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Case report

Non-tuberculous mycobacteria infection presenting as a hepatic allograft abscess

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ABSTRACT

Nontuberculous mycobacteria (NTM) are mycobacterial species other than Mycobacterium tuberculous and Mycobacterium leprae [1]. They are environmental organisms which have been implicated in a wide array of clinical syndromes. Here we describe a case of a Mycobacterium fortuitum complex liver abscess in a liver transplant recipient.

Introduction

Nontuberculous mycobacteria (NTM) are ubiquitous environmental organisms but may be implicated in a variety of clinical syndromes in both immunocompetent and immunocompromised hosts [1]. Prevalence of infection due to NTM has increased in recent years [2], possibly due to enhanced diagnostics, an aging population with increasing immunocompromise and more frequent environmental exposures. Disease manifestations vary from cutaneous, osteoarticular, or pulmonary involvement to disseminated disease. Due to the lack of mandatory reporting, the true incidence of these infections is unknown.

Solid organ transplantation and the associated impaired cell mediated immune response may predispose to NTM infection and disseminated disease [3]. Despite this, NTM infection is still a relatively infrequent complication of solid organ transplantation. However, when it occurs it poses a challenge as associated symptoms may be insidious or non-specific leading to delayed diagnosis, and treatment requires multiple drug therapy with significant risk of toxicity and drug interactions. Diagnosis requires a multi-modal approach with recognition of clinical syndrome, radiological imaging, and specific microbiologic testing of relevant samples.

Case

A 70-year-old male presented for evaluation of fever and abdominal discomfort. Medical history was notable for acute myeloid leukemia in remission and hepatitis C complicated by cirrhosis and hepatocellular carcinoma, with sustained viral response with sofosbuvir and ribavirin and subsequent orthotopic liver transplant 7 years ago. He had a *Klebsiella pneumoniae* bacteremia with an associated liver abscess 2 years prior treated with oral ciprofloxacin. He was immunosuppressed with low dose tacrolimus monotherapy.

The patient had been experiencing intermittent fevers and night sweats increasing in frequency in the six weeks prior to presentation associated with persistent and progressive right upper quadrant pain, decreased appetite and 10 kg weight loss. He also described having a longstanding non-productive cough. Of note he had a history of travel to eastern Africa in the past; 4 years ago. He did not smoke, consume alcohol or recreational substances.

On initial evaluation, the patient appeared generally weak, but was in no acute distress, with a temperature of 38.3 °C, blood pressure 170/70 mmHg, heart rate of 106 beats per minute, respiratory rate of 19 breaths per minute and saturating 99% on room air. His lungs were clear to auscultation bilaterally, with no murmurs or extra heart sounds noted on cardiovascular exam. Abdominal exam revealed right upper quadrant tenderness with negative Murphy's sign. The rest of his exam was

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unremarkable.

Complete blood count showed a white blood cell count of 8.8 × 10^9 /L (range 3.4–9.6 ×10^9 /L) with normal differential, hemoglobin of 11.2 g/dL (range 13.2–16.6 g/dL) and platelet count of 161 × 10^9 /L (range 135–317 ×10^9/L). Metabolic panel and liver chemistries were within reference limits. Right upper quadrant ultrasound revealed a 9 cm right hepatic lobe heterogenous mass. CT scan on the abdomen with intravenous contrast confirmed a 9 cm loculated hepatic abscess (Fig. 1). An ultrasound guided liver aspiration was done, and the patient was subsequently admitted to the medical floor. The patient was started on cefepime and vancomycin for broad spectrum antimicrobial coverage. The patient continued to spike fever 72 h after initiation of antibiotics. Liver aspirate culture showed growth of *Mycobacterium conceptionense/houstonense/senegalense*. After the positive growth on culture this was identified using MALDI TOF Mass Spectrometry. A liver MRI was done for pre-operative planning, and a left lung lower lobe opacity was noted. CT scan of the chest revealed a new 7 × 11 mm nodule (Fig. 2) along with other smaller, multiple nodules through both lungs with surrounding ground glass opacities. These nodules were deemed to be likely infectious in nature. Pulmonary tuberculosis was ruled out by 3 negative acid-fast bacilli smears, 2 negative mycobacterium tuberculosis PCR testing, and negative mycobacterial cultures. Further infectious workup, including serologic testing for endemic fungi, echinococcus, entamoeba and HIV was negative. The patient was subsequently taken to the operating room for right sided liver lobectomy. Acid fast bacilli staining of the tissue was focally positive for mycobacteria (Fig. 3). Tissue culture showed growth of the same organism. Susceptibilities are shown in Table 1. The patient was transitioned to intravenous amikacin, oral levofloxacin, and oral trimethoprim-sulfamethoxazole. Levofloxacin was later substituted for moxifloxacin due to nausea, with subsequent improvement of this symptom. His post-operative course was complicated by a bile leak, and subsequently had a biliary plastic stent place via ERCP. The patient continued to improve and was subsequently discharged. He had a follow up visit after completing 7 weeks of antibiotics, where his cough, fever and night sweats had improved, but continued to have poor appetite. Chest imaging showed improvement of the previously seen pulmonary nodules and CT of the abdomen showed improvement of bile leak. IV amikacin was discontinued with a plan to continue moxifloxacin and trimethoprim-sulfamethoxazole for 12 months completion. He continues to be followed closely in the outpatient setting.

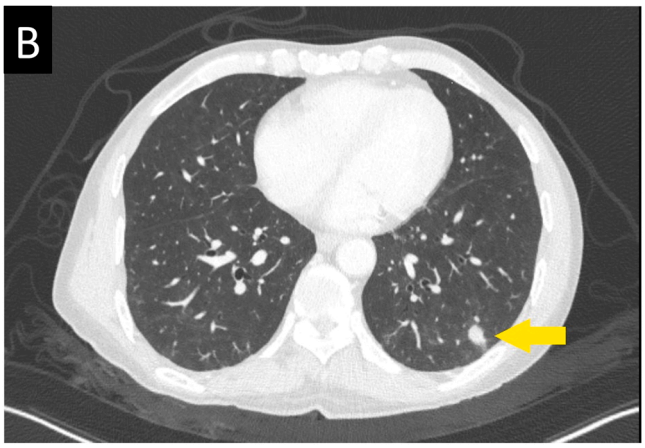

Fig. 2. CT scan of the chest showing 7 × 11 mm nodule (yellow arrow).

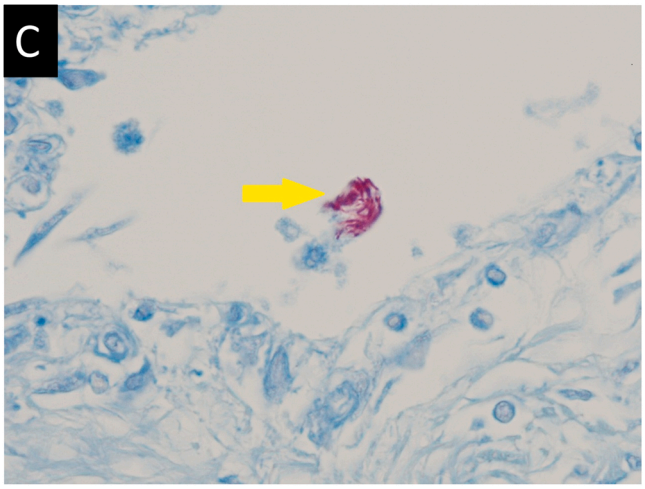

Fig. 3. Acid fast bacilli staining on liver tissue sample focally positive for mycobacteria.

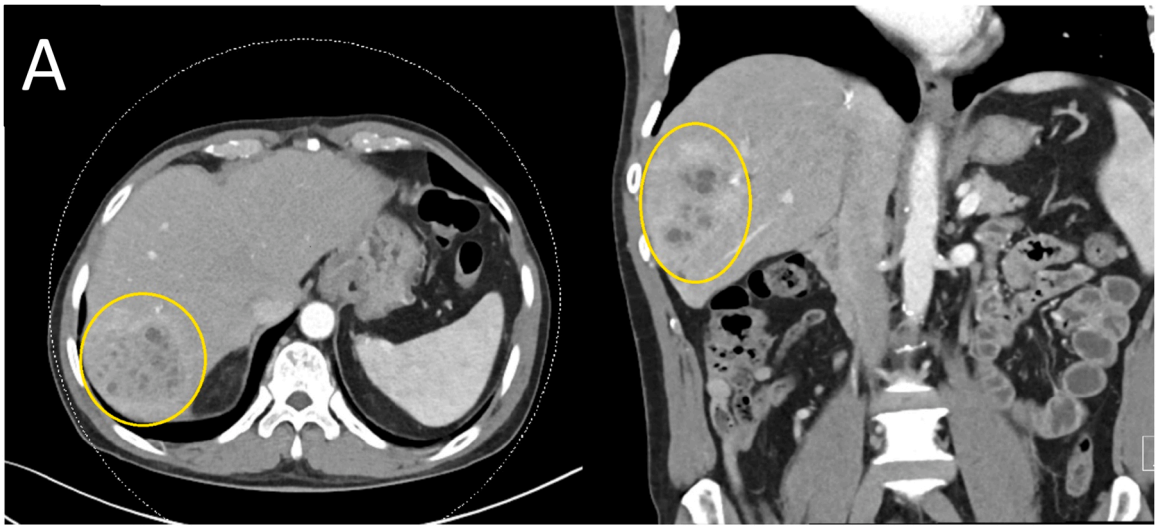

Fig. 1. A CT scan of the abdomen with intravenous contrast showing 9 cm loculated hepatic abscess, highlighted by yellow circle.

Table 1
Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

	Mycobacterium conceptionense/houstonense/ senegalense SUSCEPTIBILITY, BP (MCG/mL)
Amikacin	< =1 mcg/mL Susceptible
Cefoxitin	32 mcg/mL Intermediate
Ciprofloxacin	0.5 mcg/mL Susceptible
Clarithromycin	1 mcg/mL Susceptible
Clofazimine	0.12 mcg/mL
Doxycycline	< =0.12 mcg/mL Susceptible
Imipenem	2 mcg/mL Susceptible
Linezolid	4 mcg/mL Susceptible
Moxifloxacin	1 mcg/mL Susceptible
Tigecycline	0.06 mcg/mL
Tobramycin	16 mcg/mL Resistant
Trimethoprim + Sulfamethoxazole	2/38 mcg/mL Susceptible

Discussion

NTM are ubiquitous organisms that are an uncommon cause of human disease. Based on laboratory surveillance data in the United States, it is estimated that the annual rate of NTM isolation is 7.5–8.2 cases of NTM isolation per 100,000 population [4]. While NTM can cause infection in healthy individuals, the risk is higher among immunocompromised patients. Amongst solid transplant recipients, the incidence of NTM infection in patients with liver transplant is lower when compared to those with kidney, heart, or lung transplant [5]. NTM is a rare cause of liver abscess and should be considered when not responding to standard antibiotic regimens.

As previously stated, diagnosing NTM infection can be challenging. Due to their ubiquitous nature in the environment, microbiologic isolation does not always represent disease. Clinical diagnosis requires an appropriate clinical syndrome, supportive radiologic findings, and detection of the organisms from representative samples. Processes for staining and culture of NTM are similar to *M. tuberculosis*. Acid fast staining does not distinguish between *M. tuberculosis* and other mycobacteria. NTM are often fastidious and optimal conditions for culture vary between species. They are broadly classified into either rapid (<7 days) or slow (>7 days) growers based on the time it takes them to cultivate on solid media in subculture. Identification of the mycobacterial species is crucial to interpreting the clinical significance of the isolate. Currently techniques utilize hybridization probes, MALDI TOF Mass Spectrometry or targeted DNA sequencing to facilitate identification. Histopathology offers further diagnostic information as AFB staining may demonstrate the presence of the organism as in this case or characteristic granulomatous inflammation may be seen.

Treatment of NTM infection can be arduous. Current guidelines for NTM are based on relatively limited data and are largely centered on expert opinion [6]. The role of surgical intervention depends on the site and extent of disease but may be considered where feasible, as in this case, for localized disease control. In terms of antimicrobials, treatment choices should be driven by drug susceptibilities. Prolonged treatment duration is often required, including multidrug regimens which can be associated with significant toxicity. Treatment is often biphasic with an induction phase using 3 or more antimicrobials for 1–3 months with a maintenance phase of fewer drugs. The duration of the maintenance phase depends on the species and the clinical course. The combination of symptom improvement, radiographic findings, or sputum clearance for pulmonary NTM are all useful markers for monitoring response to therapy. In our case, the patient had induction with a combination of amikacin, moxifloxacin, and trimethoprim-sulfamethoxazole and showed clinical and radiological improvement at 7 week follow up, when it was decided to discontinue amikacin and continue moxifloxacin and trimethoprim-sulfamethoxazole- as maintenance therapy. For patients with solid organ transplant who are on immunosuppressive therapy, careful consideration of drug interactions is needed, as this can lead to toxic side effects or decreased effectiveness of immunosuppressive drugs. In this case, the combination of amikacin and tacrolimus can act synergistically to increase risk of renal impairment [7], which required close drug level and renal function monitoring for our patient.

Our current understanding on outcomes and survival of patients with NTM infections after solid organ transplant is limited largely to case series and retrospective studies. In a retrospective cohort study of 33 solid organ transplant recipients with NTM infection, Longworth et al. noted a significant association between early NTM infection within the first year of transplant and three-year mortality [8]. In our case, our patient is 7 years post-transplant, and his degree of immunosuppression was likely augmented by his history of acute myeloid leukemia. Whilst longitudinal follow up is still ongoing, he has had a promising clinical and radiologic response with combined medical and surgical therapy. This case demonstrates a rare presentation of a rare pathogen; diagnosed and managed through collaborative, multidisciplinary care.

Ethical approval

Ethical approval not needed for this cases report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Financial disclosures

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CRediT authorship contribution statement

Anthony Robateau Colón: Conceptualization, Writing – original draft, Writing – review & editing. **Eibhlin Higgins:** Writing – original draft. **Nicholas Boire:** Writing – original draft. **Nathan Cummins:** Writing – original draft, Supervision. **Kymberly D Watt:** Writing – original draft, Supervision.

Author contribution

ARC: Case design, chart review, manuscript preparation; EH: Case design, chart review, manuscript preparation; NB: expert pathologist, provided histological images, manuscript preparation; NC: Expert ID physician, manuscript preparation; KW: Liver transplant expert, case report design, manuscript preparation.

Conflicts of interest

None to disclose

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