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Case Report

A case of relapsing polychondritis solely presenting with chronic cough

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Abstract: Relapsing polychondritis (RP) is a rare autoimmune disease affecting multiple organ systems. Since the spectrum of clinical manifestations of RP is complex and diverse, patients may initially present with general, non-specific symptoms. Here, we report a case of RP presented as chronic cough. According to the chronic cough diagnostic protocol, we excluded the common causes of chronic cough. Chest high-resolution computed tomography (HRCT) scan revealed mild tracheal calcification, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) showed increased FDG uptake in bilateral auricular cartilages, nasal cartilage, larynx cartilage and costal cartilage. A left auricular cartilage biopsy revealed chondritis with chronic inflammation and necrosis. The patient was diagnosed as RP and treated with corticosteroids effectively. This unique case highlights that RP should be taken into consideration in the differential diagnosis of chronic cough with tracheal calcification, after ruling out common etiologies.

Keywords: Relapsing polychondritis, chronic cough, tracheal calcification, PET/CT

Introduction

Relapsing polychondritis (RP), first described by Jaksch-Wartenhorst in 1923 [1], is a rare autoimmune disorder with inflammation of cartilaginous structures and other tissues throughout the body [2, 3]. To date, the etiology of RP remains unknown, and immunological mechanisms might play a relevant role in the disease pathogenesis. Anti-cartilage antibodies are detected in at least 33% of RP patients, and their titers appear to correlate with disease severity. The pathogenesis of RP involves an autoimmune reaction to type II collagen, presents in the cartilage and sclera [4, 5]. The disease affects different cartilaginous structures, including the ear, nose, larynx, trachea, bronchi, peripheral joints, eye, heart and skin [1, 6, 7]. The incidence of RP is about 3.5 in 1,000,000/year [7], and the 5- and 10-year probabilities of survival after diagnosis are 74% and 55% respectively [7]. However, RP can be life-threatening if there is airway involvement. Laryngotracheal involvement is a major cause of morbidity and mortality in RP patients [8, 9].

RP has no pathognomonic clinical, radiologic, or histopathological features. Hence, the diagnosis depends on a constellation of clinical features and various diagnostic tests [10]. No standardized therapeutic protocol for RP has been established. Current medical therapy is largely empirical and based on case reports [3].

Case report

A 54-year-old man was presented with a 2-year history of dry cough. He had been treated with antibiotics but it did not relieve the symptoms. He did not report dyspnea, expectoration, hemoptysis, stridor, chest discomfort or sore throat. Moreover, odynophagia, neck pain, hoarseness, anorexia, fever, sweats, rash, arthralgia, or weight loss were not reported. The medical history of the patient was unremarkable apart from his 30-pack-year smoking his-

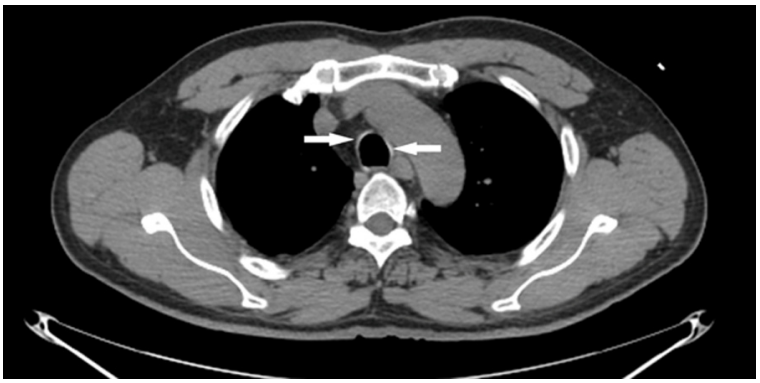

Figure 1. Chest high-resolution computed tomography (HRCT) scan revealed mild tracheal cartilage calcification (arrows).

tory. He took no regular medications, kept no pet, worked as an official in an office environment and had no history of occupational inhalational exposure. Physical examination on the patient did not reveal anything unusual.

The patient had normal results for white blood cell (WBC) count, hematocrit and platelet levels, coagulation study, complete metabolic panel values and urinalysis. Erythrocyte sedimentation rate (ESR) (10 mm/1 h) and C-reactive protein (CRP) level (0.03 mg/dl) were normal. Antinuclear antibody (ANA), rheumatoid factor (RF), antineutrophilic cytoplasmic antibody (ANCA), and anti-cyclic citrullinated peptide antibody were not detected. Sputum cultures for fungus, acid-fast bacilli, and other bacteria were negative. The results from sputum induction and differential cell analysis, paranasal sinus CT, electrocardiograph (ECG), echocardiogram and 24-hour esophageal potential hydrogen (PH) monitoring identified no abnormality. In addition, results from pulmonary function test (PFT), bronchial provocation test and test on diffusing capacity of lung for carbon monoxide and chest radiograph were also normal. Chest HRCT scan revealed mild calcification in trachea but no other obvious abnormal signs (**Figure 1**). Bronchoscopy showed moderate edema and swelling of the tracheal and bronchial walls which did not affect the membranous portion. However, PET/CT showed increased FDG uptake in bilateral auricular cartilages, nasal cartilage, larynx cartilage (cricoids cartilage, arytenoids cartilage, thyroid cartilage) and costal cartilage with maximum standardized uptake values (SUV_{max}) of 4.0, 3.3, 3.8 and 4.2, respectively (**Figure 2**). A left auricular cartilage biopsy revealed chondritis with chronic inflammation and necrosis (**Figure 3**).

Based on the clinical, radiological and histological findings, a diagnosis of RP was finally established. As soon as diagnosis of RP was identified, prednisolone treatment was initiated (50 mg daily). A rapid improvement in the patient's symptoms was observed. The prednisolone dose was slowly reduced as symptoms improved.

A follow-up ^{18}F-FDG PET/CT scan after 3 months of treatment showed that ^{18}F-FDG uptake either significantly decreased or disappeared in the affected cartilages. Fifteen months after the beginning of treatment he remained well on a decreased dose of prednisolone.

Discussion

The clinical manifestation of RP is complex and may vary from asymptomatic to severe progressive multi-organ damage or fatal cardiopulmonary presentations such as airway collapse and valvular regurgitation [11]. There is a high risk of misdiagnosis due to the rarity of this disorder, spatiotemporal variation of lesions, and unpredictability of episodes. Furthermore, the non-specificity of involved sites and comorbidities of patients also contributed to potential misdiagnosis. The respiratory tract involvement in RP was investigated in a retrospective study by McAdam et al. [12]. The study showed that 14% of patients had respiratory symptoms at initial presentation. Half of these patients had clinical symptoms such as dyspnea, cough, wheezing, stridor, and dysphonia. However in our case, the only symptom presented in the patient was chronic cough for two years, this atypical and rare sign led to delayed diagnosis and the case was initially misdiagnosed as chronic bronchitis at local hospitals.

To our knowledge, RP with chronic cough as the sole manifestation has not been reported in the literature previously. A plausible explanation for the absence of other symptoms in this case could be that the airway involvement was in an early stage or still relatively mild condition and other common airway manifestations such as dyspnea, wheezing, stridor, and dysphonia had yet to appear. Obviously, to report and

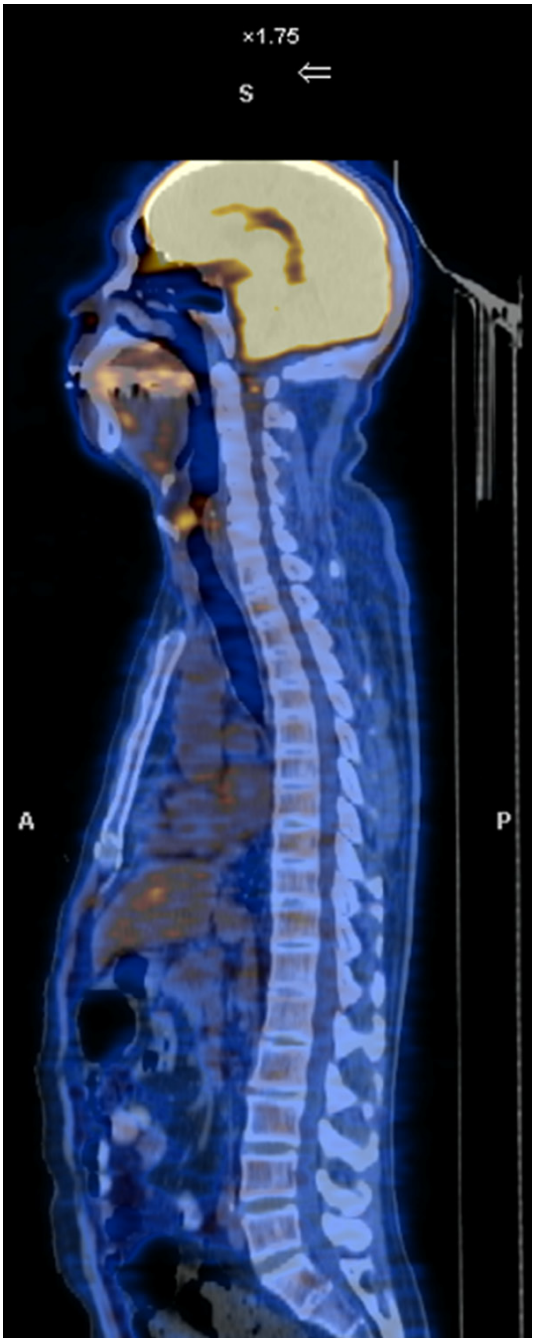

Figure 2. PET/CT showed increased FDG uptake in bilateral auricular cartilages, nasal cartilage, larynx cartilage and costal cartilage.

expound this case of RP only presented as chronic cough can improve the understanding of the diagnosis strategy of this disease.

In the clinical setting, chronic cough is defined as cough being sole or predominant symptom and lasting for more than 8 weeks with normal chest X-ray [13]. Lai et al. [13] showed that 81% of patients with chronic cough were misdiagnosed with chronic bronchitis, pharyngitis or laryngitis. 93% of patients were treated with antibiotics and/or antitussives. The most common causes of chronic cough are cough variant asthma, eosinophilic bronchitis, upper airway cough symptoms, atopic cough and gastroesophageal reflux cough. Following the chronic cough diagnostic protocol [14], we assessed our patient's history, career, environmental exposure and physical examinations carefully and arranged a series of laboratory examinations. This included sputum induction, differential cell analysis, pulmonary function test, bronchial provocation test, 24-hour esophageal pH monitoring, chest X-ray, bronchoscopy and cardiac examination. The negative findings and ineffective empirical treatments excluded the common causes of chronic cough mentioned above.

The PET/CT scan performed allowed thorough investigations of underlying etiologies. It played a significant role in assessing almost all cartilages and led to the diagnosis of RP. Although we have previously reported PET/CT as a valuable tool for RP diagnosis especially in early identification and differential diagnosis [15, 16], its cost-effectiveness and radiation risk associated must also be taken into account if the patient solely presented with chronic cough.

In recent years, a number of other unusual causes of chronic cough were identified in our Institute, such as cervical spondylosis and heterotopic salivary gland at the base of the tongue [17, 18]. To our knowledge, this is the first report of chronic cough caused by RP. Mild tracheal calcification revealed by HRCT also offered a clue to suggest this was a RP case initiating with chronic cough since tracheal calcification was often seen in RP [19].

Conclusion

This report detailed a RP case solely presenting with chronic cough which is a rare presentation of a rare disease. This case also highlights that RP should be taken into consideration in the differential diagnosis of chronic cough with tracheal calcification, after ruling out common etiologies.

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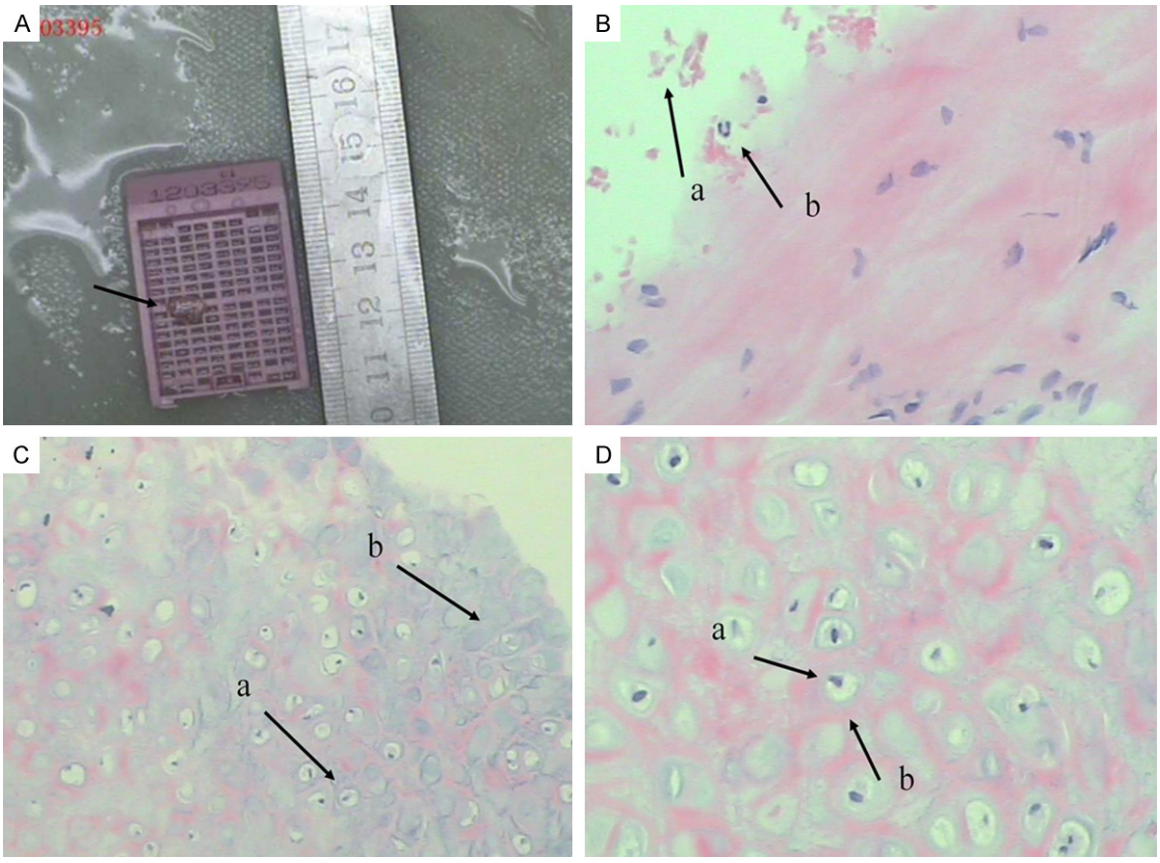

Figure 3. Histopathologic findings in left auricular cartilage biopsy specimen. A: The high-quality digital picture of pathologic gross specimen; B: H&E 400× fibrino exudation (a) and neutrophil (b); C: H&E 200× normal chondrocyte (a) and necrosis of chondrocyte (b); D: H&E 400× Cartilage cell nucleus (a) and cytoplasm of acidophilic degeneration (b).

Disclosure of conflict of interest

None.

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