

Pediatric Patient With Ulcerative Colitis-Associated Bronchiectasis

Abigail Russi, MD, PhD¹, Neepa Gurbani, DO^{1,2}, Michael J. Rosen, MD, MSCI^{1,3}, Daniel Mallon, MD^{1,3}, and Francis R. LeBlanc, MD, PhD¹

¹Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH

²Division of Pulmonary Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

³Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

ABSTRACT

We report a unique case of ulcerative colitis-associated bronchiectasis in a pediatric patient 6 years after colectomy. The patient presented with a chronic cough and had a computed tomography demonstrating bronchiectasis. She was treated with sputum expectoration (airway clearance) via chest physiotherapy and pulse-dose steroids with a prolonged oral taper. Her initial response was excellent; however, she experienced a recurrence of symptoms with de-escalation of airway clearance. Pulmonary extraintestinal manifestations of inflammatory bowel disease are most often diagnosed later in life. Both the severity of this patient's presentation and her age are unique to this case.

INTRODUCTION

Extraintestinal manifestations affect 25%–40% of individuals with inflammatory bowel disease (IBD). Although muscles, joints, and skin are most commonly affected, pulmonary involvement is more prevalent than previously appreciated.^{1–4} It is estimated that 40%–60% of patients with IBD have abnormal pulmonary function tests, but most of these patients are asymptomatic.^{5,6} The large airways are most commonly involved; however, the small airways, lung parenchyma, and pulmonary vasculature may be affected.^{5,6} Pulmonary symptoms rarely precede a diagnosis of IBD, and there is some evidence that colectomy is a risk factor for pulmonary involvement.⁷ We report a case of ulcerative colitis-associated bronchiectasis in a pediatric patient 6 years after a colectomy.

CASE REPORT

A 17-year old girl with a medical history of infliximab and steroid-refractory ulcerative colitis (UC) status postcolectomy with ileal-pouch anal anastomosis presented with a 5-month history of chronic purulent cough. Most significantly for this patient, it prevented her from playing the saxophone. She denied fevers, wheezing or difficulty breathing, and difficulty swallowing. There was no history of frequent infections or neonatal respiratory distress. Family history was negative for pulmonary disease. She had traveled to the Bahamas 2 months before onset.

From an IBD standpoint, she was originally diagnosed with UC 6 years before this hospitalization, after presenting with weight loss and rectal bleeding. Despite treatment with multiple courses of oral steroids, aminosalicylates, and 2 months of infliximab, she had a clinical relapse and continued colitis leading to total colectomy 5 years before this presentation with an ileal-pouch anal anastomosis the following year.

Outpatient workup for the chronic cough consisted of a negative chest radiograph, purified protein derivative skin test, sweat chloride test, histoplasmosis serum antigen, and pertussis polymerase chain reaction with a normal immunoglobulin E, complete blood count, and an electrolyte panel. She received 3 courses of antibiotics (amoxicillin, azithromycin, and amoxicillin-clavulanate) without improvement. She also trialed albuterol, dexamethasone, ranitidine, and fluticasone propionate without benefit. She

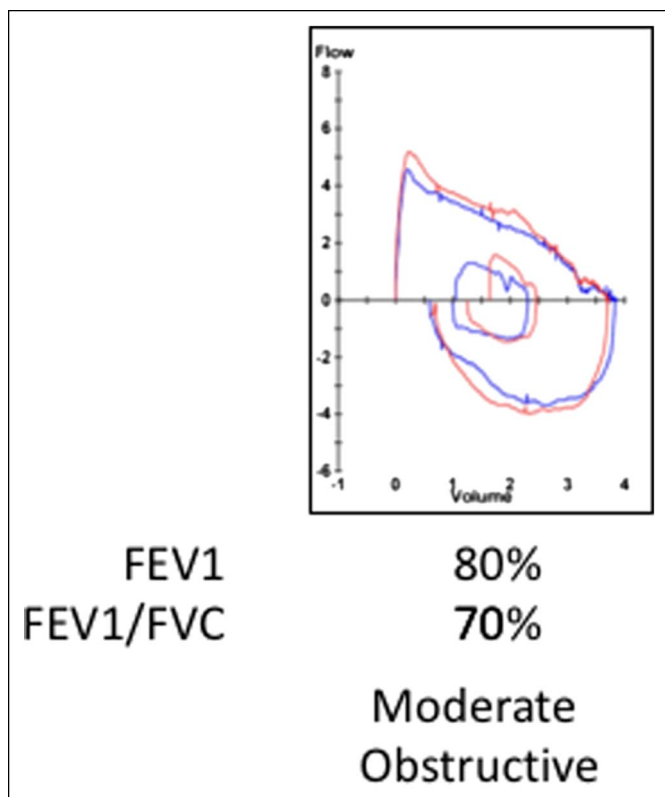


Figure 1. Pulmonary function testing demonstrating a moderate obstructive pattern with no response to bronchodilators. FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

underwent a diagnostic flexible bronchoscopy, which demonstrated purulent bronchitis. The bronchoalveolar (BAL) cytology was 99% neutrophils. BAL cultures, including fungal, were negative. Pulmonary function testing (PFT) demonstrated a moderate obstructive defect (forced expiratory volume in 1 second [FEV1]: 75% predicted) with no bronchodilator response (7% change).

She presented to the emergency department with a worsening cough. She was afebrile with appropriate oxygen saturation. On

examination, she had scattered wheezes that improved with a cough. A chest radiograph was normal. Intravenous (IV) ceftriaxone was initiated after sputum cultures were sent. Rheumatologic studies, including inflammatory markers, antinuclear antibody, perinuclear antineutrophil cytoplasmic antibody, rheumatoid factor, myeloperoxidase antibodies, and proteinase-3 antibodies, were negative. Bacterial and fungal blood cultures were both negative, and no acid-fast bacilli were detected. Repeat PFTs again demonstrated a moderate obstructive defect (Figure 1).

A high-resolution thoracic computed tomography demonstrated scattered centrilobular “tree-in-bud” opacities with mild bronchiectasis and bronchial wall thickening (Figure 2). After consultation with the pulmonology, gastroenterology, and infectious disease services, the diagnosis of UC-associated bronchiectasis was considered most likely. Ceftriaxone was discontinued, and the patient was treated with pulse-dose methylprednisolone 1 g IV daily for 3 days. Vest therapy with albuterol and 3% hypertonic saline was also performed twice daily. PFTs after 2 doses of steroids showed normal spirometry with an FEV1 of 88% predicted (Figure 3). The patient was discharged home with a 13-day steroid taper and an oscillating positive expiratory pressure device for airway clearance. At follow-up a month later, she had resolution of her cough and the ability to play wind-instruments again. However, at her most recent visit nearly 1 year after the initial admission, she reported worsening cough and dyspnea on exertion. Her PFTs were again abnormal, with an FEV1 of 71% of predicted (Figure 3). She had de-escalated airway clearance on her own in the interim. She was started on oral prednisone daily for 5 days and a 10-day course of amoxicillin-clavulanate and was ultimately hospitalized for IV antibiotics and improved again.

DISCUSSION

In addition to pulmonary extra-intestinal manifestations, the differential for this patient with a chronic cough and obstructive

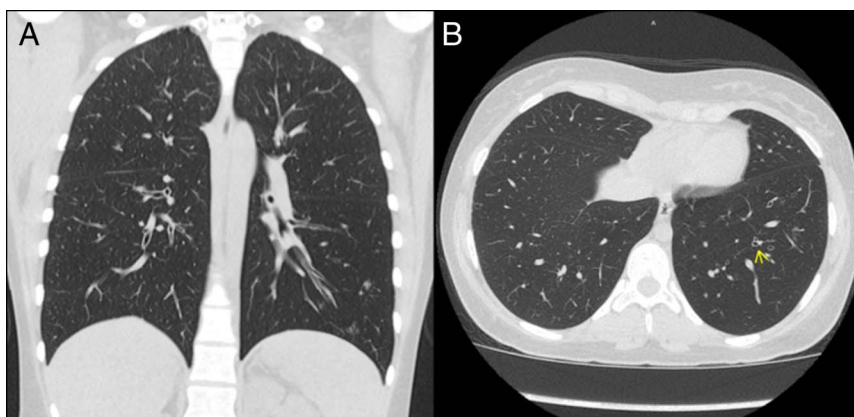


Figure 2. High resolution thoracic computed tomography showing (A) scattered centrilobular “tree-in-bud” opacities in the left lower lobe and (B) bronchial wall thickening demonstrating bronchiectasis.

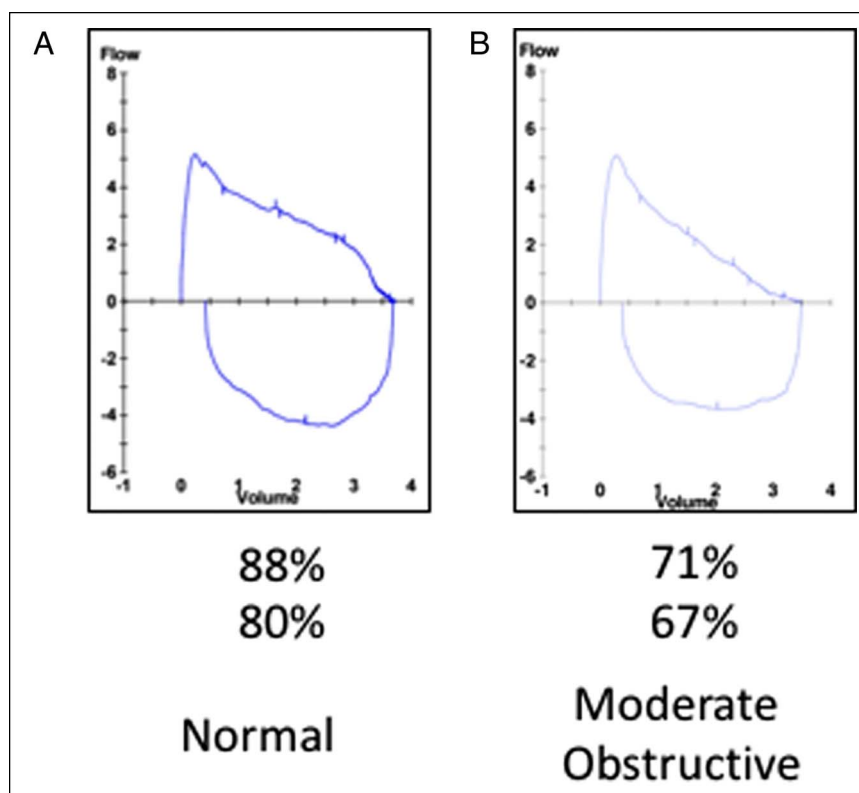


Figure 3. (A) Repeat pulmonary function testing after 2 of 3 days of pulse dose steroids demonstrating normal spirometry. (B) Pulmonary function testing taken after 1 year during acute pulmonary flare.

lung disease include asthma, immunodeficiency, infectious, anatomical abnormality, foreign body, and autoimmune etiologies. She had no response to bronchodilators eliminating asthma. She had no history of recurrent infections, which reassured against an immunodeficiency. Serum testing and the absence of skin and joint involvement made rheumatologic disease less likely. Her bronchoscopy was reassuring against vascular anomalies or foreign bodies. Furthermore, the negative repeat BAL cultures essentially ruled out an infectious etiology. Her testing was negative for fungal and mycoplasma etiologies.⁸

Pulmonary involvement in patients with IBD ranges from asymptomatic to severe.⁹ In patients with UC, pulmonary involvement, as detected by abnormal PFTs, is approximately 60%.¹⁰⁻¹² However, most of these patients are asymptomatic. The large airways are the most commonly affected, with bronchiectasis being the most common finding.⁹ In 1 study of 14 patients with UC and respiratory symptoms, 11 (79%) had bronchiectasis on computed tomography, and of those, 5 (45%) had “tree-in-bud” opacities.¹³ Furthermore, there is evidence that colectomy is a risk factor for developing pulmonary involvement.¹⁴ In 2 retrospective studies of patients with IBD and respiratory symptoms, 60% and 80% were postcolectomy.^{7,15} Interestingly, a survey of the case report literature for IBD and lung disease identified 9 patients with UC who developed bronchiectasis within 1 year of colectomy, much earlier than our patient.¹⁶

The young age of our patient, presentation 6 years post-colectomy, and the neutrophilic predominance of the BAL fluid are each unique aspects of our case. Most studies are in older adults; however, 1 study in children demonstrated PFT abnormalities with active Crohn’s disease compared with quiescent disease.¹⁷⁻¹⁹ A neutrophilic predominance in the BAL fluid accurately identifies patients with clinically symptomatic bronchiectasis; whereas, abnormal lymphocytes are most commonly isolated from the lungs of patients with asymptomatic IBD.²⁰⁻²²

The pathogenesis of UC-associated bronchiectasis is not well understood, but some suggest that it involves molecular mimicry or aberrant cell homing from the shared embryological origin of the pulmonary and intestinal system from the primitive foregut.¹⁸ This theory offers a partial explanation for why colectomy is a risk factor for pulmonary involvement. Perhaps the pulmonary system becomes the focus of sensitized lymphocytes after a colectomy. Another contributing theory is the de-escalation of immune-modulating therapy after surgery.

This case demonstrates a rare diagnosis of UC-associated bronchiectasis responsive to steroid therapy and chest physiotherapy with airway clearance. Most patients, such as ours, have a positive short-term response to systemic steroids and the potential for relapse. This highlights the importance of early involvement of pulmonologists in the care of any patients with IBD experiencing pulmonary symptoms. In addition, this

highlights that pulmonary symptoms associated with UC can present at any point during illness.

DISCLOSURES

Author contributions: A. Russi wrote the manuscript. N. Gurbani, MJ Rosen, and D. Mallon revised the manuscript for important intellectual content. FR LeBlanc wrote the manuscript and is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received November 8, 2019; Accepted February 12, 2020

REFERENCES

1. Ponder A, Long MD. A clinical review of recent findings in the epidemiology of inflammatory bowel disease. *Clin Epidemiol*. 2013;5:237–47.
2. Danese S, Semeraro S, Papa A, et al. Extraintestinal manifestations in inflammatory bowel disease. *World J Gastroenterol*. 2005;11:7227–36.
3. Mendoza JL, Lana R, Taxonera C, Alba C, Izquierdo S, Díaz-Rubio M. Extraintestinal manifestations in inflammatory bowel disease: Differences between Crohn's disease and ulcerative colitis. *Med Clin (Barc)*. 2005;125:297–300. [Spanish.]
4. Ott C, Taksas A, Obermeier F, Schnoy E, Muller M. Smoking increases the risk of extraintestinal manifestations in Crohn's disease. *World J Gastroenterol*. 2014;20:12269–76.
5. Cozzi D, Moroni C, Addeo G, et al. Radiological patterns of lung involvement in inflammatory bowel disease. *Gastroenterol Res Pract*. 2018;2018:5697846.
6. Papanikolaou I, Kagouridis K, Papiris SA. Patterns of airway involvement in inflammatory bowel diseases. *World J Gastrointest Pathophysiol*. 2014;5:560–9.
7. Camus P, Piard F, Ashcroft T, Gal AA, Colby TV. The lung in inflammatory bowel disease. *Medicine (Baltimore)*. 1993;72:151–83.
8. Casella G, Villanacci V, Di Bella C, Antonelli E, Baldini V, Bassotti G. Pulmonary diseases associated with inflammatory bowel diseases. *J Crohns Colitis*. 2010;4:384–9.
9. D'Andrea N, Vigiariolo R, Sanguinetti CM. Respiratory involvement in inflammatory bowel diseases. *Multidiscip Respir Med*. 2010;5:173–82.
10. Goyal A, Ghoshal UC, Nath A, Jindal S, Mohindra S. Pulmonary function in patients with ulcerative colitis and its relationship with disease severity. *JGH Open*. 2017;1:32–7.
11. Storch I, Sachar D, Katz S. Pulmonary manifestations of inflammatory bowel disease. *Inflamm Bowel Dis*. 2003;9:104–15.
12. Kuzela L, Vavrecka A, Prikazska M, et al. Pulmonary complications in patients with inflammatory bowel disease. *Hepatogastroenterology*. 1999;46:1714–9.
13. Mahadeva R, Walsh G, Flower CD, Shneerson JM. Clinical and radiological characteristics of lung disease in inflammatory bowel disease. *Eur Respir J*. 2000;15:41–8.
14. Spira A, Grossman R, Balter M. Large airway disease associated with inflammatory bowel disease. *Chest*. 1998;113:1723–6.
15. Kelly MG, Frizelle FA, Thornley PT, Beckert L, Epton M, Craig Lynch A. Inflammatory bowel disease and the lung: Is there a link between surgery and bronchiectasis? *Int J Colorectal Dis*. 2006;21:754–7.
16. Black H, Mendoza M, Murin S. Thoracic manifestations of inflammatory bowel disease. *Chest*. 2007;131:524–32.
17. Xie F, Fang QH, Bu XN. Clinical features of 12 cases of respiratory diseases associated with inflammatory bowel diseases. *Zhonghua Jie He He Hu Xi Za Zhi*. 2018;41:724–7. [Chinese.]
18. Maglione M, Aksamit T, Santamaria F. Paediatric and adult bronchiectasis: Specific management with coexisting asthma, COPD, rheumatological disease and inflammatory bowel disease. *Respirology*. 2019;24(11):1063–72.
19. Munck A, Murciano D, Pariente R, Cezard JP, Navarro J. Latent pulmonary function abnormalities in children with Crohn's disease. *Eur Respir J*. 1995;8:377–80.
20. Drost N, D'silva L, Rebello R, Efthimiadis A, Hargreave FE, Nair P. Persistent sputum cellularity and neutrophils may predict bronchiectasis. *Can Respir J*. 2011;18:221–4.
21. Wallaert B, Colombel JF, Tonnel AB, et al. Evidence of lymphocyte alveolitis in Crohn's disease. *Chest*. 1985;87:363–7.
22. Sarioğlu N, Türkel N, Sakar A, et al. Lung involvement in inflammatory bowel diseases. *Ann Saudi Med*. 2006;26:407–8.

Copyright: © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.