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Case Report

Comparison of pathological findings and accumulation of fluorin-18 fluorodeoxyglucose on positron emission tomography/computed tomography: A case of relapsing polychondritis

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ABSTRACT

A 70-year-old woman with a hoarse voice and dry cough was referred to our hospital. Positron emission tomography/computed tomography showed abnormal accumulation of fluorine-18 fluorodeoxyglucose (FDG) at the nasal septum, larynx, trachea, bronchus, and costal cartilages. The maximum standard uptake values of FDG accumulation in the nasal septum and costal cartilage were similar. Biopsies of the nasal septum and costal cartilage were performed. The patient was diagnosed with relapsing polychondritis (RP) based on the clinical features and pathological findings. Histopathological examination revealed progressive initial RP findings. The disease progression was different, even with the same FDG accumulation.

1. Introduction

Relapsing polychondritis (RP) is a chronic inflammatory disease of unknown cause, characterized by a recurrent and progressive disorder in the cartilage and proteoglycan-rich organization. The diagnosis is made on the basis of clinical features and pathological findings of chondritis [1].

Positron emission tomography/computed tomography (PET/CT) has been reported to be useful for diagnosing RP and monitoring therapeutic response [2]. It is also suggested that PET/CT is a radiological tool in selecting biopsy sites [3]. However, a recent study by Zeng et al. [4] found that 55 % of 30 RP cases were PET/CT-positive and non-diagnostic on PET/CT-guided biopsy. Few reports have compared the pathological findings with fluorine-18 fluorodeoxyglucose (FDG) accumulation on PET/CT.

Herein, we report the case of a patient with RP, in whom histopathologically, the progression of inflammation differed even with similar levels of FDG accumulation in each involved organ.

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2. Case report

In July 2021, a 70-year-old woman was referred to our hospital with a hoarse voice and dry cough for 2 weeks. She had a medical history of uveitis and had never smoked. Physical examination findings were as follows: body temperature, 37.1 °C; pulse rate, 93/min; respiratory rate, 20/min; blood pressure, 143/88 mmHg; and oxygen saturation, 97 %. Both the auricles were normal; however, a saddle nose was observed. Respiratory and cardiac sounds were clear. Otolaryngological examination revealed swelling of the arytenoid and subglottis. CT revealed tracheal wall thickening (Fig. 1A). FDG PET/CT revealed intense FDG accumulation in the nasal septum (maximum standard uptake value [SUVmax], 5.11), larynx, trachea, bronchus, and costal cartilage (Fig. 1B). White blood cell count was 8.2×10^9/L with 76.0 % neutrophils, 18.5 % lymphocytes, 5.0 % monocytes, and 0.5 % basophils. C-reactive protein (CRP) level was elevated to 13.27 mg/dL. Results of liver and kidney function tests were normal, and urinalysis showed no abnormal findings. Furthermore, serum proteinase-3-anti-neutrophil cytoplasmic antibody (ANCA) and myeloperoxidase-ANCA levels were <1.0 U/mL. Antibodies against type II collagen were also detected.

Biopsy of the auricle and nasal septum revealed normal findings and inflammatory granulation with the disappearance of cartilagionous tissue (Fig. 2A). The pathological findings of the nasal septum were considered non-specific. Bronchoscopy revealed vocal cord constriction and stenosis of the trachea and right main bronchus (Fig. 3A and B). Biopsy was not performed in this case because it was deemed to increase the risk of airway obstruction in cases of bleeding. A biopsy of the costal cartilage that showed strong accumulation of FDG (SUVmax: 6.61) revealed slight infiltration of lymphoid cells around the cartilage with partial destruction, consistent with RP (Fig. 2B and C). Histopathology of the nasal septum was also determined to be an RP lesion. Therefore, the patient was diagnosed with RP according to the criteria of McAdam [1]. Oral prednisolone (PSL) 50 mg/day (1 mg/kg) was initiated in September 2021. After 2 weeks, her condition improved, and the CRP level decreased to 0.01 mg/dL. Subsequently, the corticosteroid dose was gradually tapered. However, when PSL therapy was switched to 15 mg/day 7 months after starting the therapy, the CRP level increased to 5.87 mg/dL. Additionally, CT images showed aggravation of airwall thickness. Therefore, cyclosporine A (CYA) was administered. One months later, the CRP level returned to normal. In June 2022, the second FDG PET/CT scan showed that FDG accu-

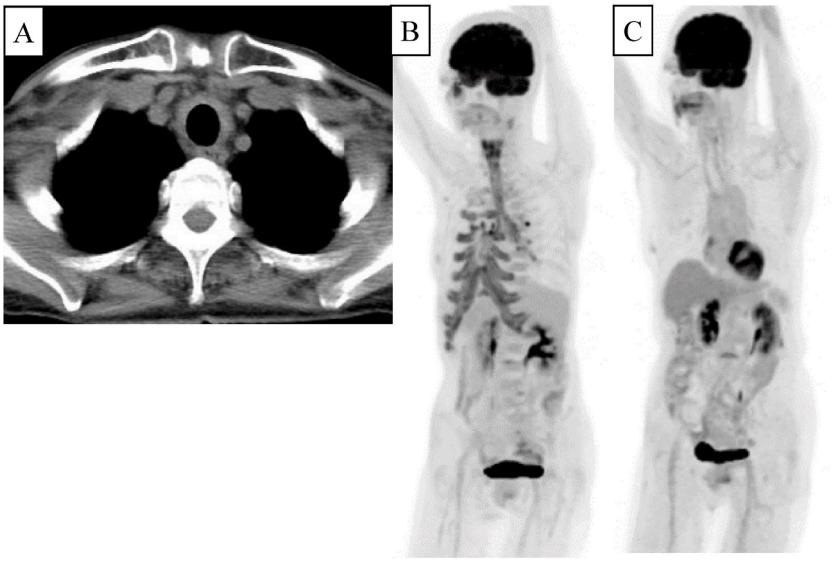

Fig. 1. Chest computed tomography images at initial presentation shows thickening of the tracheal walls (A). Initial image of FDG PET/CT shows intense FDG accumulation in the nasal sputum, larynx, trachea, bronchus, and costal cartilages (B). The second FDG PET/CT scan shows that FDG accumulation in the cartilaginous tissues had almost disappeared (C).

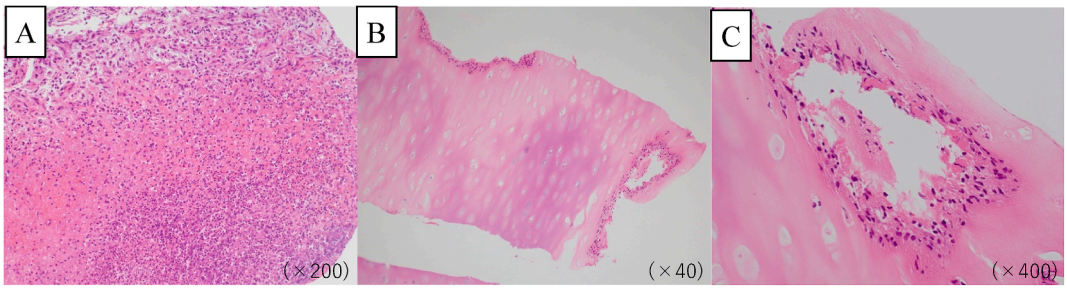

Fig. 2. Histological examination of nasal septum biopsy specimens reveals inflammatory granulation with disappearance of cartilaginous tissue (A). Histological examination of costal cartilage biopsy specimens reveals slight infiltration of lymphoid cells around the cartilage with partial destruction (B, C).

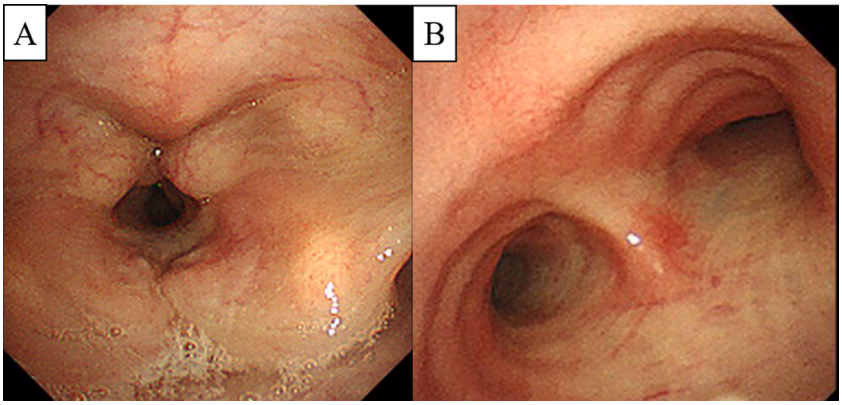

Fig. 3. Bronchoscopy shows swelling of the arytenoid, vocal cord constriction (A), and stenosis of the right main bronchus (B).

mulation in the cartilaginous tissues had almost disappeared (Fig. 1C). After 7 months of combination therapy, CRP was slightly elevated to 1.16 mg/dL, and the third FDG PET/CT scan showed FDG accumulation in the cartilaginous tissues. The CYA was replaced with methotrexate (MTX). However, the CRP levels remained low as an abnormal value (Fig. 4).

3. Discussion

RP is a multisystem disorder of unknown etiology characterized by recurrent inflammation and destruction of cartilage tissues. RP can also inflame other proteoglycan-rich structures such as the eye, heart, blood vessels, and inner ear. Airway involvement has been detected in up to 50 % of patients with RP, and respiratory failure and pulmonary infection are the major causes of death in patients of Japan [5]. Shimizu et al. conducted an epidemiological survey of 239 Japanese patients with RP and found a positive association between nasal cartilage and airway involvement and a strong inverse relationship between airway and auricular involvement [6]. Patients with airway involvement frequently exhibit a progressive disease course.

PET/CT revealed FDG accumulation in the cartilaginous structures of patients with RP, reflecting the infiltration of lymphocytes with variable proportions of polymorphonuclear cells, monocytes, and plasma cells. PET/CT has been reported to be useful in the diagnosis of RP and monitoring of the therapeutic response [2,7]. In our patient, FDG uptake before diagnosis was noted in nasal, tracheal, bronchial, and costal cartilages but not in the auricular cartilages. Moreover, our patient showed nasal involvement without auricular involvement, which was histologically confirmed.

The pathological presentation of RP depends on the timing of the biopsy. Therefore, a pathological diagnosis may be difficult when typical chondritis cannot be confirmed. In the early histological findings of RP, inflammatory infiltrates are found adjacent to the involved cartilage and consist predominantly of mononuclear cells and occasional plasma cells. At advanced stage, the destruction of the cartilage begins at the outer edges and advances centrally with infiltration of inflammatory cells into the cartilage. Basophilic staining was absent in the cartilage matrix and chondrocytes. With the progression of RP, degenerating cartilage is replaced by granulation tissue, followed by fibrosis and focal areas of calcification [8]. In our case, histological examination of costal cartilage biopsy specimens revealed destruction of the cartilage at the outer edges and infiltrations of mononuclear cells into the area, indicating ini-

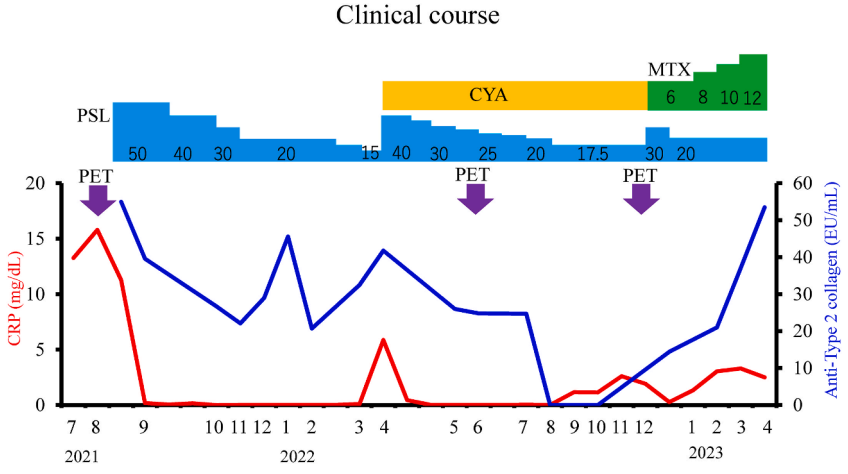

Fig. 4. Clinical course.

tial findings of RP. However, the nasal septum revealed inflammatory granulation with disappearance of cartilaginous tissue, showing the progressive findings of RP.

Zeng et al. analyzed 30 patients with RP who underwent PET/CT before steroid-based therapy [4]. In the study, the median of SUVmax in the cartilages was 3.8 (range, 1.9–17.9), and 55 % of cases were PET-positive, and biopsies were non-diagnostic. Interestingly, in our case, the degree of FDG uptake was the same in both the involved nasal and costal cartilages, but the histopathological findings showed different degrees of disease progression. Therefore, attention might be required when selecting biopsy sites using PET/CT.

Corticosteroid administration is the gold standard therapy for RP. Horie et al. investigated 56 RP cases reported in detail between 1980 and 2002 in the Japanese literature [9]. In the analysis, the PSL dose at the time of RP recurrence during steroid tapering was an average of 20.4 mg, and the average of the time to relapse was 12.8 months. Immunosuppressants, such as MTX, azathioprine, and CYA, have been proposed as steroid-sparing agents, but their efficacy has yet to be established. Petitdemange et al. investigated 177 patients with RP who were exposed to 247 lines of treatments [10]. In the present study, the pooled response rate to MTX was 54 % (n = 28). Oka et al. conducted a survey of 239 patients with RP in Japan [5]. In this study, MTX or CYA were used in 19.7 % and 8.4 % of patients with RP, in addition to oral PSL, with clinical response rates of 64.0 % and 73.7 %, respectively. In our case, in combination with PSL, CYA was able to render CRP, which is closely associated with disease activity in RP, and was negative for 7 months; however, MTX was not. Although some biologics have been used for the treatment of RP with airway involvement, there is insufficient evidence to support their general use. A French national study examining biologics in RP did not demonstrate any trends that could help guide use of biological agents [11]. In a study by Petitdemange et al., abatacept (n = 14), tocilizumab (n = 26), and tumor necrosis factor inhibitors (n = 92) were associated with the best outcomes and had pooled response rates of 72 %, 66 %, and 56 %, respectively [10].

Herein, we report a case of RP in which we compared the pathological features and degree of FDG accumulation. Both early and advanced lesions exhibited the same accumulation.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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