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Stenosis of the Subglottic Trachea Revealing Relapsing Polychondritis of a Young Adult

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Abstract

Relapsing polychondritis is a rare inflammatory disease involving essentially cartilaginous structures. Other systemic manifestations can be encountered as the eye and ear disturbance. Aortic aneurysms affect few cases. If affection of airway cartilages occurs, prognosis may be worsened by eventual stenotic lesions. We report a 22-year-old woman with Relapsing polychondritis. When she was referred to our hospital 4 weeks after the onset of respiratory symptoms, she was having severe breathing difficulty. Immediate tracheostomy followed by steroid therapy improved her respiratory condition, although the treatment was complicated because of her diabetes. While airway involvement of Relapsing polychondritis can be life threatening, it is curable with steroid therapy. Clinicians should keep in mind that airway obstruction could be caused by this disease.

Keywords

Relapsing Polychondritis, Airway Narrowing, Prognosis

1. Introduction

Relapsing polychondritis (RP) is a disease of unknown etiology characterized by recurrent non-infectious inflammation of cartilaginous and connective tissues. It is an uncommon, chronic, and potentially life-threatening multisystem disorder in case of laryngeal and tracheobronchial disturbance. The etiology of RP is still unknown, but the pathogenetic role of the autoimmunity is suggested by frequent overlaps with various autoimmune diseases, and by the presence of autoantibody against cartilage in the serum of patients with RP [1] [2].

Clinical presentations of RP vary considerably from patient to patient, and the involvement of multiple organs has been reported. Although several reports have demonstrated the clinical signs, pathologic manifestations and

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radiologic findings of RP, there are no specific features of RP. Therefore, it is difficult to show the diagnosis of RP [1] [2].

Although several reports have demonstrated the clinical signs, pathologic manifestations and radiologic findings of RP, there are no specific features of RP.

Therefore, it is difficult to show the diagnosis of RP. RP is clinically diagnosed; there are no specific biological or radiological signs to confirm the diagnosis.

Radiographic study of the airway is of great value in detection and evaluation of upper respiratory involvement. Airway involvements are major causes of morbidity and mortality, and they have accounted for most of the deaths due to RP. To suppress the inflammation of airway mucosa and cartilage is extremely important in the successful treatment for RP.

RP is a polymorph multisystem pathology with various manifestations, inducing thus serious and refractory damage such as trachea stenosis due to lateness in the diagnostic delay and therapeutic management. Only rapid diagnosis and efficient therapy are guarantors of improving the prognosis and avoiding sequelae.

The aim of this study is to show that RP diagnosis should be considered in case of airway narrowing. Only an early diagnosis and an adapted treatment may improve prognosis.

2. Observation

A 27-year-old woman presented with eight-months history of fever, productive cough, and dyspnea. A radiographic lateral view of the neck showed subglottic tracheal stenosis. A computed tomography (CT) scan of the neck also showed narrowing of the larynx (approximately 3 cm until the carena). An arterial blood gas test showed a pH: 7.4, $PaCO_2$: 37 mmHg, PaO_2: 60 mmHg, SaO_2: 94%, and HCO_3: 24 mEq/L in room air. The CRP rate was 62 mg/L and ferritin was at 560 ng/L. Other laboratory findings were in the normal range. The laryngeal biopsy showed a non-specific catarrhal laryngitis Computed tomography (CT) depicted diffuse bronchotracheal stenosis, which deteriorated in exhalation. The MRI revealed airway stenosis from the trachea to the lobar bronchi. She was treated with glucocorticoid without success and the intubation was indicated. Owing to potential risks of airway compromise during intubation and/or extubation and the regression of tracheal edema, she was extubated 5 days after. Tracheotomy was made with Shiley canule. Few months later, she developed bilateral anterior uveitis and left auricular chondritis treated with glucocorticoid with success. In conjunction with nasal, which was previously overlooked, RP was finally diagnosed We made a diagnosis of relapsing polychondritis (RP) based on the following criteria set by MacAdam *et al.* and Damiani and Levine: 1) bilateral auricular chondritis; 2) nonerosive seronegative inflammatory polyarthritis; 3) nasal chondritis; 4) ocular inflammation; 5) respiratory tract chondritis; and 6) audiovestibular damage. Administration of high-dose glucocorticoid and azathioprine resolved the symptoms and the bronchial stenosis was stabilized. She developed 6 months later diabetes treated with metformine.

3. Discussion

RP is a relapsing degenerative disease of cartilaginous tissues characterized by the involvement of multiple organs and vessels, including the nose, ears, throat, trachea, eyes, joints and cardiac valves; however, the etiology of RP is still not fully understood [1]-[3].

RP is a Th1-mediated disease marked by high serum levels of interferon γ, interleukin 12 and interleukin 2. In addition, serum levels of vascular endothelial growth factor and matrix metalloproteinases-3 are high in RP and are correlated with disease activity. Auto-immune reaction can be induced by infectious

Mechanical and chemical aggressions implicating cartilaginous structure may induce the occurrence of RP. Genetic Susceptibility to RP has been also reported.

Previous studies have suggested that autoimmunity may be associated with the pathogenesis of RP. No ethnicity, sex or age differences have been reported for RP, but most patients with RP are between 40 and 60 years of age [1] [2]. Currently, most medical practitioners and researchers apply the criteria proposed by Damiani *et al.* [3] for the diagnosis of RP. As RP is a rare disease with clinical manifestations that vary from patient to patient, it is very hard to diagnose, especially in patients with atypical symptoms. The early diagnosis of RP is even more challenging [1]. Laboratory investigations in this case revealed increased CRP, in accordance with previous studies [4]; interestingly, we also found an increased ferritin level, consistent with the findings of Fujiki *et al.* [5].

Airway involvement by RP is generally considered ominous and has been reported to portend a poor prognosis [6] [7]. Tracheobronchomalacia (TBM), due to loss of the supportive cartilaginous scaffolding of the upper respiratory airways, can be seen as chronic sequelae of RP due to recurrent inflammation [8]. TBM may also be the sole airway abnormality recognized during the early stages of RP. Respiratory compromise stemming from fixed airway obstruction or hyperdynamic collapse may cause significant morbidity and mortality [9]. Despite aggressive medical therapy, many patients experience symptom progression and eventually require tracheotomy, which may not be fully palliative due to frequent obstruction and malacia of more distal airways beyond the tracheotomy site [3] [10].

Lower airway manifestations of RP can be the only sign of the disease. RP has to be considered in the differential diagnosis of patients with recent onset of progressive dyspnea and severe airflow limitation even without other systemic signs of cartilage damage [9].

Unfortunately, our knowledge about airway involvement in RP is limited and is based on anecdotal reports and small case series. Purcelli *et al.* [11] described the first case report of RP with tracheal collapse in 1962, and McAdam *et al*. [8] reported in a case series in 1976 that the majority of patients with RP and a known cause of death had respiratory tract involvement. In many of those patients, airway problems were in fact the complaints leading to the diagnosis of RP, underscoring the fact that clinically significant airway compromise does not necessarily present late in the course of the disease. The majority of patients with respiratory symptoms who were referred for airway evaluation were women (70%) like our case, a finding that differs from those in some reports that have described an equal gender distribution in patients with a clinical diagnosis of RP as a whole but is similar to those in other reports in the literature [10].

RP is a disorder that has a variety of clinical manifestations and is considered an autoimmune disease resulting in cartilage breakdown. In this case, the patient demonstrated severe airway stenosis on CT that was well correlated with her severe respiratory symptoms. The most common causes of death among patients with RP are infection, airway compromise, and cardiac complications [12].

Symptomatic tracheobronchial involvement implies a poor prognosis. Laryngotracheal symptoms are present in approximately 25% of the patients in the initial course of the disease, however, airway symptoms eventually occur in 50% of all patients with RP [13]. The disorder causes airway obstruction by two mechanisms. The first is a stricture due to inflammatory swelling or scar formation in the glottic and subglottic areas. The second is dynamic airway collapse during respiration due to destruction of tracheal cartilage [14]. Accordingly, radiographic and bronchoscopic examinations may provide incorrect information for determining the degree of tracheal obstruction, as dynamic airway collapse occurs during respiration [15].

A review of few series of patients with RP illustrates the frequency of airway involvement and the female predominance (**Table 1**).

The CT findings in patients with RP consisted mainly of airway wall thickening, airway stenosis, airway malacia, airway wall calcification, and air trapping. The most common CT manifestations were increased attenuation and smooth corticosteroid sickening of airway walls. Tracheal or bronchial stenosis was less common. Airway collapse and lobar air trapping were seen in half of patients examined with expiratory CT [9].

The utility of fluorodeoxyglucose positron emission tomography/computed tomography for early diagnosis and evaluation of disease activity of RP was reported by Yamashita *et al.* It seems to be a potentially powerful tool for the early diagnosis of RP, especially in patients without easily biopsied organ involvement [21]. Respiratory function test is sensitive in early detection of airway involvement in RP. Bronchoscopy and CT are useful

Table 1. Review of literature of RP cases.

Author	n	Period	Age	Female	Airway involvement	Deaths
Gao L *et al.* [16]	23	1996-2011	-	-	10	3
Hong G *et al.* [17]	12	2004-2011	48	5	12	9
Zhang JQ *et al.* [18]	13	2000-2006	50	4	12	1
Shi XH *et al.* [19]	56	2006	45	18	38	
Maimon N *et al.* [20]	3	1995-2007	44	3	3	2

in evaluation of the severity of airway involvement in patients with RP.

In this case, subglottic stenosis was found during a bronchoscopic examination and emergency tracheostomy was performed. Other chondritis and bilateral scleritis developed 3 months after tracheostomy. Chang *et al*. described the same features leading to tracheostomy but the patient's upper airway was completely collapsed [22]. In fact, tracheostomy was once the most likely surgical procedure in RP. However, this procedure is only effective in patients with upper subglottic involvement. In cases of extensive tracheobronchial involvement, tracheostomy is ineffective because the distant tracheal collapse below the tracheostomy is still unresolved [23].

There are a number of treatments available for RP. Immunosuppression including steroid medication and chemotherapy with drugs is considered the primary option. A tracheostomy or surgical interventions, such as airway stenting, are indicated for patients with aggravated tracheobronchial symptoms like our patient. Airway management such as laryngotracheal reconstruction can improve quality of life and palliate patients effectively [24].

Corticosteroids remain the major treatment. Other therapies include nonsteroidal anti-inflammatory drugs, dapsone, colchicine, azathioprine, methotrexate, cyclophosphamide, hydroxychloroquine, cyclosporine, and infliximab [25]. Corticosteroid therapy is effective in improving the symptoms and delaying the progression of relapsing polychondritis with involvement of the respiratory tract at early stage. At later stage of the disease, airway interventional therapy, such as metallic stent placement, tracheostomy or positive airway pressure support, can be used to treat airway obstruction and to improve the survival. The successful use of infliximab is reported by some authors [26].

The airway tract involvement is known to be one of the most important prognostic factors in patients with RP [27]. The possibility that airway obstruction in the initial stages of RP is due to airway inflammation and that early, aggressive immunosuppressive treatment of RP may delay or prevent irreversible cartilaginous destruction and airway collapse is discussed [28].

This case is reported with the hope of increasing awareness about the potential for early upper airway involvement in RP [23] [29]-[35].

4. Conclusion

Symptomatic airway involvement in patients with RP is common, diverse, has a female predominance, and may occur throughout the course of disease. Dynamic CT scans are useful tools for the detection and surveillance of airway involvement in this population. The treatment of airway problems encountered in patients with RP can be challenging and needs to be individualized. Therefore, accurate diagnosis and referral to a specialized center for full multidisciplinary workup, medical treatment, and possible endoscopic intervention are important.

Conflict of Interest

There are no conflicts of interest.

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