Refractory disseminated coccidiodomycosis and mycobacteriosis in interferon-gamma receptor 1 deficiency. Clin Infect Dis. 2009;49(6):e62–e65.