**Crohn’s disease-associated interstitial lung disease mimicking sarcoidosis: a case report and review of the literature**

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**Abstract.** Respiratory involvement in Crohn’s disease (CD) is a rare manifestation known to involve the large and small airways, lung parenchyma, and pleura. The clinical presentation is nonspecific, and diagnostic tests can mimic other pulmonary diseases, posing a diagnostic challenge and delay in treatment. We report a case of a 60-year-old female with a history of CD and psoriatic arthritis who presented with dyspnea, fever, and cough with abnormal radiological findings. Diagnostic testing revealed an elevated CD4:CD8 ratio in the bronchoalveolar lavage fluid, and cryoprobe lung biopsy results showed non-necrotizing granulomatous inflammation. We describe here the second reported case of pulmonary involvement mimicking sarcoidosis in Crohn’s disease and a review of the literature on the approaches to making a diagnosis of CD-associated interstitial lung disease. *(Sarcoidosis Vasc Diffuse Lung Dis 2016; 33: 288-291)*

**Key words:** interstitial lung disease, Crohn’s disease, sarcoidosis, cryoprobe lung biopsy

**Introduction**

Pulmonary involvement in Crohn’s disease (CD) is relatively rare and can be difficult to diagnose. Kraft et al. was the first to report one of six cases of respiratory manifestations of CD (1). Pulmonary manifestations include bronchiectasis (most common), granulomatous bronchiolitis, tracheobronchitis, cryptogenic organizing pneumonia (COP), cellular nonspecific interstitial pneumonia, and unspecified interstitial lung disease (2-6). Airway involvement in CD also is uncommon with a prevalence of 0.4% of cases (7). Some of the immunosuppressants used to treat CD also can cause pulmonary toxicity (2, 3, 8). Moreover, certain diagnostic tests such as bronchoalveolar lavage (BAL) cell analysis and tissue biopsy results may mimic other granulomatous lung diseases, posing a diagnostic dilemma (9-11).

This review will focus on the general approaches required to make a diagnosis of interstitial lung disease (ILD) in CD and the complexity of diagnostic possibilities mimicking other pulmonary diseases.

**Case report**

A 60-year-old Caucasian female with a history of CD and psoriatic arthritis presented with a five-day history of progressively worsening dyspnea on exertion, fever and non-productive cough. Three weeks prior to admission, she was hospitalized at another hospital facility for an upper respiratory tract infection presumed to be secondary to community-acquired pneumonia and had some improvement after antibiotic treatment.
Her past medical history was significant for Crohn's disease diagnosed 13 years ago, and she had undergone multiple small bowel resections/dilations for strictures and was currently in remission on vedolizumab. She was also diagnosed with psoriatic arthritis in 2008 and had been taking methotrexate 22.5 mg/week with no flares. Physical examination was significant for bilateral inspiratory crackles and mid to end inspiratory high pitched squeaks. A chest high resolution computed tomography (HRCT) showed bilateral multiple small ground glass nodules with mosaic attenuation in the upper lungs (Figure 1) and traction bronchiectasis and diffuse ground glass opacities in the lung bases (Figure 2).

Laboratory data showed a white blood cell count of 12.8X10^9/L (normal range, 4-11), C-reactive protein 96 mg/L (normal range, 0-8), and procalcitonin 0.2 ng/mL (normal range, 0.05-0.49). Bronchoalveolar (BAL) fluid cell analysis revealed lymphocyte predominance (35%) with a CD4:CD8 ratio 11.25 (normal range, 1.4-2.6). Cultures of the BAL fluid (right middle lobe) were negative for fungal, bacterial, viral and mycobacterial infections. No malignant cells were seen on BAL fluid cytology. Cryoprobe lung biopsies of the right middle and lower lobes showed a pattern of non-necrotizing granulomatous inflammation and organizing pneumonia (Figures 3 and 4). Pulmonary function tests were performed after the bronchoscopy and showed forced expiratory volume in 1 second (FEV1) 2.13 (76% of predicted), forced vital capacity (FVC) 2.79 (76% of predicted), FEV1/FVC 76%, and diffusing capacity for carbon monoxide (DLCO) 9 mL/min/mmHg (38% of predicted). Her methotrexate was stopped presuming that it could be the etiology of her interstitial lung disease, and she was discharged on home oxygen therapy.

Six weeks later, she presented again to our hospital with worsening dyspnea on exertion, fever, and hypoxia requiring more oxygen. Repeat HRCT showed worsening ground glass opacities in the lung bases (Figures 1 and 2). Serum hypersensitivity pneumonitis panel was negative. At this time, methotrexate-associated ILD was felt to be unlikely given no improvement six weeks after stopping the medication. The cryoprobe lung biopsies were reviewed...
again with a pulmonary pathologist, and Crohn’s-associated ILD was felt to be consistent with the findings. She was started on prednisone (1 mg/kg) and had significant improvement of her symptoms within three days. She was subsequently discharged from the hospital and scheduled to follow-up with Interstitial Lung Disease Clinic in four weeks.

Discussion

Pulmonary manifestations of CD are unusual, making diagnosis challenging and potentially resulting in delayed treatment. In our patient, clinical symptoms, physical examination findings and HRCT suggested ILD. Her abnormal HRCT was consistent with previous reports of HRCT findings in Crohn’s-associated ILD (2, 12, 13). In CD-associated ILD, PFTs may reveal a restrictive pattern with reduced diffusion capacity (4, 5, 13, 14), similar to the PFT results in our patient.

A BAL is important to rule out infection, malignancy and alveolar hemorrhage. Increases in certain BAL cell types can help narrow down certain disorders. Our patient had a lymphocytic predominance that suggested drug-induced pneumonitis, hypersensitivity pneumonitis, sarcoidosis or COP (15). Elevated CD4:CD8 ratio is suggestive of sarcoidosis, but can also be seen in CD. One study of twenty-two patients with CD reported that 54% had a lymphocyte predominance (>18%), and three of the twenty-two patients were found to have elevated CD4:CD8 ratio (10). Moreover, a previous case showed BAL cell analysis suggestive of sarcoidosis, but the patient later developed a perianal abscess indicative of CD (11).

A lung biopsy can further help to elucidate the diagnosis. Histological patterns of pulmonary involvement associated with CD have variable appearance. Organizing pneumonia with granulomatous features, non-necrotizing granulomatous inflammation and neutrophil rich bronchopneumonia have been reported (16).

Our patient was on methotrexate on her initial presentation, therefore, drug-induced pneumonitis cannot be ruled out. However, methotrexate was stopped for six weeks with no symptomatic improvement and worsening of HRCT findings, suggesting methotrexate was the unlikely cause. Infectious etiology was excluded given the negative culture results. Vedolizumab, a monoclonal antibody that binds to integrin α4β7, has never been reported to cause any kind of pulmonary toxicity, although we cannot exclude it.

To our knowledge, this is the second reported case of pulmonary involvement associated with CD mimicking sarcoidosis based on the BAL and lung biopsy results. Further studies will be needed to assess whether there is any link between sarcoidosis and Crohn’s-associated ILD and if there are any diagnostic studies that may be more suggestive of one disease or the other.

This case illustrates the complexity in diagnosing Crohn’s-associated ILD in a patient who is on a
medication known to cause pneumonitis and findings that may be suggestive of other diagnoses. Initially an accurate diagnosis may be difficult, but using a multidisciplinary approach can be helpful to make an accurate diagnosis.

References