Nontuberculous Mycobacteria
Skin and Soft Tissue Infections

Tania M. Gonzalez-Santiago, MD, Lisa A. Drage, MD*

KEYWORDS

• Nontuberculous mycobacteria • Atypical mycobacteria • Skin and soft tissue infections
• Rapidly growing mycobacteria • *Mycobacterium chelonae* • *Mycobacterium fortuitum*
• *Mycobacterium abscessus* • *Mycobacterium marinum*

KEY POINTS

- Skin and soft tissue infections caused by nontuberculous mycobacteria (NTM), especially the rapidly growing mycobacteria, appear to be increasing in incidence.
- Consider NTM as a cause of skin and soft tissue infection after trauma, surgery, or a cosmetic procedure, especially if the infection is not responding to typical antibiotic regimens.
- Skin signs can include abscesses, sporotrichoid nodules, or ulcers, but may not be distinctive, necessitating a high index of clinical suspicion.
- Obtain tissue cultures and susceptibility studies specifically for mycobacteria.
- Management is via prolonged antibiotic treatment that is species specific, generally based on antimicrobial susceptibility studies and may include surgical intervention.

INTRODUCTION
Definition and Classification

Mycobacteria species other than those of the *Mycobacterium tuberculosis* complex or *Mycobacterium leprae* are known as nontuberculous mycobacteria (NTM), environmental mycobacteria, or atypical mycobacteria. NTM are a diverse group of ubiquitous, environmental, acid-fast organisms that can produce a wide range of diseases, including infections of the skin and soft tissues. More than 170 species of NTM have been identified, most of which have been incriminated in skin and soft tissue infections (SSTI).[1,2] Traditionally, NTM have been classified into Runyon groups based on colony morphology, growth rate, and pigmentation.[3,4] As technology moves forward, this classification system has become less useful and identification is now made using rapid molecular diagnostic systems.[5] Nonetheless, growth rates continue to provide practical means for grouping species of NTM. On this basis, NTM can be categorized into rapidly growing mycobacteria (RGM) and slowly growing mycobacteria (SGM).

RGM include species that produce mature growth on media plated within 7 days. These are subdivided into 5 groups based on pigmentation and genetic similarity: *Mycobacterium fortuitum, Mycobacterium chelonae/abscessus, Mycobacterium mucogenicum, Mycobacterium smegmatis*, and early pigmenting RGM. SGM include species of mycobacteria that require more than 7 days to reach mature growth. Examples of SGM

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Department of Dermatology, Mayo Clinic College of Medicine, Mayo Clinic, 200 First Street Southwest, Rochester, MN 55905, USA
* Corresponding author.
E-mail address: drage.lisa@mayo.edu

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are *Mycobacterium marinum, Mycobacterium ulcerans, Mycobacterium kansasii, Mycobacterium haemophilum,* and *Mycobacterium scrofulaceum.* Some species require nutritional supplementation of routine mycobacteria media, grow best at lower/higher temperatures or require prolonged incubation.

Most NTM species are easily isolated from the environment, including water (both natural and municipal systems), soil, plants, animals, and birds.[6] Exceptions to this include *M haemophilum* and *M ulcerans*, which are rarely isolated. Tap water is considered the major reservoir for NTM pathogens in humans and as such is of increasing public health concern.[7] Species typically recovered from tap water include *Mycobacterium gordonae, M kansasii, Mycobacterium xenopi, Mycobacterium simiae, Mycobacterium* avium complex (MAC), and the RGM. NTM develop and are protected within biofilms, the filmy layer between the solid and liquid interface, in municipal water systems. Carson and colleagues[8,9] showed that 83%of the incoming city water in hemodialysis centers throughout the United States contained NTM. The presence of mycobacteria in up to 90% of samples taken from piped water systems has been described.[10] Furthermore, biofilms may make the mycobacteria resistant to common disinfectants. NTM are difficult to eradicate with common decontamination techniques and are relatively resistant to standard disinfectants such as chlorine, glutaraldehyde, gigasept, and virkon.[11–13] They can grow in hot and cold water systems. In some cases, temperatures of up to 70°C are required to inhibit the organism.[14,15] Importantly, no evidence of person-to-person spread has been reported with NTM.[16]

Clinical Syndromes

Four clinical syndromes account for most infections with NTM: pulmonary disease, lymphadenitis, disseminated disease, and SSTIs.[17]

Pulmonary disease

The most common form of localized NTM infection is chronic pulmonary disease in human immunodeficiency virus (HIV)-negative hosts. Signs and symptoms of NTM lung disease are often nonspecific, making this a challenging diagnosis that requires extensive laboratory and imaging workup. MAC followed by *M kansasii*, and *M abscessus* are the most common pathogens in the United States.

Lymphadenitis

Localized cervical lymphadenitis is the most common NTM disease in children and is typically caused by MAC and *M scrofulaceum*.[18] It occurs in children between 1 and 5 years of age. The cervicofacial nodes, particularly the submandibular nodes, are most frequently involved.[10] These can enlarge rapidly with the formation of fistulas to the skin, and prolonged drainage may occur. As with all other NTM infections, definitive diagnosis of lymphadenitis is made by recovery of the etiologic organism from cultures.[7]

Disseminated Disease

Disseminated NTM infections occur almost exclusively in immunocompromised patients.

Disseminated disease in patients with human immunodeficiency virus

Although *M tuberculosis* continues to be the most prevalent mycobacterial disease in HIV-AIDS, disseminated NTM is well documented and is associated with increased mortality in this patient population.[19] The most commonly implicated NTM is MAC and although the incidence has decreased significantly with the introduction of highly active antiretroviral therapy, it remains an important complication of AIDS.[20] *M kansasii, Mycobacterium genavense, M scrofulaceum, M xenopi, M fortuitum,* and *M gordonae* are among many other NTM responsible for disseminated disease in patients with HIV.[21] Symptoms are not specific and in most cases resemble those seen in disseminated tuberculosis. These include intermittent or persistent fever, night sweats, weight loss, fatigue, malaise, and anorexia.[22]

Disseminated disease in the severely immunocompromised

Disseminated disease in patients without HIV is rare and seen in the setting of significant immunosuppression (eg, transplant recipients, chronic corticosteroid use, leukemia). Systemic dissemination of a primary cutaneous NTM can occur. In most cases, disseminated disease presents with disseminated cutaneous lesions. The RGM species *M chelonae* is the most commonly isolated organism, presenting with multiple, red, draining, subcutaneous nodules or abscesses. *M kansasii, M haemophilum, M fortuitum, M abscessus,* and others have also been reported.[23]

Skin and soft tissue infections

The increasing reports of SSTI NTM infections in recent years have attracted significant attention in the medical community. Initially thought to reflect the increased immunosuppressed population, numerous reports document infection in healthy individuals. The exact incidence of SSTI NTM infections is yet to be determined. The largest