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Three Cases of Relapsing Polycondritis with Isolated Laryngotracheal Stenosis

Case Report

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Abstract

Relapsing polychondritis (RP) is a rare autoimmune and inflammatory disease, particularly characterized by recurrent inflammation of the hyaline cartilage. Laryngotracheal involvement in RP is the most serious complication that is observed in 50% of the patients and may lead to a life-threatening condition. The most common cause of death is laryngotracheal stenosis associated with lung infections or severe respiratory insufficiency that may be observed in 10%-50% of the patients. In this study, three RP patients comprising a child with isolated laryngotracheal stenosis have been presented.

Keywords: Relapsing polychondritis, laryngotracheal stenosis, larynx, trachea

Introduction

Relapsing polychondritis (RP) is a very rare autoimmune and inflammatory disease characterized by recurrent inflammation of hyaline cartilage. Jaksch-Wartenhorst (1) used the term "policondropathy" in 1923, and Pearson et al. (2) used the term "relapsing polychondritis" in 1960 for the first time. While the incidence of RP is three in a million, it is observed five times more frequently in women (2). The incidence of RP increases between the ages of 20-60 and peaks at the age of 40, and only 5% of cases are seen in childhood (3, 4). Although today, it is thought that there is a genetic transmission, familial inheritance still remains uncertain (5). Specific antibodies and triggered immunological responses against type 2 collagen that develop in two-thirds of patients are thought to be responsible for the pathogenesis of RP (6). At the same time, additional autoimmune, rheumatologic, and hematologic pathologies are observed in 30% of patients (7). In addition to the uncertainty in etiology, the duration and severity of the disease and the symptoms that occur can vary significantly. Larynx and trachea involvement is seen in 50% of RP patients, and laryngotracheal stenosis (LTS) can develop in some of these cases, which can be life threatening (8). In this study, three cases of RP were presented, one being a child with symptoms similar to isolated LTS.

Case Presentations

Case 1

A 32-year-old female patient applied to the hospital with complaints of breathlessness, dry cough, and wheezing that had been gradually increasing for about 3 days. Previously, there was no similar discomfort in the family of the patient who reported having hoarseness and shortness of breath occasionally for the past 5 years and who did not report any complaints of past history of surgery or intubation or any additional disease.

On fiberoptic endoscopic laryngeal examination, a spindle-shaped stenotic area with smooth mucosal surface was observed in the

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subglottic area (Figure 1a). The computed tomography (CT) examination of the patient showed a 1.7 mm stenosis in the anterior of the subglottic region and a 3.5 mm stenosis in the posterior, but no additional lesion or pathology was found (Figure 1b). Her neurological, ophthalmologic, and orthopedic examinations were normal through auricle, nasal, and skin examinations. Vestibular system and audiological examinations were normal. Chest x-ray, abdominal ultrasonography, and echocardiography examinations were within normal limits. While the antinuclear antibody (ANA) and rheumatoid factor (RF) were negative in laboratory tests, elevated levels of anti-neutrophil cytoplasmic antibody (ANCA) (7.4 AU/mL) and c-reactive protein (CRP) (10.2 mg/L) were detected. After the immunologic markers that were examined showed no additional autoimmune disease, corticosteroid, azothiopurine, and cyclophosphamide were started after considering RP in accordance with current clinical, histopathological, and radiological findings. Three months after the treatment, the stenosis was clearly observed to regress in terms of the patient's complaints and the endoscopic examination findings (Figure 1c). In the repeated CT scan, it was seen that the anterior diameter of the subglottic area reached 2 mm, and the posterior reached 4 mm (Figure 1d).

The patient, who had been on follow-up for 3 years, did not have any complaints during this period. Written informed consent was received from the patient for the purpose of sharing this information.

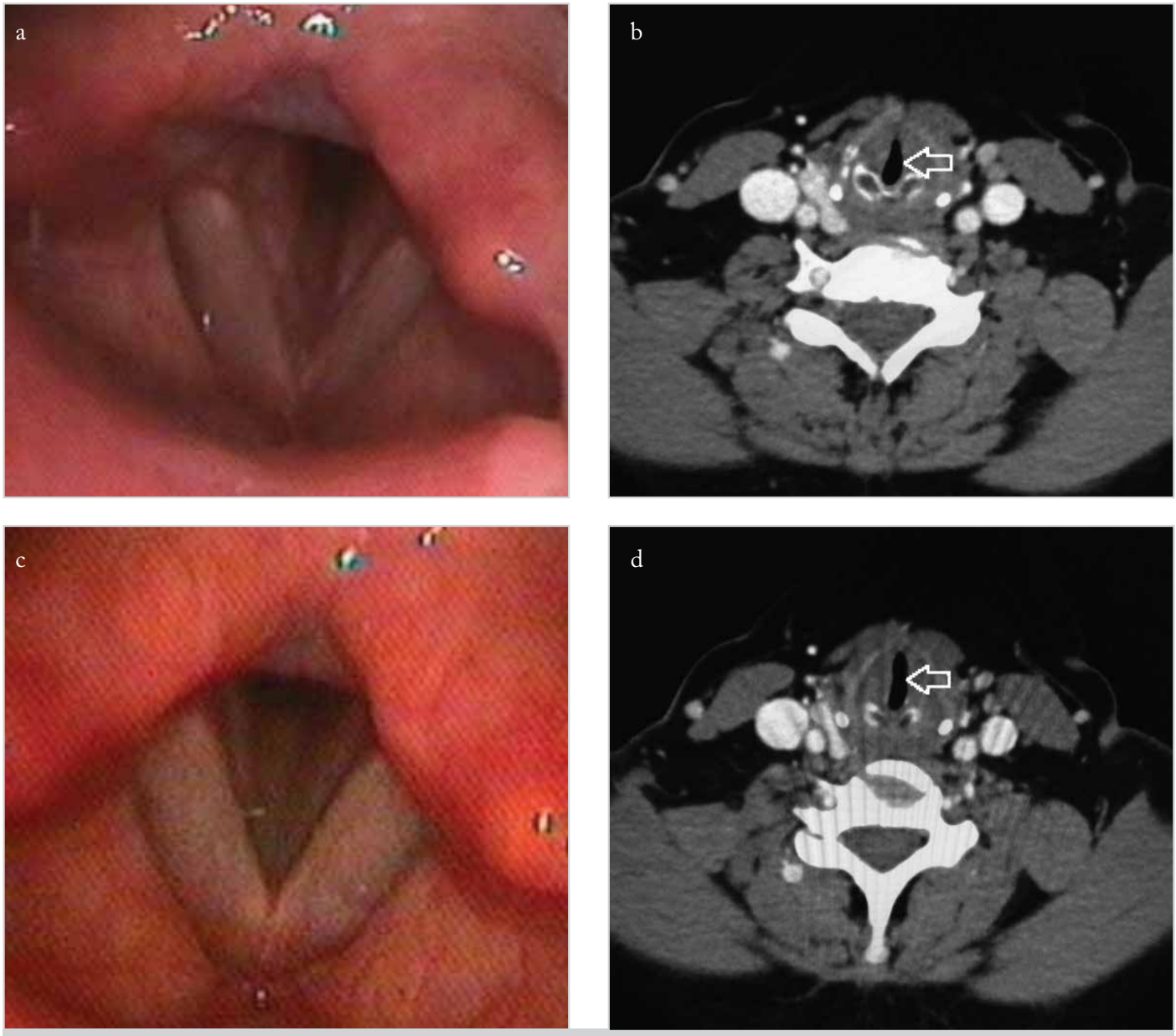

Figure 1. a-d. (a) On fiberoptic endoscopic laryngeal examination, a spindle-shaped stenotic area with smooth mucosal surface was observed in the subglottic area. (b) In computed tomography axial section, the arrow shows stenosis in the subglottic region (the subglottic area is 1.7 mm in the anterior and 3.5 mm in the posterior). (c) At the third month of the control examination, stenosis was seen to significantly regress. (d) After the treatment, LTS was seen to regress (at the tip of the arrow, the subglottic area is 2 mm in the anterior and 4 mm in the posterior)

Case 2

A 30-year-old male patient applied to our hospital with complaints of breathlessness and wheezing that had been gradually increasing for about 2 months. There was no similar disease in the family of the patient who did not report any previous surgery, intubation, or additional disease. The arterial oxygen saturation of the patient, whose general condition was evaluated as moderate and who used assistive respiratory muscles during respiration, decreased to below 90% even with mild effort. There was a gap of about 3 mm between the vocal cords of the patient, and both vocal cords were evaluated as fixed in the paramedian line in the endoscopic examination (Figure 2a).

In the CT scan, we observed an 18 mm circular stenosis that was 3 cm below the vocal cords. There were areas that had unclear borders in the thyroid/cricoid cartilages and that did not appear as a mass but led to severe destruction in the cartilages (Figure 2b). The patient, whose symptoms gradually increased, underwent tracheotomy under general anesthesia, and multiple incisional biopsies were taken from the destroyed areas of the cartilage. At the same time, direct laryngoscopy revealed an LTS area almost totally obliterating the airway about 3 cm inferior to the vocal cords (Figure 2c), and multiple punch biopsies were taken from this area. Histopathological examination revealed extensive lymphocytes, monocytes, and plasma cells, and the biopsies were interpreted in favor of a

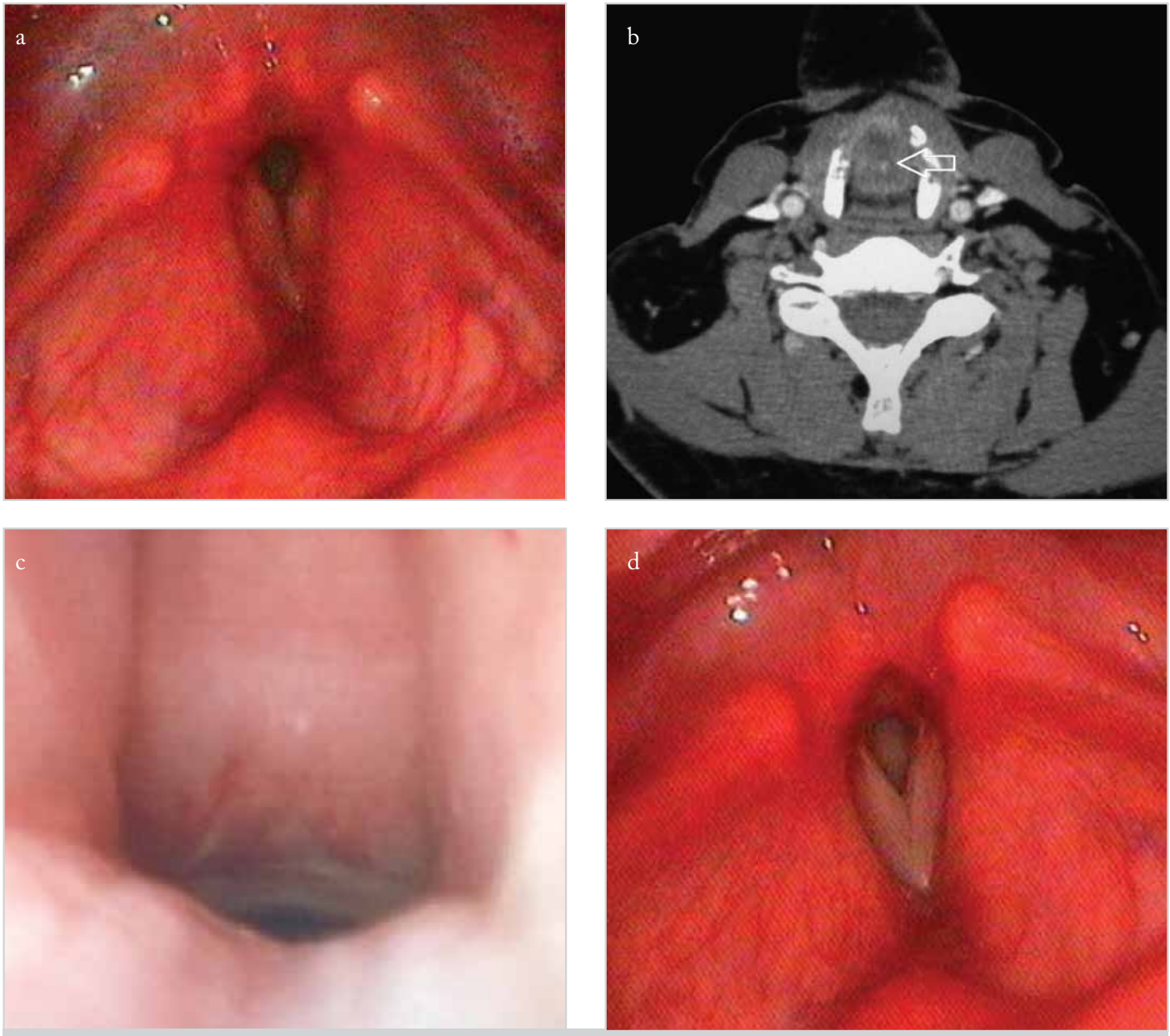

Figure 2. a-d. (a) Bilateral vocal cord paralysis was observed prior to the fiberoptic endoscopic examination. (b) In computed tomography axial section, circular stenosis 3 cm below the vocal cords and severe destruction occurring in the thyroid/cricoid cartilage can be seen at the arrow tip (c) The stenotic area almost totally obliterating the airway is seen about 3 cm inferior to the glottis in direct laryngoscopy. (d) Bilateral vocal cord paralysis was observed in the sixth month of follow-up

chronic inflammatory process. ANA, RF, and ANCA were negative in the patient, and auricle and nasal examinations were evaluated as normal. Neurological, ophthalmological, and orthopedical examinations were normal. Chest x-ray, abdominal ultrasonography, and echocardiography examinations were within normal limits.

Considering RP, corticosteroid and cyclophosphamide were started. Posterior cordotomy, tracheal resection, end-to-end anastomosis, and decannulation operations were suggested to the patient whose general condition was evaluated as good in the third month after the treatment. No change was observed in terms of LTS, but there was continued destruction in the thyroid/cricoid cartilage. The patient did not accept surgery but continued with the corticosteroid and cyclophosphamide treatments. No changes were observed in the sixth month follow-up (Figure 2d). Written informed consent was received from the patient to share this information.

Case 3

A nine-year-old male patient was brought to our clinic with complaints of breathlessness and wheezing that had gradually increased for about 6 months. There was no laryngotracheal surgery or intubation in the patient's history. During this 6-month period, inhaled steroid treatments were administered after the patient was diagnosed with asthma, but the complaints did not regress. The patient's complaints gradually increased in the week prior to coming to our clinic, and his general condition worsened and he experienced difficulty during breathing using the assisted respiratory muscles. Laryngoscopy showed a common LTS area that was thought to extend through the trachea and narrowed the airway by about 60% in the subglottic area. After the biopsy was taken from this area, the patient underwent tracheotomy. The endoscopic examination performed from the tracheotomy revealed that there was a widespread collapse in the entire trachea, which became evident especially with inspirium. ANA, RF, and ANCA were negative. Neurological, ophthalmological, and orthopedical examinations and pure-tone audiometry, chest X-ray, abdominal ultrasonography, and echocardiography examinations of the patient were within normal limits. As a result of histopathologic examination, corticosteroid treatment was started in the patient in whom chronic inflammation findings of the cartilage tissue were detected and who was thought to have RP.

After tracheotomy, the general condition of the patient was moderate and the use of assisted respiratory muscles improved and the complaint of dyspnea was somewhat decreased. The overall condition of the patient in whom systemic corticosteroid therapy continued and who was followed up under intensive care conditions deteriorated on the ninth day after the operation. The patient suffered acute respiratory failure, and the cannula was removed from the tracheotomy line and an appropriate-size intubation tube was inserted into the collapsed area deep enough to ventilate both lungs. Nonetheless, the patient in whom the collapse was observed to affect both main bronchi died of acute respiratory failure on the ninth postoperative day. In order to share information about this case, written informed consent was received from the parents of the patient.

Discussion

Laryngotracheal involvement in RP is the most serious complication that can be seen in 50% of patients and can pose a life-threatening risk (8). The most common causes of death are LTS, which is seen in 10%-50% of patients, and pulmonary infections or severe respiratory failure that develop due to LTS. In LTS, edema develops in the airway during the active period of the disease, and fibrous tissue develops due to chronic inflammation in the late period and the airway collapses due to the destruction of the laryngotracheal cartilages (6). Lung infections develop more frequently secondary to obstruction, which occurs as a result of infection and scarring (6). While the auricle (83%) is classically affected most commonly in adults, the larynx and trachea (50%), nasal, costal cartilage, joints, eye (20–60%), skin (36%), and heart (<%10) are other anatomical structures that can be affected (4). Joints (36%), auricles (27%), and airway (25%) are more commonly affected in children (9). Although the pathogenesis of RP remains uncertain, the response that emerges with the deterioration of the immune balance and the association with HLA-DR4 are believed to be at least partially responsible (5). In this study, no additional autoimmune disease was found in any case, whether child or adult.

Because of the inadequacy of immunologic markers and imaging modalities in the diagnosis of RP, the diagnosis is mostly made in the light of the patient's history and clinical findings. Auricular, nasal cartilage, larynx, trachea, ocular and auditory-vestibular involvement and the presence of seronegative arthritis have an important place in the diagnostic algorithms developed by various authors (Mc Adam et al. (7), Damiani and Levine (10) and Michet et al. (11)). Histopathologic examination is not pathognomonic, but helps diagnosis (8). There were histopathologic diagnoses of airway chondritis that were giving symptoms only through LTS in all of our cases. In addition, fiberoptic or direct endoscopic examination, CT, magnetic resonance imaging, cine tracheography, and laryngotracheograms are very helpful in detecting stenotic segment width and localization in LTS diagnosis (6). Both direct laryngoscopy and CT examination were performed for the diagnosis in the adult cases presented in this study.

Other than trauma, neoplastic, infectious, inflammatory, and granulomatous pathologies may be considered in the differential diagnosis of isolated LTS. Traumatic LTS, which sometimes develops after intubation or tracheotomy, was not considered because none of the patients had a history of previous surgery or intubation. Neoplastic pathologies were excluded because the imaging methods and biopsy results did not suggest neoplasia. The most common inflammatory and granulomatous pathology in LTS etiology is Wegener granulomatosis (WG), which can cause both nasal and airway involvement. Unlike RP, granulomatous vasculitis and c-ANCA antibody elevation are detected in WG. Pericarditis, pleuritis, and abdominal complaints come into prominence in polyarteritis nodosa, which is another granulomatous disease, and oral and genital ulcers are common symptoms in Behçet's disease (4). No additional pathology was detected in the cases presented in our study, and the only finding was isolated LTS.

A standard protocol has not been proposed for the treatment of RP, and the activity and severity of the disease determine the management strategy. While medical treatment is preferential in asymptomatic and minimally symptomatic patients, emergency tracheotomy or laryngotracheal reconstruction with medical treatment may be required in patients with severe airway obstruction. If there is local active involvement and there is no organ involvement, non-steroidal anti-inflammatory drugs can be used. If laryngotracheal, bronchial, cardiovascular, renal, ocular, and neurological involvement is seen, immunosuppressants such as glucocorticoids, dapsone, cyclophosphamide, azathioprine, cyclosporine, and methotrexate, which are more aggressive treatment choices, can be used. Elective surgical interventions are corticosteroid injections, recurrent dilatations, stenting, tracheotomy, Montgomery T-tube placement, and tracheal resection with end-to-end anastomosis (6). In this study, medical treatment was initiated in the first case without severe airway obstruction and without tracheotomy. However, severe airway obstruction occurred in the other two cases and tracheotomy was required. The tracheotomy cannula was withdrawn in the third patient whose general condition worsened after the treatment, and the intubation tube was placed in the stenotic segment with the help of fiberoptic endoscopy. For this reason, a Montgomery T-tube or tracheal stent was not preferred in the patient.

Laryngotracheal stenosis, which is more frequently seen in children, is the most common cause of mortality in these patients (3). Early diagnosis and treatment is critical to prevent possible complications and for improving prognosis. The prognosis was quite good due to early diagnosis and treatment in the first case, and no complications were observed. In the other two cases, especially in the child patient, the prognosis was poor, and this situation can be explained by the time lost between the onset of symptoms and the diagnosis. In addition, more frequent laryngotracheal involvement in pediatric patients and higher necessity for tracheotomy might be considered as other factors that worsen the prognosis.

Conclusion

It should not be forgotten that RP, which is very rare and attracts attention with more auricular involvement, may be life threatening by giving rise to symptoms due to isolated LTS that requires emergency surgical intervention and tracheotomy. To be able to avoid possible complications during the evaluation of LTS cases, RP should be considered in the differential diagnosis.

Informed Consent: Written informed consent was obtained from patients and one pediatric patient's parents who participated in this study.

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