Open Forum Infectious Diseases

NOVEL ID CASES

A Patient With Mycobacteremia Due to Two Different Nontuberculous Mycobacteria

Eddie Hill[1] **and Darcy Wooten**[1]

[1]Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California, San Diego, La Jolla, California, USA

Disseminated nontuberculous mycobacterial infections are most common in patients with severe immunosuppression, such as people with human immunodeficiency virus (HIV) and low $CD4^+$ T-cell counts. In this report, we present a rare case of a person with HIV who was hospitalized for mycobacteremia due to 2 different nontuberculous mycobacteria. We also provide a comprehensive summary of published case reports describing nontuberculous mycobacterial coinfections.

Keywords. *Mycobacterium avium-intracellulare*; *Mycobacterium kansasii*; nontuberculous mycobacteremia.

Nontuberculous mycobacteria (NTM) are ubiquitous in the environment and can be found in natural waters, drinking waters, biofilms, soils, and aerosols [1]. Nontuberculous mycobacteria can be contracted via inhalation or ingestion. They are recognized as potential pathogens that can cause significant morbidity, particularly in patients with immunosuppression or structural lung disease. Multiple epidemiological studies have shown that the prevalence of disease from NTM is increasing [2–4]. Coinfection due to multiple species of NTM is rare. In this report, we present a case of a person with human immunodeficiency virus and asthma who was hospitalized for concurrent mycobacteremia due to *Mycobacterium avium-intracellulare* (MAI) and *Mycobacterium kansasii*.

CASE PRESENTATION

A 58-year-old man with a history of human immunodeficiency virus (HIV) and asthma was admitted to the hospital for grave disability and failure to thrive. He had last been seen in clinic 2 years prior. At that time, the patient was taking bictegravir/emtricitabine/tenofovir-alafenamide for antiretroviral therapy and trimethoprim-sulfamethoxazole for *Pneumocystis jiroveci* pneumonia prophylaxis; his $CD4^+$ T-cell count was 136 cells/mm^3 (5%) and HIV-1 viral load was 2780 copies/mL.

Upon arrival to the hospital, the patient reported experiencing chills, malaise, dyspnea on exertion, productive cough of clear sputum, odynophagia without dysphagia, 20-pound weight loss, and nonbloody diarrhea for the past 2 months. He also noted the development of a painful rash on his extremities over the past 1 month. Besides HIV and asthma, the patient had no other significant past medical history. He had not been taking any medications for the past year. He reported no drug allergies. He did not use tobacco or drink alcohol but did smoke methamphetamine occasionally. The patient was not sexually active and was currently unemployed.

The patient's physical exam was notable for a temperature of 37.8°C, heart rate of 110 beats per minute, respiratory rate of 30 breaths per minute, blood pressure of 147/71 mmHg, and oxygen saturation of 96% on room air. His weight was 67.5 kilograms, down from 80.4 kilograms 2 years prior. He had white plaques on the oropharyngeal mucosa, tender lymphadenopathy in the right supraclavicular and left cervical regions, tachycardia, and inspiratory rhonchi throughout his lungs. He had erythematous nodules on his right arm, distal left arm, and left foot. The patient's abdominal and genitourinary, neurologic, and psychiatric exams were unremarkable.

Initial laboratory tests revealed a white blood cell count of 9000/mm^3 (neutrophils 80%; bands 8%; lymphocytes 7%; and eosinophils 0%), hemoglobin level of 11.1 gm/dL, platelet count of 423 000/mm^3, creatinine of 1.09 mg/dL, aspartate aminotransferase of 91 U/L, alanine aminotransferase of 50 U/L) and normal alkaline phosphatase and total bilirubin levels. A computed tomography (CT) scan of the chest with contrast showed a 1.7 × 2.1-centimeter thick-walled cavitary lesion in the upper lobe of the right lung, multiple enlarged and necrotic right hilar and mediastinal lymph nodes, and diffuse ground-glass opacities in all lobes of the left lung. A CT scan of the abdomen with contrast showed hepatosplenomegaly and severe bladder wall thickening.

On the day of admission, a broad infectious work-up was initiated. The patient also started having daily fevers (as high as 39.5°C). His $CD4^+$ T-cell count was undetectably low (<10 cells/mm^3), and his HIV-1 viral load was 384 000 copies/mL.

The patient's infectious work up revealed 2 disseminated nontuberculous mycobacterial infections. Acid-fast bacilli (AFB) sputum, blood, and urine cultures were positive for *Mycobacterium kansasii* and *Mycobacterium avium-intracellulare* (MAI). A punch biopsy of a skin nodule on the patient's right arm

Received 24 August 2022; editorial decision 27 September 2022

Correspondence: E. Hill, MD, Division of Infectious Disease and Global Public Health, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0507 (e2hill@health.ucsd.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofac519

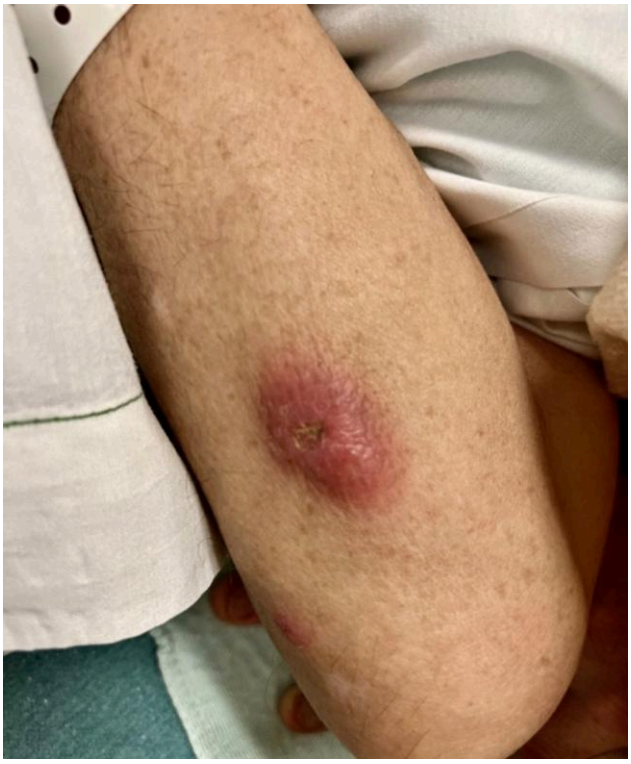

Figure 1. Skin nodule on right arm.

(Figure 1) showed suppurative dermatitis with necrosis, a positive AFB smear, and AFB culture growing MAI. Cultures were collected within 27 hours of each other, positive by mycobacterial growth indicator tubes (MGIT) 8 to 9 days after collection, and identified sequentially 8 to 37 days after collection; MAI was identified before *M kansasii* in urine and blood cultures. Organisms were identified via matrix-assisted laser desorption/ionization with time-of-flight mass spectrometry; MAI was unable to be speciated to *M avium* or *Mycobacterium intracellulare*.

Random biopsies of his colon were positive on AFB smear, but no cultures were sent. Testing for *Mycobacterium tuberculosis* (MTB) of the sputum was negative by both culture and polymerase chain reaction. The patient was initially started on treatment for disseminated MAI, disseminated *M kansasii*, and possible culture-negative MTB with rifabutin, isoniazid, pyrazinamide, and ethambutol (RIPE) and azithromycin while organism identification and antimicrobial susceptibility testing were pending. The patient's fevers began to improve 5 days after initiation of treatment.

During his hospitalization, the patient was also diagnosed and treated for biopsy-proven cytomegalovirus esophagitis. He was restarted on antiretroviral therapy 8 days after initiation of antimycobacterial therapy. Upon confirmation that both the MAI and *M kansasii* were macrolide-susceptible, the patient's antimycobacterial regimen was consolidated to rifabutin (minimum inhibitory concentration breakpoint [MIC BP] of 1 μg/mL], ethambutol (MIC BP >20 μg/mL), and azithromycin. The patient was discharged with a treatment plan for at least 12 months of antibiotics pending infection clearance and meaningful $CD4^+$ T-cell count recovery.

At a follow-up office visit 4 months after discharge, the patient reported medication adherence, resolution of his fevers, and improvement of his cough and rash. The patient's $CD4^+$ T-cell count was 41 cells/mm^3 (3%), and his HIV-1 viral load was undetectable (<20 copies/mL). The most recent AFB sputum culture was positive for MAI, but the patient's most recent AFB blood, urine, and stool cultures were negative. An interval CT scan of his chest showed resolution of the cavitary lesion and improvement of hilar and mediastinal lymphadenopathy.

Patient Consent Statement

This study was reviewed by the University of California San Diego Human Research Protection Program or Institutional Review Board (IRB) and was deemed to be exempt from IRB requirements under category 45 CFR 46.104(d). It was determined that patient consent is not required because the identity of the human subject cannot readily be ascertained directly or through identifiers linked to the subject.

DISCUSSION

Disseminated NTM infections are characterized by mycobacteremia or seeding of multiple organs. In the United States, they are most commonly caused by *M avium* complex (MAC), which includes *M avium* (responsible for more than 90% of these infections) and *M intracellulare* [5]. The second most common cause of disseminated NTM is *M kansasii*.

Disseminated NTM infections are typically seen in the setting of severe immunocompromise. In people with HIV, disseminated NTM infections occur when the $CD4^+$ T-cell count is less than 50 cells/mm^3 [6]. The risk increases with progressively lower $CD4^+$ T-cell counts [7]. Our patient had some of the most commonly described signs and symptoms of disseminated NTM: fever, night sweats, weight loss, abdominal pain, diarrhea, anemia, and hepatosplenomegaly [8]. The majority of people with disseminated NTM will have positive blood cultures, but multiple blood cultures may be required for diagnosis in cases of low-grade mycobacteremia [7]. If blood cultures are negative, bronchoalveolar lavage or biopsies of involved organs may be required.

Coinfection with 2 different species of NTM is rare [9, 10], and the majority of coinfections occur in patients with advanced immunosuppression (Table 1). To our knowledge, this is the first case report in the literature of a patient with concurrent MAI and *M kansasii* mycobacteremia. The case is particularly unique because both MAI and *M kansasii* were cultured in 3 different bodily fluids—sputum, blood, and urine—on the day of admission. This demonstrates a high

Table 1. Case Reports of NTM Coinfections

First Author (Year)	Mycobacterial Species: Site(s) of Positive Culture	Host Characteristics	Antibiotic Regimen
Agrawal (2022) [11]	*M kansasii* and MAC: Transbronchial nodal aspiration	HIV, hepatitis C, tobacco use	Not specified
Conville (1989) [12]	*M avium* and *M intracellulare*: Blood	HIV	Not specified
Hirayama (2022) [13]	*Mycobacterium arupensis*: Blood, cervical lymph node, sputum; *M avium*: Cervical lymph node and bone marrow	Anti-interferon-γ neutralizing autoantibody-associated immunodeficiency syndrome	Clarithromycin, ethambutol, rifabutin
Ishii (1998) [14]	*Mycobacterium peregrinum* and *Mycobacterium scrofulaceum*: Skin	Fish-fancier who owns multiple tropical fish	Sparfloxacin, minocycline
Kwan (2010) [15]	*Mycobacterium chelonae* and *Mycobacterium fortuitum*: Left forearm wound	Recent open distal radius and ulna fracture	Levofloxacin, amikacin
Lao (2022) [16]	*M peregrinum*: bone marrow; MAC: Blood, sputum	HIV	Clarithromycin, ciprofloxacin, linezolid
Lévy-Frébault (1987) [17]	MAI, *Mycobacterium simiae*: Jejunal fluid, feces, rectal biopsy, blood	HIV	Lost fo follow-up after diagnosis
Massenkeil (1992) [18]	MAC: liver abscess, blood; *M kansasii*: blood, feces; *Mycobacterium xenopi*: BAL fluid	HIV	Isoniazid, rifampin, ethambutol, amikacin
Narang (2010) [19]	*M avium*: Blood, stool; *Mycobacterium wolinskyi*: Stool	HIV	Lost to follow-up after diagnosis
Sharma (2017) [20]	*M fortuitum*, *Mycobacterium bovis*: Vitreous fluid	Chronic steroid use, farmer	RIPE
Singh (2015) [21]	*Mycobacterium szulgai* and *Mycobacterium intermedium*: Pus from abdominal sinus tracts	Healthy	Rifampicin, ethambutol, clarithromycin
Tabaja (2022) [22]	*M abscessus* complex: Skin; M. avium and *M simiae*: Blood	GATA2 mutation, myelodysplastic syndrome	Azithromycin, imipenem, tigecycline, amikacin
Thimmareddygari (2020) [23]	MAC, *Mycobacterium abscessus* complex: BAL	COPD, tobacco use	Tigecycline, delafloxacin, linezolid, azithromycin
Wang (2021) [24]	*Mycobacterium yongonense*, MTB, *Mycobacterium* sp *MOTT36Y*, and *M abscessus* complex: Sputum	Not specified	RIPE, amikacin, tigecycline, azithromycin
Wang (2011) [25]	*M fortuitum* and *M abscessus* complex: Synovial fluid of right knee	Right knee replacement, farmer	Doxycycline, ciprofloxacin, clarithromycin, amikacin

Abbreviations: BAL, bronchoalveolar lavage; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; MAC, *Mycobacterium abscessus* complex; MTB, *Mycobacterium tuberculosis*; NTM, nontuberculous mycobacteria; RIPE, rifamycin, isoniazid, pyrazinamide, and ethambutol.

mycobacterial burden and highlights the severity of the patient's immunosuppression in the setting of untreated HIV.

Although NTM coinfection is a rare occurrence, it is important for clinicians to be aware of this possibility when evaluating people with advanced HIV or other forms of immunosuppression. Depending on the identified NTM species, empiric therapy with multiple agents may be required while additional culture data are pending.

CONCLUSIONS

We describe a case of mycobacteremia due to MAI and *M kansasii* in a person with advanced HIV. We also summarize published case reports demonstrating NTM coinfections. Although these cases are rare, they are important to be aware of and may significantly impact treatment options.

Notes

Author contributions. All authors contributed to the manuscript concept, drafting, and content review.

Financial support. The authors received no financial support.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

1. Falkinham JO. Nontuberculous mycobacteria in the environment. Clin Chest Med **2002**; 23:529–51.
2. Prevots DR, Shaw PA, Strickland D, et al. Nontuberculous mycobacterial lung disease prevalence at four integrated health care delivery systems. Am J Respir Crit Care Med **2010**; 182:970.
3. Jones MM, Winthrop KL, Nelson SD, et al. Epidemiology of nontuberculous mycobacterial infections in the U. S. Veterans Health Administration. PLoS One **2018**; 13:e0197976.
4. Adjemian J, Olivier KN, Seitz AE, Holland SM, Prevots DR. Prevalence of nontuberculous mycobacterial lung disease in U. S. Medicare beneficiaries. Am J Respir Crit Care Med **2012**; 185:881.
5. Horsburgh CR, Selik RM. The epidemiology of disseminated nontuberculous mycobacterial infection in the acquired immunodeficiency syndrome (AIDS). Am Rev Respir Dis **1989**; 139:4–7.
6. Mycobacterioses and the acquired immunodeficiency syndrome. Joint Position Paper of the American Thoracic Society and the Centers for Disease Control. Am Rev Respir Dis **1987**; 136:492–6.
7. Griffith DE, Aksamit T, Brown-Elliott BA, et al. An official ATS/IDSA statement: diagnosis. Treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med **2012**; 175:367–416.
8. Tortoli E. Clinical manifestations of nontuberculous mycobacteria infections. Clin Microbiol Infect **2009**; 15:906–10.
9. Hannah CE, Ford BA, Chung J, Ince D, Wanat KA. Characteristics of nontuberculous mycobacterial infections at a Midwestern Tertiary Hospital: a retrospective study of 365 patients. Open Forum Infect Dis **2020**; 7:ofaa173.
10. Kobayashi T, Nishijima T, Teruya K, et al. High mortality of disseminated nontuberculous mycobacterial infection in HIV-infected patients in the antiretroviral therapy era. PLoS One **2016**; 11:e0151682.
11. Agrawal N, Gekhman D, Guy ES, Alapat PM. Non-tuberculosis mycobacterium co-infection presenting as a thoracic mass. Available at: www.atsjournals.org. Accessed July 10, 2022.

12. Conville PS, Keiser JF, Witebsky FG. Mycobacteremia caused by simultaneous infection with Mycobacterium avium and Mycobacterium intracellulare detected by analysis of a BACTEC 13A bottle with the gen-probe kit. Diagn Microbiol Infect Dis **1989**; 12:217–9.
13. Hirayama K, Kanda N, Suzuki T, et al. Disseminated Mycolicibacter arupensis and Mycobacterium avium co-infection in a patient with anti-interferon-γ neutralizing autoantibody-associated immunodeficiency syndrome. J Infect Chemother **2022**; 28:1336–9.
14. Ishii N, Sugita Y, Sato I, Nakajima H. A case of mycobacterial skin disease caused by Mycobacterium peregrinum and M. scrofulaceum. Acta Derm Venereol **1998**; 78:76–7.
15. Kwan K, Ho ST. Mycobacterium chelonae and Mycobacterium fortuitum infection following open fracture: a case report and review of the literature. Indian J Med Microbiol **2010**; 28:248–50.
16. Lao CK, Wu TS, Lin KY, Lee MH. Disseminated Mycobacterium peregrinum and Mycobacterium avium infection in a patient with AIDS: a case report and review of literature. J Clin Tuberc Other Mycobact Dis **2022**; 27:100314.
17. Levy-Frebault V, Pangon B, Bure A, Katlama C, Marche C, David HL. Mycobacterium simiae and Mycobacterium avium-M. intracellulare mixed infection in acquired immune deficiency syndrome. J Clin Microbiol **1987**; 25: 154.
18. Massenkeil G, Opravil M, Salfinger M, Von Graevenitz A, Lüthy R. Disseminated coinfection with Mycobacterium avium complex and Mycobacterium kansasii in a patient with AIDS and liver abscess. Clin Infect Dis **1992**; 14:618–9.
19. Narang R, Narang P, Jain AP, et al. Mycobacterium avium bacteremia and dual infection with Mycobacterium avium and Mycobacterium wolinskyi in the gut of an AIDS patient—first case report. Indian J Tuberc **2010**; 57:148–51.
20. Sharma K, Gautam N, Sharma M, et al. Ocular mycobacteriosis—dual infection of M. tuberculosis complex with M. fortuitum and M. bovis. J Ophthalmic Inflamm Infect **2017**; 7:1–5.
21. Singh AK, Marak RSK, Maurya AK, Das M, Nag VL, Dhole TN. Mixed cutaneous infection caused by Mycobacterium szulgai and Mycobacterium intermedium in a healthy adult female: a rare case report. Case Rep Dermatol Med **2015**; 2015:1–4.
22. Tabaja H, Jensen KL, Rivera CG, Misra A, Pruthi RK, Vergidis P. Multiple simultaneous infections with nontuberculous mycobacteria in the setting of GATA2 mutation and myelodysplastic syndrome. Open Forum Infect Dis **2022**; 9:ofac309.
23. Thimmareddygari DM, Ajao S, Patel R, Miller R, Slim J. Fulminant respiratory failure in multi-drug resistant Mycobacterium abscessus complex with mycobacterium avium complex co-infection. Chest **2020**; 158:A459–60.
24. Wang L, Liu D, Yung L, et al. Co-infection with 4 species of mycobacteria identified by using next-generation sequencing. Emerg Infect Dis **2021**; 27:2948.
25. Wang SX, Yang CJ, Chen YC, Lay CJ, Tsai CC. Septic arthritis caused by Mycobacterium fortuitum and Mycobacterium abscessus in a prosthetic knee joint: case report and review of literature. Intern Med **2011**; 50:2227–32.