CLINICAL VIGNETTE

Diffuse Panbronchiolitis in a Caucasian Male

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A 65-year-old male with hypertension and recurrent sinusitis presented with two weeks of exertional shortness of breath, low-grade fevers, fatigue, and worsened cough with mucus. He denied chills, arthralgias, nausea, vomiting, or abdominal discomfort. The patient reported similar symptoms one-year prior which partially improved spontaneously, but not back to his baseline. Social history includes 30 pack-years smoking and prior heavy dust exposure working as a carpenter. The patient had prior allergy testing with a highly positive reaction to most woods, but denied personal or family history of lung disease or lung infections.

Upon presentation the patient was hypoxic with initial room air oxygen saturation of 81%. Supplemental oxygen was rapidly escalated to high flow nasal cannula (HFNC) with an FiO2 of 100%. Physical examination was notable for diffuse, coarse breath sounds with decreased air movement at the bases without respiratory distress. Initial blood labs included a leukocytosis, thrombocytosis, moderate eosinophilia, with normal comprehensive metabolic panel. ABG on 100% FiO2 revealed PaO2 of 96 mmHg. In addition to HFNC, the patient was started on antibiotic coverage for a community acquired pneumonia.

Chest CT showed bilateral diffuse centrilobular tree-in-bud nodules, some of which appeared more confluent and consolidative. He underwent further lab evaluation with infectious and autoimmune serologies, and a hypersensitivity pneumonitis panel. The tests were unremarkable other than an "indeterminate" result for MTB-Quantiferon Gold test. Subsequent bronchoscopy with bronchoalveolar lavage also did not reveal the etiology of hypoxemia or the nodularity on radiographic imaging. Bronchoscopic respiratory cultures and viral panels remained negative with cell counts showing mostly alveolar macrophages. He also completed transthoracic echocardiogram with bubble study which was also unremarkable.

Patient was eventually started on high dose oral steroids on hospital day 5 and antibiotics were discontinued. He improved and by hospital day 8, oxygen support was weaned to 8 L/min via oxymizer nasal cannulae. He was discharged on hospital day 10 on 2 L/min nasal cannula with a prednisone taper. The patient was seen in pulmonary clinic and started on macrolide therapy with a continued slow prednisone taper. He weaned off oxygen 2 weeks after hospital discharge. Follow up chest CT scan one month after presentation showed improvement in radiologic findings. The patient continued to report improvement in exercise tolerance on subsequent outpatient follow-up visits.

Discussion

Panbronchiolitis was first described in Japan in 1969 as a distribution of pulmonary nodules with involvement of all layers of the respiratory bronchioles.[1] The exact pathogenesis remains unknown with likely contributions from genetic, environmental, and systemic factors. The prevalence of panbronchiolitis in Japan, based on a 1982 government survey was 11 cases per 100,000 people with a male to female ratio of 1.4-2:1. Two thirds of patients were non-smokers with no history of inhalation of toxic fumes.[1] This disease is predominantly found in the Japanese population and has rarely been reported outside East Asian populations.[2] Interestingly, in Western countries half of cases are among Asian immigrants. A genetic predisposition is noted with HLA-B54 identified in 63% of Japanese patients compared to 11% of control subjects.[2]

Pathologic findings on lung biopsies can show transmural and peribronchial infiltration by lymphocytes, plasma cells, and lipid-laden "foamy macrophages" in the respiratory bronchioles.[2] These findings are not specific for diffuse panbronchiolitis but in other diseases the most marked changes are in the proximal membranous bronchioles.[3] There are no other histologic lesions, like granulomas, that are usually identified on pathology in diffuse panbronchiolitis. Clinical features include symptoms of exertional dyspnea, wheezing, and productive cough. Over 80% of patients have current or past history of chronic rhinosinusitis which often can precede any lower airway symptoms. Haemophilus influenzae and Pseudomonas aeruginosa are common organisms that can cause infections in this patient population.[2]

Diagnostic criteria for diffuse panbronchiolitis[2,4] includes three of the major criteria with at least two of the minor criteria outlined in the table below:

Major Criteria	Persistent cough, sputum, and exertional dyspnea	History of paranasal sinusitis	Bilateral diffuse small nodular shadows on a plain chest radiography or centrilobular micronodules on chest CT images
Minor Criteria	Coarse crackles on respiratory examination	FEV1/FVC less than 70% and PaO2 <80 mmHg	Titer of cold hemagglutinin > 64

FEV1 = forced expiratory volume in one second, FVC = forced vital capacity, PaO2 = partial pressure of oxygen in arterial blood

Macrolides are the mainstay of therapy for panbronchiolitis.[2] There are no data for use of beta-lactams, systemic corticosteroids, mucolytic agents, or bronchodilators. Prior to macrolide therapy, patients with this disease had poor prognosis. The first open-label trial for treatment with low dose, long term use of erythromycin was published in 1987.[4] Subsequent trials demonstrated improvement in respiratory symptoms, body weight, pulmonary function tests, and in PaO2. Changes in radiographic findings include reduction in small nodular opacities, severity of peri-airway thickening, and degree of mucus plugging.[4]

The 10-year survival prognosis is currently over 90%. The mechanism of action for macrolides includes: inhibition of mucus hypersecretion, inhibition of neutrophil migration, and significant decrease in CD4 and CD8 T-cells. Clinical response can usually be assessed 2-3 months after initiation of therapy.[5] Medication should be stopped: when no longer effective; or due to adverse effects, or drug interactions. Treatment should be completed after 2 years if there has been improvement in clinical symptoms, radiographic findings, and pulmonary function tests. Therapy can be resumed if symptoms recur after cessation of macrolide therapy. Extending treatment for longer than 2 years should be considered in patients with extensive bronchiectasis or respiratory failure.[5] There are reports of lung transplantation for these subset of patients.[6]

Interestingly, our patient was a Caucasian male but met diagnostic criteria for diffuse panbronchiolitis. He had a robust response to initial therapy with steroids which could be attributed to possible allergic component from his wood exposure. It is also possible that different genetic variants exist in different ethnic populations.

Figures

Figure A

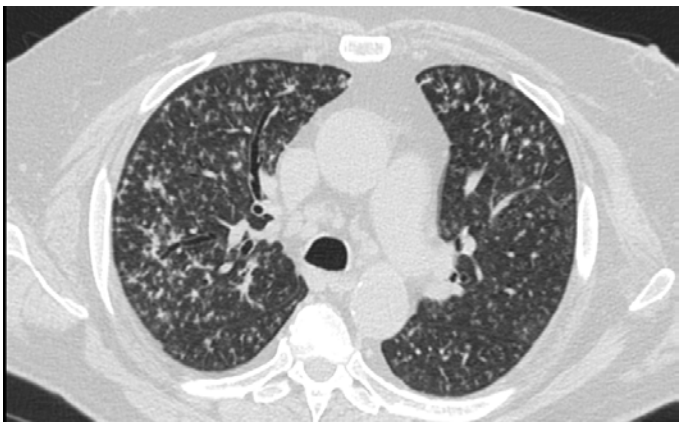
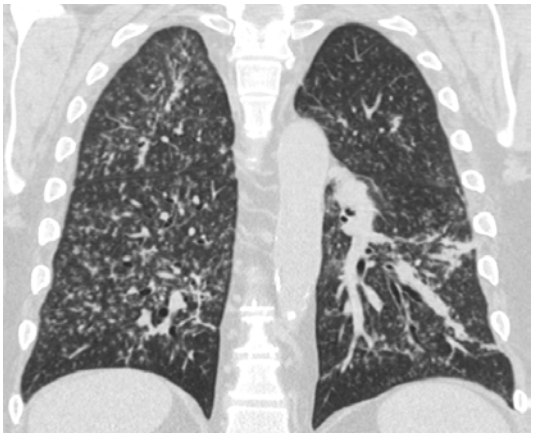


Figure B



Figures A and B demonstrate computed tomography images demonstrating bilateral diffuse centrilobular tree-in-bud nodules in the axial and coronal views, respectively

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