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CASE REPORT

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Disseminated *Mycobacterium bovis* infection after deceased donor liver transplantation: A case report

Kayvon Sotoudeh | **Samantha Quon** | **Eric P. Hsieh** | **John Donovan** | **Shefali Chopra**

Keck Medical Center, University of Southern California, Los Angeles, CA, USA

Correspondence
Eric P. Hsieh, Keck Medical Center of USC, 1450 San Pablo Street, Los Angeles, CA 90033 USA.
Email: ephsieh@med.usc.edu

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Abstract

This case demonstrates the significance, and ongoing relevance of mycobacterial infections, especially in patients who have recently been started on immunosuppression.

KEYWORDS

immunosuppression, Mycobacterium bovis, liver transplantation infection

1 | CASE REPORT

Mycobacterium bovis is the causative agent of tuberculosis in cattle. It is known to jump the species barrier and cause tuberculosis-like infections in humans. This case describes a patient with disseminated *M. bovis* who had recently undergone a deceased donor liver transplantation.

A 66-year-old woman with a past medical history of type 2 diabetes and NASH cirrhosis was admitted to the hospital due to 2 weeks of progressive shortness of breath, decreased appetite, and lethargy. She had undergone a deceased donor liver transplantation one month prior. Her post-operative course had been complicated by renal insufficiency requiring a brief period of hemodialysis, and a persistent right pleural effusion which was managed with a thoracentesis. Per the patient's family, she had initially been doing well after being sent home from an acute rehab center after her liver transplantation. She had been compliant with all of her post-transplant medications; however, roughly one week after going home, she started to develop worsening fatigue, poor appetite, and worsening shortness of breath at rest, becoming bedbound in the process. Initial laboratories on hospital admission were notable for a normocytic anemia with hemoglobin of 7.5 g/dL, a BUN of 67 mg/dL, creatinine of 1.48 mg/dL, and notably an elevated calcium of 13.4 mg/dL. Chest X-ray showed stable mild pleural effusions, and initial infectious workup including blood cultures, urine cultures, and a lumbar puncture was unremarkable. Serologies including RPR, Epstein Barr virus quantitative DNA, and cytomegalovirus quantitative DNA were negative. CSF studies including cryptococcal antigen, coccidioides antibody, herpes simplex virus 1 and 2 PCR, West Nile virus IgG, and mycobacterium TB were negative. Despite IV fluid resuscitation, the patient's hypercalcemia persisted, and further laboratory analysis revealed a very low parathyroid hormone level, low 25-OH vitamin D, and elevated 1,25 OH vitamin D level. Coincidently, pleural fluid culture that was obtained 1 month prior grew *M. bovis* (identified by DNA probe and PCR), sensitive to isoniazid, rifambin, and ethambutol but resistant to pyrazinamide. The patient was started on a regimen of rifabutin, isoniazid, and ethambutol. Additionally, a liver core biopsy was performed due to concerns for disseminated mycobacterial infection, which was notable for granulomatous

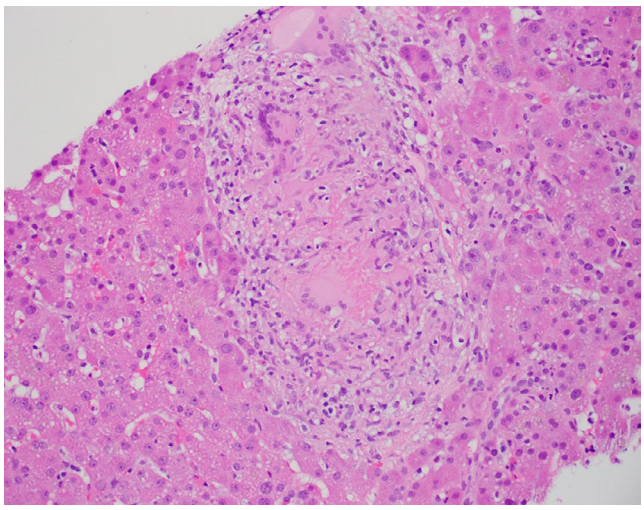

FIGURE 1 Liver core biopsy showing hepatic parenchyma with an epithelioid granuloma including a multinucleated giant cell. H & E stain, 200×

hepatitis most likely secondary to disseminated *M. bovis* infection (Figure 1). On further discussions with the patient's family, it became apparent that she had grown up on a rural farm in Mexico, where she and her family consumed mostly unpasteurized dairy products from their livestock. This exposure history led us to believe that this patient had harbored a latent *M. bovis* infection, which disseminated after she started taking immunosuppressive medications after her liver transplant.

2 | DISCUSSION

This case demonstrates the significance, and ongoing relevance of mycobacterial infections in the United States, most notably in patients who have recently been started on immunosuppression. *M. bovis* infections can be particularly difficult to diagnose, due to the relative rarity of the infection in the western world. In a recent longitudinal study conducted from 2006 to 2013, *M. bovis* accounted for only 1.3%-1.6% of all tuberculosis cases (N = 59,273) in the United States.[1] Recent investigations into the epidemiology of *M. bovis* have pointed to certain specific risk factors for the disease. In a retrospective review of the California tuberculosis registry, a multivariate analysis of TB case patients showed hispanic ethnicity, extrapulmonary disease, diabetes, and immunosuppressive conditions (excluding HIV co-infection) as being independently associated with *M. bovis* infection.[2] In addition to obtaining a thorough social and exposure history, understanding the similarities and differences between M. Tuberculosis and *M. bovis* can be helpful in elucidating the natural history of the disease. From a clinical and radiological perspective, *M. bovis* and M. tuberculosis are indistinguishable from one another. Both organisms can lead to primary and reactivated infections, and both may involve pulmonary, extrapulmonary, or disseminated disease. One important difference between the organisms is the increased propensity for *M. bovis* to manifest with extrapulmonary findings, particularly when the route of infection is through the ingestion of contaminated food or dairy products.[3] Typical sites of *M. bovis* dissemination include lymph nodes, the pleural space, joints, eyes, the central nervous system, and abdominal organs such as the liver as was described in this case. Diagnostic testing for *M. bovis* and M. Tuberculosis is identical, and involves acid-fast bacilli staining and mycobacterial culturing of relevant tissues, and molecular testing for mycobacterial DNA. Both the tuberculin skin test and interferon-gamma release assays can also detect *M. bovis* infection.[4] Despite these diagnostic similarities, identification of the correct type of mycobacterium is critical from a treatment standpoint. The treatment for *M. bovis* differs from that of M. tuberculosis, primarily due to the widespread resistance of *M. bovis* to pyrazinamide. The typical regimen of choice for both pulmonary and extrapulmonary *M. bovis* infection includes two months of daily isoniazid, rifampin, and ethambutol, followed by seven months of isoniazid and rifampin alone.[5] When there is a concern for resistance to antibiotics other than pyrazinamide, further susceptibility testing and expert consultation may be needed. This particular case of disseminated *M. bovis* infection reflects the persistent diagnostic challenges that continue to exist in the modern day. It also serves as a reminder of the risk posed to at-risk individuals, even in non-endemic countries such as the United States.

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CONFLICT OF INTEREST

All authors have no conflict of interest.

AUTHOR CONTRIBUTIONS

The authors confirm contribution to the paper as follows: Kavyon Sotoudeh: draft manuscript preparation and primary author. Samantha Quon: draft manuscript preparation and editing. Eric Hsieh, John Donovan and Shefali Chopra: interpretation of clinical data and case. All authors reviewed the manuscript and approved the final version.

ETHICAL STATEMENT

All ethical standards and consent were obtained for this manuscript.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed for this manuscript.

ORCID

Eric P. Hsieh https://orcid.org/0000-0002-3704-9436

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