A Case of Tracheal Involvement of Crohn’s Disease: the first case in Korea

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Running title: Tracheal Involvement of Crohn’s Disease

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Abstract

Respiratory involvement of Crohn’s disease (CD) is rare condition which reported only around a dozen. We report the first case of tracheal involvement of CD in the Korea. An 18-year-old woman had been CD was hospitalized for cough, dyspnea and fever sustained for 3 weeks. Because she showed stridor on her neck, computed tomography of neck was performed and it showed circumferential wall thickening of larynx and hypopharynx. Bronchoscopy showed mucosal irregularity, ulceration, exudates debris at the proximal trachea. The bronchial biopsy showed chronic inflammation with granulation tissue. From all these findings, we thought tracheal involvement of CD, and started to administer intravenous (IV) methyl-prednisolone 1 mg/Kg/day to her. Then, her symptoms and bronchoscopic findings were improved.

Key words: Crohn’s disease; Inflammatory bowel disease; Tracheobrochial involvement
Introduction

Crohn’s disease (CD) is a chronic inflammatory disease which mainly affects gastrointestinal (GI) tract. However, it may have various extraintestinal manifestations including uveitis, arthritis, pyoderma gangrenosum, erythema nodosum, episcleritis, sclerosing cholangitis, hemolytic anemia. Symptomatic tracheobronchial involvement is not common manifestation, however have been reported including chronic bronchitis, bronchiectasis, upper airway obstruction, granulomatous interstitial pneumonitis, bronchiolitis obliterans, granulomatous lung disease and interstitial lung disease. This report describes a case of tracheal involvement of CD.

Case report

An 18-year-old Korean woman was diagnosed with CD 4 months ago. She had been treated with prednisolone 50mg/day for 1 month and after tapering and discontinuation of prednisolone, mesalazine 3g/day was started for maintenance. She visited a primary clinic for prolonged symptoms of purulent cough, fever and dyspnea. She never smoked before and had no history of environmental or occupational exposure which can cause respiratory symptoms. The Montreal classification of CD of the patient is A2L3B1 and Crohn’s disease activity index was 71.92 at that time. She was treated with antibiotics for 5 days along with symptomatic treatment but her dyspnea and fever persisted and stridor was found on her physical examination. Then, she was referred to our hospital for further evaluations.

On physical examination, she had stridor at her neck. Blood pressure was 110/70 mmHg, heart rate 100/min, body temperature 36.7 °C, and SpO2 was 97% (room air). The electrocardiogram and chest radiographs were normal. Laboratory data on admission included the following: white blood cell count 18,770/μL (polymorphonuclear neutrophil 67.6%, eosinophil 0.4%), hemoglobin 10.4 g/dl, platelet 628,000/μL, C-reactive protein 5.75 mg/dl. The remainder of serum chemistries, and coagulation profile were all normal. The computed tomography of neck performed for exploring the cause of stridor and cough. And it revealed circumferential wall thickening of larynx and hypopharynx (Fig. 1).

Initially, it was thought that the patient had bacterial trachitis. Therefore she was treated with antibiotics, Amoxacillin/Clavulanate 3.6 g/day for 4 days. However, her symptoms and stridor were not improved. Flexible
fibrotic bronchoscopy (FFB) were performed and showed mucosal irregularity, edema and yellowish patch-like mucosal lesion on the proximal part of trachea (Fig. 2). Bacterial culture and AFB stain/culture, Tuberculosis (TB)-Polymerase chain reaction (PCR) of bronchial washing fluid were negative. Result of interferon-gamma release assays (IGRA) to M. tuberculosis was also negative. The results of bronchoscopic biopsy were non-specific inflammatory reactions including dense inflammatory cell infiltration, necrotic detritus representing tissue destruction, and granulation tissue manifesting healing of damaged tissue. However, this biopsy specimen contained no granulomas, relatively well known histopathologic feature of Crohn’s disease (Fig. 3). Considering the negative results of each study, we suspected tracheal involvement of CD. Then methyl-prednisolone IV 1 mg/kg/day was started for treatment.

4 days later, her cough and dyspnea was relived. Fever and stridor was also disappeared. After 2 months, bronchoscopic findings were revealed marked improvement in tracheal lesion (Fig.4). The patient was treated with oral corticosteroid for 4 weeks and the corticosteroid was discontinued. After that, she has not been recurred lung involvement of CD over one year.

Discussion

We found the first case tracheobronchial involvement of CD in Korea which is rare even in global perspective. Since Kraft et al\textsuperscript{5} reported bronchopulmonary involvement of IBD in 1976 , only 13 cases including the present case (7 men and 6 women, ages 18-59 year, average 28)\textsuperscript{3} have been reported and the patient of our case is the youngest one (Table 1).

In the present case, other disease which could cause a similar clinical manifestation such as bacterial trachitis, tracheal tuberculosis and sarcoidosis had to be excluded. In this patient, bacterial trachitis could be excluded by negative result of bacteriologic studies and unresponsiveness to antibacterial agent. Mycobacterial infection could be excluded by no growth of mycobacteria in repeated sputum and bronchial washing fluid, negative result of IGRA and nested TB-PCR and the absence of caseating granuloma. Sarcoidosis could be ruled out by no evidence of extrapulmonary sarcoid involvement and the absence of typical sarcoid granuloma in bronchial biopsies.
Tracheobronchial involvement of CD is rare, however several cases have been reported.\textsuperscript{1, 2, 5, 6, 8, 9, 11-13} As shown in this case, bronchoscopic findings were mucosal irregularity, elevation, edema and yellowish patch-like lesion which are similar to colonoscopic findings of CD. These are also characteristic findings in previous reports\textsuperscript{2, 6, 9, 13, 14}. As the present case, the pathologic findings of bronchial biopsy showed epithelial and subepithelial infiltrates of diverse inflammatory cells such as neutrophils, macrophages, lymphocytes, and plasma cells\textsuperscript{2, 6, 9, 13, 14}, as the previous cases. As suggested by Asami T et al\textsuperscript{3}, those pathologic and bronchoscopic findings suggest that the tracheobronchial inflammation may be provoked by mechanism similar to that of colon, associated with activation of macrophage and T lymphocyte\textsuperscript{3}. Then, authors of previous reports suggest that it is possible to think that there exists common antigen which could trigger mucosal immune response of both GI tract and airway\textsuperscript{2, 6, 9, 13, 14}. In this case, when tracheal involvement of CD was exacerbated, colonic condition of the patient was stable. Thus, it seems to be the clinical courses of tracheobronchial and GI involvement could be unparallel\textsuperscript{3, 11}. Plataki et al\textsuperscript{11} explained the mechanism of this unparallel clinical course as in the following. Although the antigen which trigger the immune response could be basically same between the GI tract and respiratory tract, amplification of the inflammatory process might be different, which results in unparallel clinical courses between those organs\textsuperscript{3, 11}. Usually, before the presentation of pulmonary manifestations the patients have been diagnosed with CD. However, patient who had not diagnosed with CD presenting with airway involvement has also been reported.\textsuperscript{15} Pathologically, airway infiltration by inflammatory cells and mucosal ulceration may be found. However, non-caseating granulomas are not always present, like colon involvement of CD\textsuperscript{4, 6}. In this case, there was only granulation tissue, not granuloma.

It is reported that the treatment with both inhaled and systemic corticosteroid therapy of upper airway involvement of CD was effective. From the previous reports, 6 cases were treated with oral steroids\textsuperscript{2, 5, 8, 12}, 2 cases were treated with inhaled steroids\textsuperscript{3, 9}, 4 cases were treated with oral and inhaled steroids\textsuperscript{1, 6, 11, 13} (Table 1). Regardless of the method of administration, all cases treated with steroid, showed improvement of both respiratory and GI symptoms\textsuperscript{3}. In this case, we used IV steroids, because she refused oral steroids because of nausea, abdominal pain and sore throat, and she had trouble in using inhaled corticosteroids (ICS). We started methyl-prednisolone 1mg/kg/day IV. 4 days later, her symptoms were improved and after 2 months FFB findings were markedly improved.

The clinical course of the tracheobronchial involvement of CD tends to be more responsive to corticosteroids than lower respiratory tract involvement such as bronchiectasis in CD\textsuperscript{4}. This is especially true when high dose
systemic corticosteroids were administered early in the course of upper respiratory tract involvement. Clinical sequelae of residual tracheal stenosis and respiratory failure have been reported with delayed diagnosis and consequent delayed treatment with systemic steroids. We report the first Korean case of tracheobronchial involvement of CD with dramatic response to systemic steroid. As this case, if CD patient presents unexplained respiratory symptoms, pulmonary involvement of CD should be considered.

REFERENCES


Table 1. The previous reports of tracheobronchial involvement in patients with Crohn's disease

<table>
<thead>
<tr>
<th>Author</th>
<th>Sex</th>
<th>Age</th>
<th>Type of involvement</th>
<th>Treatment</th>
<th>Response to treatment</th>
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<tr>
<td>Kelly J.H. et al</td>
<td>25</td>
<td>M</td>
<td>Laryngitis</td>
<td>Systemic CS</td>
<td>Complete clearance of symptoms, then steroid-dependence</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>M</td>
<td>Laryngitis</td>
<td>Systemic CS</td>
<td>Some initial improvement, then upper airway obstruction requiring tracheotomy</td>
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<td>Kuzniar T. et al</td>
<td>29</td>
<td>M</td>
<td>Tracheobronchitis</td>
<td>ICS &amp; Systemic CS</td>
<td>Improvement of tracheobronchitis, persistence of tracheobronchial deformity</td>
</tr>
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<td>Kraft S.C. et al</td>
<td>59</td>
<td>F</td>
<td>Tracheobronchitis</td>
<td>Systemic CS</td>
<td>Marked improvement</td>
</tr>
<tr>
<td>Iwama T. et al</td>
<td>26</td>
<td>M</td>
<td>Tracheobronchitis</td>
<td>ICS</td>
<td>Dramatic improvement</td>
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<td>Lemann M. et al</td>
<td>24</td>
<td>F</td>
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<td>Systemic CS</td>
<td>Dramatic improvement</td>
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<tr>
<td></td>
<td>19</td>
<td>F</td>
<td>Tracheobronchitis</td>
<td>Systemic CS</td>
<td>Marked improvement</td>
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<td>Plataki M. et al</td>
<td>34</td>
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<td>Tracheobronchitis</td>
<td>ICS &amp; Systemic CS</td>
<td>Dramatic improvement</td>
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<td>Lamblin C. et al</td>
<td>37</td>
<td>M</td>
<td>Tracheobronchitis</td>
<td>ICS &amp; Systemic CS</td>
<td>Dramatic improvement</td>
</tr>
<tr>
<td>Takashi A. et al</td>
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<td>F</td>
<td>Tracheobronchitis</td>
<td>ICS</td>
<td>Dramatic improvement</td>
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<td>Henry M.T. et al</td>
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<td>F</td>
<td>Tracheobronchitis</td>
<td>Systemic CS</td>
<td>Marked improvement</td>
</tr>
<tr>
<td>Spira A. et al</td>
<td>30</td>
<td>M</td>
<td>Tracheobronchitis</td>
<td>ICS &amp; Systemic CS</td>
<td>Marked improvement</td>
</tr>
<tr>
<td>Current case</td>
<td>18</td>
<td>F</td>
<td>Tracheobronchitis</td>
<td>Systemic CS</td>
<td>Dramatic improvement</td>
</tr>
</tbody>
</table>

*CS: corticosteroid; † ICS: inhaled corticosteroid
Figure 1. Computed tomography of neck showed abrupt narrowing of proximal trachea. (arrows)
Figure 2. Flexible bronchoscopy showed mucosal irregularity, edema and yellowish patch-like mucosal lesion on the proximal part of trachea.
Figure 3. Bronchoscopic biopsy: Dense inflammatory cell infiltration in the mucosa and submucosa of trachea. [Haematoxylin and eosin (H&E) stain; magnification x 10(A)]. Granulation tissue representing healing of damaged tissue. [H&E stain; magnification x 100(B)].
Figure 4. Flexible bronchoscopy findings after treatment show marked improvement.