Provisionally accepted for publication

NARRATIVE REVIEW

Respiratory involvement in inflammatory bowel disease in children: a case-based narrative review

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Doi

10.56164/PediatrRespirJ.2026.13

ABSTRACT

Pediatric Inflammatory Bowel Disease (IBD) is increasingly recognized as a systemic disorder, yet its respiratory implications remain frequently overlooked. While clinical data suggests a lung involvement rate below 1%, subclinical anomalies may affect up to 40% of young patients. We present the case of a 15-year-old boy with Crohn's disease and chronic tracheobronchitis to highlight the diagnostic challenges in distinguishing primary extraintestinal manifestations from

treatment-related toxicity or opportunistic infections. We analyze the spectrum of pediatric pulmonary involvement, where airway disease and interstitial lung disease often fluctuate independently of intestinal activity. Our synthesis suggests that tools such as impulse oscillometry and diffusing capacity of the lung for carbon monoxide (DLCO) are more sensitive than standard spirometry for early detection. A multidisciplinary approach and structured follow-up are essential to ensure early recognition, individualized management, and the prevention of long-term pulmonary sequelae.

IMPACT STATEMENT

Although pulmonary involvement in pediatric IBD is often considered rare, it is frequently underdiagnosed and can lead to irreversible lung damage. This perspective highlights the "gut-lung axis" and the critical role of early diagnostic tools, such as DLCO and impulse oscillometry, in identifying subclinical respiratory manifestations. Our work emphasizes that a high index of clinical suspicion and a multidisciplinary approach are essential for the timely recognition and management of these systemic complications in children and adolescents.

KEY WORDS

Pediatric inflammatory bowel disease; extraintestinal manifestations in pediatric IBD; pulmonary involvement in pediatric IBD; gut-lung axis; pulmonary function tests.

INTRODUCTION

Inflammatory Bowel Disease (IBD), including Crohn’s Disease (CD), Ulcerative Colitis (UC), and IBD-unclassified (IBD-U), is recognized as a complex systemic inflammatory condition (1-

3). With the global incidence of pediatric IBD rising, particularly in Europe and North America (2), nearly 25% of all diagnoses now occur before the age of 18 (4). In children, IBD presents distinctive challenges, including growth impairment, delayed puberty (5), and a high burden of extraintestinal manifestations (EIMs) (3, 4). While EIMs are well-documented in the skin and joints, pulmonary manifestations (PM) remain underrecognized and likely underdiagnosed (6). Although it is established that lungs and gut share a common mucosal immune system (4), it remains clinically controversial whether respiratory involvement represents a direct extension of IBD or a secondary effect of immunosuppressive therapies (7). The clinical relevance of this distinction is paramount: misidentifying PM as drug toxicity may lead to the unnecessary discontinuation of effective treatments. Here, we provide a focused, case-based narrative review of pulmonary involvement in pediatric IBD, highlighting diagnostic challenges and implications for clinical practice.

METHODS

A comprehensive literature search was performed, dating from 1982 up through April 2026, in PubMed. The search strategy utilized Medical Subject Headings (MeSH) and keywords, including: “inflammatory bowel disease”, “Crohn’s disease”, “ulcerative colitis”, “pulmonary manifestations”, “extraintestinal manifestations” and “gut-lung axis”, combined with age related filters to identify pediatric-population studies. We included original research articles, systematic and narrative reviews, and significant case series involving pediatric populations (age < 18 years). Only English-language publications were considered. Exclusion criteria included studies focusing exclusively on adult populations and abstracts from conferences without full-text availability.

CASE PRESENTATION

A 15-year-old boy with a one-year history of CD was followed at our institution for severe ileocolonic involvement. Because of persistent disease activity, he required several therapeutic interventions, including mesalamine, azathioprine with systemic corticosteroids, methotrexate, and subsequently biological therapy with the anti-TNF agent infliximab. Despite intensive medical treatment, the disease progressed and the patient ultimately underwent surgical resection of the terminal ileum, cecum, and ascending colon. The postoperative course was initially uneventful.

Shortly after discharge, the patient developed a febrile respiratory illness with sore throat and symptoms consistent with acute bronchitis. Empirical therapy with azithromycin was initiated by his primary care physician. Although the fever resolved, a persistent productive cough remained, prompting referral to a pulmonology outpatient clinic.

At presentation, the patient was afebrile, eupneic, and maintained an oxygen saturation of 98% on room air. Pulmonary auscultation revealed diffuse bilateral rhonchi with occasional wheezing. Laboratory tests showed mildly elevated inflammatory markers. Spirometry demonstrated a mild obstructive ventilatory pattern with a positive bronchodilator response. Sputum culture yielded *Staphylococcus aureus*, and chest radiography showed enlarged pulmonary hila with increased bilateral hilobasal bronchovascular markings. Treatment with inhaled bronchodilators, airway clearance techniques, and targeted antibiotic therapy with amoxicillin/clavulanic acid resulted in partial clinical improvement, but the cough persisted.

Given the persistence of symptoms, an extended diagnostic evaluation was performed. Repeat pulmonary function testing showed a mild restrictive ventilatory pattern, while bronchodilator testing, fractional exhaled nitric oxide measurement, DLCO, and methacholine challenge were within normal limits. Extensive investigations excluded alternative causes, including allergic disease, gastroesophageal reflux, immunodeficiency, cystic fibrosis, tuberculosis, and atypical respiratory infections.

High-resolution computed tomography (HRCT) of the chest demonstrated bronchial wall thickening with intraluminal secretions but no evidence of bronchial stenosis, bronchiectasis or parenchymal lung disease. Flexible bronchoscopy revealed tracheobronchial mucosa with a pronounced vascular pattern and abundant thick whitish secretions. Cytological analysis of bronchoalveolar lavage (BAL) fluid showed granulocyte predominance. Based on the clinical presentation, exclusion of infectious and systemic etiologies, and bronchoscopic and radiologic findings, a diagnosis of chronic tracheobronchitis as a respiratory manifestation of IBD was established. Treatment with inhaled corticosteroids was initiated, resulting in complete resolution of symptoms and normalization of pulmonary function tests (PFTs) at follow-up.

A major diagnostic challenge in this patient was differentiating between persistent infection, drug-related pulmonary toxicity, and an extraintestinal manifestation (EIM) of CD. The initial isolation of *Staphylococcus aureus* and partial response to antibiotic therapy raised the possibility of prolonged bacterial tracheobronchitis. However, persistence of symptoms despite adequate antimicrobial treatment, absence of radiologic evidence of pneumonia or bronchiectasis, and lack of ongoing systemic inflammatory response argued against an active infectious process. Similarly, pulmonary toxicity associated with methotrexate or anti-TNF therapy was carefully considered. Methotrexate-related lung disease typically presents with

diffuse interstitial involvement and restrictive impairment accompanied by radiologic infiltrates, which were absent in our patient. Anti-TNF-associated pulmonary complications, including opportunistic infections and granulomatous disease, were also excluded through microbiological and radiological investigations. Importantly, the patient did not demonstrate imaging findings suggestive of hypersensitivity pneumonitis, interstitial lung disease (ILD), or pulmonary granulomatosis.

The diagnosis of chronic tracheobronchitis as a pulmonary manifestation of IBD was ultimately supported by several converging findings: chronic productive cough resistant to standard anti-infective therapy, bronchoscopic evidence of diffuse tracheobronchial inflammation with excessive secretions, exclusion of alternative etiologies, and rapid clinical response to inhaled corticosteroid therapy. The predominance of granulocytes in BAL fluid further supported ongoing airway inflammation rather than isolated infection. Notably, the respiratory symptoms developed in the setting of severe and refractory intestinal disease requiring surgery, which is consistent with previous observations that pulmonary EIMs may occur during periods of heightened systemic inflammatory activity.

Although chronic tracheobronchitis is a recognized pulmonary manifestation of IBD, pediatric cases remain infrequently reported, particularly in patients with severe CD receiving multiple immunomodulatory and biologic therapies. The added value of this case lies in the detailed diagnostic reasoning process used to distinguish inflammatory airway disease from infectious and treatment-related complications in an immunosuppressed adolescent. The case also underscores the importance of bronchoscopy and HRCT in evaluating persistent respiratory symptoms in children with IBD, even in the absence of significant parenchymal abnormalities.

This case highlights the importance of considering respiratory manifestations in patients with IBD who present with persistent pulmonary symptoms and illustrates the diagnostic approach required to establish this uncommon but clinically relevant EIM.

Informed consent was obtained before publication.

Pathophysiology: the gut-lung axis

The pathogenesis of PM in IBD is complex and not yet fully understood, though it is primarily attributed to the bidirectional communication known as the gut-lung axis (3, 8, 9). While their shared embryological origin from the primitive foregut provides a structural template (3, 4), current evidence suggests that this relationship is driven by functional immune crosstalk rather than mere developmental similarity (10, 11). Shared susceptibility genes (*NOD2, ATG16L1, IL23R*), likely act as a "priming" stage (8, 12). From an analytical perspective, this genetic background lowers the threshold for EIMs (8) when triggered by environmental factors (dysbiosis, smoking, or drugs) (3). The resulting breakdown of the intestinal barrier allows microbial products, such as short-chain fatty acids, to enter systemic circulation and alter the lung microenvironment (9). This mechanism may explain the high prevalence of subclinical lung abnormalities even during periods of gastrointestinal remission (9, 11). Crucially, the recruitment of inflammatory cells is an active driver of damage. Neutrophils activated within the inflamed gut mucosa enter the systemic circulation and become sequestered in pulmonary capillaries (3). This process reflects a failure of the lung's normal regulatory mechanism (13). Similarly, memory T-lymphocytes sensitized to gut antigens can undergo miss-homing to the bronchus-associated lymphatic tissue (BALT) via chemokine receptors (CCR4, CCR6) (11). This process is sustained by a cytokine cascade involving TNF-α, IL-1, IL-6 and the Th17/IL-17 axis (3, 4).

Together, these mechanisms support a model where the lung acts as an immunological extension of the gut (**Figure 1**).

Epidemiology

The reported prevalence of PM in IBD varies significantly based on the detection method and study design. While clinically overt disease is traditionally reported in less than 1% of patients, systematic screening using PFTs or radiological imaging identifies subclinical involvement in up to 40% of cases (4), revealing that the lungs are a frequent but often "silent" target of systemic inflammation. Importantly, higher prevalence estimates (up to 75%) reported in some cohorts refer to the cumulative incidence of all EIMs, rather than pulmonary involvement specifically (14)**.** In pediatric-onset IBD, EIMs are more frequently reported and may follow a more aggressive course, potentially reflecting both longer cumulative disease duration and distinct disease phenotypes compared to adults (15). Specifically, while airway disease is more commonly reported in adult UC, pediatric data show a stronger association between CD and interstitial manifestations (4, 15).

Spectrum of pulmonary manifestations and clinical presentations

Pediatric IBD can potentially affect every anatomical component of the respiratory system (3), from the upper and lower airways to the lung parenchyma and pleura (5). The clinical presentation can vary notably, with symptoms ranging from occult physiological alterations to acute, life-threatening respiratory distress (7). Clinical manifestations may range from completely asymptomatic disease to severe respiratory compromise, most commonly including

chronic cough, dyspnea, wheezing, and reduced exercise tolerance (16). Furthermore, while airway involvement is a frequently documented feature in adults (17), emerging evidence suggests that ILD represents the most prevalent respiratory manifestation within the pediatric population (18, 19).

The onset of these manifestations is unpredictable. Respiratory symptoms, such as chronic cough, dyspnea, or chest discomfort, do not strictly correlate with intestinal disease activity (7); they may precede the IBD diagnosis, emerge concurrently, or develop years later during periods of gastrointestinal remission (8). Importantly, a subset of pediatric patients may remain clinically asymptomatic despite the presence of abnormal PFTs or radiologic findings, which may delay recognition of respiratory involvement (20). A significant diagnostic challenge involves distinguishing primary PM from secondary lung injuries, such as medication-induced toxicity or opportunistic infections resulting from therapeutic immunosuppression (16).

Involvement of the large airways includes conditions such as tracheobronchitis, chronic or suppurative bronchitis and glottic or subglottic stenosis (8). Bronchiectasis is the commonly observed feature in this category, reported up to 66% of confirmed cases (21). Patients typically present with dyspnea, productive cough, wheezing, sputum production, stridor (3). In some cases, airway disease may mimic more common pediatric conditions such as asthma, potentially leading to delayed or inappropriate treatment.

Chronic, unmanaged inflammation of the tracheobronchial tree can lead to irreversible structural damage, including the formation of webs or nodular stenosis, which may present clinically as stridor or hoarseness (21). If not recognized early, these changes may result in persistent airflow limitation and long-term respiratory morbidity. Small airway involvement, such as bronchiolitis obliterans or granulomatous bronchiolitis, typically presents more insidiously with a non-specific

dry cough (8). Exercise intolerance and subtle declines in pulmonary function may be the only early indicators of small airway disease.

The lung parenchyma may also be the site of manifestation. Organizing pneumonia (OP) is the most frequently observed subtype (22). Other less common manifestations include non-specific interstitial pneumonia (NSIP), necrobiotic nodules or pulmonary vasculitis (8). Patients typically present with fever, dyspnea, dry cough, chest pain and acute respiratory failure (3). These presentations may be accompanied by systemic inflammatory features and can occasionally progress rapidly, requiring prompt recognition and management.

Although less common, clinicians should also be aware of additional thoracic manifestations, including thromboembolic complications (19), pleural disease and the rare formation of enteric-pulmonary fistulas (23). These entities, while rare, may represent severe and potentially life-threatening complications and require a high index of clinical suspicion.

A summary of respiratory manifestations in pediatric IBD is presented in **Table 1**.

Diagnostic evaluation: approaches and functional assessments

The diagnostic workup for pulmonary involvement in pediatric IBD requires a high index of suspicion (5), as symptoms often correlate poorly with the severity of tissue damage (7). We propose a tiered diagnostic approach, moving from non-invasive screening to specialized imaging and invasive procedures.

Functional assessment (first line)

PFTs represent the primary screening tool for detecting early involvement, although their sensitivity varies significantly. While spirometry is widely accessible, conventional indices such as Forced Expiratory Volume in 1 second (FEV1) and Forced Vital Capacity (FVC) are often maintained in children, making obstructive patterns an inconsistent finding across pediatric cohorts (20, 24). DLCO is established as the most sensitive functional parameter (24), with impairments reported in over 50% of patients (25), correlating with histopathological severity (26, 27). Among emerging tools, Impulse Oscillometry (IOS) offers a valuable alternative for assessing small-airway resistance (20), particularly in younger children (28). However, its routine application remains investigational due to the limited availability of large-scale pediatric reference data. In contrast, fractional exhaled nitric oxide (FeNO) is not considered a reliable marker for latent pulmonary involvement in children (20).

Imaging (second-line)

Imaging is indicated when functional abnormalities or persistent symptoms are present. Conventional chest X-rays are frequently insufficient, often appearing normal even in cases of active tracheobronchitis or subclinical alveolitis (7, 11). HRCT remains the gold standard for detecting structural lung changes, including early bronchiectasis or "tree-in-bud" opacities (27). Despite its diagnostic accuracy, the use of HRCT in children must be carefully balanced against the risks of ionizing radiation (5). To mitigate these risks, low-dose HRCT protocols and lung Magnetic Resonance Imaging (MRI) are currently the most promising alternatives for longitudinal assessment in the pediatric population (29, 30).

Invasive diagnostics (third-line)

Invasive procedures are reserved for complex cases, primarily to exclude infection or drug-related toxicity (5). The initial assessment must prioritize the exclusion of infectious etiologies (5), with a specific focus on atypical pathogens and fungi through molecular diagnostics and biomarkers like galactomannan (31, 32).

Bronchoscopy with BAL serves as a critical third-line tool in this differential process. Rather than providing a definitive diagnosis of IBD-related involvement, the primary role of BAL is the exhaustive exclusion of opportunistic infections or drug-induced toxicity (33, 34). Finding a sterile neutrophilic or lymphocytic inflammatory phenotype provides strong indirect evidence for a primary PM, facilitating the decision to escalate or adjust IBD therapy.

Management and prognosis

Management of PM in pediatric IBD remains a significant clinical challenge, primarily due to the complete lack of randomized controlled trials (RCTs). Consequently, current therapeutic strategies are largely adapted from adult literature or based on retrospective case series and expert consensus, representing a low level of evidence (35). While corticosteroids remain the cornerstone of therapy, effective in approximately two-thirds of cases (35), the choice between inhaled and systemic administration depends on the anatomical pattern of disease (7). Inhaled corticosteroids are generally preferred for isolated airway disease, whereas systemic therapy is indicated for diffuse or interstitial involvement (5). However, a significant pediatric-specific gap remains in defining the optimal duration of therapy and the exact dosage required to prevent irreversible damage while minimizing steroid-related side effects in the growing child.

In refractory or severe cases, the introduction of biologic therapies, particularly anti-*TNF* agents like infliximab, has expanded the therapeutic landscape (5). While infliximab has demonstrated efficacy in cases unresponsive to conventional treatment, its use for PM remains largely anecdotal in the pediatric population, as these drugs are typically initiated to control gastrointestinal activity rather than respiratory symptoms (35, 36). A major clinical dilemma arises from the dual nature of these agents: while they can resolve severe PM, they are also potential triggers for drug-induced ILD (37). This uncertainty necessitates a rigorous diagnostic process to distinguish between a primary manifestation requiring treatment escalation and drug toxicity requiring cessation (37).

Antibiotic therapy, particularly with macrolides, is often employed in patients with bronchiectasis and bacterial colonization (7). Beyond their antimicrobial activity, macrolides are valued for their immunomodulatory properties in neutrophilic airway inflammation, contributing to reduction in exacerbation frequency (38). Supportive care, including pulmonary rehabilitation, and airway clearance, is essential for symptomatic patients (39); however, its impact on long-term disease progression has not been systematically evaluated in IBD cohorts (7).

The most controversial aspect of management concerns the subclinical nature of many pediatric cases. Since pulmonary involvement is frequently asymptomatic, it remains unclear whether isolated functional abnormalities, such as a reduced DLCO, warrant early pharmacological intervention to prevent chronic sequelae in adulthood (20, 24). This represents a major unresolved clinical question in pediatric practice. Given this uncertainty, a structured multidisciplinary follow-up and longitudinal functional monitoring are established as essential components of care to mitigate the risk of progressive respiratory impairment as the patient transitions into adulthood (6, 40).

Future directions

Despite increasing recognition of PM in pediatric IBD, significant gaps remain in its early detection, pathophysiological understanding, and management. Future research should focus on establishing standardized screening strategies for at-risk pediatric patients, particularly those with persistent respiratory symptoms or high inflammatory burden.

The development of non-invasive biomarkers, including advanced pulmonary function indices (*e.g.* DLCO, IOS) and circulating inflammatory markers, may facilitate earlier identification of subclinical lung involvement. In addition, further studies are needed to better define the role of emerging imaging modalities, such as lung MRI and low-dose HRCT protocols, in longitudinal monitoring while minimizing radiation exposure.

A deeper understanding of the shared immunopathological mechanisms between the gut and lung may open new therapeutic avenues. Targeted biologic therapies and precision medicine approaches tailored to specific inflammatory pathways represent promising areas for future investigation.

Finally, prospective multicenter pediatric studies are essential to better characterize the natural history, treatment responses, and long-term respiratory outcomes of IBD-related pulmonary involvement.

CONCLUSIONS

PM of pediatric IBD represents a significant, yet frequently overlooked, component of the disease's systemic burden. As demonstrated by our case, respiratory involvement can fluctuate independently of intestinal activity and often presents with non-specific symptoms, such as persistent cough. To improve clinical practice, it is essential that pediatricians consider the lung as an immunological extension of the gut. Any persistent respiratory symptom, even during gastrointestinal remission, should be viewed as a sentinel indicator of systemic inflammation, necessitating a structured diagnostic evaluation that prioritizes sensitive tools like DLCO and, when indicated, targeted imaging or bronchoscopy. This proactive multidisciplinary approach is critical not only to establish a timely diagnosis, but also to differentiate primary EIMs from drug-induces toxicity, thereby preventing the unnecessary discontinuation of effective IBD therapies. Overall, increased clinical awareness and structured follow-up strategies are essential to optimize individualized management and mitigate the risk of long-term pulmonary sequelae.

COMPLIANCE WITH ETHICAL STANDARDS

Conflicts of interest

The authors declare no conflicts of interest.

Financial support

None.

Author contributions

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Ethical approval

Human studies and subjects

Specific ethical approval was not required for this case report in accordance with institutional guidelines.

Data sharing and data accessibility

N/A.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data corresponds to the real.

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Table 1. *Respiratory manifestations in pediatric inflammatory bowel disease.*

Respiratory site	Typical manifestations	Clinical presentation / symptoms	Subclinical findings	Notes / frequency
Large airways	Tracheobronchitis, chronic or suppurative bronchitis, glottic/subglottic stenosis	Dyspnea, wheezing, productive cough, stridor, hoarseness	Airway narrowing detectable on imaging or bronchoscopy before symptoms	Bronchiectasis is common (up to 66% of cases); irreversible if untreated
Small airways	Bronchiolitis obliterans, granulomatous bronchiolitis	Non-specific dry cough, mild dyspnea, exercise intolerance	Reduced FEV1 or DLCO, subtle imaging changes	Often insidious; may remain asymptomatic for years
Lung parenchyma	Organizing pneumonia (OP), non-specific interstitial pneumonia (NSIP), necrobiotic nodules, pulmonary vasculitis	Fever, dyspnea, dry cough, chest pain, acute respiratory failure	Abnormal HRCT patterns, mild PFT changes	OP most common in children; other patterns rarer
Pleura	Pleural effusion	Chest pain, dyspnea	Often asymptomatic if small	Rare
Rare / severe complications	Thromboembolic events, enteric–pulmonary fistulas	Acute respiratory compromise, hypoxemia	N/A	Life-threatening; requires high clinical suspicion

DLCO: Diffusing capacity of the lung for carbon monoxide; FEV1: Forced expiratory volume in 1 second; HRCT: High-resolution computed tomography; NSIP: Non-specific interstitial pneumonia; OP: Organizing pneumonia; PFT: Pulmonary function tests.

Simplified model of gut–lung axis–mediated pulmonary involvement in pediatric IBD