Case Report

Mycobacterium Avium Complex: A Rare Cause of Pancytopenia in HIV Infection

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Abstract

Opportunistic infections in HIV infection are challenging to diagnose and treat, especially when the prevalence of disease is rare. Mycobacterial infections can have debilitating morbidity and mortality in HIV individuals if prompt diagnosis and treatment is not done. A 33-year-old African-American female presented for the complaints of easy fatigability, unintentional weight loss, and diarrhea of 3-month duration. Initial laboratory results suggested bicytopenia; however, there was an initial delay of a couple of months in evaluation because of her poor compliance. A final diagnosis of HIV with a low CD4 count of 9 cells/mm^3 and disseminated *Mycobacterium avium* complex (MAC) infection was made. She was started on anti-MAC therapy, followed by antiretroviral therapy however soon succumbed to her illness.

Keywords: HIV, *Mycobacterium avium* complex, pancytopenia

Introduction

Mycobacterium avium complex (MAC) was rare until 1982 when it was found to be associated with HIV infection. Thereafter, due to increased awareness, there was a sharp rise in reporting of MAC infection.[1] MAC incidence rate amongst the individuals with HIV was reported as high as 43% in one of the studies conducted in 1992.[2] Currently, it has gone down significantly (0.2%) due to the impact of effective antiretroviral therapy (ART) and good patient compliance.[3]

Case Report

A 33-year-old African-American female with no significant past medical history was evaluated as an outpatient for the complaints of 3-month duration of tiredness, diarrhea, and weight loss. Clinical examination suggested pallor, bilateral cervical lymphadenopathy, and splenomegaly. Further laboratory and imaging studies were ordered, but the patient did not follow-up for the next 2 months. Later, she reported to the emergency room for worsening symptoms. On examination, she was found to be apprehensive with vital signs of temperature of 98.9°F, a pulse rate of 140 beats/min, blood pressure of 90/60 mmHg, and a respiratory rate of 18 breaths/min. Laboratory examination showed a sodium level of 127 mmol/L, a potassium level of 3.9 mmol/L, a chloride level of 98 meq/L, a bicarbonate level of 19 meq/L, a blood urea nitrogen level of 21 mg/dL, a creatinine level of 1.11 mg/dL, a hemoglobin level of 4 gm/dL, a platelet count of 21,000 cells/mm^3, and a total leukocyte count of 6100 cell/mm^3 (DLC-P56, L11, M13, band cells 14, E3, and B3). Peripheral blood smear showed many hypochromic red blood cells (RBCs), many polychromatophilic RBCs, moderate teardrops, few target cells, and spherocytes.

In view of hypotension, breathlessness, severe anemia, and thrombocytopenia, she received urgent packed RBC transfusions (4 units) and single-donor apheresis platelets (SDAPs) (2 units). Computed tomography (CT) suggested massive splenomegaly and retroperitoneal, mediastinal, and cervical lymphadenopathy [Figure 1a-c]. Her rapid HIV test came positive with a CD4 count of 9 cells/mm^3 and HIV viral load of 147,830 copies/ml. She was started on PCP prophylaxis problem (trimethoprim/sulfamethoxazole)

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and MAC prophylaxis (tablet azithromycin 1200 mg once a week).

In view of immunosuppression and ongoing suspected infection, laboratory works for opportunistic diseases were carried out including blood, urine cultures and lymph node and bone marrow (BM) biopsies. Both BM and lymph node aspirates were positive for acid-fast bacillus (AFB) stain [Figure 2] based on which she was started on preemptive treatment for disseminated MAC (tablet azithromycin 500 mg once daily, tablet ethambutol 15 mg/kg/day, and tablet rifabutin 300 mg once daily). Later, blood and BM cultures confirmed *M. avium intracellulare*. During her hospital stay, she gradually started feeling better with improving laboratory parameters [Graph 1]. Two weeks later, she was started on ART (efavirenz, emtricitabine, and tenofovir) and was discharged. At follow up, she expired a month later probably related to nonadherence to medications and superadded infections.

Discussion

MAC refers to the infection caused by either *M. avium* or *M. intracellulare*. MAC presentation is variable and depends on the level of immunity in an individual. Isolated pulmonary infection is the most common form in an immunocompetent individual.[4] In contrast, focal lymphadenitis and DMAC are the common forms of MAC infection in HIV-positive individuals.[5]

HIV infection has a well-known association with MAC. Among HIV patients, individuals with CD4 count <50 cells/μL are at highest risk. Our patient was recently diagnosed with HIV infection and had low CD4 count, putting her at high risk of acquiring MAC infection. Other than HIV, individuals suffering from hematological malignancies, myelofibrosis, and hemophagocytic lymphohistiocytosis are also prone to acquire MAC infection.[6] Important to note that risk of

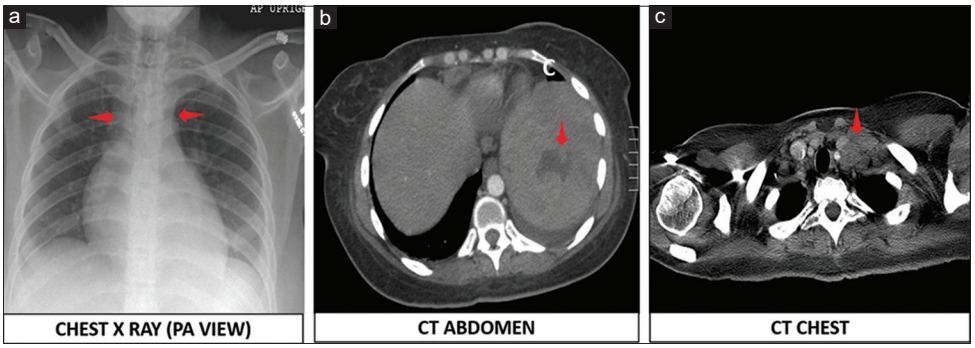


Figure 1: (a) Chest X-ray showing mediastinal fullness. (b) Transverse view of computed tomography pelvis showing hypoechoic lesion with splenomegaly. (c) Transverse view showing mediastinal lymph nodal enlargement

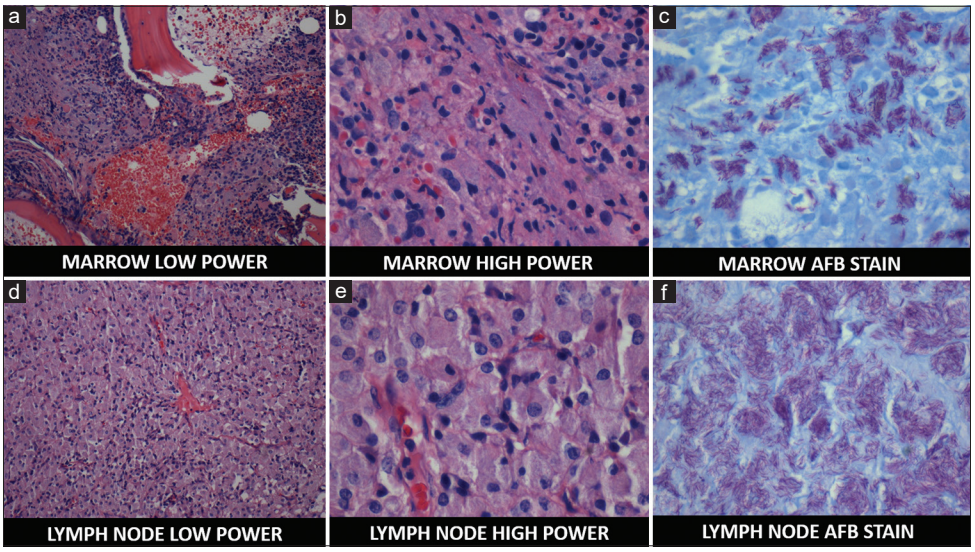
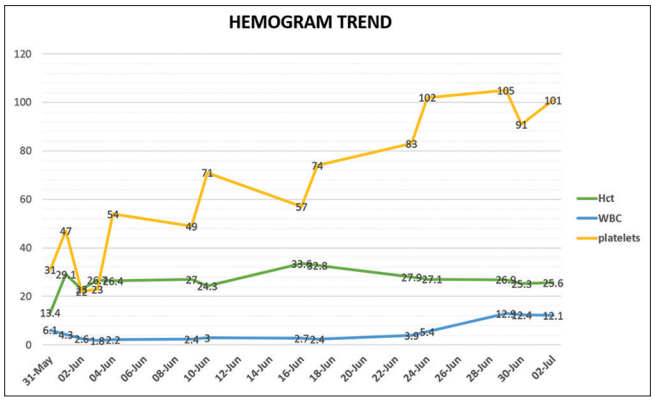


Figure 2: (a) Section from the bone marrow trephine biopsy showing vaguely nodular aggregates of foamy histiocytes along with lymphocytic cell infiltrates. The normal hematopoietic lineage elements are markedly reduced (Hematoxylin and Eosin, ×200). (b) Closer view of the bone marrow trephine biopsy section showing foamy histiocytic cell infiltrates along with lymphocytes and plasma cells (Hematoxylin and Eosin, ×400). (c) Abundant acid-fast bacilli are seen within the histiocytes (Ziehl–Neelsen stain, ×1000). (d) Section from the lymph node biopsy showing effaced nodal architecture with sheets of foamy histiocytes and many lymphocytic cell infiltrates (Hematoxylin and Eosin, ×200). (e) High-power view of the section from the lymph node biopsy showing foamy histiocytes (Hematoxylin and Eosin, ×400). (f) Numerous acid-fast bacilli are seen within the histiocytes (Ziehl–Neelsen stain, ×1000)



Graph 1: Graphical trend in the hematological parameters (hematocrit, platelet count, and leukocyte count)

acquiring infection does not vary by ethnicity, gender, or route of transmission (inhalation vs. ingestion).

As mentioned above, disseminated MAC and focal lymphadenitis are the most common presentations for MAC in HIV. Interesting to note that localized lymphadenitis is usually the result of immune reconstitution inflammatory syndrome and not the infection *per se*, which occurs approximately 4 weeks after starting ART. Symptom wise, diarrhea, abdominal pain, fever, and weight loss are the most common symptoms. Although rare, it is important to remember the unusual presentations of MAC infection such as spinal mass, mastitis, osteomyelitis, and granulomatous hepatitis.

The most important challenge in MAC infection is the early detection and prompt treatment. Radiological imaging constitutes an integral component of investigational tool for MAC infection. CT helps in differentiating focal lymphadenitis from disseminated MAC.

Microbiological identification is the most crucial part of diagnosis as imaging and clinical examinations are supportive but not confirmatory for MAC diagnosis. Isolation and culture of MAC can be from anywhere, for example, blood, lymph node, and BM aspirates (BMAs). Blood culture is the preferred initial diagnostic test due to its simplicity and less invasive technique. However, BACTEC cultures have their own limitations – (1) Unlike in disseminated MAC, in localized MAC infection, blood culture is almost always negative, (2) it takes at least 1–2 weeks for detection of mycobacterial growth, and (3) there are no differentiating features in colony morphology to differentiate between *Mycobacterium tuberculosis* (MTB) versus non-MTB species. Nowadays, DNA probes detecting polymerase chain reaction-amplified tuberculosis DNA fragments are used for the subclassification.

Hussong *et al*. compared the blood and BMA culture yield in their institutional retrospective study of 86 HIV-positive patients. Among 30 MAC-positive blood cultures, only 17 had concomitant positive BMA cultures and only 9 BM specimens were positive for AFB staining.[7] In another study, Farhi *et al*. found that only one case of 14 positive BM biopsy culture specimens was AFB stain positive.[8] Detection of granulomas in BM trephine biopsies can assist in the diagnosis of MAC but is nonspecific and can occur in many other infectious diseases such as those caused by *Cryptococcus neoformans* and histoplasmosis. It is very important to know that granuloma may be missed if not searched properly. Farhi *et al*. reported to have missed granuloma during initial microscopic examination in 6 of 14 MAC cases.[8] Similarly, Hussong *et al*. found that only 50% of MAC-infected patients were positive for granulomas.[7] These findings suggest that blood culture has the highest yield and BM cultures, AFB stain, and granuloma detection are good complementary investigations, especially in cases of pancytopenia. Detection of rare infections is challenging, especially in immunocompromised states.[9-11]

Combinations of antimycobacterial are available, and treatment regimen depends on the severity of MAC disease. Macrolides in combination with rifampin and ethambutol are considered as the cornerstone for the treatment of MAC.

Conclusion

MAC is one of the important differentials while evaluating pancytopenia in an immunocompromised individual. While blood and BM culture might take time for results, AFB stain of BMA can be quick and might be helpful in guiding treatment.

Take-home message

1. Blood cultures have the highest yield and should be the initial investigation of choice
2. All BM biopsy specimens from HIV patients should also be tested with AFB staining as it has the fastest detection rate, and if positive, it allows for prompt initiation of anti-MAC therapy
3. Cytopenia can be due to a variety of causes and it is necessary to work up for all differentials including MAC, autoimmune diseases, and malignancies.[12]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nightingale SD, Byrd LT, Southern PM, Jockusch JD, Cal SX, Wynne BA. Incidence of *Mycobacterium avium-intracellulare* complex bacteremia in human immunodeficiency virus-positive patients. J Infect Dis 1992;165:1082-5.
2. Chaisson RE, Moore RD, Richman DD, Keruly J, Creagh T. Incidence and natural history of *Mycobacterium avium*-complex infections in patients with advanced human immunodeficiency virus disease treated

with zidovudine. The zidovudine epidemiology study group. Am Rev Respir Dis 1992;146:285-9.
3. Buchacz K, Lau B, Jing Y, Bosch R, Abraham AG, Gill MJ, *et al.* Incidence of AIDS-defining opportunistic infections in a multicohort analysis of HIV-infected persons in the United States and Canada, 2000-2010. J Infect Dis 2016;214:862-72.
4. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, *et al.* An official ATS/IDSA statement: Diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367-416.
5. Fordham von Reyn C, Arbeit RD, Tosteson AN, Ristola MA, Barber TW, Waddell R, *et al.* The international epidemiology of disseminated *Mycobacterium avium* complex infection in AIDS. International MAC study group. AIDS 1996;10:1025-32.
6. Griffith DE. Treatment of *Mycobacterium avium* complex (MAC). Semin Respir Crit Care Med 2018;39:351-61.
7. Hussong J, Peterson LR, Warren JR, Peterson LC. Detecting disseminated *Mycobacterium avium* complex infections in HIV-positive patients. The usefulness of bone marrow trephine biopsy specimens, aspirate cultures, and blood cultures. Am J Clin Pathol 1998;110:806-9.
8. Farhi DC, Mason UG 3rd, Horsburgh CR Jr. The bone marrow in disseminated *Mycobacterium avium-intracellulare* infection. Am J Clin Pathol 1985;83:463-8.
9. Dhibar DP, Sahu KK, Dhir V, Singh S. Immune thrombocytopenia as a presenting manifestation of tuberculosis- challenge in resource constraint settings. J Clin Diagn Res 2016;10:OD01-2.
10. Sharma S, Singh P, Sahu KK, Rajwanshi A, Malhotra P, Naseem S. Histoplasmosis in pleural effusion in a 23-year-old man with mixed-phenotype acute leukemia. Lab Med 2017;48:249-52.
11. Sahu KK, Yanamandra U, Kakkar N, Malhotra P. Rare presentation of mucormycosis in aplastic anaemia: Isolated hepatic mucormycosis. Mycopathologia 2019;184:347-8.
12. Lal A, Mishra AK, Sahu KK, Noreldin M. Scurvy of modern age: Rare presentation with pancytopenia. Blood Cells Mol Dis 2019;77:76-7.