Disseminated *Mycobacterium avium-Intracellular* Complex in an HIV Patient with HIV with Massive Splenomegaly

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Background	Disseminated *Mycobacterium avium-intracellulare* complex (MAC) infection typically occurs in HIV-infected individuals with CD4+ T lymphocyte counts below 50 cells/mm³, manifesting as fever, chills, weight loss, fatigue, diarrhea, and night sweats. Massive splenomegaly in the context of disseminated MAC is a rare finding.
Summary	We present a case of an HIV-positive patient with a CD4+ T lymphocyte count of 10 cells/mm³ exhibiting massive splenomegaly and bulky mesenteric and retroperitoneal lymphadenopathy. Disseminated *Mycobacterium avium* complex was diagnosed following splenectomy.
Conclusion	The incidence of disseminated MAC has declined significantly due to advances in antiretroviral therapy (ART), though the prognosis remains poor. In HIV-infected patients with CD4+ counts below 50 cells/mm³ presenting with massive splenomegaly and bulky intra-abdominal lymphadenopathy, disseminated MAC should be strongly considered. Confirmation of the diagnosis requires a positive culture, which can be challenging due to the prolonged culture time. While treatment may involve CT-guided aspiration of mesenteric or retroperitoneal lymph nodes, splenectomy should be considered for both diagnostic and therapeutic purposes when aspiration is not feasible.
Key Words	HIV; splenomegaly; Mycobacterium avium-intracellulare complex
Abbreviations	human immunodeficiency virus (HIV-1) *Mycobacterium avium-intracellulare* complex (MAC) *Pneumocystis* pneumonia (PCP) antiretroviral therapy (ART) Grocott's methenamine silver (GMS) Periodic acid-Schiff (PAS)

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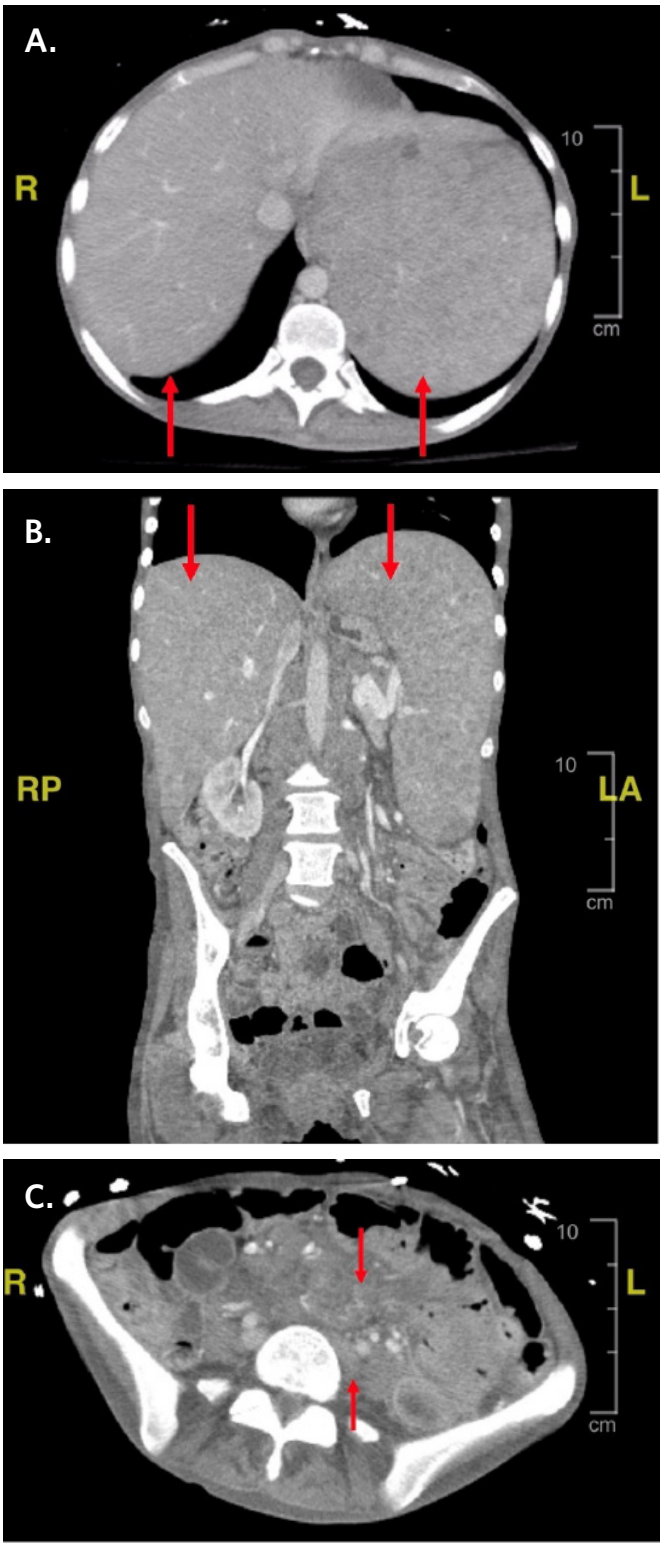
Case Description

A 37-year-old Caucasian female with known HIV-1 presented to the emergency room with a one-week history of shortness of breath, bilateral lower extremity edema, abdominal fullness, nausea, vomiting, and a 30-pound weight loss. She reported non-compliance with her prescribed HIV medication, Biktarvy. On examination, she was afebrile, pale, and cachectic, with a BMI of 16. Physical exam revealed a distended abdomen and palpable hepatosplenomegaly. Laboratory studies were notable for pancytopenia (hemoglobin 5.2 g/dL, white blood cell count 2.6 × 10^3/mm^3), hypoalbuminemia (2.3 g/dL), and a CD4+ T lymphocyte count of 10 cells/mm^3.

A CT scan of the abdomen (Figure 1) demonstrated marked hepatosplenomegaly (spleen measuring 23 × 15 × 9 cm) and retroperitoneal and mesenteric lymphadenopathy. The differential diagnosis included metastatic lymphoma, disseminated *Mycobacterium avium-intracellulare* complex (MAC), Castleman disease, and tuberculosis. The patient was started on PCP prophylaxis (atovaquone) and broad-spectrum antibiotics (vancomycin and cefepime). Cardiology was consulted, and a transthoracic echocardiogram showed no acute abnormalities. A multidisciplinary team (hematology/oncology, infectious disease, internal medicine, and general surgery) recommended splenectomy for both diagnostic and therapeutic purposes.

Pre-splenectomy vaccinations were deferred due to the low CD4+ count. The splenic artery was embolized by interventional radiology, and an open splenectomy was performed. The open approach was favored due to the concern for malignancy, the patient's body habitus, and the massive splenomegaly. Postoperatively, infectious disease recommended continuing atovaquone and resuming Biktarvy. Blood cultures obtained on admission subsequently grew *Mycobacterium avium* complex approximately three weeks later.

Figure 1. Abdominal and Pelvic CT Imaging with IV Contrast. Published with Permission



(A) *Axial view demonstrating hepatosplenomegaly. The spleen measures approximately 23 × 15 × 9 cm at its largest dimensions.* ***(B)*** *Coronal view confirming hepatosplenomegaly.* ***(C)*** *Axial view of the pelvis demonstrating mesenteric and retroperitoneal lymphadenopathy.*

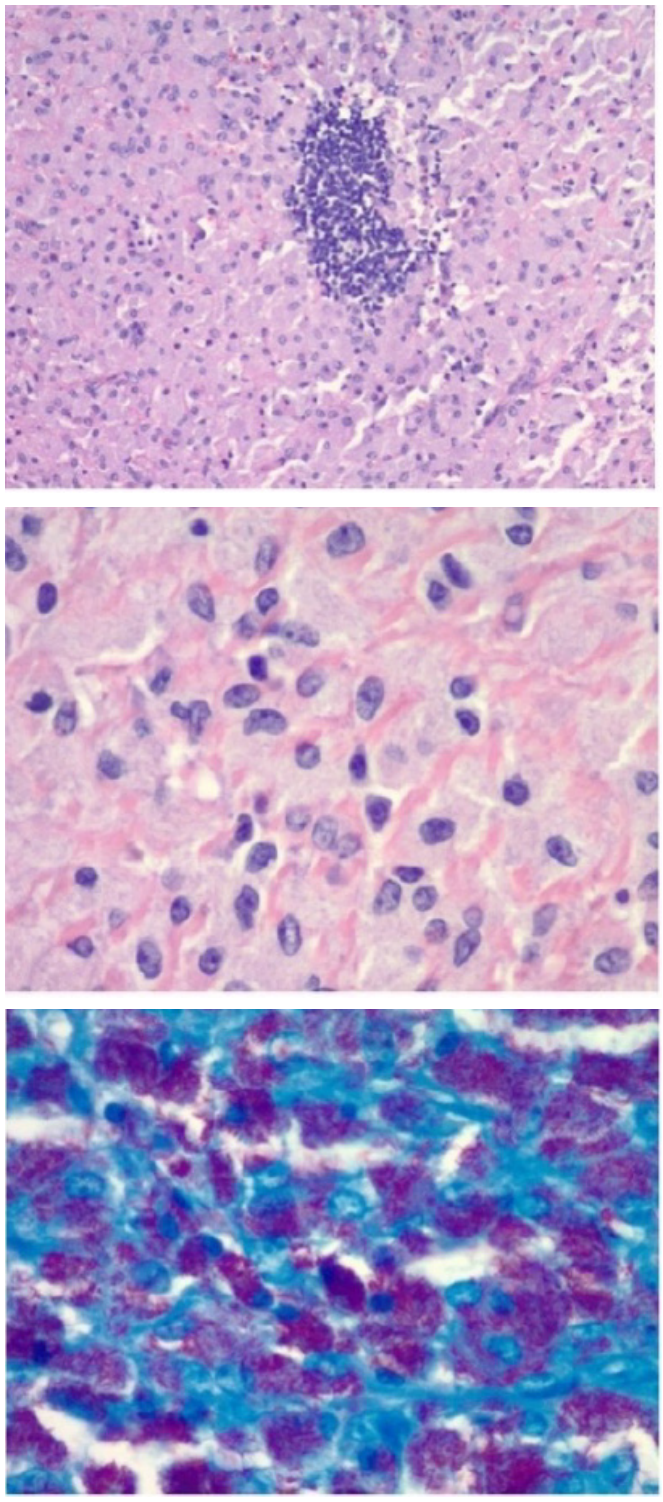
Pathology revealed a spleen measuring 26.0 × 17.0 × 11.5 cm and weighing 2201 grams. Ziehl-Neelsen staining demonstrated macrophages engorged with acid-fast organisms (Figure 2). Grocott methenamine silver (GMS) and periodic acid-Schiff (PAS) stains were negative. Given the positive acid-fast bacilli, disseminated MAC was presumed, and the patient was started on azithromycin, rifabutin, and ethambutol. The patient was discharged with a plan for post-splenectomy vaccinations in clinic.

Discussion

Disseminated *Mycobacterium avium-intracellulare* complex (MAC) infection occurs in HIV-infected patients with CD4+ T lymphocyte counts below 50 cells/mm^3. In the pre-HAART era, the reported incidence of disseminated MAC in patients with advanced immunosuppression ranged from 20% to 40%,[1,2] but has significantly decreased with advances in ART. Disseminated MAC typically presents with fever, weight loss, fatigue, diarrhea, night sweats, abdominal pain, anemia, and elevated alkaline phosphatase.[3] Massive splenomegaly as a manifestation of disseminated MAC in HIV-infected individuals is rare, with only a few cases reported in the literature through retrospective reviews,[4] imaging analysis,[5] and individual case presentations.[6–8] The criterion for massive splenomegaly is enlargement of the spleen measured by size or weight. The European Association for Endoscopic Surgery defines massive splenomegaly based on preoperative imaging, with a maximum splenic diameter exceeding 20 cm.[9,10] Alternatively, a weight criterion can also be used, defining massive splenomegaly as a spleen weighing more than 1000 g.

CT findings in disseminated MAC often include marked hepatomegaly, splenomegaly, multiple intra-abdominal lymph nodes larger than 10mm in diameter, and jejunal wall thickening.[5] Nyberg et al. reported that 84% of patients with disseminated MAC have CT findings of large, bulky retroperitoneal and mesenteric lymphadenopathy, with often normally-sized peripheral lymph nodes.[11] Our patient's CT scan demonstrated both hepatosplenomegaly and mesenteric and retroperitoneal lymphadenopathy. Furthermore, a significant proportion of patients with disseminated MAC have a history of at least one prior AIDS-defining illness, such as Kaposi sarcoma, lymphoma, *Pneumocystis carinii* pneumonia, cytomegalovirus infection, esophageal candidiasis, toxoplasmosis, or cryptosporidiosis.[5]

Figure 2. Histopathological Analysis. Published with Permission



(A) *Hematoxylin and eosin (H&E) stain, 10x magnification.* ***(B)*** *H&E stain, 45x magnification.* ***(C)*** *Ziehl-Neelsen (acid-fast bacillus) stain, 45x magnification.*

Treatment of disseminated MAC requires a positive culture for appropriate antibiotic selection, but obtaining cultures can be challenging due to the prolonged time required for mycobacterial growth. Nyberg et al. recommend CT-guided percutaneous needle aspiration of intra-abdominal lymph nodes as a method to obtain tissue for diagnosis of MAC.[11] Due to the rarity of massive splenomegaly in disseminated MAC, there is no established surgical consensus. In our case, a multidisciplinary approach guided the decision for open splenectomy, considering factors such as spleen size, preoperative malnutrition, and low body mass index. Laparoscopic splenectomy for massive splenomegaly has been associated with increased morbidity, longer postoperative stays, higher conversion rates, and a substantially greater risk of postoperative complications compared to open splenectomy.[12,13]

Diagnosing MAC infection relies on culturing the organism from a normally sterile body site. While cultures from any such site can be diagnostic, blood, bone marrow, lymph nodes, and liver are the most commonly involved tissues and, thus, the preferred samples for culture.[14] The histopathological findings in this case are consistent with disseminated MAC infection. The presence of poorly defined granulomas with pale blue, striated histiocytes harboring mycobacteria is characteristic of this disease.[15] While Klatt et al. describe necrotic areas filled with inflammatory cells and nuclear debris as a potential histological feature of disseminated MAC, the observed findings, in this case, support a diagnosis nonetheless.[15]

In patients presenting with massive splenomegaly, disseminated MAC should be a high consideration in the differential diagnosis. Due to the critical need for a definitive diagnosis to guide potentially life-saving treatment and the often lengthy turnaround time for positive cultures, a combined diagnostic and therapeutic splenectomy should be strongly considered in this setting to obtain tissue for definitive diagnosis of MAC, allowing for the prompt initiation of appropriate targeted therapy.

Conclusion

Disseminated MAC infection has become increasingly rare due to advances in antiretroviral therapy (ART). However, in HIV-infected patients with CD4+ counts below 50 cells/mm^3 presenting with massive splenomegaly and bulky intra-abdominal lymphadenopathy, disseminated MAC should remain a diagnostic consideration. A positive culture is required for definitive diagnosis and targeted treatment. The prolonged time required for culture growth can pose a diagnostic challenge. Treatment strategies include CT-guided aspiration of mesenteric or retroperitoneal lymph nodes. When CT-guided aspiration is not feasible, splenectomy should be considered for both diagnostic and therapeutic purposes.

Lessons Learned

Disseminated MAC should be included in the differential diagnosis for patients presenting with massive splenomegaly, particularly in the context of advanced HIV infection. Given the poor prognosis associated with disseminated MAC, prompt diagnosis and treatment are crucial. While a positive culture is the gold standard for diagnosis, treatment should not be delayed solely due to the time required for culture growth.

Therefore, in cases of massive splenomegaly where less invasive diagnostic methods are inconclusive or unavailable, diagnostic and therapeutic splenectomy should be strongly considered to obtain tissue for analysis and expedite the initiation of appropriate therapy.

In patients exhibiting resistance or non-compliance with HIV treatment, a broader differential diagnosis, including other opportunistic infections and potential lymphomas, must be considered alongside disseminated MAC. This underscores the importance of a comprehensive diagnostic approach and emphasizes the need for patient adherence to ART for optimal management and improved outcomes.

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