CASE REPORT | PATHOLOGY

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

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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.[1,2] 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).

Figure 1. CT showing a large, solid mass (arrow) in the porta hepatis concerning for primary malignancy or metastasis.

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

Figure 2. 7.5 MHz EUS image of the same mass undergoing EUS-FNA with a 22-gauge core needle. The lesion is heterogeneous and hypoechoic.
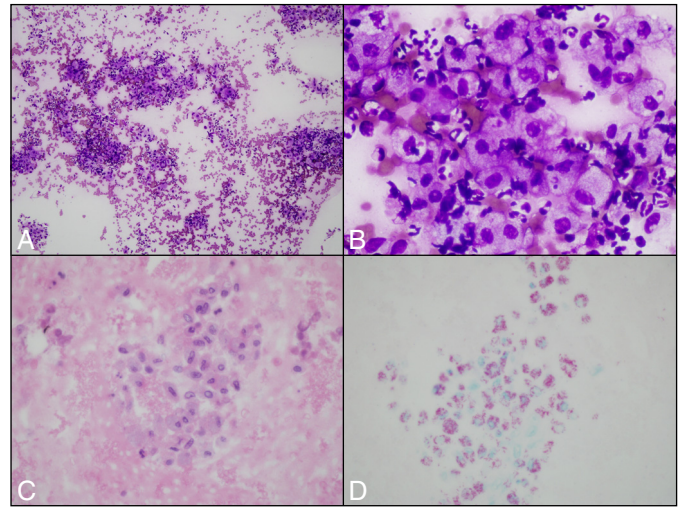

Figure 3. Cytologic images. (A) Diff Quick stain 100x showing clusters of epitheloid histiocytes with expanded granular eosinophilic cytoplasm. The clusters of histiocytes are surrounded by acute neutrophilic inflammation and occasional lymphocytes and red blood cells. (B) Diff Quick stain 600x showing the granular cytoplasmic contents of the epithelioid histiocytes. The histiocytes have large, coarse nuclei and abundant eosinophilic granular cytoplasm. Within the cytoplasm of the histiocytes are numerous filamentous organisms that aggregate in some of the histiocytes. Associated with the histiocytes are neutrophils and occasional lymphocytes. (C) H&E stain 600x showing a cluster of epithelioid histiocytes with expanded granular eosinophilic cytoplasm at the center of the image. Necrosis and degenerating inflammatory cells surround this cluster of histiocytes. (D) Acid-fast bacilli stain 600x showing a cluster of epithelioid histiocytes all containing numerous mycobacterium in their cytoplasm. The mycobacterium are the thin filamentous to aggregating magentastaining organisms contained within the cytoplasm of the histiocytes. Since the organism burden is heavy, the organisms appear as aggregates in most of the histiocytes on this stain. The histiocyte nuclei stain pale blue. The pink to tan background surrounding the histiocyte aggregate is necrotic material.

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.[1,2] Overall incidence of disseminated MAC has fallen more than 10-fold since the introduction of effective HAART.[7] 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/mm^3, at which point primary prophylaxis is indicated.[7,8,3] 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).[7] 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.[4,9] 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.[10] Secondary prophylaxis guidelines suggest that risk of recurrence is low after 12 months of successful MAC treatment and a CD4 count of 100 cells/mm^3 for at least 6 months after initiating HAART therapy.[7,9,10] Studies have shown a low 11% relapse rate after discontinuation of secondary prophylaxis.[9]

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.[6,7] 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.[11-13] 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 interferon gamma deficiency, which persisted despite T-cell increase. In such cases, administration of interferon gamma has been sucessful in stimulating a protective immune response.[14]

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