Case Reports

Nontuberculous Mycobacterial Pulmonary Disease in an Immunocompetent Adolescent

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We report a 16-year-old previously healthy boy who presented with a 6-week history of fever, anorexia, weight loss, and respiratory distress. The chest radiograph showed bilateral upper infiltrates and cavitations indistinguishable from *Mycobacterium tuberculosis* infection. He was actually infected with *M. kansasii*. Treating *Mycobacterium* in an immunocompetent child requires multiple antimycobacterial drugs, including isoniazid, rifampicin, and ethambutol for at least 12 months after negative sputum culture. *Key words: mycobacteria, pulmonary disease, Mycobacterium tuberculosis, Mycobacterium kansasii, children, pediatric.* [Respir Care 2008;53(7):908–911. © 2008 Daedalus Enterprises]

Introduction

Diseases caused by nontuberculous mycobacteria are uncommon in the pediatric population. Most nontuberculous mycobacteria infections in children are localized to the cervical and submandibular regions.[1] There are few published data on nontuberculous mycobacteria pulmonary diseases in children.[2-9] We report a previously healthy adolescent boy with cough, fever, bilateral apical pulmonary infiltrates, and sputum culture positive for *M. kansasii*.

Case Summary

A 16-year-old Taiwanese student seen in the out-patient clinic of our hospital had cough and intermittent low-grade fever for several weeks, during which he had been anorexic and had lost 1.5 kg. His history included no smoking, alcohol consumption, or illicit drug use. Physical examination revealed an acutely ill-looking adolescent boy with a temperature of 36.9°C and mild tachypnea (respiratory rate 20 breaths/min). Chest auscultation revealed fine inspiratory crackles in both upper lung fields. There was no cyanosis or clubbing of the fingers. He had received bacillus of Calmette and Guérin vaccination on the day of his birth, and he had no family member with tuberculosis and no known tuberculous contacts. He had not traveled to foreign countries. His hemogram showed a white blood cell count of 6.6×10^3 cells/μL, hemoglobin 13 g/dL, platelet count $32.8 \times 10^3/\mu$L, and a normal differential count (64% neutrophils, 24% lymphocytes, 8.7% monocytes, 3% eosinophils). Serum aspartate aminotransferase and alanine aminotransferase values were 26 IU/mL and 24 U/L, respectively. A plain chest radiograph (Fig. 1) showed bilateral upper-lobe infiltrates with multiple cavitations. A high-resolution computed tomogram (Fig. 2) showed multiple air-fluid cystic lesions, dilated bronchi, thickened bronchial walls, and bilateral diffuse reticulonodular infiltrates. A tuberculin skin test revealed 15 mm of induration 72 hours after placement. Expectorated sputum had 1+ to 2+ acid-fast staining bacilli on 3 occasions. Sweat chlorine test (with the pilocarpine inophoresis method) showed a concentration < 60 mEq/L. Serum immunoglobulin (IgG, IgA, and IgM) were within normal limits. Human immunodeficiency virus enzyme-linked immunosorbent assay was negative. Further immunological studies showed 64% cluster of differentiation 3 (CD3+) cells, 19% CD19+ cells, and a CD4+/CD8+ ratio of

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The authors report no conflicts of interest related to the content of this paper.

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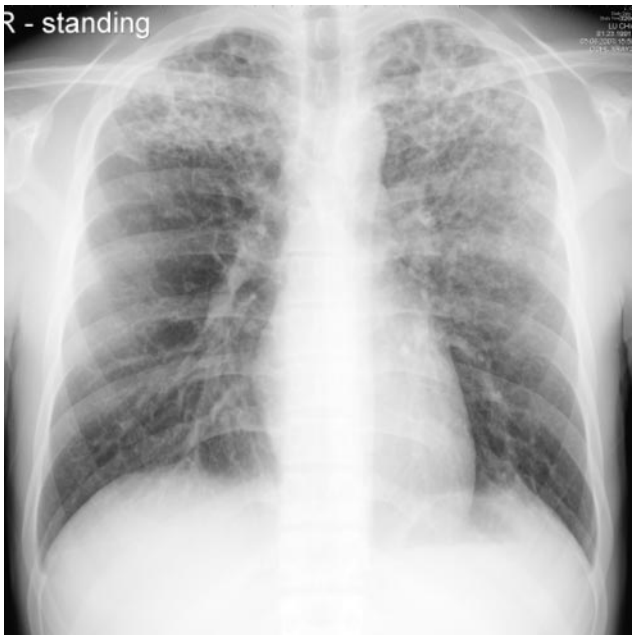

Fig. 1. Plain chest radiograph shows bilateral upper-lobe infiltrates and multiple cavitations.

1:1.2. Interferon gamma productions to Candida antigen and Concanavalin A were normal, as compared to normal controls. Interleukin-12 receptor assay was not done because the test was not available in our laboratory.

Four weeks later, *M. kansasii* was isolated in 3 sputum specimens. Initially, the patient had been put on multiple anti-tuberculosis medications, including isoniazid (300 mg/d), rifampicin (600 mg/d), and pyranizamide (1,500 mg/d). That regimen was subsequently modified: pyranizamide was replaced with ethambutol (15 mg/kg/d). Follow-up chest radiograph 1 month later revealed regression of the apical infiltrates and cystic lesions.

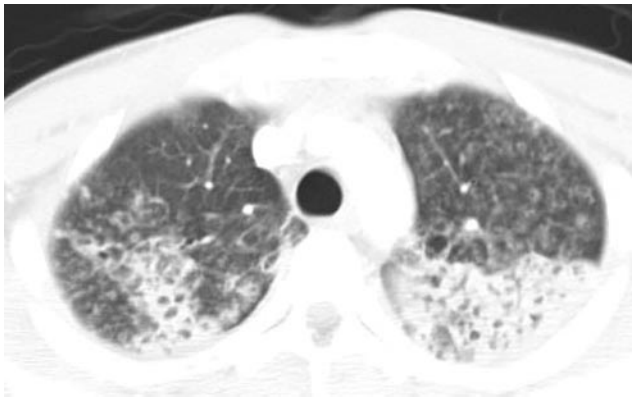

Fig. 2. Computed tomogram shows ill-defined air-space opacities, dilated bronchi, bronchial-wall thickening, and air-filled cavitations.

Discussion

Nontuberculous mycobacteria are ubiquitous in soil, water supplies, domestic and wild animals, dust, and plants. The prevalence of nontuberculous mycobacteria disease varies geographically.[10-12] In the central United States, parts of the United Kingdom, and South Africa the commonest slow-growing nontuberculous mycobacteria that cause pulmonary disease in adults are *M. avium intracellulare* complex, *M. xenopi*, and *M. kansasii*, respectively.[11] The true prevalence of nontuberculous mycobacteria pulmonary disease in Taiwan is not known. All previously reported local cases were in adults.[12]

Risk factors that predispose adults to nontuberculous mycobacteria pulmonary infection include industrial dusts (eg, from mining), chronic pulmonary diseases (eg, from smoking, bronchiectasis, chronic obstructive pulmonary disease, or previous pulmonary tuberculosis), and congenital or acquired immunodeficiency (human immunodeficiency virus).[11] In a study of 262 adult patients who did not have human immunodeficiency virus, the majority of patients with *M. avium intracellulare* complex infection had preexisting immunodeficiency.[11] Though half of the patients with *M. kansasii* pulmonary disease were immunocompetent, most of them had preceding heavy smoking, chronic obstructive pulmonary disease, and alcohol misuse.[11]

In children with nontuberculous mycobacteria infection, common predisposing conditions are primary immunodeficiency disorders, cystic fibrosis, and immunosuppressive therapy for malignancies.[2-9] Immunodeficiency due to mutations in the interferon gamma receptor, interleukin-12 receptor β_1, and interleukin-12 receptor p40 genes have been reported and are associated with disseminated nontuberculous mycobacteria or bacillus of Calmette and Guérin.[13] Nonetheless, nontuberculous mycobacteria infections also occur in seemingly healthy adult and pediatric patients.[14,15] Our patient had been previously healthy, had exclusively pulmonary involvement, and had quick response to anti-tuberculosis therapy. Complete interferon gamma and interleukin-12 receptor deficiency is not likely, but partial deficiency cannot be totally excluded.

We searched the MEDLINE and PubMed databases from 1970 to 2007 for cases of nontuberculous mycobacteria pulmonary disease in children, with the words "nontuberculous," "mycobacteria," "atypical," "children," "pediatric," and "pulmonary." Only articles reported in English were included. We considered only cases in patients < 18 years old. Cases confined to the cervical region were excluded. Table 1 summarizes 8 cases of pulmonary *M. kansasii* infection.

Dore and colleagues reported 10 children with nontuberculous mycobacteria pulmonary disease < 5 years old, the majority of whom presented with mediastinal lymph-

Table 1. Seven Case Reports of *Mycobacterium kansasii* Pulmonary Disease in Pediatric Patients, Published 1970–2007

First Author	Age	Sex	Underlying Disease	Clinical Features	Radiographic Findings	Outcome
Wong (present report)	16 y	M	Normal	Fever, cough	Bilateral apical infiltrates and cavities	Improved
Lincoln[7]	7 mo	M	Probable immunodeficiency	Fever, respiratory distress	Disseminated pulmonary abscess and progressive skeletal and spine lesions	Died
Lincoln[7]	4 y	F	Normal	Fever, cough, wheezing	Irregular pulmonary infiltrates and blunting of costophrenic angle	Not stated
Lincoln[7]	10 y	F	Normal	Fever, cough, weight-loss	Left-upper-lobe infiltrates and left-hilar enlargement	Improved
Lincoln[7]	Not stated	Not stated	Normal	Acute pneumonia	Consolidation and pleural effusion	Improved
Lincoln[7]	8 y	F	Normal	Not stated	Diffuse bilateral infiltrates	Improved
Oermann[8]	20 y	M	Cystic fibrosis	Fever and pulmonary exacerbation	Bronchiectasis and infiltrates	Return to baseline function of cystic fibrosis
Cuppen[16]	14 y	M	Hypoplastic myelodysplastic syndrome	Hemoptysis and broncholithiasis	Bilateral pulmonary infiltrates with large calcified bronchial tumor	Died

adenopathy and extrinsic bronchial obstruction, but none of those were due to *M. kansasii*.[2]

The largest number of cases of nontuberculous mycobacteria pulmonary disease in the pediatric population was detailed by Nolt et al.[9] However, in that series of 43 cases there were no cases of *M. kansasii*. Five cases of *M. kansasii* pulmonary disease in children were reported by Lincoln and Gilbert, in the 1970s, and those patients had good outcomes, except for one patient with primary T cell deficiency, who died.[7] Oermann et al reported improvement of a 20-year-old man with cystic fibrosis and concomitant *M. kansasii* pulmonary infection after therapy.[8]

In adult patients, upper-lobe infiltrates and cavitary lesions have appeared in about three quarters of nontuberculous mycobacteria infections that were indistinguishable from *M. tuberculosis* infection.[11] The radiographic findings of nontuberculous mycobacterial pulmonary disease in children range from pulmonary infiltrates to obstructive emphysema by hilar lymphadenopathy.[2-4] In an adolescent boy with cough, malaise, weight loss, bilateral apical infiltrates, and cavitations, pulmonary tuberculosis should be highly suspected, even without preliminary laboratory confirmation, so early institution of multiple anti-tuberculous medications (isoniazid, rifampicin, ethambutol, and pyrazinamide) is necessary. Subsequent isolation of *M. kansasii* should not be regarded as contamination or colonization if multiple specimens reveal heavy growths of the organism, and this infection must be treated accordingly.

Various regimens for different nontuberculous mycobacteria infections have been suggested, using combinations of clarithromycin, quinolones, cephalosporins, amikacin, and imipenem. For adult patients, *M. kansasii* pulmonary infection should be treated with isoniazide (300 mg/d), rifampician (600 mg/d), and ethambutol (15 mg/kg/d) for 18 months, and the patient should have at least 12 months of negative sputum culture.[17,18] There is no standard regimen for children, but strategic therapy for pulmonary nontuberculous mycobacteria infections in pediatric patients has been based largely on adult studies and anecdotal pediatric case reports.

In summary, in children with clinical and radiographic features of pulmonary tuberculosis but lack of contact his-

tory and negative sputum culture, nontuberculous mycobacteria infection should be highly suspected, despite its uncommon occurrence. Immunodeficient patients with nontuberculous mycobacteria pulmonary disease have a poor prognosis, so screening for human immunodeficiency virus and primary immunodeficiency is mandatory. Despite the lack of standard regimen for nontuberculous mycobacteria infection in children, multiple drugs (isoniazide, rifampicin, and ethambutol) should be given for at least 12 months after sputum culture is negative.

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