A Patient with Relapsing Polychondritis who Had Been Diagnosed as Intractable Bronchial Asthma

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Abstract

A 62-year-old woman, diagnosed as bronchial asthma 3 years previously, was admitted due to acute severe dyspnea. Physical examination revealed saddle nose, flare/swelling of the ear auricles, and stridor. Computed tomography demonstrated thickening of tracheal/bronchial walls and stenosis of the lumen that deteriorated on expiration, suggesting tracheobronchomalacia. Auricle biopsy indicated cartilage destruction. Based on these findings, the patient was diagnosed as relapsing polychondritis. As demonstrated in this case, relapsing polychondritis involving airways might be misdiagnosed as bronchial asthma due to stridor and transient corticosteroid-related improvement. Early diagnosis is necessary to prevent irreversible airway stenosis and progression to tracheobronchomalacia.

Key words: intractable bronchial asthma, saddle nose, takotsubo cardiomyopathy, tracheobronchomalacia, relapsing polychondritis


Introduction

Relapsing polychondritis (RPC), considered to be an autoimmune disease (1), involves general cartilage and tissues containing a high concentration of mucopolysaccharides. This is a rare disorder with an estimated incidence of 3.5/1,000,000 persons/year (2), and the treatment has not been established. When tracheal/bronchial cartilages are affected, respiratory symptoms such as dyspnea and stridor may appear (3), which can be misleading, prompting an improper diagnosis as bronchial asthma (4). It could take long until correct diagnosis was made (5). Here, we report a patient with RPC who had been diagnosed as intractable bronchial asthma for a long period of time. Since RPC could be fatal, it is important to differentiate this disorder from bronchial asthma.

Case Report

A 62-year-old woman was admitted to our hospital because of severe acute dyspnea, one month after she was referred to our hospital because of intractable bronchial asthma. Neither medical nor family history was contributory. She had a 22-year history of smoking (10 cigarettes/day). At the age of 59, she was admitted to another hospital with dyspnea, with no demonstration of saddle nose or flare/swelling of the ear auricles at that time. Based on elevated ST in an extensive area on electrocardiography and increases in serum and plasma biomarkers of cardiac injury, a tentative diagnosis of myocarditis was made in addition to bronchial asthma. Subsequently, asthma treatment with oral prednisolone was initiated. When prednisolone was decreased in dose or discontinued, her asthma condition was exacerbated until ventilator assistance was required. During this clinical
course several times she noticed flare/swelling of the ear auricles although she or her doctor did not realize that the symptom could be related with the dose of the corticosteroid. As for her saddle nose, she realized it when she was about 60 years old.

On admission, her height, weight and body temperature were 149.5 cm, 35.3 kg and 37.1°C, respectively. Her blood pressure was 154/92 mmHg with SpO2 80% under 12 L/min of oxygen flow by reservoir mask. Slight flare/swelling of the bilateral ear auricles as well as saddle nose (Fig. 1) was observed without abnormal findings in the palpebral or bulbar conjunctivae. By auscultation, stridor was audible on the bilateral sides with no abnormal heart sounds. Edema was not detected in either lower limb. Laboratory data on admission is listed in Table 1. The white blood cell (WBC) count was markedly increased to 23,000/μL while the C-reactive protein (CRP) level was 0.91 mg/dL. The patient’s serum was negative for antinuclear antibody and antineutrophil cytoplasmic antibody (ANCA). Although the chest X-ray (Fig. 2) demonstrated no abnormalities in the bilateral lung fields, stenosis of the left and right principal bronchi was noted.

Due to respiratory failure, she was intubated and connected to a ventilator on the day of admission. Treatment with methylprednisolone at a dose of 500 mg/day for 3 days was initiated. After confirming improvement in respiratory condition, the dose of corticosteroid was gradually decreased. Extubation was conducted 7 days after admission. The pattern of a flow-volume curve (Fig. 3) recorded at an outpatient clinic before this admission indicated reversible intrathoracic stenosis, which became flat in the descending limb after a sharp peak associated with the collapse of central airways (6, 7), suggesting tracheobronchomalacia had been present. In addition, the swelling of the auricles and saddle nose lead to a tentative diagnosis of RPC.

Thoracic computed tomography (CT) (Fig. 4) performed after extubation revealed thickening of airway walls from trachea to bilateral principal bronchi with the luminal diameter reduced to approximately 5 mm, consistent with RPC. CT on expiration exhibited applanation of the lumen, more marked stenosis, and tracheobronchomalacia in comparison with findings on inhalation.

Electrocardiography after admission (Fig. 5) revealed negative T waves and QT prolongation with I-, aVL-, II-, III-, aVF-, and V2- to V6-lead with a slight increase in the

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**Table 1. Laboratory Findings on Admission**

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Biochemistry</th>
<th>Serology</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 23,000 /μL</td>
<td>TP 7.1 g/dL</td>
<td>CRP 0.91 mg/dL</td>
</tr>
<tr>
<td>Neut 88 %</td>
<td>Alb 4.2 g/dL</td>
<td>ANA &lt;40</td>
</tr>
<tr>
<td>Lym 11 %</td>
<td>LDH 303 IU/L</td>
<td>RF &lt;10 IU/mL</td>
</tr>
<tr>
<td>Mon 1 %</td>
<td>AST 47 IU/L</td>
<td>PR-3-ANCA &lt;3.1 EU</td>
</tr>
<tr>
<td>Bas 0 %</td>
<td>ALT 33 IU/L</td>
<td>MPO-ANCA &lt;3.1 EU</td>
</tr>
<tr>
<td>Eos 0 %</td>
<td>BUN 23.5 mg/dL</td>
<td>IgG 871 mg/dL</td>
</tr>
<tr>
<td>RBC 474 ×10^4 /μL</td>
<td>Cre 0.56 mg/dL</td>
<td>IgA 167 mg/dL</td>
</tr>
<tr>
<td>Hb 13.6 g/dL</td>
<td>Na 141 mEq/L</td>
<td>IgM 112 mg/dL</td>
</tr>
<tr>
<td>Ht 43.5 %</td>
<td>K 4.0 mEq/L</td>
<td>IgE &lt;35 mg/dL</td>
</tr>
<tr>
<td>Plt 36.3×10^4 /μL</td>
<td>Cl 103 mEq/L</td>
<td>Troponin T 0.038 ng/mL</td>
</tr>
<tr>
<td>CPK 95 IU/L</td>
<td></td>
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</tr>
</tbody>
</table>
myocardial troponin-T level but without any increase in the other serum biomarkers of cardiac injury. In addition, echocardiography indicated akinesis of the left ventricular anterior wall and ventricular septum (intermediate to cardiac apex regions) and a decrease in the ejection fraction. Both the electrocardiographic and echocardiographic findings gradually and spontaneously subsided; echocardiography confirmed recovery of cardiac systolic function within a
week, and negative T in electrocardiography persisted for about a month and was gradually normalized. Contrast-enhanced coronary CT revealed the absence of arteriosclerosis and stenosis in 3 vessels. Therefore, the cardiologists diagnosed she had takotsubo cardiomyopathy.

Since biopsy of the auricle (Fig. 6) demonstrated destruction of the cartilage and rupture of elastic fibers, a definitive diagnosis of RPC was made on 28th days after admission, based on the clinical and pathological findings. On the same day, the dose of oral prednisolone was increased to 30 mg combined with 100 mg of cyclosporine. The dose of prednisolone was decreased by 5 mg every 2 weeks until the maintenance dose was established as 15 mg.

The anti-type-II-collagen antibody was revealed to be negative at the concentration of 8.9 EU/mL (positive: >25 EU/mL) on the 62nd day after admission. Bronchoscopy (Fig. 7), performed on the 105th day after admission, did not indicate flare or swelling on the tracheal luminal surface although the disappearance of the tracheal cartilage rings was noted.

**Discussion**

RPC causes repetitive inflammation in the cartilage tissues of the whole body and in ocular/cardiovascular systems, which contain a high concentration of mucopolysaccharides, and it is likely to respond to steroids and immunosuppressive agents. Anti-type-II-collagen antibody was de-
ected in approximately 30 to 50% of patients with RPC (8), suggesting an autoimmune disease.

McAdam et al. (9) established the diagnostic criteria in which patients with RPC were defined as having 3 or more of the following 6 items plus histological evidence of cartilage inflammation: 1) bilateral auricular chondritis, 2) non-erosive sero-negative inflammatory polyarthritis, 3) nasal chondritis, 4) ocular inflammation, 5) respiratory tract chondritis and 6) audiovestibular damage. In the present patient, auricular chondritis, nasal chondritis, and respiratory tract chondritis were noted in addition to cartilage destruction identified with the auricular cartilage biopsy, leading to a diagnosis of RPC. Although there was no increase in the anti-type-II-collagen antibody level, this could be because steroids had been frequently administered under a diagnosis of bronchial asthma.

Trentnam and Le reported that the mean interval from the first visit to the diagnosis of RPC was 2.9 years (5). The present patient had been treated for bronchial asthma for about 3 years after her first visit at a local clinic with dyspnea at the age of 59 years. Since then, corticosteroid was administered for the treatment of suspected asthma attack and decreased and discontinued after symptoms subsided. The steroid dose-reduction or discontinuation had deteriorated not only her respiratory conditions but auricular swelling and saddle nose, which emerged during the course involving remission and exacerbation of her “asthma”. As Segel et al. indicated (4), steroid administration to RPC patients might transiently improve a respiratory symptom that was related to RPC.

In the present case, the diagnosis may have been delayed for the following reasons: 1) auricular chondritis and saddle nose emerged after the onset of airway symptoms, 2) symptoms (auricular swelling/saddle nose) other than airway symptoms were underestimated, and 3) the patient had been diagnosed as bronchial asthma due to steroid therapy-related improvement. Previous case reports of relapsing polychondritis misdiagnosed as bronchial asthma (10-12) suggested similar reasons for the misdiagnosis. The present case exhibited saddle nose and flare/swelling of ear auricles, which was not connected with her airway symptoms by her doctor. Several studies reported that the incidence of airway symptoms in RPC patients ranged from 20 to 50%, and that airway symptoms were initially present in 10 to 15% (3, 9). Other common sites involved in RPC included the auricles, joints, and nasal cartilage although many patients might not show all symptoms at onset.

Clinical features of relapsing polychondritis, different from typical bronchial asthma, include the following: 1) inhaled bronchodilator and corticosteroid are ineffective and oral corticosteroid is required, 2) lung function test reveals upper airway obstruction, and 3) CT scan demonstrates stenosis and edema of large airways. Based on the present case report, we strongly suggest that relapsing polychondritis should be differentiated from intractable bronchial asthma by physical examination, lung function test, and imaging technique.

Concerning the prognosis of RPC patients, the 5- and 10-year survival rates were 74 and 55%, respectively (13). Airway involvement is considered to be a major prognostic factor (14). Inflammation and destruction of tracheobronchial cartilages caused airway edema, airway collapse (tracheobronchomalacia), and cicatricial stenosis of the airways. In patients without advanced cartilage destruction, treatment might normalize respiratory function (4). In the present case, repeated airway chondritis led to irreversible tracheobronchomalacia. The disappearance of the tracheal cartilage ring by bronchoscopy suggested advanced cartilage destruction, consistent with a flow-volume curve indicating the pattern of intrathoracic airway stenosis. Since common causes of death in RPC patients included respiratory failure and airway infection, insertion of a tracheobronchial stent must be considered (3, 14).

In the present case, the results of coronary CT, electrocardiography, echocardiography, and serum biomarkers of cardiac injury suggested the concomitant development of takotsubo cardiomyopathy. According to studies reported (15, 16), aortic regurgitation, mitral valve regurgitation, or pericarditis was detected in approximately 10% of patients with RPC while no study has reported the concomitant development of takotsubo cardiomyopathy. Physical/mental stress may be involved in the pathogenesis. In the present patient, severe dyspnea may have induced takotsubo cardiomyopathy. Furthermore, β2 stimulants administered before and after admission may also have been an etiological factor (17). This is the first report of takotsubo cardiomyopathy in the patient with RPC. Takotsubo cardiomyopathy should be considered when differentiating heart diseases in patients with RPC.

As described above, early diagnosis/drug therapy for RPC may prevent or delay progression to tracheobronchomalacia. On the other hand, RPC is easily misdiagnosed as bronchial asthma because of its response to corticosteroid. It is important to differentiate RPC from bronchial asthma based on physical examination, detailed imaging, and respiratory function test findings.

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

Acknowledgement

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