

Clinical Assessment of Respiratory Complaints in Patients with Inflammatory Bowel Disease

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Original Research Article

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Article History

Received: 02.08.2018

Accepted: 10.08.2018

Published: 30.08.2018

DOI:

10.36348/sjimps.2018.v04i08.008



Abstract: Complications involving the lungs as a sequela of a systemic disease process are not uncommon, and in fact, pulmonary involvement could be the first or even the only manifestation of systemic disease in a handful of clinical cases. Inflammatory bowel diseases are characterized by mucosal inflammation involving the GI tract that can follow a relapsing-remitting course. Respiratory tract diseases in the setting of IBD can be quite variable and warrants clinical recognition and proper treatment as it could have a significant impact on the patients' health. Here I summarize the potential pathological involvements of the respiratory system in the cohort of IBD patients and summarize the clinical assessment steps necessary to achieve the proper diagnosis.

Keywords: Inflammatory bowel disease, airway disease, pulmonary function test, chest images.

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory bowel diseases (IBD) that have variable clinical course and well recognized multiple extraintestinal manifestations. The concomitant relationship between IBD and respiratory system pathology has been demonstrated and more recognized in the clinical setting. When a patient with IBD presents with a respiratory complaint, the physician should keep in mind the possibility that the patient's respiratory symptoms might be related to or caused by his underlying IBD. Airway, parenchymal and pleural pathologies have been reported in these patients with diverse clinical presentations and clinical course. Interestingly, a high proportion of patients with IBD were asymptomatic from a respiratory perspective despite the presence of radiographic or lung function abnormalities [1-3].

Starting with airway diseases, a concomitant involvement of this vital part of the respiratory system in patients with IBD is an essential diagnosis to make given that there has been growing evidence on the presence of what seems to be a bidirectional relationship between the development of airway diseases and IBD. Moreover, the burden of the respiratory symptoms including a cough, sputum expectoration, and breathlessness can be quite debilitating to the patients warranting appropriate diagnosis and treatment. Thus, proper diagnostic steps have to be conducted to ascertain the diagnosis of airway involvement in these patients. Environmental factors, immunological dysregulation, and genetic predisposition are most likely the common platforms in the underlying pathological process of IBD and airway disease besides the fact that they share a common embryonic origin and similar histology, i.e., mucosal lining epithelial cells and goblet glands [4-6]. The various airway diseases that have been commonly observed in IBD patients include asthma, chronic bronchitis, and structural abnormalities like bronchiectasis [7-9], and tracheal stenosis which was

rarely reported in these patients [10, 11]. In addition, small airway diseases such as bronchiolitis with its different pathological features, i.e., granulomatous bronchiolitis, concentric obliterans and diffuse panbronchiolitis have been described in the literature in association with IBD. Bronchiolitis manifest mainly with breathlessness and airflow limitation on lung function, with sometimes subtle imaging findings [5, 12, 13].

When evaluating patients with respiratory complaints in general, and in a relevant discussion, patients with IBD, assessment of lung function is an essential first step to take as a diagnostic tool, an integral component of lung physiology could be obtained by performing this noninvasive test. Variable pulmonary function test (PFT) abnormalities have been described in patients with IBD on multiple published papers with a high proportion of patients being asymptomatic despite the finding of lung function abnormalities. The lung dysfunction varied among obstructive defect, restrictive impairment, and low gas transfer capacity [14-18]. Of note, not all previous

authors correlated the results of PFT with chest images to precisely identify the cause of lung function abnormalities. Moreover, some authors reported that PFT abnormalities were changing with the activity of the underlying IBD [14, 19] which might indicate the presence of a subtle chronic pulmonary inflammation that is in line with the ongoing gastrointestinal inflammatory process.

In practice, it is reasonable to assess for airway hyperresponsiveness in patients with IBD complaining of breathlessness, chest tightness, cough or wheezing, by performing a methacholine challenge test. This airway abnormality has been reported in these patients, and in fact, some of them were asymptomatic from respiratory perspective [1, 2, 20]. The significance of the presence of airway hyperresponsiveness in patients with IBD can support the diagnosis of bronchial asthma in symptomatic patients; however, it is clinical significance when the patients lack respiratory symptoms are unclear.

The utility of sputum analysis for cell count and differential in diagnosing airway disease, in general, can be helpful in providing a good insight into the type and degree of the airway inflammation. Different types of airway inflammations have been detected in patients with IBD, some of them lacked respiratory symptoms and had a normal lung function. Lymphocytic (CD4+T-cell) and eosinophilic bronchitis, the latter in some patients was unrelated to the presence of airway hyperresponsiveness or atopy, have been identified in IBD patients [17, 21-23]. Given the demonstration in few studies of the relationship between an increase in these inflammatory cells in the airway and IBD activity, monitoring these cells might be of value as a noninvasive surrogate test for IBD activity. Including sputum cell count analysis in the workup of IBD patients with respiratory complaints can guide treatment therapy, i.e., the finding of eosinophilic airway inflammation warrants treatment with an inhaled corticosteroid to help improve the patient symptoms.

Chest –x-ray is reasonable to obtain if a patient with IBD developed any respiratory symptoms to assess for significant lung abnormality like infiltrate, mass or apparent airway changes. In case it is not diagnostic, it should be followed by High-Resolution Computed Tomography (HRCT) of the chest with inspiratory/expiratory hold images as radiographic changes might be subtle and won't be detected easily on CXR. Sato *et al.*, have recently characterized the radiographic abnormalities on chest CT in patients with IBD; they demonstrated that these patients have wide varieties of lung abnormalities including bronchial wall thickening which was more common in CD than UC group, centrilobular nodules, bronchiectasis, ground-glass opacities, consolidation, organizing pneumonia and less commonly fibrotic parenchymal changes [3].

Evaluation of lung nodules and opacities in these patients should thoroughly be undertaken. Infections, especially with opportunistic pathogens, and malignancies are the two serious conditions that should be ruled out given that the patients with IBD are usually immunocompromised as a part of their disease-directed therapy and they are more prone to these two complications. Other lung pathologies to be considered when evaluating parenchymal lung lesions in IBD patients include organizing pneumonia, necrobiotic nodules, granulomatous reaction reported in CD and necrotizing nodules resembling granulomatosis with polyangiitis reported in patients with UC [5, 24]. Bronchoscopy to obtain samples for culture, cell count differential and cytology assessment is the appropriate step to take in an attempt to identify a cause of the lung abnormality with consideration for tissue sample for histology assessment especially if the lung lesion persists despite initial treatment with an appropriate antibiotic.

As an interesting observation, pulmonary sarcoidosis and Cohn's disease have rarely been reported to coexist in the same patients. It was demonstrated that CD could be associated with lymphocytic alveolitis as evident by the presence of a high proportion of CD4+ T-lymphocyte cells on Bronchoalveolar lavage fluid analysis [25]. This type of T- lymphocyte is characteristic of sarcoidosis. Knowing that they share a common pathological feature of granulomatous inflammation of unknown etiology makes the possibility that there is an underlying unique immunological/inflammatory trigger responsible for both conditions [26].

Various interstitial lung diseases were reported in patients with IBD include organizing pneumonia (OP). OP can present on chest images in a nodular pattern, solitary mass, ground-glass opacities, airspace disease or reticular lesions. Other different ILD patterns reported in IBD cases include non-specific interstitial pneumonia, eosinophilic pneumonia and very rarely usual interstitial pneumonia and upper lobe predominant fibrosis, all have been described as well [3, 5, 27].

The risk of venous thrombosis has been demonstrated to be elevated in patients with IBD; pulmonary embolism definitely would be in the differential diagnosis when evaluating IBD patients with respiratory complaints [28].

As the case with any other chronic conditions where the patients are chronically treated with maintenance medications, drug reaction and side effects have to be born in mind as a differential diagnosis when assessing lung pathology. Different medications used for IBD treatment have been implicated in the

development of variable lung pathologies summarized by Ji XQ *et al.*, [29] including eosinophilic pneumonia, hypersensitivity pneumonitis, pleural effusion and interstitial lung disease. The challenge is to discriminate between the IBD- related lung involvement and drug reaction which is sometimes difficult to ascertain even in the presence of lung tissue biopsy.

In summary, the presence of a respiratory complaint in patients who has underlying IBD whether it is an active disease or is under remission should prompt a thorough clinical evaluation beside consideration of lung function assessment and obtaining an appropriate chest image as a necessary evaluation step in these patients. Various lung pathologies could be seen and detected in patients with IBD and could imply significant comorbidity in this cohort of patients.

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