Progressive stridor: extraintestinal airway manifestations in a pediatric patient with inflammatory bowel disease.

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CASE REPORT

Progressive stridor: extraintestinal airway manifestations in a pediatric patient with inflammatory bowel disease

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Abstract

Airway manifestations of inflammatory bowel disease are rare in pediatrics. This case describes a nine-year-old female with ulcerative colitis (UC) with progressive stridor and dyspnea for two months. Severe upper airway obstruction was noted on spirometry. CatScan (CT) of the neck and chest revealed tracheal narrowing with circumferential, heterogeneous soft tissue thickening, and posterior wall nodularity. Bronchoscopy visualized the granulation tissue of the large airways and an ulcerative lesion to the right mainstem. Consultation and evaluation by gastroenterology, oncology, and rheumatology determined a diagnosis of extraintestinal manifestations of UC. Systemic steroids led to symptom resolution and improvement in lung function.

Keywords Stridor · Tracheal stenosis · Tracheal nodularity

Abbreviations

CBC	Complete blood count
CRP	C-Reactive Protein
FEV1	Forced expiratory volume in one second
IBD	Inflammatory bowel disease
GPA	Granulomatosis with polyangiitis
PFT	Pulmonary function test
RP	Relapsing polychondritis
TSH	Thyroid-stimulating hormone
UC	Ulcerative colitis

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Introduction

Ulcerative colitis (UC) has been known to cause pulmonary symptoms and complications since 1976 when Kraft et al. described 6 patients with inflammatory bowel disease (IBD) who had copious secretions with and without bronchiectasis [1]. Since that time, the pulmonary manifestations of IBD are documented in the adult population and can include bronchiectasis, cryptogenic organizing pneumonia, interstitial pneumonia, tracheitis, pulmonary embolism, and drug-induced pulmonary fibrosis [2]. However, literature describing pulmonary involvement in children is rare. Further, tracheal involvement in UC is rare and infrequently reported in case reports over the span of decades and even less frequently in children [3]. Here, we present a case of a pediatric patient with extensive tracheal involvement leading to progressive stridor, dyspnea, and increased work of breathing secondary to an extraintestinal manifestation of underlying ulcerative colitis.

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Case report

A 9-year-old female with a history of mild persistent asthma and ulcerative colitis diagnosed at age 7 presented to the pediatric pulmonology office with two months of worsening stridor and dyspnea. Spirometry revealed mild airway obstruction with forced expiratory volume in one second (FEV1) of 68% and a mildly flattened expiratory limb (Fig. 1A, Table 1A). The patient was started on inhaled bronchodilator therapy and encouraged to perform breathing exercises, such as diaphragm breathing. The patient showed little improvement, had repeat FEV1 of 61% (Fig. 1B, Table 1B), and was started on inhaled corticosteroids. After experiencing worsening symptoms, repeat spirometry showed an FEV1 of 41% with flat inspiratory and expiratory limbs (Fig. 1C, Table 1C). The patient's symptoms were not well controlled on inhaled albuterol every 4–6 h as needed or two puffs of inhaled fluticasone propionate 110 mcg twice daily despite reported adherence to therapy. As she complained of no active gastrointestinal symptoms, no treatment specific to her IBD was initiated at that time.

On presentation, the patient was visibly dyspneic with retractions, tachypnea, and tracheal tugging. A chest X-ray was normal, but airway fluoroscopy noted fixed, diffuse tracheal narrowing measuring 4.7 mm in diameter prompting a CT neck and chest. The CT revealed circumferential, heterogeneous tracheal soft tissue thickening from the thoracic inlet to the mediastinum with a diffuse nodular appearance of the posterior trachea and mainstem bronchi (Fig. 2). There was no noted parenchymal lung disease or lymphadenopathy in neck or chest. With these imaging findings and continued symptoms, the patient underwent a flexible and rigid bronchoscopy. Bronchoscopy revealed circumferential stenosis at the mid-cervical trachea and extending down to the carina with white endophytic granulation tissue involving the tracheal wall (Fig. 3A–D). The right mainstem bronchus revealed an ulcerative lesion with central erythema and surrounding purulent inflammatory tissue (Fig. 3B).

The ulcerative lesion was biopsied, and a routine BAL was performed to investigate for bacterial, fungal, and viral infection. Cytologic studies revealed normal cell counts. All cultures, including AFB, fungal, and bronchial cultures, resulted negative. The biopsy confirmed granulation tissue, fibrin, and leukocytes most consistent with the base of a chronic ulcer.

Table 1 Sequential evaluation of pulmonary function testing

Parameter	June 2019 Loop A	July 2019 Loop B	August 2019 Loop C	September 2019 Loop D
FVC	2.19 (90)	2.5 (102)	2.07 (84)	2.61 (106)
FEV1	1.45 (68)	1.32 (61)	0.89 (41)	2.21 (103)
FEV1/FVC%	66	53	43	85
FEF25-75 L/S	1.13 (42)	0.77 (29)	0.68 (25)	2.40 (89)

Data in parentheses are the percentage of the predicted value for age, ethnicity, and height. Measurements taken in June and July 2019 were performed in the pulmonology outpatient office. The July 2019 values represent the change noted after initiation of inhaled bronchodilators. The measurement from August 2019 demonstrates decreased lung function despite inhaled corticosteroids. The measurements in September 2019 represent improvement after 14 days of oral corticosteroids after bronchoscopic diagnosis of pulmonary manifestations of IBD

FVC forced vital capacity, *FEV1* forced expiratory volume in one second, *FEF25-75* forced mixed expiratory flow

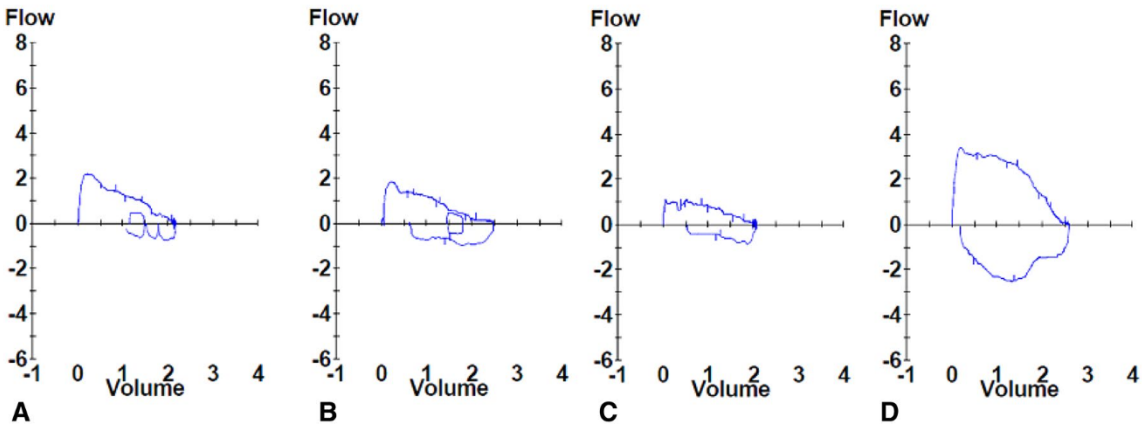

Fig. 1 Sequential pulmonary function testing—flow volume loops **A**, **B**, and **C** represent pretreatment gradual worsening of fixed upper airway obstruction in chronological order from the time of presentation to the time of diagnosis. Flow volume loop **D** represents improvement after treatment with systemic steroids

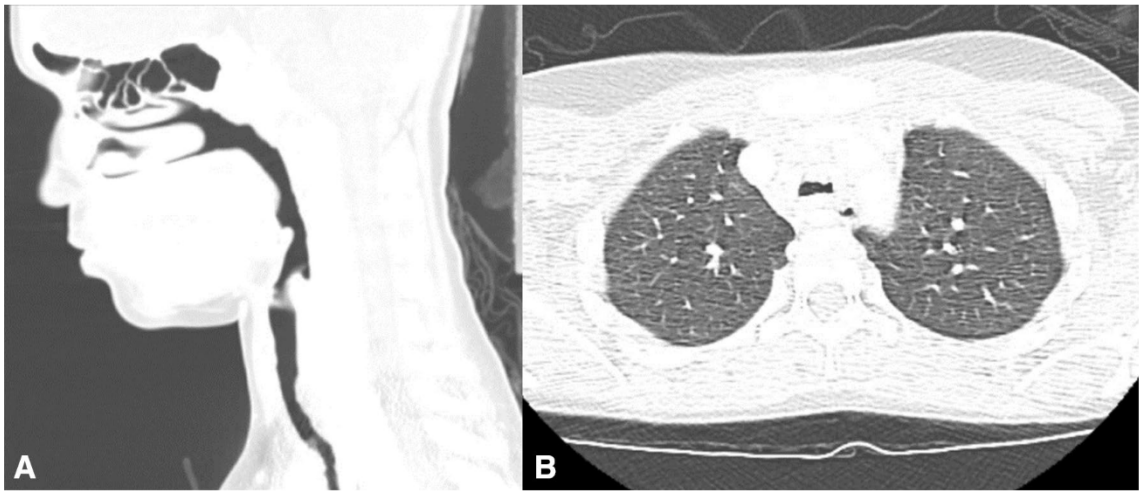

Fig. 2 **A**- Extensive, circumferential soft tissue thickening and heterogeneous enhancement of the tracheal wall. These findings began at the level of the thoracic inlet and extended into the upper mediastinum. There was moderate, diffuse stenosis of the imaged aspect of the trachea on neck CT. **B**- Axial slice of chest CT showed narrowing of the trachea with nodularity. This started at C6–C7 level and extended along the trachea to the carina and involved portions of the right and left mainstem bronchi. The wall of the trachea was thickened and demonstrated scattered nodularity and irregularity. The posterior wall of the trachea was partially involved

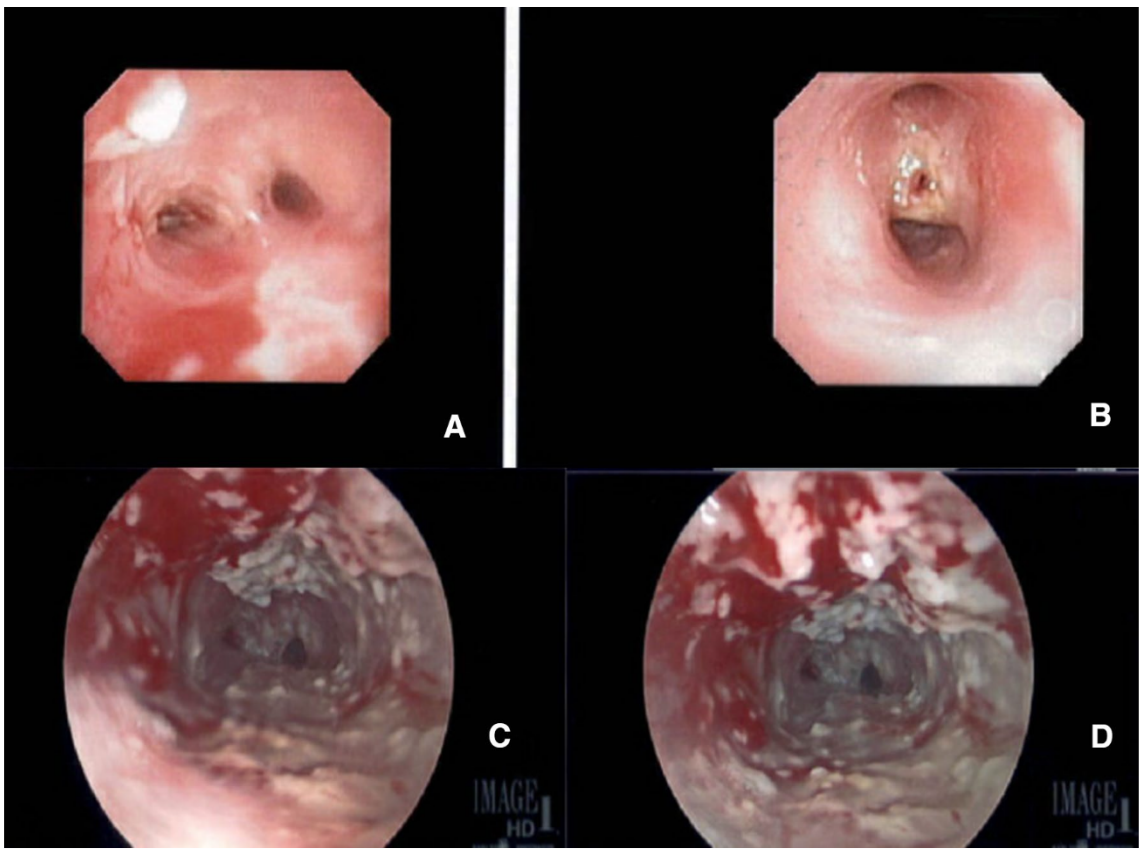

Fig. 3 **A**- Visualization of the right mainstem bronchus revealed thick, white tissue with yellow, purulent secretions. **B**- Branching of the bronchus showed ulceration with circumferential inflammatory tissue. Pathology revealed tiny fragments of inflamed granulation tissue and large fragments of fibrin with leukocytes, most likely representing the bottom of a chronic ulcer. **C**, **D**- The proximal tracheal mucosa and tracheal rings were intact, and there was visible friable tissue with white, cystic-like tissue protruding from the anterior and lateral walls

A rheumatologic evaluation was performed to investigate the possibility of relapsing polychondritis (RP) or vasculitis, such as granulomatosis with polyangiitis (GPA) as potential cause for the large airway inflammation. This workup revealed high titer antineutrophil cytoplasmic antibodies in atypical perinuclear pattern, typical of UC. She had mild elevation of her erythrocyte sedimentation rate. The remaining rheumatologic workup was unrevealing, including negative rheumatoid factor and myeloperoxidase, proteinase 3, and antinuclear antibodies. She had a normal CRP, CBC, TSH, iron level, ferritin, and quantitative immunoglobulins. Ophthalmology consultation found no ocular inflammation. Gastroenterology determined that the UC was unlikely to be active, as she had no gastrointestinal symptoms and a normal fecal calprotectin.

The patient received fourteen days of prednisone with symptom resolution. Repeat spirometry four weeks after treatment showed an improved FEV1 of 103%, with a bell-shaped expiratory limb (Fig. 1D, Table 1D). She was also continued on her medium dose inhaled corticosteroid throughout the treatment period. The combination of systemic and inhaled steroids led to resolution of her stridor and dyspnea. In conjunction with the multidisciplinary team, it was determined that the origin of the airway abnormalities was extraintestinal manifestation of ulcerative colitis. Prior to the onset of her pulmonary symptoms, her gastrointestinal symptoms were well managed without daily medications. At the time of initial diagnosis of UC, the patient was started on olsalazine 250 mg twice daily for disease maintenance. This was discontinued after 6 weeks as she had no active symptoms, including abdominal pain, loose stool, or bloody stool. However, when the complications of the extraintestinal manifestations arose, specialists proposed the addition of balsalazide for anti-inflammatory effect. Per parental preference, the medication was not started and the patient only completed the fourteen days of systemic steroids. The patient will be followed closely by pulmonology and gastroenterology for surveillance, including routine pulmonary function tests (PFT), lab evaluation, and imaging or bronchoscopy as clinically indicated. The patient currently remains asymptomatic two years later with stable lung function. The patient's fecal calprotectin is serially monitored and parents continue to prefer homeopathic approaches to care without the addition of daily medications.

Discussion

Extraintestinal manifestations of IBD are well characterized in the literature and affect approximately 21–41% of patients with IBD [4, 5]. These symptoms typically include musculoskeletal, dermatologic, and ocular symptoms, but emerging literature proposes that respiratory tract involvement is underrecognized. In the past, it was thought that only 0.4% of patients suffered pulmonary complications, though now studies suggest subclinical findings can be found in up to 50% of patients with IBD [5–7]. These studies, however, focus on the adult population with only rare case reports in the pediatric population. The leading theories linking the respiratory and gastrointestinal manifestations of IBD stem from the related embryological origin of the two systems. Both systems originate from the primitive foregut, share epithelial and immune characteristics, and are exposed to the same allergens and triggers that can sensitize and inflame the tissues [2, 4, 8].

The presentation varies from subclinical, asymptomatic PFT changes to progressive and limiting stridor or respiratory distress. Subclinical abnormalities, such as increased bronchial hyperresponsiveness, PFT changes, and increased lymphocytes in BAL, and sputum samples are well characterized, though not diagnostic, in patients with IBD [4, 9]. There are no definitive findings on BAL or direct tissue biopsy to confirm the diagnosis IBD in the airway; however, upper airway friability, cobblestoning, edema, ulceration, hemorrhage within the trachea and large airways, and histologic appearance similar to colonic epithelium in ulcerative colitis have been noted in case reports [2, 4]. The degree of pulmonary involvement has no direct correlation to the degree of intestinal involvement, and the patient can present with respiratory complaints even in the absence of GI symptoms [3, 7, 8, 10]. Some patients can also present with pulmonary symptom onset prior to GI manifestations of IBD [3]. The early recognition of the etiology for pulmonary symptoms is pivotal as the complications can affect the entire pulmonary system from the nasopharynx to the small airways. The untreated inflammation can lead to irreversible destruction, including tracheal stenosis, bronchiolitis obliterans, and fixed airway obstruction [4, 7, 8, 11]. Bronchiectasis is reported in up to 66% of patients found to have pulmonary system involvement [5, 8].

In this case, the diagnosis was one of exclusion given the patient's age and lack of similar documented pediatric presentations in the literature. Prince et al. describes conditions and complications that can affect the tracheobronchial wall. They discuss infectious, post-infectious, inflammatory, and idiopathic causes of tracheal lesions [12]. The patient had no infectious symptoms or history of exposures, but the infectious workup was still warranted as infectious etiologies are typically the most common cause of pulmonary complications in this patient population [8]. After infectious workup was negative, the differential was expanded to include rheumatologic conditions that affect the large airways, including RP, sarcoidosis, and GPA. The posterior wall of the patient's trachea showed nodularity and irregularity which would be atypical of RP since the posterior wall of the trachea is non-cartilaginous. Furthermore, there was no auricular, nasal,

or laryngeal involvement and thus the patient failed to meet clinical criteria for RP [12]. Bronchial involvement is more common than tracheal involvement in sarcoidosis, and our patient had no lung parenchymal involvement or lymphadenopathy [13]. Proteinase 3 antibodies were negative, and she had no other manifestations of GPA, such as sinus or renal involvement. Consultation among pediatric rheumatology, gastroenterology, and pulmonology led to a diagnosis of extraintestinal manifestation of IBD affecting the large airway.

Management of the pulmonary involvement of IBD is not well delineated given the rarity of this condition [14]. The treatment depends on patient presentation. While most respiratory complications do respond to systemic steroids, no surgical or medical intervention has been proven to prevent the development of pulmonary complications of IBD [15]. Unfortunately, managing the underlying disease with disease modifying immunosuppressive agents can also lead to pulmonary complications due to the immunosuppression increasing the risk of infectious pulmonary complications [5]. The goal for managing the gastrointestinal manifestations of ulcerative colitis is to achieve histologic remission, suppress inflammation, and manage symptoms with the least amount of side effects from the medications chosen. Treatment regimens can include antibiotics, anti-inflammatory medications, corticosteroids, immunomodulators, and biologics. The medications are chosen based on disease severity. There are no dosing recommendations for systemic steroids or antibiotics, so current recommendations remain empirical and driven by patient response [4]. Our patient experienced complete symptom resolution after 14 days of systemic corticosteroids and will continue to require close follow-up by the various involved specialists to maintain disease control. Additionally, patients can be considered as surgical candidates based on disease severity.

Conclusion

In conclusion, pediatric patients with inflammatory bowel disease should be monitored for extraintestinal manifestations of their disease, including airway manifestations. Classically, the extraintestinal manifestations include skin rashes, arthritis, uveitis, liver inflammation, anemia, and side effects of medications typically used to treat IBD. However, this case also presents the possibility that children can be afflicted with airway manifestations of IBD. The granulation tissue and airway ulceration manifested as stridor on physical exam, but any presentation of airway compromise in patients with IBD should prompt further workup or referral by the pediatrician.

Declaration

Conflict of interest All authors declare that they have no conflict ofinterest.

Statement on human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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