CASE REPORT

Successful treatment of ulcerative bronchiolitis in a woman with refractory *Mycobacterium intracellulare* infection

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SUMMARY

We present a case of a woman with medically refractory ulcerative colitis (UC) who developed severe bronchiectasis, bronchitis, bronchiolitis and *Mycobacterium intracellulare* (MAC) infection 2 years after total colectomy. Despite being on optimal therapy for her MAC and sterilising multiple consecutive sputum cultures, she remained highly symptomatic, and this led to further investigations that revealed the presence of UC-related airways disease. Addition of immunosuppressive therapy to her antimycobacterial treatment resulted in sustained and complete clinical remission of her disease. To our knowledge, this is the only case published in the literature that describes a case of successful treatment of concomitant UC-related pulmonary disease and symptomatic MAC.

BACKGROUND

Extraintestinal manifestations of inflammatory bowel disease (IBD) are common, occurring in up to 20–60% of all cases of IBD.^{1–8} Clinically recognised pulmonary manifestations of IBD are extremely rare,^{5 9–11} with an estimated prevalence of 0.21%.^{12 13} Unlike non-pulmonary extraintestinal manifestations, IBD-related pulmonary disease is much more common in ulcerative colitis (UC) than Crohn's disease.^{2 3 6 10 11 14} Thoracic manifestations are likely under-reported and under-recognised, as subclinical pulmonary manifestations may be present in up to 50–60% of patients with IBD.^{1 2 7 15 16} It is important to consider IBD-related pulmonary patients with disease in IBD whose pulmonary pathology may not be completely explained by more common pulmonary diseases.^{2 6 8}

CASE PRESENTATION

A 49-year-old woman, a former smoker, was diagnosed with UC at age 37. Her symptoms were refractory to steroids, mesalamine and azathioprine, so she underwent a total colectomy at age 43. At age 45, she developed cough, shortness of breath and wheeze. Pulmonary function tests revealed mild obstruction and reduced diffusing capacity for carbon monoxide.

INVESTIGATIONS

Chest CT revealed centrilobular nodules, bronchiolitis and peribronchial wall thickening without evidence of fibrosis or air trapping (figure 1). After

the onset of bronchiolitis, multiple sputum cultures were obtained and noted to be positive for *Mycobacterium intracellulare* (MAC). As such, therapy with clarithromycin, ethambutol and rifampin was initiated. While the patient initially experienced clinical, microbiological and radiographic improvement, she subsequently developed recrudescence dyspnoea and productive cough associated with night sweats and weight loss. Sputum cultures again grew MAC, and the patient's regimen was expanded to include inhaled amikacin, hypertonic saline and aggressive chest percussion therapy.

Despite sterilising her sputum cultures, the patient's clinical and respiratory status continued to deteriorate. Repeat chest imaging revealed marked progression of bronchiectasis in the right middle lobe and bronchiolitis (figure 2). A rheumatological work up including rheumatoid factor, antinuclear antibody and anti-Sjögrens-related antigen A/B were all negative. Quantitative and qualitative immunoglobulin levels were within normal limits. *Mycoplasma pneumoniae* IgM and IgG were noted to be slightly elevated though the patient had been on azithromycin for nearly 12 months, and so infection was felt to be unlikely. The patient also had a normal barium swallow but declined further work up for occult aspiration.

Ultimately, she underwent fiberoptic bronchoscopy, which revealed copious purulent secretions, marked oedema and cobblestoning of the trachea and bronchi (figure 3). Endobronchial biopsies

Figure 1 High-resolution CT (HRCT) demonstrating centrilobular nodules, bronchiolitis and bronchial wall thickening of right lower lobe.

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Figure 2 High-resolution CT (HRCT) demonstrating severe right middle lobe bronchiectasis that developed in over less than 2 years.

demonstrated severe submucosal inflammation, lymphoplasmacytic infiltration, squamous metaplasia, peribronchial fibrosis and absence of granulomatous inflammation (figure 4).

TREATMENT

The clinical, radiographic and histopathological findings were consistent with UC-related bronchitis and bronchiolitis. Anti-MAC antibiotics were continued, and the patient underwent resection of her severely bronchiectatic right middle lobe. Surgical cultures were negative, and azathioprine was added to her regimen.

OUTCOME AND FOLLOW-UP

Azathioprine resulted in intolerable side effects, and it was changed to low dose prednisone and mycophenolate mofetil, which was well tolerated and, in combination with the anti-MAC antibiotics, has resulted in sustained clinical remission of the patient's disease.

Figure 3 Right upper lobe segmental bronchi with mucosal oedema and cobblestoning.

Figure 4 Marked chronic inflammation with lymphoplasmacytic infiltration (200×H&E).

DISCUSSION

Our patient had an unusual combination of UC-related pulmonary disease and MAC infection. UC-related airway disease can occur anywhere in the tracheobronchial tree, with bronchiectasis, chronic bronchitis and chronic bronchiolitis accounting for nearly half of UC-related pulmonary disease after medication-related pulmonary toxicity is excluded (table 1).^{2-5 16 17} UC-related pulmonary complications appear to have a female predominance and onset occurs in the fifth decade of life, or, as in this case, after colectomy.^{2 15 18}

The pathogenesis of airway inflammation in UC is poorly understood, but is likely mediated by immune mechanisms similar to those causing colonic inflammation. This may be related to the shared derivation of lung and colonic epithelium from the primitive foregut.¹⁰ Another hypothesis is that circulating inflammatory mediators originate from inflamed bowel mucosa and drive lung disease.⁶ Finally, it may be that inflamed gastrointestinal mucosae leading to systemic absorption of luminal contents such as dietary antigens, enzymes and even bacterial products, such as lipopolysaccharide, contribute to pulmonary disease.⁶ However, this latter mechanism fails to explain the onset of UC-related pulmonary disease following colectomy.^{2 4 6 12 19}

Pulmonary complications may develop and progress independently of intestinal disease, and often occur years after colectomy, as observed in our patient.^{5 6 9 12 13 17 19} This may be related to the withdrawal of immunosuppressive medications

Table 1 Frequencies of most common inflammatory bowel disease-related pulmonary manifestations⁵

Manifestations	Percent (%)
Chronic bronchitis	22.6
Bronchiectasis	20.3
Interstitial lung disease	17.9
Bronchiolitis obliterans	12.4
Chronic suppurative bronchitis	7.8
Subglottic stenosis	6.7
Necrobiotic nodules	5.6
Chronic bronchiolitis	3.4
Pulmonary infiltrates and eosinophilia (PIE)	3.3

following definitive UC therapy with colectomy, or by the shifting of inflammatory epitopes and targets to the pulmonary epithelium following colectomy.^{1 2 5 6 12 15 16}

The mainstay of ulcerative bronchitis/bronchiolitis treatment is immunosuppressive therapy, usually with systemic or high dose inhaled glucocorticoids, sometimes in combination with steroid sparing agents such as infliximab, azathioprine or mycophenolate mofetil.^{10 14–16 20} Since pulmonary symptoms in a patient with UC may represent complications of the medications used to treat the disease, especially mesalamine, sulfasalazine and methotrexate, it is essential to exclude drug toxicity.^{2 9}

This case highlights the fact that UC-related lung pathology (eg, bronchiectasis) can predispose to pulmonary infection, which must be aggressively investigated and managed along with treating the UC-related lung disease.³

Patient's perspective

I have been managing the effects of illness in my life for over a decade now, and am aware I spent most of my 40 s either very ill or in recovery. I am convinced that research into Auto Immune Disorders is among the most important work that can be done at this time to unlock the puzzles of these diseases and infections, and I hope that this research can help ease the pain of those who come after me. It may be too late to reverse the toll that Auto Immune Disorders have taken on my health, but this research will benefit many others and I am grateful to be a part of this work.

Learning points

- It is important to consider pulmonary complications in patients with inflammatory bowel disease (IBD).
- Pulmonary complications may develop and progress independently of gastrointestinal disease, and in patients with ulcerative colitis, may present years after a colectomy.
- Immunosuppressive therapy and treatment of any underlying infections are the mainstays of therapy for IBD.

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Competing interests None declared.

Patient consent Obtained.

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