Tracheobronchitis with Dyspnea in a Patient with Ulcerative Colitis

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Abstract

We herein report the case of a 42-year-old man with a one-year history of ulcerative colitis who presented with exacerbated bloody diarrhea, a productive cough and increasing breathing difficulties. Colonoscopy revealed typical deep ulcers in the rectosigmoid colon and atypical multiple sucker-like ulcers in the transverse colon, and computed tomography of the chest demonstrated wall thickening of the trachea and bronchi. In addition, bronchoscopy showed ulcers in the trachea, and histopathology disclosed findings of necrosis and inflammation of the subepithelial tissue of the trachea. Based on these findings, the patient’s respiratory symptoms were strongly suspected to be due to ulcerative colitis-related tracheobronchitis. Treatment with systemic corticosteroids subsequently resulted in a rapid clinical improvement.

Key words: ulcerative colitis, tracheobronchitis, inflammatory bowel disease, extraintestinal manifestations

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Introduction

Extraintestinal manifestations of inflammatory bowel disease (IBD) are relatively frequent, although clinically evident pulmonary disease associated with IBD is uncommon. Tracheobronchitis is a particularly rare extraintestinal manifestation of ulcerative colitis (UC) and is often diagnosed incorrectly and treated as asthma (1). We herein report a case of fulminant tracheobronchitis associated with exacerbation of UC in which colitis developed with atypical sucker-like ulcers. In this report, we describe our difficulties in the selecting the treatment plan and provide the details of the patient’s complex clinical course.

Case Report

A 42-year-old man visited our hospital complaining of increasing bloody diarrhea and mild abdominal pain. He had been diagnosed with UC by his family doctor a year earlier (Fig. 1), after which time he had received treatment with oral mesalazine (3.6 g/day). He had also experienced a productive cough and nose pain with purulent nasal discharge for a few days prior to the current admission. He was a non-smoker and had no history of pulmonary disease.

Computed tomography (CT) indicated diffuse colonic bowel wall thickening and mild inflammation of the paranasal sinuses, without abnormal findings in the thoracic region. Blood tests showed severe inflammatory changes, with a white blood cell count of 16,500 cells/mm³ (82% neutrophils; 2.0% eosinophils; 6.0% monocytes; 10% lymphocytes), an erythrocyte sedimentation rate of 94 mm/h and C-reactive protein level of 21.15 mg/dL. Due to the highly elevated inflammatory reaction, the patient was hospitalized with a diagnosis of exacerbation of UC complicated by sinusitis.
Figure 1. Endoscopic (a) and histological findings (b) of the rectum at the initial diagnosis. The biopsy specimen showed a crypt abscess.

Figure 2. Colonoscopy of the transverse colon. Sucker-like ulcers in transverse colon (a). Typical deep ulceration was observed continuously from the sigmoid colon to the rectum (b).

Figure 3. No abnormal findings were detected on an X-ray examination, even when the patient’s sensation of dyspnea and stridor worsened.

Colonoscopy revealed both typical deep ulcers in the rectosigmoid colon and atypical multiple round ulcers in the transverse colon (Fig. 2). A microscopic examination of the biopsy specimens showed acute inflammation with crypt abscesses, although neither cytomegalovirus nor dysentery amoebas were detected on immunostaining. Initially, the patient was treated with empirical antibiotics; however, the administration of this therapy for one week did not improve the inflammatory reaction, as observed on blood tests. Instead, the patient’s respiratory symptoms worsened, with the appearance of dyspnea and hoarseness. Although the chest X-ray findings remained within the normal limits (Fig. 3), a reexamination using chest CT showed wall thickening of the trachea and bronchi (Fig. 4). Flexible bronchoscopy disclosed the presence of mucosal irregularities and ulcers in the trachea, findings indicative of ulcerative colitis (Fig. 5). A tracheal biopsy showed necrosis and mild inflammation of the subepithelial tissue, with no infectious features (Fig. 6). Hence, the patient’s respiratory symptoms were strongly suspected to be extraintestinal manifestations of UC rather than infectious bronchitis.

The patient was treated with 1,000 mg of intravenous methylprednisolone for three days followed by 30 mg of methylprednisolone. The corticosteroids quickly improved the patient’s respiratory status, with marked regression of the tracheal wall and bronchi thickening (Fig. 4). The digestive symptoms related to UC also improved simultaneously. Follow-up colonoscopy performed eight months later showed the disappearance of the sucker-like ulcers in the transverse colon, without scars. At that time, the deep ulcers in the sigmoid colon and rectum had also healed with residual scars and inflammatory polyps. The dose of corticoste-
Figure 4. Chest CT images obtained before (a, b) and after (c, d) corticosteroid treatment. Wall thickening of the trachea and bronchi (white arrows) was relieved by treatment.

Figure 5. Bronchoscopy performed five days after steroid pulse therapy. Irregular thickening of the mucosa, edema and ulcer-like lesions were observed in the trachea and bronchi.

Figure 6. A biopsy of the trachea showed necrosis and mild inflammation of the subepithelial tissue (Hematoxylin and Eosin staining). No infectious etiology was found.

Discussion

Extraintestinal manifestations may develop in 21% to 41% of patients with IBD; this incidence is higher in subjects with Crohn’s disease (CD) than in those with UC (2, 3). However, pulmonary involvement as an extraintestinal manifestation of UC is rare, occurring in only 0.21% of IBD patients (4). The colonic and bronchial epithelia may exhibit a common inflammatory response, as both tissues are derived from the primitive gut (5). Therefore, any part of the respiratory system may be involved in airway-associated diseases, such as subglottic-glottic stenosis, tracheitis, tracheobronchitis, chronic bronchitis, bronchiectasis and pulmonary disorders, including bronchiolitis with organizing pneumonia, interstitial lung disease and serositis (6, 7).

Tracheobronchitis is characterized by the presence of submucosal inflammation of large airways and the proliferation of the reserve cell layer (7), usually as a result of viral or bacterial infection with underlying lung disease (7). This condition is a rare pulmonary complication of UC, with only 16 reported cases, including the present case (nine men...
and seven women; age: 23-64 years, average: 46 years) (Table 1, 6-15). In most of these cases, pulmonary involvement and colonic exacerbation developed simultaneously, as in our patient, whereas tracheobronchitis developed after colectomy in a few cases (8, 10, 11) or after UC remission of more than 30 years (1, 15). The relationship between smoking and IBD is well established (16), although the role of more than 30 years (1, 15). The relationship between smoking and IBD is well established (16), although the role of smoking in the onset of pulmonary manifestations of IBD remain unclear.

In the present case, mucosal irregularities and UC-like ulcers in the trachea were observed on bronchoscopy, without the detection of granuloma formation or infection in the biopsy specimens. A wide variety of bronchoscopic findings have been reported, including severe tracheal narrowing, erythematous, irregular and ulcerated mucosa (13), a cobblestone appearance (14) and exuberant pus (11). Active inflammation with marked lymphoplasmacytic infiltration within the epithelium and lamina propria without evidence of granuloma formation are typical histopathological findings (15).

In the 16 previously reported cases, including ours, all patients were treated with corticosteroids, with an immediate response to therapy in all but one case (8), in which only a limited improvement was achieved with systemic steroids. Although bronchial dilation was attempted in that case, the procedure resulted in tracheal rupture and death (8). While gastrointestinal and respiratory symptoms were relieved simultaneously in most cases (9, 13), the clinical courses of the upper airway and digestive diseases were not always entirely parallel (17). For example, in one case, the patient’s respiratory status improved markedly with corticosteroid therapy, whereas the exacerbation of UC worsened, resulting in emergency colectomy for toxic megacolon (7).

Infectious bronchitis, drug-related disease and granulomatosis with polyangitis should be considered as differential diagnoses. Because treatment with corticosteroids is essential for UC-associated tracheobronchitis and can also promote infection, ruling out infectious diseases is particularly important. In the present case, an infectious cause of bronchitis was excluded based on the findings of repeated sputum and blood cultures with no evidence of infection. Mesalazine, the principal drug for IBD treatment, is also responsible for respiratory complications, such as interstitial disease and eosinophilic pleuritis or pneumonia (18). However, the present patient’s respiratory symptoms remitted without interruption of this drug. Because the biopsy of the bronchial mucosa obtained via bronchoscopy showed no granulomas, there was little possibility of the presence of granulomatosis with polyangitis, leading to a diagnosis of tracheobronchitis as an extraintestinal manifestation of UC.

The current patient had originally been diagnosed with proctitis type UC; however, by the time of the current episode, the UC had progressed to the pancolitis type. The manifestation of ulcers in the rectosigmoid colon was typical of UC, whereas that in the transverse colon was atypical, including sucker-like ulcers that appeared to line up with the intestinal axis with normal mucosa interposed between the lesions. We initially considered the coexistence of amoebic colitis. However, a biopsy specimen obtained from the edge of the sucker-like ulcer showed only mildly inflamed colonic mucosa, and the findings for amoebas were negative, even on PAS staining. We also suspected cytomegalovirus

<table>
<thead>
<tr>
<th>Sex</th>
<th>Smoking status</th>
<th>Duration of UC, yrs.</th>
<th>UC activity</th>
<th>Treatment</th>
<th>Outcome</th>
<th>[Ref.]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M(55)</td>
<td>Ex-smoker</td>
<td>30 remission</td>
<td>steroids, azathioprine</td>
<td>partial improvement</td>
<td>[1]</td>
<td></td>
</tr>
<tr>
<td>F (44)</td>
<td>Ex-smoker</td>
<td>5 remission</td>
<td>steroids</td>
<td>improvement</td>
<td>[6]</td>
<td></td>
</tr>
<tr>
<td>M(50)</td>
<td>N/A</td>
<td>0 active</td>
<td>steroids</td>
<td>marked improvement</td>
<td>[7]</td>
<td></td>
</tr>
<tr>
<td>F (24)</td>
<td>Never</td>
<td>10 active</td>
<td>steroids</td>
<td>rapid improvement</td>
<td>[9]</td>
<td></td>
</tr>
<tr>
<td>F (51)</td>
<td>Never</td>
<td>20 active</td>
<td>steroids</td>
<td>rapid improvement</td>
<td>[9]</td>
<td></td>
</tr>
<tr>
<td>F (45)</td>
<td>Never</td>
<td>27 active</td>
<td>N/A</td>
<td>N/A</td>
<td>[10]</td>
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</tr>
<tr>
<td>M(54)</td>
<td>Never</td>
<td>12yr prior</td>
<td>N/A</td>
<td>N/A</td>
<td>[10]</td>
<td></td>
</tr>
<tr>
<td>M(52)</td>
<td>Never</td>
<td>21 remission</td>
<td>N/A</td>
<td>N/A</td>
<td>[10]</td>
<td></td>
</tr>
<tr>
<td>M(50)</td>
<td>None for 12 yr</td>
<td>22 colectomy, 8yr prior</td>
<td>steroids</td>
<td>improvement</td>
<td>[11]</td>
<td></td>
</tr>
<tr>
<td>M(64)</td>
<td>None for 10 yr</td>
<td>5 colectomy, 4yr prior</td>
<td>steroids</td>
<td>improvement</td>
<td>[11]</td>
<td></td>
</tr>
<tr>
<td>F (23)</td>
<td>Never</td>
<td>8 remission</td>
<td>steroids</td>
<td>improvement</td>
<td>[12]</td>
<td></td>
</tr>
<tr>
<td>F (29)</td>
<td>N/A</td>
<td>0 active</td>
<td>mesalazine, steroids, antibiotics</td>
<td>improvement</td>
<td>[13]</td>
<td></td>
</tr>
<tr>
<td>M(47)</td>
<td>None for 3yr</td>
<td>12 active</td>
<td>steroids, antibiotics</td>
<td>rapid improvement</td>
<td>[14]</td>
<td></td>
</tr>
<tr>
<td>M(57)</td>
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<td>30 remission</td>
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<td>partial improvement</td>
<td>[15]</td>
<td></td>
</tr>
<tr>
<td>M(42)</td>
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<td>1 active</td>
<td>steroids</td>
<td>rapid improvement</td>
<td>[present case]</td>
<td></td>
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</table>

Data in curved parentheses are patient age. UC: ulcerative colitis; F: female; M: male; N/A: data not available.
colitis; however, cytomegalovirus immunostaining was negative. Nevertheless, we were unable to completely exclude the potential of infectious enteritis and thus continued the treatment with antibiotics and mesalazine. Consequently, the initiation of corticosteroid therapy due to the need to treat the patient’s rapidly deteriorating airway symptoms also gradually stopped the bloody stools. Furthermore, colonoscopy performed four days after the initiation of corticosteroids confirmed that the active bleeding in the rectosigmoid colon had stopped and that the ulcers in the transverse colon had decreased in size along with a reduction in redness and the findings of a depressed ulcer margin. Hence, corticosteroid therapy was effective for these ulcers. On follow-up colonoscopy performed eight months later, the ulcers in the transverse colon had healed without any scarring. Therefore, we suggest that the sucker-like ulcers reflected a specific subtype of ulcerative colitis or another form of autoimmune colitis.

In conclusion, large airway involvement, such as that due to tracheobronchitis, is a rare but potentially critical extraintestinal manifestation of UC. This complication should be kept in mind when diagnosing respiratory symptoms in patients with UC, particularly because treatment with corticosteroids can quickly improve these symptoms.

The authors state that they have no Conflict of Interest (COI).

References