Intrathoracic Mycobacterium avium Complex Infection in Immunocompetent Children: Case Report and Review

Jaime E. Fergie, Thomas W. Milligan, Bruce M. Henderson, and Wesley W. Stafford

Mycobacterium avium complex (MAC) infection is a rarely recognized cause of intrathoracic infection in immunocompetent children. The incidence of this disease is unknown but is likely underestimated among children in whom MAC infection is not usually considered. An increase in the number of cases of MAC infection in adults has been noted since the late 1970s. The number of these cases in children with AIDS has also increased. There are currently no guidelines for the treatment of these children. We describe a previously healthy 14-month-old boy with a mediastinal mass for whom tuberculosis was initially diagnosed; subsequently, biopsy-proven infection with MAC was demonstrated. He received no specific therapy after surgical excision of his intrathoracic mass and has done well since. We reviewed eight additional cases of intrathoracic nontuberculous mycobacteria infection in children that were reported from 1979 to 1994 and found excellent outcomes for seven immunocompetent children who received diverse methods of treatment.

Mycobacterium avium complex (MAC), a Runyon group III nonphotochromogenic mycobacterium, is a common environmental isolate found in soil, water, and house dust [1]. These organisms are usually considered to have low virulence in the normal host [2]. MAC infection in children usually manifests as cervical lymphadenitis [1, 3, 4]. Disseminated MAC infection has been increasingly recognized as a significant problem in children with advanced HIV infection and in children with other underlying causes of immunosuppression [4, 5]; less frequently described are infections in otherwise healthy children in whom intrathoracic infection develops. We describe a child with MAC infection who presented with supravacular lymphadenitis and a mediastinal mass; he was initially treated for presumptive Mycobacterium tuberculosis infection.

Case Report

A previously healthy 14-month-old boy was admitted to Driscoll Children’s Hospital (Corpus Christi, TX) because of respiratory distress. He had been well until 2 weeks earlier when rhinorrhea and cough but no fever developed; he received therapy with trimethoprim-sulfamethoxazole, but his condition did not improve. Physical examination revealed mild intercostal retractions and expiratory wheezes. He was treated with inhaled bronchodilators and iv methylprednisolone with moderate improvement in his condition. An initial chest radiograph detected a soft-tissue density overlying the right hilum and right upper mediastinum. CT of the chest characterized this density as an inhomogeneous enhancing mass present in the mediastinum along the right paratracheal region; its largest dimensions were 2.5 X 2.5 cm (figure 1). The mass was clearly separated from the thymus and was not calcified.

At the time of CT, a small (1 cm in diameter) nontender right supraclavicular node was noted and surgically excised. Pathological examination of the node revealed chronic granulomatous lymphadenitis, and stains for fungi and acid-fast bacilli (AFB) were negative. Bacterial culture of a node specimen showed no growth, but culture for AFB was not performed. The patient’s family history revealed no known cases of tuberculosis, but the patient was attending a day-care center. The patient and both parents underwent Mantoux tests; all tests were negative.

Laboratory studies disclosed the following values: WBC count, 16,700/µL (26% neutrophils, 66% lymphocytes, 6% monocytes, and 2% eosinophils); hemoglobin level, 11.6 g/dL; and platelet count, 812,000/µL. Serological tests were negative for Histoplasma capsulatum, Blastomyces dermatitidis, and Coccidioides immitis. Three consecutive early morning gastric aspirates were cultured for AFB. Stains for AFB were negative. Therapy with daily isoniazid and rifampin was started, and the patient was discharged home; the presumptive diagnosis was tuberculosis.

Two months after the patient’s initial admission, cultures of gastric aspirates were negative for mycobacteria, the local health department found that the Mantoux tests for the adults at the patient’s day-care center were negative, and he was admitted to the hospital for further study. At this time, he was...
mycobacteria infection in children that was published in 1972, Lincoln and Gilbert [6] found that 13 cases of proven, 5 of probable, and 3 of possible pulmonary disease were reported from 1930 until 1969. It is of interest that four of the five children with probable disease presented with cervical adenitis, and intrathoracic disease was discovered by subsequent chest roentgenography. In contrast to these few cases, Lincoln and Gilbert found 447 cases of infections of superficial lymph nodes in children.

Lymphadenitis is recognized as the most common presentation of nontuberculous mycobacteria infection in children. Other described syndromes are otologic, skin and soft tissue, catheter-associated, pulmonary, and disseminated infections [3]. A review of intrathoracic (pulmonary, endobronchial, and mediastinal) cases reported after 1969 produced only nine additional cases (including our patient). Eight of these patients had no recognized underlying immunodeficiency (table 1).

In 1979, Herrod et al. [7] described two children aged 7 and 11 years, respectively, who had pulmonary infiltrates associated with the isolation of nontuberculous mycobacteria (Mycobacterium fortuitum and Mycobacterium intracellulare); one of these children (the 11-year-old) had associated acquired hypogammaglobulinemia. In 1980, Powell and Walker [8] described a 30-month-old boy who had a 90% obstruction of the right upper bronchus with consolidation of the right upper lobe and a 15-month-old girl with a 90% obstruction of the left main stem bronchus; cultures of resected mass specimens from both patients yielded MAC.

In 1981, Kelsey et al. [9] described a 6-month-old boy who underwent bronchoscopy during which an intraluminal mass was detected in the right main stem bronchus. Thoracotomy revealed that “a large, rubbery, gray-white mass involving the anterior portion of the trachea and both mainstem bronchi, and compressed the anterior portion of the trachea and the right mainstem bronchus.” Cultures of a specimen from the mass yielded MAC, and the child recovered completely after surgery without antimycobacterial therapy.

In 1986, Krause et al. [10] described a 2.5-year-old girl with left lower lung and left upper lung pneumonia caused by M. intracellulare. The child had apparently normal immunity and received 14 months of therapy with ansamycin, isoniazid, and ethionamide. At 6 months of therapy, excision of a nonfunctioning left lower lobe was required. Cultures and smears of specimens from the resected lobe were negative for AFB.

More recently, in 1994 Gupta and Katz [11] reported two cases of chest disease due to nontuberculous mycobacteria. The first case occurred in a 26-month-old boy who presented with a 2-month history of cough and shortness of breath; this boy was found to have an anterior mediastinal mass. Bronchoscopy demonstrated compression of the right main stem bronchus that was caused by M. avium/M. intracellulare. The second case occurred in a 20-month-old girl with a 2-month history of cough and wheezing that was unresponsive to therapy with bronchodilators and oral antibiotics; she was found to have a...
M. tuberculosis these children have an induration (<10 mm) after tuberculin
dence is likely underestimated because the symptoms and ra-
the pediatric literature [5].

infection in otherwise healthy children is unknown; this inci-
cdence is likely underestimated because the symptoms and ra-
the pediatric literature [5].

infection in otherwise healthy children is unknown; this inci-
cdence is likely underestimated because the symptoms and ra-
the pediatric literature [5].

mass in the right main stem bronchus. Culture of biopsy mate-
material yielded M. avium/M. intracellulare.

Both of these children were otherwise healthy. Although bronchoscopy was not done in our case, it is likely that the cough and wheezes were secondary to external compression due to the mediastinal mass, particularly considering the abatement of symptoms after surgery.

An increase in the number of cases of MAC infection in adults from Europe and the United States has been noted since the late 1970s [12, 13]. This change is due to an increased number of infections in patients with AIDS and other immuno-compromised hosts as well as increased recognition of disease in immunocompetent patients with other underlying illnesses (e.g., chronic obstructive pulmonary disease, chronic bronchi-
tis, bronchiectasis, healed or active tuberculosis, pneumoconio-
sis, cystic fibrosis, and bronchogenic carcinoma).

At the same time, pulmonary disease caused by MAC has also been increasingly recognized in elderly women without predisposing conditions; many of these women are initially thought to have chronic bronchitis [13]. Iseman [14] suggested that the observed increase in the number of MAC infections could be related to multisystem connective tissue disorders, increased virulence of the organisms, and increased environmental exposure. Similar increases in the number of cases of MAC infection in children with AIDS have been reported in the pediatric literature [5].

The incidence of intrathoracic nontuberculous mycobacteria infection in otherwise healthy children is unknown; this incidence is likely underestimated because the symptoms and radiographic findings of this infection are similar to those of M. tuberculosis infection. Furthermore, on many occasions, these children have an induration (<10 mm) after tuberculin administration [11], and histological examination of excised tissues shows granulomatous inflammation. As in our case, stains for AFB are often reported to be negative.

There are no guidelines for the management of intrathoracic nontuberculous mycobacteria infection in immunocompetent children [4]. Children with nontuberculous mycobacteria lymphadenitis are successfully treated with surgical excision in 95% of the cases; antimycobacterial therapy is rarely used [3]. A 7-year-old child in whom a recurrent parotid abscess due to MAC developed after initial needle aspiration was successfully treated with clarithromycin and ethambutol [15].

The combination of clarithromycin and rifabutin was successfully used to treat eight children with nontuberculous mycobacteria lymphadenitis [16]. In five cases, there was resolution of chronic sinus infection and discharge after incomplete excision, and in two of three patients treated without surgery, signs and symptoms abated within 2 months. Three patients had a brownish film on the teeth that resolved 1 month after completion of therapy.

Children with disseminated MAC infection and immunode-
ficiencies including HIV infection have received treatment with four- and five-drug regimens, including ethambutol, rifampin, ciprofloxacin, amikacin, rifabutin, clofazamine, and clarithromycin [4, 5]. On the basis of mainly case reports and the in vitro susceptibility of the isolates [1, 14], the treatment of immunocompetent adults with MAC infection is empirical; traditional regimens have included combinations with three to four different drugs.

More recently, it has become clear, particularly from studies with HIV-infected patients, that clarithromycin and azithromycin are two of the most effective drugs available for preventing and, in the case of clarithromycin, treating MAC infec-

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (y)/</th>
<th>Risk factor</th>
<th>Type of infection</th>
<th>Isolate</th>
<th>Treatment (duration)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [7]</td>
<td>7/M</td>
<td>None</td>
<td>Pulmonary</td>
<td>M. fortuitum</td>
<td>INH, PAS, Em (1 y)</td>
<td>Cured</td>
</tr>
<tr>
<td>2 [7]</td>
<td>11/M</td>
<td>Acquired hypogammaglobulinemia</td>
<td>Pulmonary, endobronchial generalized</td>
<td>M. intracellulare</td>
<td>INH, Cyse, Etb, Eth, Vio, Cpm</td>
<td>Died (after 7 y)</td>
</tr>
<tr>
<td>3 [8]</td>
<td>2/M</td>
<td>None</td>
<td>Endobronchial</td>
<td>M. avium/M. avium/ M. intracellulare complex</td>
<td>Partial resection; INH, Rif (14 mo)</td>
<td>Cured</td>
</tr>
<tr>
<td>4 [8]</td>
<td>1/F</td>
<td>None</td>
<td>Endobronchial</td>
<td>M. avium/M. intracellulare complex</td>
<td>Partial resection; INH, Rif (16 w)</td>
<td>Cured</td>
</tr>
<tr>
<td>5 [9]</td>
<td>0.5/M</td>
<td>None</td>
<td>Endobronchial, mediastinal</td>
<td>M. intracellulare</td>
<td>Partial surgical resection</td>
<td>Cured</td>
</tr>
<tr>
<td>6 [10]</td>
<td>2/F</td>
<td>None</td>
<td>Pulmonary</td>
<td>M. avium/M. intracellulare</td>
<td>INH, Rif, Stm (1 mo); Ansa, INH, Etb (1 y)</td>
<td>Cured</td>
</tr>
<tr>
<td>7 [11]</td>
<td>2/M</td>
<td>None</td>
<td>Endobronchial</td>
<td>M. avium/M. intracellulare</td>
<td>Surgical resection; INH, Rif, Pza (4 mo)</td>
<td>Cured</td>
</tr>
<tr>
<td>8 [11]</td>
<td>1/F</td>
<td>None</td>
<td>Mediastinal</td>
<td>M. avium/M. intracellulare</td>
<td>INH, Rif, Pza (6 mo)</td>
<td>Cured</td>
</tr>
<tr>
<td>9 [PR]</td>
<td>1/M</td>
<td>None</td>
<td>Mediastinal</td>
<td>M. avium complex</td>
<td>INH, Rif, Pza (2 mo); surgical resection</td>
<td>Cured</td>
</tr>
</tbody>
</table>

NOTE. Cases were reported after 1969. Ansa = ansamycin; Cpm = capreomycin; Cyse = cycloserine; Em = erythromycin; Eth = ethambutol; Ethi = ethionamide; INH = isoniazid; PAS = p-aminosalicylic acid; PR = present report; PZA = pyrazinamide; Rif = rifampin; Stm = streptomycin; Vio = viomycin.
tions [17–21]. In a recent report, Wallace et al. [22] described 30 HIV-negative patients with lung disease due to MAC who received clarithromycin monotherapy (500 mg twice daily for 4 months). Twenty patients completed therapy. There were 19 cases in which pretreatment MICs of clarithromycin were <16 μg/μL; improvement was demonstrated by sputum cultures, chest radiographs, or both in 18 of these cases. Two patients discontinued therapy because of adverse events, and clarithromycin resistance developed in three isolates. Perhaps the most effective form of treatment for pulmonary infection due to MAC is surgery. Four of the 21 patients without predisposing conditions who were described by Prince et al. [13] were cured after surgical resection.

In our review, five of nine children with intrathoracic nontuberculous mycobacteria disease (eight with MAC infection and one with M. fortuitum infection) underwent surgical resection (table 1). To our knowledge, there are no randomized studies of children that address the choice of therapy for intrathoracic MAC infection in immunocompetent children. Our patient was initially treated for 2 months with isoniazid and rifampin without any clinical benefit. Believing that our patient was immunocompetent, we elected not to give him specific antitycobacterial therapy after surgical resection and to observe him clinically and radiographically as in the report by Kelsey et al. [9]. One year after surgery, he was asymptomatic, and his chest roentgenogram was normal.

As can be seen from this review, immunocompetent children with MAC infection did well despite diverse therapies including agents with poor activity against MAC. We can only extrapolate information from the adult literature and from cases of MAC lymphadenitis in children to help us guide therapy for intrathoracic MAC infection. Because surgical resection will be performed to diagnose the lesion in some instances, the most important part of therapy is removal of as much of the infected tissue as possible. When there are multiple lesions or when surgical resection is not complete, monotherapy with clarithromycin or combination therapy with rifabutin or ethambutol can be used. The duration of therapy will depend on clinical and radiographic resolution but will probably be from 4 to 12 months.

References