Widespread cutaneous nontuberculous mycobacterial infection in the absence of bacteremia mimicking leukemia cutis

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INTRODUCTION
Ten percent to 15% of patients with acute myeloid leukemia (AML) go on to have leukemia cutis, a papular or papulonodular cutaneous eruption caused by leukemic cells invading the dermis. Acute leukemics are also prone to a plethora of infectious processes in the context of their immune dysfunction. Here we present a perplexing case of a generalized nontuberculous mycobacterial (NTM) papulonodular eruption mimicking leukemia cutis that persisted and progressed despite proven clearance of the patient’s preceding Mycobacterium massiliense bacteremia.

CASE REPORT
A 69-year-old white man with a history of AML in remission was admitted to the hospital for a third hematopoietic stem cell transplantation (HSCT). The patient initially received a diagnosis of primary hypocellular AML not otherwise specified, without significant karyotypic or genotypic abnormalities 2 years before presentation. He underwent conventional conduction chemotherapy with cytarabine and daunorubicin (also known as 7 + 3). Remission was proven by multiple subsequent negative bone marrow biopsies.

Over the next 2 years, the patient exhibited persistent pancytopenia and transfusion dependence despite his remitted state. The etiology of this marrow failure was unclear despite an extensive evaluation; however, a smoldering AML recurrence remained on the differential diagnosis throughout his clinical course, especially given its hypocellular nature at initial presentation. The patient eventually underwent 2 match-unrelated donor HSCTs, both of which failed to engraft. The patient was then admitted for a third, haploidentical HSCT, which also failed to engraft.

During this prolonged admission, the patient had fevers, dyspnea, and a nonproductive cough over several days. He was febrile to 38.8°C but otherwise hemodynamically stable and nontoxic in appearance. The patient’s total white blood cell count was less than 100. Computed tomography scan of the chest showed findings concerning for an atypical pneumonia. The patient underwent bronchoscopy with bronchoalveolar lavage, and the respiratory culture grew Mycobacterium abscessus chelonae complex. Concurrent blood cultures also grew M abscessus chelonae complex within 4 days. The respiratory pathogen was sent for speciation and antibiotic susceptibility testing and speciated as M massiliense.

Concurrent to this systemic illness, the patient had a generalized cutaneous eruption. It began on his thighs and spread to his proximal arms, abdomen, and back. His mucosae, distal extremities, neck, and head were spared. On examination, there were numerous, discrete, 5- to 10-mm, violaceous, and

Abbreviations used:
AFB: acid-fast bacilli
AML: acute myeloid leukemia
HSCT: hematopoietic stem cell transplantation
NTM: nontuberculous mycobacterial

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slightly tender papules and papulonodules (Fig 1). The 2 diagnoses primarily under consideration were a hematogenously disseminated NTM infection versus leukemia cutis.

The patient was empirically treated with intravenous imipenem, amikacin, and tigecycline as well as oral clarithromycin. Amikacin was discontinued within several days secondary to ototoxicity. The patient defervesced, and his respiratory symptoms improved with this antimicrobial therapy. Further, the bacteremia cleared, proven by multiple pairs of negative blood cultures. Another bone marrow biopsy failed to demonstrate AML recurrence. Despite his clinical improvement systemically, his eruption continued to progress. New cutaneous lesions continued to develop, and both new and preexisting lesions became thicker and more tender. He completed a 6-week course of intravenous imipenem and was maintained on intravenous tigecycline and oral clarithromycin for several months. No antibiotic changes were necessary given the susceptibility profile of the cultured *M. massiliense*.

Representative skin lesions underwent biopsy 4 times over a 5-month period during and after this hospitalization. The first and third biopsies showed a mild perivascular dermatitis. Gram, acid-fast bacilli (AFB), and periodic acid–Schiff–diastase stains as well as tissue cultures for bacterial, fungal, and mycobacterial pathogens were negative. The second biopsy found a suppurative and granulomatous dermatitis, but the infectious stains and cultures were again negative. Leukemic cells were never identified in the skin. The patient was then presented at our institution's Grand Rounds for further discussion and a fourth biopsy. Hematoxylin-eosin stain showed suppurative and granulomatous inflammation, and the AFB stain was positive for mycobacteria in the dermis (Fig 2). Of note, the tissue cultures collected at this time were negative. The cutaneous mycobacteria seen histopathologically were presumed to be *M. massiliense* as detected in the patient’s respiratory tract.

The patient eventually experienced a slight improvement in his skin disease with prolonged treatment with tigecycline and clarithromycin. However, his overall health continued to decline, and the patient died at home under the care of a local hospice organization.

**DISCUSSION**

Our patient presented with a generalized papulonodular eruption requiring repeated diagnostic testing to elucidate the true underlying etiology. Our suspicion was highest for a disseminated NTM infection given the concomitant onset of his eruption and *M. massiliense* pneumonia and secondary bacteremia. However, it was puzzling to see the cutaneous disease progress when his systemic illness resolved. The morphologic features of the eruption in the context of the patient’s persistent pancytopenia raised the possibility of AML recurrence manifesting as leukemia cutis, but this was never identified despite extensive evaluation of the blood, skin, and bone marrow. We hypothesize the pharmacologic interventions for the *M. massiliense* infection were insufficient to control the cutaneous disease despite appropriate antibiotic selection given the severity of his immunocompromised state. The preference of some NTM for lower temperatures may have also been a contributing variable.3

*M. massiliense* is a rapidly growing atypical mycobacterial species first described as distinct from *M. abscessus* in 2004.4 Since then, *M. massiliense* has been isolated from patients with pneumonia and
following various invasive procedures. From a clinical perspective, it is worth noting that *M. abscessus* can develop an inducible resistance to clarithromycin, whereas *M. massiliense* cannot. This finding did not have major implications in our patient, as he only marginally responded to a multi-agent regimen that included clarithromycin. However, this finding may be relevant in other cases of cutaneous atypical mycobacterial infections and reinforces the importance of pathogen speciation and antibiotic susceptibility testing.

Finally, this case underscores the necessary persistence when evaluating a dermatologic condition in a complex patient when the underlying disease process is unclear. Four separate skin biopsies were taken at different time points for histopathology and tissue culture before the NTM pathogen was finally identified on AFB staining. Even then, the tissue cultures were negative. A high degree of clinical suspicion for the underlying disease process was thus required to empirically select an appropriate treatment regimen.

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