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CASE REPORTS

Mycobacterium simiae Complex Infection in an Immunocompetent Child▽

Andrea T. Cruz,[1,2]* Veronica K. Goytia,[1] and Jeffrey R. Starke[1]

Department of Pediatrics, Sections of Infectious Disease[1] and Emergency Medicine,[2] Baylor College of Medicine and Texas Children's Hospital, Houston, Texas

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Nontuberculous mycobacteria are ubiquitous in the environment but rarely infect immunocompetent patients. We describe a pediatric case of *Mycobacterium simiae* complex lymphadenitis in an immunocompetent child and review the natural history, clinical manifestations, diagnosis, and current management of the disease.

CASE REPORT

A 19-month-old Latin American female presented with a left-sided neck mass first noted 5 days prior to admission. She had seen her physician 3 days prior to admission and was started empirically on oral clindamycin for lymphadenitis. A tuberculin skin test (TST) was placed. On presentation to the emergency department, the TST was 20 mm. The family denied fever, cough, weight loss, night sweats, pallor, fatigue, or easy bruising.

The child was born in Houston; her parents had emigrated from Guatemala 5 years prior to admission. The family denied travel outside of Texas, but multiple relatives had visited from abroad, and a friend of the family had been incarcerated 2 months prior to contact with the patient. A maternal uncle had a history of chronic cough of unclear etiology, and a maternal grandmother, who had never had contact with the patient, had a history of a positive TST and normal chest radiograph in the past. The patient's father, who had worked in a nursing home in Guatemala, had a negative TST 5 years ago. The child had no prior TSTs and had not received a BCG vaccine.

On physical examination, she was a healthy-appearing girl. Vital signs included a temperature of 97.7°F, pulse of 124 beats/min, respiration at 26 breaths/min, blood pressure of 118/46 mm Hg, and a pulse oximetry of 99% on ambient air. Height and weight were in the 50th and 90th percentiles, respectively. The child was alert and smiling. A 3-by-3-cm left submandibular lymph node was palpable; it was not fluctuant, erythematous, or tender, and had no overlying violaceous skin discoloration. The patient had no palpable adenopathy elsewhere. A 20-mm TST induration remained visible on the left forearm; the remainder of her physical examination was normal.

The white blood count was 11,800/mm^3 with 54% neutrophils, 41% lymphocytes, 3% monocytes, and 2% eosinophils. The hemoglobin level was 13.3 g/dl, and the platelet count was determined to be 400,000/mm^3. Human immunodeficiency virus (HIV) enzyme-linked immunosorbent assay was negative; quantitative immunoglobulins and neutrophil oxidative burst assay for chronic granulomatous disease were normal.

Chest radiography demonstrated prominence of the right hilum and a soft tissue density in the left paratracheal region that suggested the presence of adenopathy. Serial gastric aspirates for an acid-fast smear were negative. Partial excisional biopsy of the cervical lymph node was performed; complete excision was not a surgical option given the deep extension of the lymph node. Histopathologic examination of the partial cervical lymph node excisional biopsy revealed multiple caseating granulomas and rare acid-fast organisms. The patient was discharged on daily directly observed therapy with isoniazid, rifampin, and ethambutol; clarithromycin was added for coverage of nontuberculous mycobacteria. Acid-fast culture of the biopsy specimen grew *Mycobacterium simiae* complex after 6 weeks, as identified by high-performance liquid chromatography (HPLC) by the city health department; the isolate was resistant to isoniazid, rifampin, streptomycin, and ethambutol and susceptible to amikacin, ciprofloxacin, and kanamycin. It was not possible to further speciate this isolate; however, the growth characteristics (niacin production) were most consistent with *M. simiae.* Medications were discontinued when culture results became available. The chest radiograph was normal, and the patient's cervical adenopathy continued to decrease in size off of therapy, with resolution by 8 months. Chest radiographs and tuberculin skin tests on the parents were negative.

M. simiae complex is comprised of several phylogenetically related species, including *M. simiae*, *M. triplex*, *M. genavense*, *M. heidelbergense*, and *M. lentiflavum* (15). The most common species associated with human pathology has been *M. simiae*, which was first isolated from rhesus macaques in 1965 (6); disease in humans was described several years later. This species is a slow-growing photochromogen, appearing rust-colored after exposure to light, and is the only nontuberculous

* Corresponding author. Mailing address: Texas Children's Hospital, Feigin Center, Suite 1150, 6621 Fannin Street, MC 3-2371, Houston, TX 77030-2399. Phone: (832) 824-5582. Fax: (832) 825-5424. E-mail: atcruz@texaschildrenshospital.org.

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mycobacterium (NTM) that, like *M. tuberculosis*, is niacin positive (14, 15). This species is less environmentally ubiquitous than other NTMs, and most isolates have been reported from the southwestern United States, Cuba, and Israel. The environmental niche for *M. simiae* is assumed to be aquatic. Although more than 400 cases from a variety of sites have been reported in the literature, the range of pathogenicity has varied widely; it is estimated that only 9 to 21% of laboratory isolates are associated with clinical disease (12).

The majority of cases of *M. simiae* complex infection reported in the last quarter century have been in HIV-infected patients, in whom disseminated disease can occur, primarily with pulmonary and reticuloendothelial system involvement (1). In HIV-uninfected adults, pulmonary manifestations are most common, although lymphadenopathy, skin lesions, and genitourinary tract involvement have also been described (12). Two pseudo-outbreaks have also been described. The first was an outbreak of *M. simiae* pulmonary colonization in 22 patients in San Antonio, TX, 3 of whom met the criteria for clinical disease. The organism was recovered from water samples obtained both in the hospital and in patients' homes (2). A second pseudo-epidemic was reported in Houston: 65 cultures were obtained over a 4-year period due to a contaminated water supply in hospital buildings. All cultures represented colonization and not clinical disease (3). One immunocompetent woman developed nodular skin disease after injection of unlicensed cosmetic products (10). Only four cases of *M. simiae* disease, as opposed to colonization, have been described in pediatric patients in the English-language literature: three immunocompetent children with cervical adenopathy (5, 9) and one HIV-infected child with immune reconstitution syndrome after initiation of antiretroviral therapy (11). *M. lentiflavum* has been documented to cause cervical adenitis in children (4).

M. simiae can be cultured on Löwenstein-Jensen or Middlebrook media and typically requires 4 to 6 weeks to grow. Mycolic acid profile via HPLC enables discrimination between *M. simiae*, *M. tuberculosis*, and *M. avium* complex (7). However, HPLC does not differentiate between members of the *M. simiae* complex (13); these can be speciated by oligonucleotide array (8). In addition, *M. simiae* is the only member of the complex that produces niacin (14). TST results are more than 15 mm in ca. 60% of children with lymphadenitis due to NTM; in children with *M. simiae* infection, the average TST induration was 20 mm (5).

There are no published clinical trials for the treatment of *M. simiae* complex disease. This group is usually resistant to many of the agents used in the treatment of *M. tuberculosis*. Agents reported to have activity against members of the *M. simiae* complex include clarithromycin, ethambutol, ethionamide, fluoroquinolones, amikacin, and cycloserine. In vitro studies in murine models have demonstrated that the combination of clarithromycin with either ethambutol or ofloxacin was superior to either agent used as monotherapy (16). Duration of antimycobacterial therapy has varied from 6 months to more than 1 year and is often based upon clinical response. However, immunocompetent patients who have an excisional biopsy performed may not require adjunctive antimicrobial therapy. Fine-needle aspiration is not recommended because of the risk of creating a chronically draining sinus tract.

In our patient, epidemiologic risk factors initially favored a diagnosis of tuberculosis. Thus, we used a four-drug combination (isoniazid, rifampin, ethambutol, and clarithromycin) that offered coverage both for *M. tuberculosis* and NTMs. The patient continued to improve clinically off of medication, with symptom resolution and chest radiograph normalization several months after partial surgical excision. Despite risk factors for tuberculosis, this child grew a rare species of NTM. In areas with a low prevalence of tuberculosis, a case of isolated adenopathy and a positive TST in an otherwise healthy child under 4 years of age is more likely to represent NTM infection.

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