All about *Mycobacterium simiae* in Brief

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**Abstract**

More than hundreds pathogens of mycobacterium have been identified till now but a minority of these bugs cause diseases in humans. *M. simiae*, an emerging bacterium that has been discovered recently, commonly recovered from human sputum especially in patients with underlying lung diseases. Most commonly this bacterium is a bystander rather than a true culprit. Such differentiation is critical to avoid unnecessary long term treatment not free of side effects.

**Keywords:** Non-tuberculous mycobacterium; *M. simiae*; Immunocompetent; Lung diseases

**Introduction**

Different terms are used to define non-tuberculosis mycobacteria [NTM] including atypical mycobaciera and mycobacteria other than tuberculosis [MOTT]. However, NTM terminology is the most used name worldwide. NTM, an emerging entity, includes more than 100 species with variable microbiological features, clinical manifestations and significances. Nevertheless, NTM therapy also differs between species.

NTMs are rods shaped bacilli similar to *Mycobacterium tuberculosis* [MTB]. In 1959, Runyon classified these bacteria into four groups according to their ability to form pigment after exposure to light or dark and the rapidity of their growth as well (Table 1) [1].

The majority of human pathogens are slowly grower like *M. kansasi*, *M. marinum*, *M. avium*, *M. intracellulare*, *M. simiae* [1]. However, *M. simiae* is the only niacin-positive MOTT, which makes it easily confused with *Mycobacterium tuberculosis* [2]. *M. simiae* like other NTM is a ubiquitous organism with huge environmental reservoirs, such as natural and municipal water, soil, aerosols, protozoan, animals, and humans [3].

In 1965, *M. simiae* was initially isolated from maccacus rhesus monkeys [4]. It was first reported in Israel, Cuba, and south western America and then reports from middle east and Asia identified the presence of this emerging specie [2,5].

**Epidemiology**

The incidence of diseases attributed to NTM is not well established, due to underreporting of new cases. On the other hand, the frequency of respiratory NTM is increasing worldwide. Data from Australia showed higher incidence in 2005 compared to 1999 [6,7].

**Clinical manifestation**

NTM have a broad spectrum of clinical manifestations. They can cause either symptomatic or asymptomatic infections. Four clinical syndromes account for nearly all cases: pulmonary diseases, lymphadenitis, skin or soft tissue diseases, and disseminated diseases especially in AIDS patients. All four clinical syndromes are increasing in frequency, particularly in immunosuppressed hosts [4]. Rarely *M. simiae* can be a cause of central line related bloodstream infection especially in immunosuppressed patients [8]. *M. simiae* is commonly isolated from respiratory specimen without being considered as a true pathogen especially in immunocompetent patients [9,10].

Pulmonary symptoms due to *M. simiae* are nonspecific. Infected patients frequently present with cough, sputum production, hemoptysis, sweating, weight loss, low grade fever, and dyspnea [4,11]. Patients with underlying lung diseases such as prior pulmonary tuberculosis or silicosis, chronic obstructive pulmonary disease [COPD], and non-cystic fibrosis bronchiectasis have higher risk for *M. simiae* than healthy people [11]. The association between *M. simiae* and cystic fibrosis was also described [12]. Furthermore, other co-morbidities, such as Diabetes Mellitus, cardiovascular diseases, and malignancies could also predispose to *M. simiae* infection [13]. Other than that, *M. simiae* can cause disseminated infection in immunocompromised patients mainly HIV [14]. For long time this organism was thought to cause disseminated infections only in immunocompromised individuals. However, recent reports showed that disseminated *M. simiae* can also be seen in immunocompetent patients [10]. *M. simiae* may rarely be a cause hematogenous spread from pneumonia, leading to multifocal osteomyelitis in immunocompetent patient [15].

**Diagnosis**

Differentiation between true *M. simiae* infection and colonization is critical since treatment of infected cases is recommended for at least one year after negative culture. Thus, the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) developed guidelines criteria to diagnose NTM pulmonary diseases (Table 2).

In addition to microbiologic information, these criteria include data about host factors, clinical, and radiological findings consistent with pulmonary diseases which mainly focused on recurrent isolation of mycobacteria from sputum or isolated from at least one bronchial wash in symptomatic patients [16]. Tuberculosis skin test (TST) is not a specific test as positive results are seen in different types of mycobacterium. TST is positive in 76.9 % of *M. simiae* pulmonary cases [4].

**Table 1: NTM Runyon Classification**

| Produce yellow pigment in light | Slowly growing | Runyon I |
| Yellow pigment in light and dark | Slowly growing | Runyon II |
| No pigment | Slowly growing | Runyon III |
| No pigment | Rapidly growing | Runyon IV |

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Radiographic findings

Radiographic findings with NTM pulmonary infections could be very similar to those seen in MTB findings. In addition, most patients with NTM have structural lung diseases. Typical radiographic features include nodular lesions (100%), cavity lesions (88.5%), and bronchiectasis (84.6%). The middle and lower lobes are commonly involved in *M. simiae* infections [4].

Treatment

Although NTM might share similar clinical and radiological findings, treatment approach is different between species. Therefore identification of mycobacterium species is extremely important whenever NTM is recovered. The choice of antibiotics depends on the susceptibility pattern obtained from in vitro susceptibility tests that includes Clinical and Laboratory Standards Institute (CLSI) E-test, agar-based testing methods, and the disk elution and diffusion method [17].

*M. simiae* isolates are susceptible to fluoroquinolones and amikacin but resistant to all others including isoniazid, capreomycin, minocycline, doxycycline, p-aminosalicylic acid, and ethionamide [17]. However, some isolates are susceptible in vitro to trimethoprim-sulfamethoxazole, ciprofloxacin [2].

To date, there is no standard treatment yet for *M. simiae*, but the following drugs: clarithromycin, quinolones, ethambutol, cycloserine, amikacin but resistant to all others including isoniazid, capreomycin, minocycline, doxycycline, p-aminosalicylic acid, and ethionamide seems to be effective. Surprisingly *M. simiae* isolates remain sensitive to moxifloxacin even if the isolates are resistant to ciprofloxacin [2].

Regimen including moxifloxacin, clarithromycin and a third drug to which the isolate is susceptible (like trimethoprim-sulfamethoxazole, clofazimine, streptomycin, amikacin) is the best treatment approach [2].

Aminoglycosides and clofazimine are promising therapeutic options [18].

Conclusion

*M. simiae* infection is uncommon and can affect immunosuppressed and immunocompetent patients as well. Its presence in respiratory specimen could represent either true infection or colonization. The clinical manifestations and radiological findings usually resemble another infectious NTM. However early diagnosis is necessary in order to implement appropriate treatment despite limited choices in such cases.

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