

Suppurative Inflammation With Microabscess and Pseudocyst Formation Is a Characteristic Histologic Manifestation of Cutaneous Infections With Rapid-Growing *Mycobacterium* Species

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Key Words: Rapid-growing *Mycobacterium*; *Mycobacterium abscessus*; *Mycobacterium chelonae*; Suppuration; Abscess

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Upon completion of this activity you will be able to:

- describe the classical findings of cutaneous involvement by classical *Mycobacterium tuberculosis*.
- list histologic features in skin biopsies that should raise suspicion of rapidly growing atypical mycobacterial infections.
- list the special stains that are indicated in the workup of inflammatory conditions of the skin to assist in defining possible mycobacterial infections.

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CME

Abstract

Mycobacterial infections of the skin classically cause a granulomatous tissue reaction. We have observed a suppurative pattern of inflammation associated with infections by rapid-growing Mycobacterium species in immunocompromised patients. We report 6 cases in skin and soft tissue with an unusual but consistent lack of a predominance of granulomatous inflammation. Of the 6 cases, 4 had predominantly (~75%) suppurative inflammation, 1 case predominantly demonstrated (~75%) a mix of acute and chronic inflammation, and 1 case showed an approximately equal contribution of suppurative and granulomatous inflammation. All 6 cases showed abscess formation and numerous acid-fast bacilli (AFB) on AFB stain and were confirmed by tissue culture. Of these 6 cases, 2 had microabscesses with central pseudocysts harboring microorganisms. Five patients were taking oral prednisone, and 1 had an uncharacterized immunodeficiency. These cases highlight the need for awareness of this unusual manifestation of infection with rapid-growing Mycobacterium species, particularly in immunocompromised patients.

Mycobacterial infections in the skin, as in other parts of the body, classically cause a granulomatous tissue reaction. Pathologists readily order acid-fast bacilli (AFB) stains, such as Kinyoun or Fite stain, along with fungal stains in the context of granulomatous inflammation. However, infection with AFB is often not considered in the differential diagnosis of prominent acute inflammation and abscess formation in skin and soft tissue. As a consequence, only Gram and fungal stains are often ordered in these cases. Herein, we describe suppurative response to infection with rapid-growing species of mycobacteria in immunocompromised patients.

Materials and Methods

We studied 6 cases of infection with rapid-growing *Mycobacterium* species in skin and soft tissue, 5 with *Mycobacterium abscessus* and 1 with *Mycobacterium chelonae*. Of the 6 patients, 5 were taking oral prednisone for various chronic illnesses and 1 had an uncharacterized immunodeficiency with a CD4 cell count of 25/μL in the face of multiple negative HIV serologic test results. This patient also had chronic hepatitis B and hepatitis C virus infections (Table 1). Of the 6 patients, 4 had multiple nodules on the bilateral lower extremities only, 1 had multiple papules and nodules on all 4 extremities and 1 abscess on the lower extremity, and 1 had a single abscess and sinus tract on the chest wall. Clinical suspicion for cutaneous mycobacterial infection was present in only 2 of the 6 cases. Additional details about the clinical manifestations for each patient are given in Table 2.

Table 1
Demographic and Clinical Data for Patients With Infection by Rapid-Growing *Mycobacterium* Species

Case No./ Sex/Age (y)	Immunosuppression	Underlying Disease
1/F/70	Oral prednisone	IPF
2/M/45	Oral prednisone	PAN
3/M/51	Oral prednisone	Bilateral lung transplantation for CF
4/M/77	Oral prednisone	CLL
5/M/54	Oral prednisone	Sarcoidosis of liver
6/M/45	Immunodeficiency of unknown etiology (HIV-; CD4 count, 25/ μ L)	HBV and HCV infection; uncharacterized immunodeficiency

CF, cystic fibrosis; CLL, chronic lymphocytic leukemia; HBV, hepatitis B virus; HCV, hepatitis C virus; IPF, idiopathic pulmonary fibrosis; PAN, polyarteritis nodosa.

Table 2
Data on Manifestations of Infection With Rapid-Growing *Mycobacterium* Species

Case No.	Initial Clinical Manifestation of Cutaneous Lesions	Systemic Involvement	Duration of Cutaneous Lesions (mo)	Size of Cutaneous Lesions (cm)
1	Multiple nodules, bilateral LE only	None	1-2	Not known
2	Multiple nodules, bilateral LE only	None	1	1-2
3	Abscess and sinus tract, chest wall	None	4	Not known
4	Multiple nodules, bilateral LE only	"Suspicious" lung opacities; patient died before lung biopsy performed; no autopsy done	1	Not known
5	Multiple nodules, bilateral LE only	None	6+	Not known
6	Multiple nodules, all 4 extremities and single abscess on 1 LE	None	4	2-4

LE, lower extremity or extremities.

The mycobacteria were cultured using liquid and solid media for growth. The specimens were inoculated into a bacT/alert bottle (bioMérieux, Durham, NC), which has a liquid medium containing Middlebrook 7H 9 broth, oleic acid, and a mixture of antibiotic and antifungal agents (polymyxin B, amphotericin B, nalidixic acid, trimethoprim, and azlocillin). Once growth was detected by an automated system, a smear with Kinyoun stain was made to confirm that the culture grew AFB. Once confirmation of AFB was made, species identification was attempted with genetic probes (Gen-Probe technology [Gen-Probe, San Diego, CA] with probes for *Mycobacterium tuberculosis* complex, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium goodnae*, and *Mycobacterium kansasii*). In our cases, the AFB were not identified with any of our probes, so the samples were submitted to the Massachusetts State Laboratory. At that facility, the mycobacteria species were identified by using growth characteristics and standard biochemical techniques.

Results

Of the 6 cases, 4 (67%) histologically showed greater than 75% suppurative inflammation and less than 25% granulomatous inflammation; 1 case (17%) showed a greater than 75% mixture of acute and chronic inflammation with less than 25%

granulomatous inflammation; and 1 case (17%) showed 50% suppurative inflammation and 50% granulomatous inflammation. All 6 cases (100%) showed frank dermal abscess or microabscess formation. When present, the granulomatous inflammation was nonnecrotizing and was intimately admixed with the suppurative inflammation. In 3 cases (50%), the inflammatory response was centered in the panniculus, and in 2 cases (33%), the response was centered in mid and deep levels of the dermis with less prominent involvement of the superficial subcutis. In 1 case (17%), the inflammatory response was present only in the superficial and mid dermis. Of the 6 cases, 2 (33%) cases, both with greater than 75% suppuration, showed formation of small pseudocysts within the abscesses. These pseudocysts were clear or filled with amorphous "fluffy" blue-gray material that on AFB staining represented AFB **Image 1** and **Image 2**. In all 6 cases, AFB staining revealed numerous microorganisms, sometimes in areas of the biopsy with minimal to no inflammation **Image 3** and **Image 4**. Of note, 1 of the 6 cases was initially misdiagnosed by a surgical pathologist as necrotizing fasciitis.

Discussion

Mycobacterial infections classically cause a granulomatous tissue reaction in most body sites, including the skin. Therefore, AFB stains are routinely performed along with

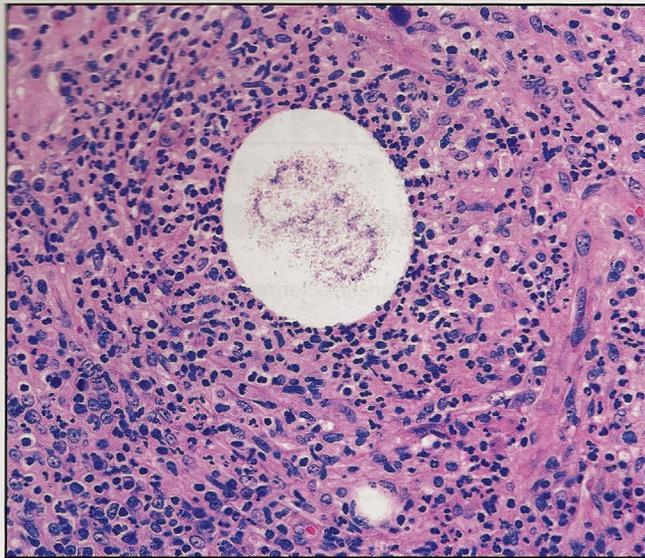


Image 1 Pseudocyst within a dermal abscess (H&E, ×400).

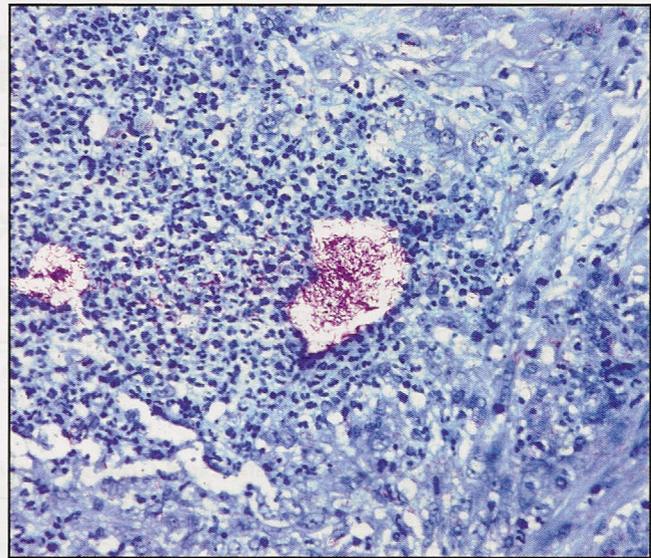


Image 2 The pseudocyst is filled with acid-fast organisms (acid-fast bacilli stain, ×400).

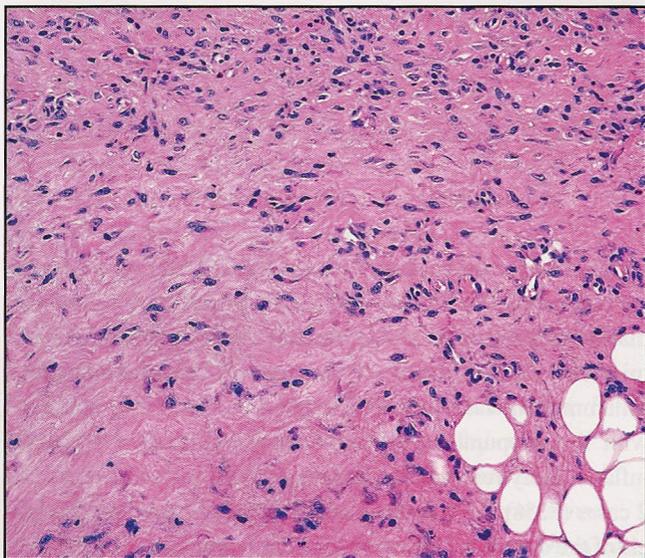


Image 3 Corresponding area for Image 4 of area with minimal inflammation away from the dermal abscess (H&E, ×200).

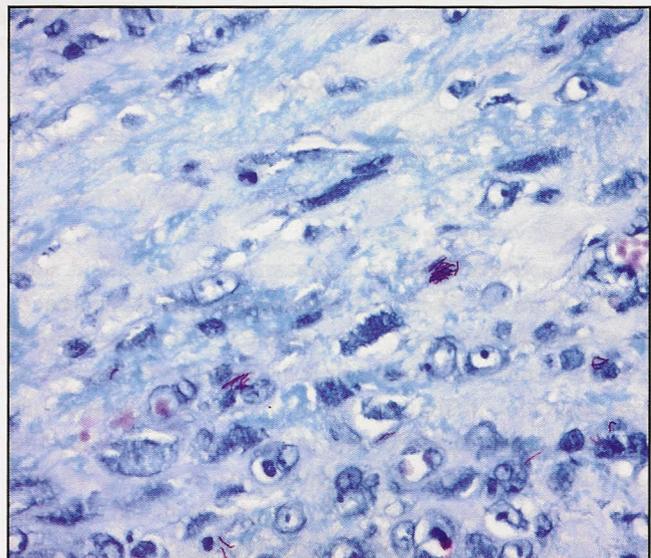


Image 4 Acid-fast bacilli (AFB) are readily seen away from the inflammation (AFB stain, ×400).

fungal stains in the context of granulomatous inflammation. However, other histologic patterns have been reported in association with cutaneous mycobacterial infections, including classical “tuberculoid” caseating granulomas,^{1,2} well-formed noncaseating (“sarcoidal”) granulomas,^{1,2} suppurative granulomas,¹⁻³ dermal abscess formation,^{1,4} diffuse histiocytic infiltration,¹ panniculitis,¹ lichenoid dermatitis mixed with granulomata,⁵ and nonspecific chronic inflammation.¹ Despite these reports, infection with AFB is often not considered in the differential diagnosis in skin and soft tissue biopsy specimens with prominent acute inflammation and abscess formation.

The rapid-growing *Mycobacterium* species, including *M abscessus*, *M chelonae*, and *Mycobacterium fortuitum*, are separated from other nontuberculous mycobacteria because of their tendency to grow out in culture in 3 to 5 days rather than the more typical 2 to 4 weeks of other *Mycobacterium* species. These organisms are ubiquitous and rarely cause significant clinical infection in immunocompetent hosts. However, in the past 2 decades with the emergence of AIDS and the increased use of immunosuppression in transplant recipients and other chronically ill patients, the recognition of infections caused by rapid-growing mycobacteria has increased.⁶ These infections often are disseminated in

immunocompromised hosts but can also be localized to the skin and soft tissue. Immunocompromised patients in whom nontuberculous mycobacterial infections develop have been reported to have an increased number of cutaneous lesions compared with immunocompetent patients with similar infections.⁷ The immunocompromised patients tend to have more prominent ulceration of and abscess formation within the cutaneous lesions.^{7,8} Histologically, immunocompromised hosts show more involvement of the subcutaneous tissue with more prominent microabscess formation.⁷⁻⁹

We report a characteristic histologic reaction pattern in cutaneous rapid-growing *Mycobacterium* infections in a series of immunocompromised patients. A high index of suspicion for AFB should be present when faced with a skin or soft tissue sample with predominantly suppurative inflammation, especially in immunocompromised patients. In some cases, small pseudocysts within the abscesses were found to be filled with acid-fast bacteria. We recommend routine use of an AFB stain, in addition to Gram and fungal stains, for the histologic evaluation of suppurative inflammations of skin and soft tissue infections.

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