

# Disseminated mycobacterium avium complex infection mimicking lymphoproliferative disorder in a kidney transplant recipient

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## Abstract

Disseminated Mycobacterium avium complex (MAC) infections are commonly reported in patients infected with the human immunodeficiency virus (HIV), although MAC infections are also reported in such immune-compromised patients as renal transplant recipients. In this group of patients, the clinical course is generally atypical, and treatment strategies can differ. Herein we present the case of a disseminated infection caused by MAC in a kidney transplant recipient who presented with abdominal pain, fever and generalized intra-abdominal lymphadenopathy.

**Keywords:** Disseminated mycobacterium avium complex; kidney; transplant

## INTRODUCTION

The term *M. avium* complex (MAC) encompasses multiple species, but specifically *M. avium* and *M. intracellulare*. Among the nontuberculous mycobacteria (NTM), MAC is the most common cause of pulmonary involvement worldwide (1). Disseminated MAC infection, on the other hand, is a common extrapulmonary presentation that occurs primarily in severely immune-compromised patients, such as those with advanced HIV infection, hematologic malignancy, a history of immunosuppressive therapy or therapy with tumor necrosis factor-alpha inhibitors (2). MAC infections have been reported in kidney transplant recipients, as presenting with diverse clinical symptoms. Here, we report on a kidney transplant recipient with disseminated MAC infection mimicking lymphoproliferative disorder who presented with abdominal pain, weight loss, nausea and vomiting.

## CASE REPORT

A 50 year old male patient with renal failure of unknown origin received a deceased donor kidney transplant in 1997. The patient underwent maintenance therapy with tacrolimus, prednisone and mycophenolate mofetil until 2017. He started hemodialysis (HD) and was told in

September 2017 to stop immunosuppressive therapy as a result of graft failure due to chronic allograft nephropathy. He was a lifelong nonsmoker with no known underlying pulmonary disease.

Upon admission at the beginning of June 2018, the patient's chief complaint was several weeks of worsening abdominal pain, accompanied by weight loss and fever. The abdominal pain was diffuse and intermittent, lasting from minutes to hours, and associated with nausea and vomiting. He reported no complaint of cough or dyspnea. Laboratory data at that time revealed a WBC count of 17800cells/mL, hematocrit of 26%, and creatinine of 11.5 mg/dL. His urinalysis was normal, revealing no infection-related finding. A human immunodeficiency virus (HIV) screen was negative. A chest X-ray was normal, revealing no mass or infiltration. Upon physical examination, the patient was afebrile, and his abdomen was tender with hypoactive bowel sounds. He had no submandibular, cervical or inguinal lymphadenopathy (LAP). A computerized tomography (CT) scan of the abdomen showed a possible thickening of the small bowel wall with enlarged mesenteric, para-aortic and paracaval multiple LAPs of about 35mm in size. A thorax CT was normal without any LAP or parenchymal involvement. The patient

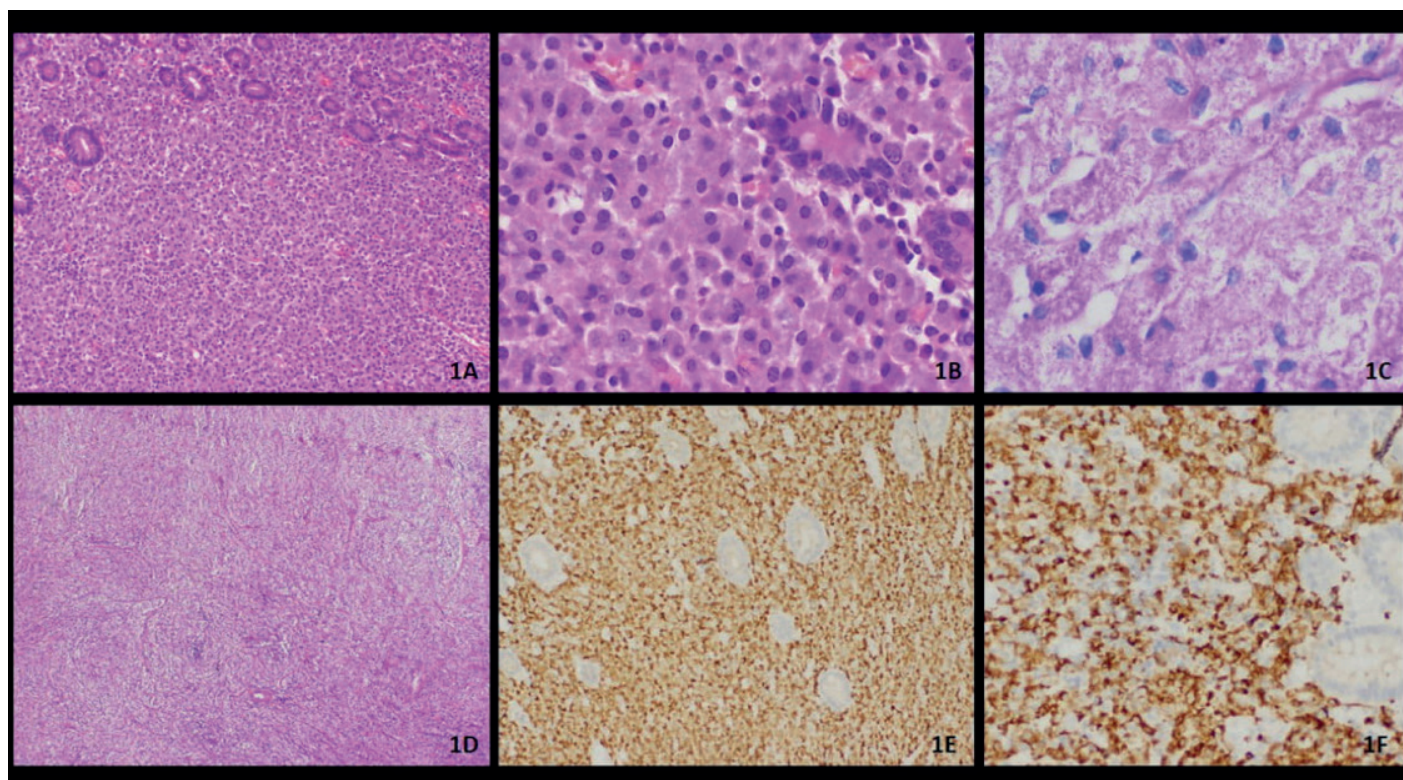
**Received:** 17.02.2020 **Accepted:** 30.09.2020 **Available online:** 22.03.2021

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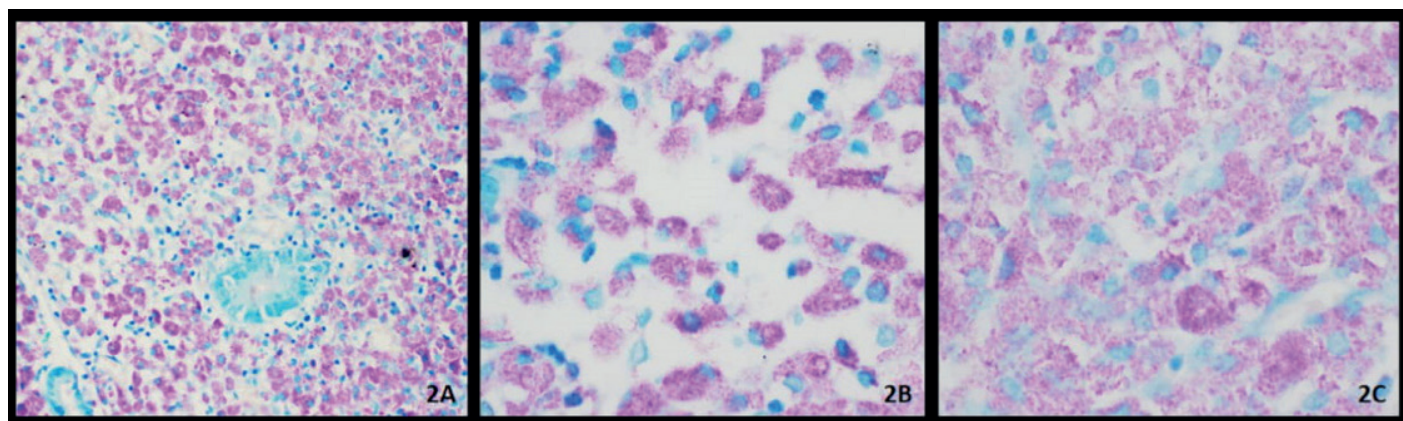
underwent an exploratory laparotomy with a small bowel resection and lymph node sampling of the ileac area.

A histopathological examination of the small bowel (ileum) and lymph node dissection material revealed diffuse CD68 positive histiocytes with focal granulomas throughout the ileum and lymph nodes (Fig 1). Many acid-fast bacilli in these histiocytes were highlighted with Ehrlich- Ziehl-Neelsen (EZN) histochemical staining (Fig 2). These histological findings were considered to be consistent with a disseminated MAC infection, although no example of the specimen was sent for culture. Subsequent blood, stool and urine cultures were all negative for MAC and other microorganisms. The patient was also evaluated with a cranial CT, which also reported normal findings.

An infectious disease consultant recommended initiating treatment for MAC with a regimen of ethambutol 25mg/kg per os (PO) three times a week after dialysis, rifampin 600 mg PO daily and azithromycin 500 mg PO daily. We learned at this time that the patient was still on tacrolimus and mycophenolate mofetil up until his last hospital admission, although we had stopped them by starting HD. After the fifth day of MAC treatment, the patient developed sustained fever. Serial blood cultures were obtained and the patient was started on meropenem and vancomycin. Upon becoming hemodynamically unstable, the patient was transferred to the intensive care unit. He continued to decline clinically, prompting intubation and the need for vasopressor support. After a hospital course, he died of resistant septicemia one month after admission.



**Figure 1.** (A) Effacement of the crypts with diffuse histiocyte infiltration throughout the mucosa and the bowel wall (H&E, x40), (B) High power view of the infiltrated histiocytes (H&E, x 200), (C) The cytoplasm of histiocytes were found to be filled with bacilli (H&E, x600), (D) Diffuse histiocyte infiltration with incomplete and complete granulomas throughout the lymph nodes (H&E, x40), (E, F) Diffuse histiocyte infiltration highlighted with CD68



**Figure 2.** Many acid-fast bacilli in the cytoplasm of histiocytes were highlighted with Ehrlich- Ziehl-Neelsen (EZN) histochemical staining



## DISCUSSION

NTM is a broad group of environmental organisms that have been often linked to infections in immune-compromised patients, such as solid organ transplantation recipients. The incidence and prevalence of NTM infections, including mainly those associated with MAC, are increased in this patient group (3). Reported data primarily takes the form of a case report or case-control form. Since clinical presentations differ significantly, delays in diagnosis are common. MAC infection usually presents in pulmonary, disseminated or lymphadenitis forms. In patients without HIV infection, underlying lung disease is a significant risk factor for MAC infection (4). MAC lymphadenitis generally occurs in children. The disseminated form is uncommon in solid organ recipients, being related rather to advanced immune-compromised conditions such as AIDS and/or lymphomas in patients whose CD4 count has fallen below 50 cells/ $\mu$ L (5).

The pathogenesis of MAC related disseminated infection in a transplantation setting is yet to be understood. The drugs used in solid organ transplantations (calcineurin inhibitor, antimetabolite, and corticosteroid) act in the early stages of T-cell proliferation and block cell-mediated immunity. The impaired cell mediated killing of MAC infected macrophages contributes to the unchecked proliferation and development of the disseminated disease. Colonization of the gut or bronchoalveolar system is the leading trigger point (6), although it is as yet unknown why over immunosuppression occurs in transplant patients evoking MAC to cause infection.

The risk factors and prognosis related to MAC infections in transplantation patients are not well defined. In a case-control study, lung transplantation, and structural lung disease with other solid organ transplantations presented as leading risk factors. In another study, it was claimed that the disseminated form was linked mainly to heart and lung transplantation (7). Prognosis is variable and dependent on the type of transplantation. In a review of disseminated NTM infections, death was reported in 5.9% of infected liver recipients, 5.6% of infected kidney recipients, 17.6% of infected heart recipients and 10.1% of infected lung recipients (8). The case presented here is an example of disseminated MAC infection in a patient with renal allograft failure. The patient applied to the hospital after a six month course of HD. It may be suggested that his over-immunosuppression may be related to the patient's continuation of calcineurin inhibitors, antimetabolite and corticosteroid, although he was told to stop. With HD, the drug effects may become stronger and may provoke the contaminated MAC to cause infection, and we have lost patients soon after a diagnosis of MAC infection.

The signs and symptoms of disseminated disease with MAC in transplantation patients may not be as apparent as in patients infected with HIV. Constitutional symptoms such as fatigue, weight loss, non-productive cough and abdominal discomfort may be the only initial complaints (9), and there may be no accompanying fever, as was

the case with the patient in the present study, who was admitted to hospital with acute abdominal discomfort. Intestinal involvement is not a common finding in the absence of lung problems in the disseminated form, although it may be isolated to the gut as a result of colonization. In one case report of intestinal MAC infection it was argued that nasogastric aspirate sampling may be critical in the diagnosis (10). Unfortunately, no gastric fluid analysis was performed in our patient. As the patient had an apparent intraabdominal LAP involvement that mimicked lymphoma, we did not suspect the presence of possible MAC or any other infection prior to making a histopathological examination. Our aim was to rule out the existence of any lymphoproliferative disease.

## CONCLUSION

In conclusion, disseminated MAC with intestinal involvement is a rare opportunistic infection in transplant patients. Even after the loss of a graft, patients should be carefully followed to ensure no misuse of drugs that may cause over immunosuppression.

*Conflict of interest : The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Informed Consent: Additional informed consent was obtained from the patient's wife since the patient is dead.*

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