Abstract

Primary cutaneous Mycobacterium avium complex (MAC) infection is a rare diagnosis in both immunocompetent and immunocompromised hosts. Disseminated MAC almost always occurs in the setting of advanced HIV infection and typically results from initial pulmonary or gastrointestinal disease. We describe a case of a 70-year-old female with systemic sclerosis and severe tumoral calcinosis that developed disseminated MAC infection secondary to deep cutaneous disease. Treatment was complicated by multiple significant drug interactions, patient comorbidities, as well as an inability to safely and completely surgically resect her infected soft tissue for source control.

Keywords: Immunocompromised host, Mycobacterium avium complex, skin infection

Introduction

Disseminated Mycobacterium avium complex (MAC) infection rarely occurs in non-HIV patients. When it does occur, it is usually in the setting of profound immunosuppression (e.g., hematological malignancy) or a genetic defect in the interferon-γ signaling pathway.[1] In addition, disseminated disease typically begins via inhalation or ingestion of MAC, resulting in local pulmonary or gut disease, respectively, before systemic spread. Dissemination from these locations typically occurs over several months.[2] We describe a case of deep skin and soft-tissue MAC infection which secondary dissemination in a HIV-negative patient. Written informed consent was obtained before publication.

Case Report

A 70-year-old female developed an erythematous papular skin lesion over her posterior right hip. She had a background of limited cutaneous systemic sclerosis with severe and extensive tumoral calcinosis of the right pelvis and lateral thigh, as well as psoriatic arthropathy (PsA) and hypogammaglobulinemia. Her medications included oral methotrexate 10 mg twice weekly, hydroxychloroquine 200 mg daily, and prednisolone 8 mg daily. She also took rivaroxaban 20 mg daily for atrial fibrillation stroke prevention and received regular subcutaneous immunoglobulin infusions. Her lesion enlarged and began to ulcerate and became painful with acute development of severe sepsis requiring hospital admission. Computed tomography (CT) pelvis revealed a right-sided flank collection overlying the lateral iliac crest and gluteal muscles measuring 16 cm × 12 cm × 8 cm, extending from her tumoral calcinosis [Figure 1]. In addition, there was a cystic or “milk of calcium” loculated fluid collection over the right quadriceps. She was admitted to the intensive care unit, was commenced on intravenous (IV) piperacillin/tazobactam 4.5 g every 8 h, and underwent emergency debridement and drainage of her deep tissue infection. Over 1 L of pus was drained with standard bacterial cultures growing Peptostreptococcus asaccharolyticus from her operative samples; multiple blood culture samples were negative for growth. Mycobacterial culture or acid-fast bacilli (AFB) staining was not performed on the operative sample or blood. She was changed to oral amoxicillin/clavulanate 875/125 mg twice daily after 11 days of IV therapy and was then discharged from hospital 10 days after her drainage procedure.

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She developed insidious anorexia, 13 kg weight loss, and increasing frailty over the next 3 months. A spontaneously draining sinus appeared over her right lateral proximal thigh, overlying her cold fluctuant “milk of calcium” collection. Fluid draining from the sinus was cultured which initially grew Enterobacter cloacae; abundant AFB were also identified in the sample. A temporary collection bag placed over the sinus was required due to high fluid output. Her CD4+ T-cell count was 860/mm³. In a short period of time, she clinically deteriorated developing fevers, rigors, and delirium with pain over her right thigh and hip. Mycobacterial blood cultures were obtained. Repeat CT imaging of her right leg revealed re-accumulation of the anterolateral thigh fluid collection measuring 27 cm × 8 cm × 12 cm. It also showed increasing calcification in her right gluteal and short adductor region. She was commenced on IV meropenem 1 g every 8 h and an incision and drainage procedure was performed. The initial Gram stain on her operative samples showed Gram-positive cocci and IV vancomycin 1 g twice daily was added. After initially responding to a repeat drainage procedure and broad-spectrum antimicrobial therapy, over the next few weeks, she continued to deteriorate with ongoing fevers, delirium, and rising inflammatory markers (C-reactive protein increased from 48 to 181). Mycobacterium intracellulare was subsequently cultured on both original sinus and intraoperative and blood cultures samples. The clarithromycin minimum inhibitory concentration was 1 mg/L measured via Sensititre method. Meropenem and vancomycin were ceased, and she was commenced on IV amikacin 500 mg thrice weekly and oral azithromycin 500 mg, rifabutin 600 mg, and ethambutol 800 mg daily. CT chest showed no evidence of lung involvement, and she had no evidence of gastrointestinal disease or malabsorption. Magnetic resonance imaging of her right thigh demonstrated a bone abscess or MAC osseous involvement in the greater trochanter. Drug interactions were a major issue and QTc monitoring was made difficult due to a long-standing left bundle branch block on her electrocardiogram (ECG). With regard to reducing her immunosuppression and avoiding adverse drug interactions, concerns regarding cessation of hydroxychloroquine and future potential flare of PsA with subsequent need for higher doses of corticosteroid were made. Hydroxychloroquine and low-dose prednisolone were continued. The QTc was carefully monitored by a modified calculation that involved subtracting 30 ms from the ECG result. Her rivaroxaban was ceased, and she was put on subcutaneous enoxaparin 40 mg daily. Surgical consultation regarding excision of her infected soft tissue, bone, and tumoral calcinosis was sort; however, it was deemed to carry a significantly high risk of morbidity and mortality and was not pursued. She was seen by a dietician and commenced on a high calorie nasogastric feeding regimen to improve her nutritional status and cachexia. After 4 weeks of therapy, she gained 2 kg in weight and is tolerating her antimycobacterial agents well with renal and auditory function remaining stable.

**Discussion**

*M. intracellulare*, like other MAC organisms, is relatively avirulent in the healthy host. It is acquired, usually via inhalation or ingestion, from many environmental sites including from water, soil, and animals. Glycolipid typing has divided MAC into 28 serovars; serovars 1, 4, and 8 cause most cases of disseminated disease and have appeared more virulent in animal infection models. A greater amount of bacteremia has been found to incur a worse prognosis. Disseminated MAC occurs almost solely in acquired immunodeficiency syndrome (AIDS), usually with a CD4+ cell count <20/mm³. This has become a largely uncommon occurrence due to improved treatment strategies and antiretroviral therapy for HIV infection.

Disseminated MAC in HIV-negative patients has been documented with identified risk factors including high-dose corticosteroid therapy, hematological malignancy, and cytotoxic chemotherapy. Various other immunocompromised states have had isolated cases reported including idiopathic T-cell lymphopenia, end-stage renal disease, renal transplantation, and myelodysplastic syndrome. There are limited data to support secondary MAC prophylaxis in these patient groups.

Very few cases of primary cutaneous MAC disease have been reported in the literature. Although usually occurring in the setting of advanced immunosuppression or HIV infection, a case in an immunocompetent recreational gardener and another occurring postskin lesion excision has been documented. Abnormal skin architecture and integument barrier function and a large inoculum of *Mycobacterium* are thought to be crucial in early pathogenesis. None of these cases reported secondary dissemination.

Although *M. intracellulare* primarily involves the pulmonary, gastrointestinal, and lymphatic systems, there was no

**Figure 1:** Deep soft tissue *Mycobacterium intracellulare* infection with draining sinus (bottom right) complicating severe heterotopic calcinosis of the right hip (top left). Suspected mycobacterial bone abscess involving the right greater trochanter on magnetic resonance imaging (top right)
evidence of their involvement in our patient clinically or radiologically. There were no other skin lesions identified to support secondary cutaneous involvement from primary disseminated MAC infection. A persistently open wound, previous instrumentation, and a chronic “milk of calcium” fluid collection with surrounding calcinosis in the context of high net immunosuppression provided enough risk for cutaneous mycobacterial infection.

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.

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