Case Report

Idiopathic constrictive bronchiolitis with rapidly progressive bronchiectasis and *Mycobacterium kansasii* infection

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1. Case report

A 58 years old man presented to pulmonary clinic with a history of worsening dyspnea and thoracic CT scan abnormalities. He was in good health without any respiratory problems until 9 months before this visit. At that time, he first noticed dyspnea on exertion followed by productive cough and wheezing several weeks after exposure to a flooded basement. One month later, he was admitted to an outside hospital with progressively worsening dyspnea. He was treated with antibiotics and bronchodilators but showed no improvement. He was a lifelong non-smoker and had no history of asthma, allergies or occupational exposures. Cardiac evaluation and chest x-ray were unremarkable. A chest CT scan revealed no infiltrates with borderline changes of bronchiectasis best seen in the lower lobes (Fig. 1). Five months before this clinic visit, his respiratory symptoms persisted and sputum was positive for *Pseudomonas aeruginosa* and *Aspergillus fumigatus*; lung biopsy showed constrictive bronchiolitis that was clinically idiopathic. His respiratory symptoms and pulmonary function rapidly improved within a week of high-dose corticosteroid therapy. We suggest that a diagnosis of constrictive bronchiolitis should be considered in patients with a combination of new rapidly progressive lung hyperinflation and worsening bronchiectasis. We hypothesize that the bronchiolitis-associated bronchiectasis may occur from a predisposition for secondary infections known to cause large airway wall damage. Identification and adequate treatment of these infections is critical if concurrent high-dose corticosteroid therapy is attempted to alleviate the constrictive bronchiolitis.

1.1. Physical examination and laboratory data

His vital signs were normal except for a heart rate of 125 beats/min. His lungs revealed diminished breath sounds and bilateral lower lung field rhonchi; the remainder of the examination was normal. The complete blood count was significant for a hemotocrit of 30% and a leukocyte concentration of 11,000/mm3 with 10% eosinophils; platelets were normal. His blood chemistries were normal. Serum IgG and IgA levels were mildly increased; the IgE level of 429 U/ml was at the upper end of the normal range. His erythrocyte sedimentation rate, alpha-1 antitrypsin, and serum precipitins for *Aspergillus, Micropolyspora faeni, Thermophilus vulgaris, Thermoactinomyces sacchari*, and pigeon proteins were normal or negative. Anti-nuclear antibodies, rheumatoid factor and...
HIV testing were also negative. Repeat sputum cultures were positive for *M. kansasii*. Pulmonary function testing revealed progressive severe obstruction with FEV$_1$ of 0.80 L, FVC 1.99 L, TLC 6.91 L (101% predicted), FRC 5.18 L (130% predicted), RV 4.14 L (171% predicted) and CO diffusing capacity that was 52% of predicted. He was started on an 18 month course of isoniazid 300 mg/day, rifampin 600 mg/day and ethambutol 15 mg/kg/day for the *M. kansasii* infection. A repeat chest CT was obtained (Fig. 3) before proceeding with thoracoscopic lung biopsy. His biopsy demonstrated constrictive bronchiolitis; no peribronchior granulomas were observed (Fig. 4). Following the biopsy, he was continued on anti-mycobacterial therapy and pulsed with 1 g/day of methylprednisolone for 3 days followed by 60 mg/day prednisone (with a slow taper) as an attempted treatment for idiopathic constrictive bronchiolitis. Thrice weekly empiric azithromycin as well as sulfa-methoxazole/trimethoprim prophylaxis for *Pneumocystis jirovecii* pneumonia were also initiated. He demonstrated a clinical response within the first week of corticosteroid treatment with less dyspnea and resolution of productive cough. One month later, his PFTs showed a marked improvement in obstruction, hyperinflation and gas exchange (FEV$_1$ 1.06 L, FVC 2.61 L, TLC 94% predicted, FRC 102% predicted, RV 129% predicted and DLCO 70% predicted). He completed 18 months of anti-mycobacterial therapy with tapering of prednisone to 15 mg/day. PFTs showed no further improvement but remained stable.

### 2. Discussion

Constrictive bronchiolitis (or obliterative bronchiolitis) is characterized by concentric peribronchior and submucosal fibrosis with luminal narrowing that is unresponsive to bronchodilators. Clinically, patients present with dyspnea, cough and have severe progressive irreversible airways obstruction with hyperinflation. The diffusing capacity for carbon monoxide can be mildly to moderately reduced. It is important to differentiate constrictive bronchiolitis from cryptogenic organizing pneumonia (previously called bronchiolitis obliterans organizing pneumonia). The latter is defined pathologically as proliferating plugs of fibrous tissue within airway lumen surrounded by an organizing pneumonia whereas constrictive bronchiolitis involves only bronchiolar walls. Radiologic studies of constrictive bronchiolitis reveal hyperinflation with or without evidence of fine nodularity on computed tomography. Expiratory CT images typically show evidence of air trapping resulting in a pattern of mosaic attenuation. A small percentage of patients with constrictive bronchiolitis, including those with idiopathic disease, present with radiographic bronchiectasis.

Lung biopsy is the gold standard test to diagnose constrictive bronchiolitis. The most common causes are connective tissue disorders (rheumatoid arthritis, eosinophilic fasciitis, systemic lupus erythematosus), allograft-related (lung or bone marrow...
transplantation), post-infectious (viruses, mycoplasma), inhalational (NH3, NO2, butter flavoring, ground zero dust), and miscellaneous (hypersensitivity pneumonitis, carcinoid tumors, paraneoplastic pemphigus, inflammatory bowel diseases). As in our case, constrictive bronchiolitis can also be idiopathic. In some clinical situations, such as rheumatoid arthritis, the rapid development of respiratory failure with airways obstruction and clear hyperinflated lungs is so likely to be secondary to constrictive bronchiolitis that a lung biopsy is not necessary. In our patient, we elected to pursue a lung biopsy because mycobacterial infection can rarely cause a granulomatous bronchiolitis6,7 which could be treated primarily with antibiotics instead of high-dose corticosteroids.

An unusual feature of constrictive bronchiolitis shown by our patient was the development of rapidly progressive bronchiectasis that occurred in association with the loss of lung function and air trapping from the more distal bronchiolar obliteration. Other causes of adult-onset bronchiectasis including connective tissue diseases, inflammatory bowel disease, common variable immunodeficiency or alpha-1 antitrypsin deficiency were excluded in our patient by absent serologies, lack of compatible clinical features, and normal serum levels of immunoglobulins and alpha-1 antitrypsin. Although the development of bronchiectasis has been reported in association with idiopathic constrictive bronchiolitis,3 our report is the first to document the time course of the large airway dilatation.

The mechanism for bronchiectasis complicating constrictive bronchiolitis is unknown. Based on our patient, one mechanism may be related to the poor airway clearance from the diminished expiratory airflow. This could, in turn, lead to secondary large airway infections with organisms known to be associated with bronchial damage such as atypical mycobacterium, P. aeruginosa or A. fumigates. There is one previous report of idiopathic constrictive bronchiolitis with an associated infection with M. kansasii.8 Thus, we would suggest that constrictive bronchiolitis should be considered in any patient with the rapid development of severe obstructive lung disease in association with new-onset bronchiectasis even if a known bronchiectasis-causing organism is identified in the airways.

M. kansasii is generally the second common cause of non-tuberculous mycobacterial lung disease in the United States.9 Tap water is likely a major reservoir for M. kansasii. Patients present with symptoms and radiological findings mimicking Mycobacterium tuberculosis infection. Risk factors include pneumoconiosis, COPD, previous nontuberculous mycobacterial infection, and an immunocompromised state. Typical radiological findings include cavitary infiltrates with an upper lobe predominance but rarely, bronchiectasis can be the only abnormality. The presence of compatible radiographic findings and a single positive bronchoscopy culture or two positive sputums are sufficient to make the diagnosis and initiate treatment for M. kansasii.9

The significance of the A. fumigates was unclear but may have just been an airway colonizer. We considered the possibility that he could have developed a concurrent allergic bronchopulmonary aspergillosis based on the presence of the proximal bronchiectasis and eosinophilia. However, his IgE was not elevated, serum precipitans to A. fumigates were negative and A. fumigates is frequently cultured from the sputum in patients with bronchiectasis and atypical mycobacterial infection, including M. kansasii.10 Moreover, eosinophilia has previously been reported in pulmonary mycobacterial infections.11 12 His sputum Aspergillus and eosinophilia have not recurred following anti-mycobacterial treatment although he has remained on corticosteroids.

In general, there is no known effective treatment for idiopathic constrictive bronchiolitis. There is some evidence to suggest that the administration of a macrolide antibiotic, such as azithromycin, could be of benefit at least in the setting of transplant-associated obliterative bronchiolitis,13,14 As in our patient, corticosteroid therapy is often tried with a highly variable response. Although we were simultaneously treating his M. kansasii infection, the rapid improvement in pulmonary symptoms and lung function that occurred within a week of initiating corticosteroids suggested that the constrictive bronchiolitis was partially steroid responsive. We are currently following him closely for evidence of further lung function deterioration with consideration for lung transplantation if further medical treatment proves to be unsuccessful.

Our report has several important clinical implications. First, the development of new rapid bronchiectasis with airflow obstruction and hyperinflation out of proportion to the bronchiectasis should raise the possibility of constrictive bronchiolitis. Second, this associated bronchiectasis could be a result of secondary infections in the large airways because of the diminished expiratory airflow from the bronchiolitis. Identifying and treating these secondary infections is critical to halt the bronchiectasis and avoid further infectious complications if an attempt is made to treat the constrictive bronchiolitis with corticosteroid therapy.

Conflict of interest statement

None declared.

References