Pediatric Dermatology Vol. 31 No. 3 292–297, 2014

Mycobacterium abscessus Hand-and-Foot Disease in Children: Rare or Emerging Disease?

Jo Linda M. Sinagra, M.D.,* Elisabeth E. Kanitz, Ph.D.,† Carlo Cerocchi, M.D.,‡ Carlo Cota, M.D.,* Ottavia Fantetti, M.D.,* Grazia Prignano, Ph.D.,* Pietro Donati, M.D.,* Enrico M. Tortoli, Ph.D.,¶ Francesco P. D'Ancona, M.D.,† and Bruno Capitanio, M.D.*

**Istituto San Gallicano, Rome, Italy, †Istituto Superiore di Sanità, Rome, Italy, ‡Azienda Unità Sanitaria Locale Roma C, Rome, Italy, ¶Istituto Scientifico Universitario San Raffaele, Milan, Italy*

Abstract: ***Mycobacterium abscessus*** **is emerging as an important cause of cutaneous infections in sporadic cases and outbreak settings. Although immunosuppressed or elderly patients are most commonly affected, in 2006 an outbreak of clinically distinct cutaneous lesions on the hands and feet caused by *M. abscessus* in a population of healthy children using a public swimming pool was reported. This article describes an outbreak of skin infection in a population of healthy Italian children attending the same school and using the same swimming pool. In January 2010 we identified three children with multiple, painful nodules on the palms and soles. *M. abscessus* was isolated from one child's lesions. A public health investigation was conducted and a team of dermatologists and public health officers visited all of the children; 514 children were screened and 29 cases were identified overall. All of the affected children had used the school's swimming pool. These children were treated with oral clarithromycin for 4 to 8 weeks. Because of the long period of time between the presentation and diagnosis of the first cases, the possibility that the number of cases may have been underestimated cannot be excluded. To our knowledge, this is the second largest reported cluster of *M. abscessus* skin infection suspected to be related to swimming pool exposure in a population of otherwise healthy children. It is unclear whether this disease is rare or should be considered as an emerging clinical entity.**

Atypical mycobacteria, or mycobacteria other than *Mycobacterium tuberculosis* (MOTT), are a group of ubiquitous microorganisms that can cause multi-organ infections, especially in immunocompromised patients (1). These organisms are classified as slow or rapid growing according to their speed of growth in the laboratory (2).

Among these microorganisms, *Mycobacterium abscessus* is an environmental rapidly growing mycobacterium that is emerging as an important cause of

Address correspondence to Jo Linda Sinagra, M.D., Pediatric Dermatology Department, San Gallicano IRCCS, Via Elio Chianesi 53, 00144 Rome, Italy, or e-mail: jlsinagra@hotmail.com.

DOI: 10.1111/pde.12333

cutaneous infections in sporadic cases and outbreak settings (3). This bacterium exhibits important biologic characteristics: biofilm production in piped waters; the ability to survive under harsh conditions; and resistance to common sterilizing agents, disinfectants, and water chlorination (4,5). The clinical manifestations are nonspecific and lack characteristic symptoms, usually consisting of suppurative lesions, such as folliculitis, furuncles, abscesses, ulcers, or nodules (6). Skin infections are described in association with invasive, traumatic, or iatrogenic procedures (e.g., Mohs micrographic surgery, cutaneous surgery, punch biopsy, acupuncture, mesotherapy, and injections) (7–9). Immunosuppressed or elderly hospitalized patients are most commonly affected (10), but in 2006, Dytoc et al (11) described an outbreak of clinically distinct cutaneous lesions on the hands and feet caused by *M. abscessus* in a population of children using a public swimming pool. This was the first description of a *M. abscessus* outbreak in a healthy, young population due to nontraumatic transmission. According to the authors, the disease was self-limiting, even without treatment.

We describe an outbreak of skin lesions due to *M. abscessus*, similar to the lesions that Dytoc et al (11) described, in a population of Italian schoolchildren using a swimming pool. To our knowledge, this is the second report of skin infection by *M. abscessus* in a population of nonimmunocompromised children. Based on our experience, this disease is not always self-limiting and may relapse and disseminate if not treated.

PATIENTS AND METHODS

Patient Identification

In January 2010 we evaluated three patients (one boy and two girls, all 4 yrs old) with multiple erythematous, violaceous, tender, painful nodules and pustules located bilaterally on the palms and soles. The patients attended the same school in Rome and used the school's swimming pool. Swabs or biopsies of the lesions were obtained for microbiologic and histopathologic examination. The skin biopsies revealed the presence of suppurative granulomas centered on the dermis. After 12 days, microbiologic examination showed the presence of deep-yellow colonies, identified as *M. abscessus*, in one sample.

All of the children attending the school were consequently examined for dermatologic lesions after their parents provided informed consent. Similarly, anamnestic data were collected regarding exposure to the school's swimming pool and skin conditions in relatives. All suspected cases were directed to our Pediatric Dermatology Department for further investigation.

The following criteria were adopted for diagnosis, considering the young age of the subjects and the traumatic nature of the procedures. Microbiologic samples were obtained from lesions in children with papules, pustules, or nodules on the palms or soles. These children were considered infected (according to the case definition by Dytoc et al (11)), even if the results of microbiologic examinations were negative. Biopsies were taken from patients with papules, pustules, or nodules located on other parts of the body for histologic and microbiologic examination. These children underwent follow-up for 1 year. Environmental samples were collected from the school and from the swimming pool.

Microbiologic Investigation

For microbiologic investigations, the purulent material from swabs or biopsies was inoculated, after appropriate digestion and decontamination, onto culture media (Lowenstein-Jensen Medium; BD Biosciences Division, Sparks, MD) in a mycobacteria growth indicator tube (BD Biosciences Division). The media were incubated at 37°C. The mycobacterial colonies were then subjected to Ziehl-Neelsen staining for acid-fast bacteria and processed for strain typing using the reverse hybridization method (INNo-Lipa Mycobacteria v2; Innogenetics, Ghent, Belgium). Environmental samples were also taken from the swimming pool, the showers, and the school's water supply.

RESULTS

Case Series

Four hundred twenty-seven of 514 schoolchildren, ages 4 to 10 years, were screened; 116 attended the nursery school (mean age 4.5 yrs, range 4–5 yrs) and 311 attended the primary school (mean age 7.8 yrs, range 6–10 yrs). Of the entire sample, 128 children were exposed to the school-annexed swimming pool (nursery school, 45/116; primary school, 83/311), 29 of whom were found to be affected (nursery school, 15/45, 33.3%; primary school, 14/83, 16.8%). No cases were found in children who had never been exposed to the swimming pool. Similarly, no cases were reported in adults visiting the school and using the swimming pool (e.g., teachers and assistants).

Excluding mycobacteriosis, all of the children presented in good health (no history of congenital or acquired immunosuppression and no surgical intervention), although eight (32%) had atopic dermatitis. None of the patients' parents or siblings had suspect lesions, despite the fact that six patients had one or more siblings attending the same school and using the same swimming pool.

Of the affected children, 16 fulfilled the case definition that Dytoc et al (11) provided (red, painful nodules on the palms and soles) and 13 others had multiple similar lesions at other body sites (knees, elbows, forearms, trunk) and a consistent histologic examination.

According to the clinical anamnestic characteristics, we were able to identify two forms, which we defined as palmoplantar type (PPT) and widespread type (WT):

- PPT ($n = 16$) (Figs. 1, 2 and 3A, B): Single or multiple lesions on the palms and soles and no lesions at other body sites. Lesion onset occurred 64.2 days (range 52–71 days) after the first swimming pool exposure.
- WT ($n = 13$) (Figs. 4A, B and 5A, B): Lesions at other body sites (knees, elbows, trunk), with or without lesions on the palms and soles.

The parents had reported onset on the hands and feet approximately 10 to 12 months earlier, 45 to 60 days after the first exposure to the swimming pool. Most of the parents had contacted other dermatologic clinics, but the patients remained undiagnosed or misdiagnosed with (and treated for) warts, without results. The lesions disappeared during the summer but reappeared at other body sites (legs, knees, forearms, abdomen) during the subsequent winter, even without further exposure to the swimming pool.

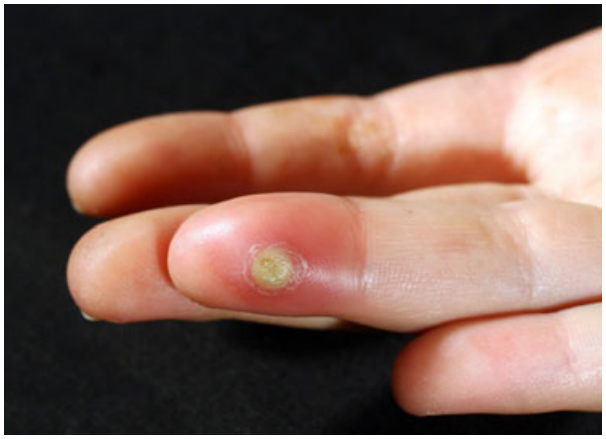

Figure 1. A 6-year-old girl presenting with a single pustule on the finger (palmoplantar type).

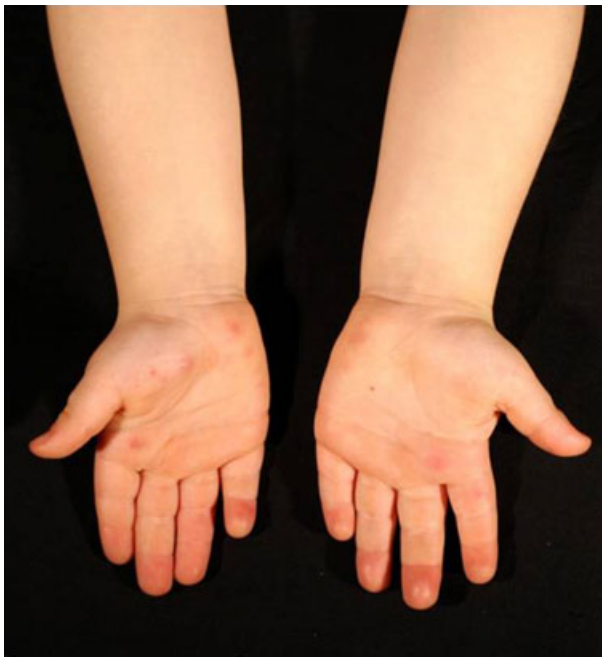

Figure 2. A 4-year-old boy with multiple bilateral lesions on the palms (palmoplantar type).

PPT was associated with younger age (mean age 4.3 yrs, range 4–6 yrs) and exclusively involved nursery school children, whereas WT was found in older children (mean age 7.8 yrs, range 6–10 yrs), all attending the primary school.

In total, 24 children were treated with oral clarithromycin at 15 mg/kg/day until remission (4–8 wks). No children experienced significant side effects during the therapy. Subcutaneous infiltrations remained until the end of the therapy but spontaneously resolved after 3 to 6 months. After 1 year (March 2011), no relapses were observed.

In the PPT group, five children were not treated because their parents did not give their consent to antibiotic therapy, so these children only underwent follow-up (their parents were instructed to contact our clinic should new lesions appear). In all these subjects, the lesions spontaneously disappeared within an average of 132.1 days (range 121–170 days) (May–July 2010), although two children experienced the appearance of new lesions on the knees and elbows during the subsequent winter (January 2011). These individuals were treated with clarithromycin in accordance with the above-mentioned protocol and were still disease free after the 1-year follow-up (January 2012).

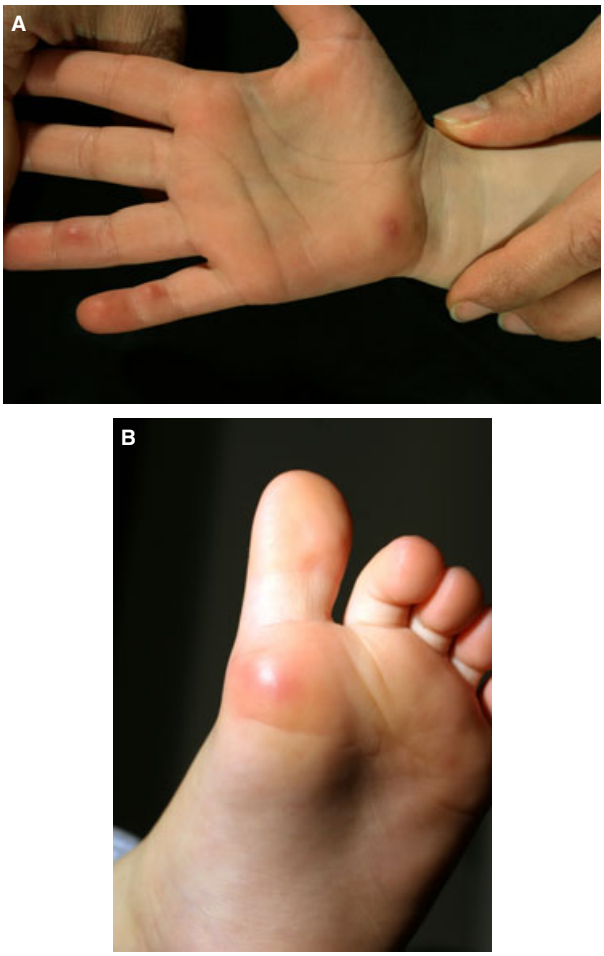

Figure 3. (**A**) Multiple bilateral lesions on the palms of a 4-year-old girl (palmoplantar type). (**B**) Single lesion on the sole of the same child.

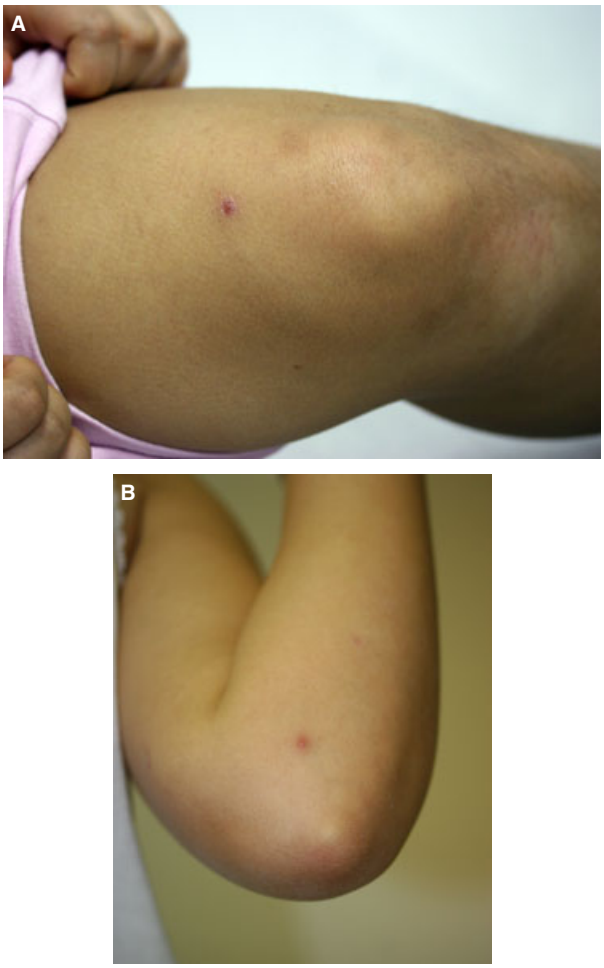

Figure 4. (**A**) An 8-year-old girl presenting with a nodular lesion of the knee (wild type). (**B**) Small nodule on the left forearm of the same patient.

Microbiology

In total, 29 samples were collected for microbiologic examination. Direct observation was negative for all samples. Deep-yellow colonies grew after 12 days from two samples taken from recently developed pustules (2–5 days). Microscopic examination showed the presence of acid-alcohol-resistant bacilli. Strain typing identified the *M. chelonae* complex (group III, *M. abscessus*). All samples obtained from older lesions were negative. The environmental samples were also negative for the isolated species.

Histopathology

Sixteen of 25 children underwent skin biopsies, which revealed a suppurative granuloma mostly centered in the middermis. Psoriasiform or pseudocarcinomatous hyperplasia of the epidermis was observed in all cases. Ziehl-Neelsen staining revealed no bacilli.

DISCUSSION

To our knowledge, this is only the second description of an outbreak of skin infections by *M. abscessus* in a population of immunocompetent children due to nontraumatic transmission. Brantley et al (12) reported a skin infection by *M. abscessus* in a child, most likely subsequent to exposure of a wound to pond water. Two other outbreaks including children were described after injections of contaminated drugs (penicillin and lidocaine) (13,14). In 2005, Dytoc et al (11) first described an outbreak characterized by tender, erythematous papules, pustules, and nodules located exclusively on the hands and feet of children, which they defined as "*M. abscessus* hand-and-foot disease." The authors considered the disease to be self-limiting, for which antibiotic therapy may be not necessary (11).

In our sample, 16 cases had clinical characteristics identical to those that Dytoc et al described (nodules,

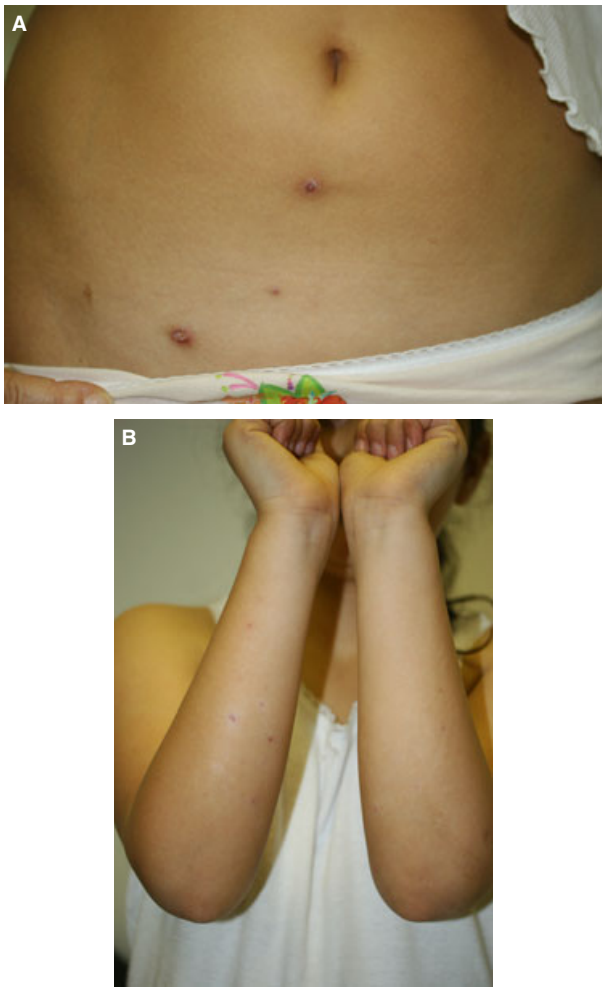

Figure 5. (**A**) Multiple nodular lesions on the abdomen of a 10-year-old girl (wild type). (**B**) Lesions on the forearms (wild type).

papules, and pustules on the hands and feet), whereas 13 had lesions at other body sites (knees, elbows, trunk). All children with WT experienced the first appearance of lesions on the hands and feet, a spontaneous remission during the summer, and a relapse at other body sites approximately 1 year after the first onset. This finding (in contrast to the observations of Dytoc et al) suggests that the disease can become chronic and relapse at sites different from the first locations, most likely by cutaneous, lymphatic, or systemic spreading.

Because of the delayed diagnosis, the possibility that a number of self-limiting cases may have been missed cannot be excluded. Despite this possibility, we found that 33.3% of the youngest children were infected, suggesting a high infection rate.

Pseudomonas hand-and-foot disease shares several clinical features with *M. abscessus* hand-and-foot disease, but usually has a more rapid (2–5 days) onset and faster resolution (15). Single lesions can be misdiagnosed as warts, foreign body granuloma, and perhaps pyogenic granuloma.

Delayed diagnosis is a common problem for MOTT infections and can be attributed to a lack of clinical suspicion (1), nonspecific clinical manifestations, a lack of familiarity with this pathogen, and inadequate laboratory services (4). We found *M. abscessus* in only two patients, based on microbiologic samples obtained from recent lesions (1–2 days). Moreover, in spite of the fact that all 29 cases were found in children who were using or had used the same swimming pool, we did not find *M. abscessus* in the swimming pool or school's water supply. Difficulties in isolating *M. abscessus* are often encountered in clinical and environmental investigations because of cultural difficulties, biases, or delays in sample collection or in the growth of competitor species (4).

Similar to the study by Dytoc et al (11), our case series involved only children, as no adults using the swimming pool (e.g., teachers and assistants) were infected. One possible explanation, in accordance with the report by Dytoc et al, is that the thinner skin of children, and perhaps microabrasions on the hands and feet, could increase the risk of inoculation.

We treated all affected children with systemic clarithromycin monotherapy until remission (6–8 wks). *M. abscessus* is naturally resistant to conventional antimycobacterial drugs (rifampicin, isoniazid, ethambutol) (16), but monotherapy with clarithromycin has been proven to be effective and is associated with a low risk of antibiotic resistance (17). No severe side effects were observed and all of the children concluded the treatment and were completely disease free after the 1-year follow-up.

M. abscessus is an emerging pathogen that is responsible for an increasing number of community- and nosocomially acquired infections, particularly in immunocompromised hosts (16), although it is unclear whether the disease that we describe is rare or an emerging clinical entity. Even if its clinical manifestations are mild, we recommend antibiotic therapy in children since it is impossible to foresee the potential risks related to acquired permanent or transient immunodepressive conditions (systemic infections, surgical interventions).

It is important to educate physicians (particularly pediatricians and dermatologists) about the disease's existence to improve diagnosis and to better define the disease's relevance and clinical and epidemiologic features.

REFERENCES

1. Bhambri S, Bhambri A, Del Rosso JQ. Atypical mycobacterial cutaneous infections. Dermatol Clin 2009;27:63–73.
2. Runyon EH. Pathogenic mycobacteria. Bibl Tuberc 1965;21:235–287.
3. Uslan D, Kowalski TJ, Wengenac NL et al. Skin and soft tissue infections due to rapidly growing mycobacteria comparison of clinical features, treatment, and susceptibility. Arch Dermatol 2006;142:1287–1292.
4. Piersimoni C, Scarparo C. Extrapulmonary infections associated with nontuberculous mycobacteria in immunocompetent persons. Emerg Infect Dis 2009;15:1351–1358.
5. van Ingen J, Boeree MJ, Dekhuijzen PNR et al. Environmental sources of rapid growing nontuberculous mycobacteria causing disease in humans. Clin Microbiol Infect 2009;15:888–893.
6. Wallace RJ Jr, Swenson JM, Silcox VA et al. Spectrum of disease due to rapidly growing mycobacteria. Rev Infect Dis 1983;5:657–679.
7. Wongkitisophon P, Rattanakaemakorn P, Tanrattanakorn S et al. Cutaneous *Mycobacterium abscessus* infection associated with mesotherapy injection. Case Rep Dermatol 2011;3:37–41.
8. Ricciardo B, Weedon D, Butler G. *Mycobacterium abscessus* infection complicating a professional tattoo. Australas J Dermatol 2010;51:287–289.
9. Steyaert S, Stappaerts G, Mareen P et al. Soft tissue infections with atypical mycobacteria in two patients with inflammatory rheumatic diseases using TNF-inhibitors and/or leflunomide. Acta Clin Belg 2011; 66:144–147.
10. Elston D. Nontuberculous mycobacterial skin infections—recognition and management. Am J Clin Dermatol 2009;10:281–285.
11. Dytoc MT, Honish L, Shandro C et al. Clinical, microbiological, and epidemiological findings of an outbreak of *Mycobacterium abscessus* hand-and-foot disease. Diagn Microbiol Infect Dis 2005;53:39–45.
12. Brantley JS, Readinger AL, Morris ES. Cutaneous infection with *Mycobacterium abscessus* in a child. Pediatr Dermatol 2006;23:128–131.
13. Villanueva A, Calderon RV, Vargas BA et al. Report on an outbreak of post-injection abscesses due to *Mycobacterium abscessus*, including management with surgery and clarithromycin therapy and comparison of strains by random amplified polymorphic DNA polymerase chain reaction. Clin Infect Dis 1997;24:1147–1153.
14. Zhibang Y, BiXia Z, Qishan L et al. Large-scale outbreak of infection with *Mycobacterium chelonae* subsp. *abscessus* after penicillin injection. J Clin Microbiol 2002;40:2626–2628.
15. Yu Y, Cheng AS, Wang L et al. Hot tub folliculitis or hot hand and foot syndrome caused by *Pseudomonas aeruginosa*. J Am Acad Dermatol 2007;57:596–600.
16. Medjahed H, Gaillard JL, Reyrat JM. *Mycobacterium abscessus*: a new player in the mycobacterial field. Trends Microbiol 2010;18:117–123.
17. Weitzul S, Eichhorn PJ, Pandya AG. Nontuberculous mycobacterial infections of the skin. Dermatol Clin 2000;18:359–377.