Mycoplasma pneumoniae Bronchiolitis Mimicking Asthma in an Adult

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Introduction

Bronchiolitis refers to an inflammatory disease primarily involving the terminal and respiratory bronchioles, and in some cases extending to the adjacent alveolar ducts and alveolar spaces.[1,2] Infectious bronchiolitis is well recognized in pediatric patients, but uncommon in adults.[3,4] Most pediatric cases are caused by respiratory syncytial virus. In adults, there are occasional reports of *Mycoplasma pneumoniae* induced bronchiolitis.[5,6] Here we report a case of *M. pneumoniae* bronchiolitis in an adult whose clinical presentation mimicked an acute attack of asthma.

Case Summary

A 42-year-old woman of east Indian ancestry was hospitalized with complaints of dyspnea, cough productive of yellowish sputum, and fever of 2 weeks duration. Her illness started as sore throat, sneezing, and nasal congestion. This was followed by high fever with chills, myalgia, wheezing, cough productive of yellowish sputum, and dyspnea. Her primary care physician had treated her with a 5-day course of amoxicillin/clavulanate, prednisone pack, and antitussives, without any benefit. She denied headache, ear ache, diarrhea, or sick contact at home.

Her medical history was notable for asthma since early childhood, but it was well controlled with maintenance dry powder fluticasone/salmeterol, 250/50 μg, one puff twice daily. She is allergic to sulfa drugs, which manifested as urticarial rash, mucosal edema, and wheeze. She is a life long non-smoker and she had not received influenza vaccine. She was born in India and immigrated to the United States 18 years ago and has been residing in the New York City since then. She is a school teacher by profession and had visited south India a month prior to her hospitalization.

Vital signs were noteworthy for tachycardia, tachypnea, and mild hypoxia (S_{pO_2} 90% on room air). Physical examination revealed a hyposthenic woman in moderate respiratory distress, with use of accessory muscles, and lung auscultation revealed bilateral diffuse coarse rales and expiratory wheeze. The peak expiratory flow was 200 L/min (predicted 400 L/min).

The white-blood-cell count was 22,800 cells/μL, with neutrophils of 82%. The chest radiograph (Fig. 1) revealed coarse reticular nodular infiltrate and thickening of bronchovascular bundles. High resolution computed tomography (CT) (Fig. 2) revealed poorly defined centrilobular nodules connected to the bronchioles, giving a tree-in-bud appearance. The tuberculin skin test was non-reactive after 72 hours. Three sputa acid-fast smears were negative. Sputum cultures grew normal flora. The spirometry revealed FVC 2.13 L (64% of reference value for whites), FEV_1 1.66 L (61%), FEV_1/FVC 78%, and forced expiratory flow during the middle half of the FVC maneuver ($FEF_{25–75}$) 1.54 L/s (53%). The static lung volumes by body plethysmography disclosed TLC 3.49 L (76%), residual volume/TLC 39% (122% of predicted). The flow-volume loop disclosed flow limitation and dynamic airway collapse at low lung volumes.

Serology was notable for cold agglutinins and serum immunoglobulin M (IgM) antibody titers that were strongly positive for *M. pneumoniae*, indicative of current infection.

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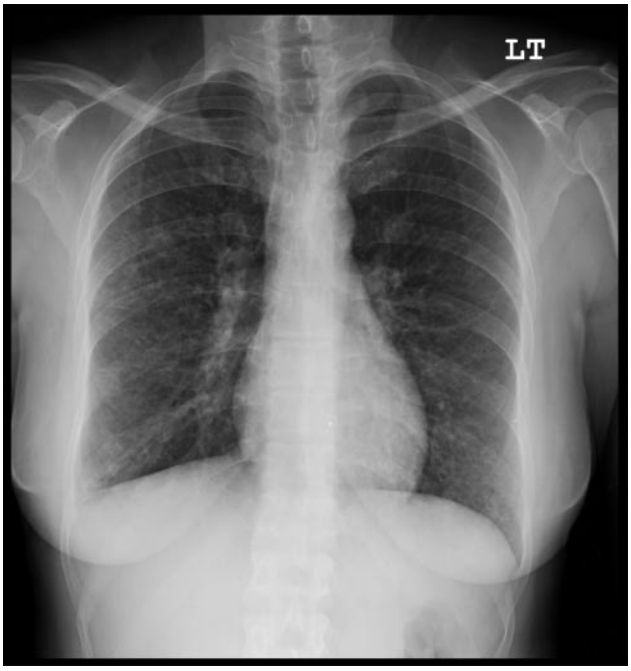

Fig. 1. The chest radiograph shows diffuse bilateral interstitial nodular opacities with thickened bronchial markings, more profuse in the right lung. The diaphragms are flattened.

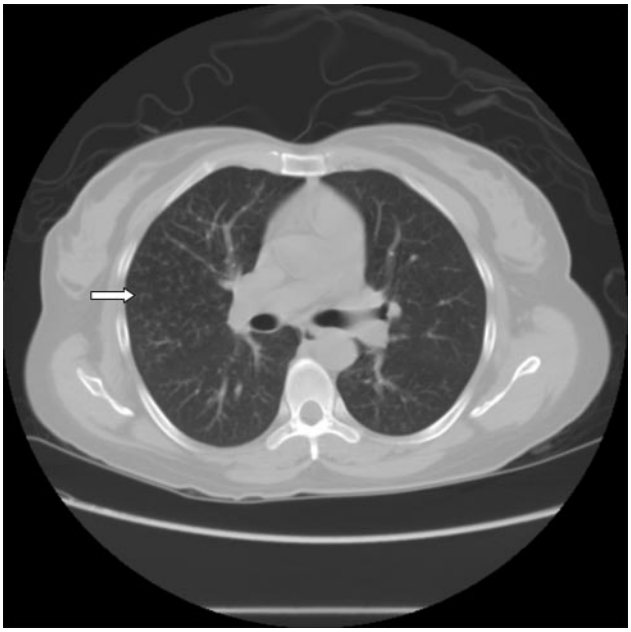

Fig. 2. High-resolution computed tomography image shows multiple centrilobular nodules, many of which connect to branching linear structures (arrow): tree-in-bud pattern.

The patient was treated with intravenous ceftriaxone and azithromycin combined with methylprednisone 80 mg every 8 hours, inhaled oxygen, and unit dose nebulized albuterol every 4 hours. Over the course of the next few days her symptoms improved and peak flow rose from 200 L/min to 360 L/min. She was discharged home on oral moxifloxacin, tapering steroids, and inhaled albuterol.

Discussion

A number of pulmonary manifestations have been reported in patients with *M. pneumoniae* infection. These include pneumonia, tracheobronchitis, cellular bronchiolitis, bronchiectasis, induction of reactive airway disease, and exacerbation of underlying airways disease.[7–11] Infectious cellular bronchiolitis, an inflammatory disease of small airways disease due to *M. pneumoniae* usually accompanies bronchopneumonia.

Clinical manifestations of *Mycoplasma* bronchiolitis include productive cough, wheeze, dyspnea, and fever. Unlike an acute attack of asthma, infectious bronchiolitis in adults is seldom severe enough to require hospitalization. The chest radiograph typically reveals coarse reticular nodular infiltrate and thickening of bronchovascular bundles. High resolution CT findings of bronchiolitis include centrilobular nodules and peribronchial thickening with a tree-in-bud pattern. This radiological appearance is correlated with the pathological findings of thickening of the bronchiolar wall by inflammatory cells and inspissated inflammatory exudates in the bronchioles, resulting in V-shaped or Y-shaped branching linear opacities that represent the tree-in-bud pattern.[12] Inflammatory cellular infiltration in the peribronchiolar alveoli, typically seen in respiratory bronchiolitis, results in poorly defined centrilobular nodules that often have attenuation less than that of soft tissue. Bronchiolectasis is a less common direct sign of bronchiolitis and is found most commonly in chronic form of bronchiolitis.[13]

Air trapping is an indirect sign of obstructive small airways disease and may be identified in some by the presence of mosaic attenuation on inspiratory CT that is accentuated with expiratory imaging.[14] Infectious bronchiolitis is characterized histologically by a pattern of acute bronchiolar injury, with epithelial necrosis and inflammation of the bronchiolar walls, and intraluminal exudates.[15]

The diagnosis of *M. pneumoniae* infection is confirmed by serologic tests. Identification of *Mycoplasma* specific IgM antibody by enzyme immunoassay in a single titer of 1:64 during acute illness or a 4-fold rise in convalescent titer has a sensitivity of 97.8% and specificity of 99.7% in the diagnosis of *M. pneumoniae*.

Literature review of *M. pneumoniae* bronchiolitis in adults identified isolated case reports and small series as described in the following paragraphs.

A case report[16] of severe *Mycoplasma* induced diffuse bronchiolitis was described in an adolescent, who presented with severe obstructive ventilatory defect. Thoracoscopic surgical lung biopsy revealed diffuse bronchioli-

tis with suppurative intrabronchiolar inflammation. The patient responded to clarithromycin, inhaled albuterol, and steroids.

Ham[17] described 7 adults with acute infectious bronchiolitis with moderate air-flow obstruction and lung hyperinflation. One patient had a diffuse and fine granular pattern on the chest radiograph, and a cold agglutinin titer of 1:1,024, consistent with bronchiolitis due to either a viral or *Mycoplasma* infection. The patient's symptoms improved with inhaled isoproterenol. O'Reilly[18] described an adult with bronchiolitis who presented with substantial hypoxemia and hypercarbia despite a normal chest radiograph. He improved clinically with bronchodilator and corticosteroid treatment, but some residual air-flow limitation persisted.

Rollins and co-workers[5] described 6 patients with open lung biopsy specimen-proven inflammatory (cellular) bronchiolitis due to *M. pneumoniae*. In 3 of the cases there was an accompanying bronchopneumonia. A lymphoplasmocytic bronchiolar wall infiltrate with a neutrophil-rich intraluminal exudate was present. Ultrastructurally there was extensive injury to the respiratory mucosa, causing loss of cilia and ciliated cells. Also noted were edema, fibrosis, and plasma cells infiltrating the bronchial and bronchiolar walls, with extension of the inflammatory exudate from the bronchiolar lumen into the alveolar spaces.

Two review articles noted that most patients with acute infectious inflammatory bronchiolitis recover without important sequelae, but some may develop constrictive bronchiolitis or reactive airways disease.[19,20] Chan et al[21] described 3 adults with *M. pneumoniae* induced bronchiolitis who were hospitalized with severe gas exchange abnormalities and restrictive ventilatory defects, with high resolution CT findings of bronchiolitis. One had associated bronchiolitis obliterans and organizing pneumonia. All responded favorably to corticosteroids and macrolide antibiotics.

Teaching Points

- Chest x-ray appearance of diffuse interstitial micronodular opacities in patients with asthma-like clinical presentation and air-flow limitation in smaller airways should alert the clinician to the diagnosis of bronchiolitis. High resolution CT findings of centrilobular nodules and a "tree-in-bud" pattern are characteristics of bronchiolitis.
- The diagnosis of *M. pneumoniae* infection is confirmed by the detection of *Mycoplasma* specific IgM antibodies on enzyme immunoassay in serum, either by an acute titer of $>$ 1:64 or 4-fold rise in convalescent titers. Surgical lung biopsy is seldom required for diagnosis.
- Macrolide, doxycycline, or respiratory quinolone antibiotics, corticosteroids, and inhaled albuterol produce resolution in most patients. Constrictive fibrotic bronchiolitis with fixed airway obstruction or induction of bronchial hyperactivity are rare sequelae.

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