Clinical Case Report

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^{18}F-FDG PET/CT is an ideal imaging modality for the early diagnosis of relapsing polychondritis

A case report

JianJie Wang, MD, XiaoFei Liu, MD*, Chaoyu Pu, MD, Yan Chen, MD

Abstract

Background: Relapsing polychondritis (RP) is a rare autoimmune disease of unknown etiology that may affect multiple cartilage throughout the body.

Case report: We report on a middle-aged man presented with cough, chest tightness, and fever of unknown origin, 18F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) was performed. And the imaging shows multiple increased FDG accumulation in tracheobronchial tree and all intercostal cartilages, as well as in nasal, right auricule, laryngeal cartilage. Based on the findings, the diagnosis of RP was made.

Conclusion: Our case demonstrates that FDG PET/CT is an useful diagnostic tool to accurately determine the extent of inflammation throughout the body and to guiding the selection of a biopsy site.

Abbreviations: ^{18}F-FDG PET/CT = 18F-fluorodeoxyglucose positron emission tomography/computed tomography, CRP = C-reactive protein, IGRA = interferon-gamma release assay, MDP = Tc-99m methylene diphosphonate, RP = relapsing polychondritis.

Keywords: fluorodeoxyglucose, positron emission tomography/computed tomography, relapsing polychondritis

1. Introduction

Relapsing polychondritis (RP) is a rare autoimmune disease without clear process. It is characterized by recurrent inflammation and destruction of cartilages, especially hyaline cartilage, and tissues throughout the body with high risk of misdiagnosis. Airway involvement is present in up to 50% of patients with RP and is a major cause of morbidity and mortality.[1,2] The clinical course of RP is irregular, the early diagnosis of RP confront great challenges due to the lack of specificity in clinical and laboratory examinations.

2. Case report

A 55-year-old man presented with a 3-month history of cough with white sputum, chest tightness, weight loss, and 10-day history of low-grade fever. He had been previously diagnosed with pulmonary pneumonia and taking cephalosporin antibiotic in a local hospital, but the treatment was ineffective. Physical examination revealed no coarse crackles in both lungs, but swelled right auricles. Blood routine test: The white-cell count was 9.9×10^9/L, with 68.3% neutrophils, the C-reactive protein (CRP) level was 182.32 mg/dL (normal level <5), and Interferon-gamma Release Assay (IGRA) for tuberculosis showed both the tuberculosis-specific antigens were positive, antigen A and B were equal to 40. The tumor markers were negative, the results of sputum culture (mycobacterium non-tuberculous) were negative, the antinuclear factor level was normal.

On plain chest CT scan, trachea and bilateral main tracheobronchial wall were thickening and airway stenosis. Bronchoscopy showed bronchial mucosa were hypertrophy, the patient underwent a transbronchoscopic biopsy on bronchial mucosa. The pathological results revealed interstitial edema and inflammatory cell infiltration, chronic mucosa inflammation was diagnosed. Both PAS stain and acid fast staining were negative. Therefore, the patient underwent an ^{18}F-FDG PET/CT as a systemic search to explain fever of unknown origin and to exclude malignancy.

The FDG PET/CT images revealed intense symmetric radiotracer uptake in tracheobronchial tree and all intercostal cartilages, as well as in nasal, right auricle, laryngeal cartilage. The maximum standard uptake value (SUVmax) of the lesions were from 2.9 to 8.1, according to the criteria proposed by McAdam et al,[1] the diagnosis of RP was suggested (see Figs. 1 and 2). The patient underwent a cartilage biopsy on right auricle, and the result showed cartilaginous lymphocytic infiltration and degeneration, being consistent with the performance of relapsing polychondritis. The patient was treated with methylprednisolone that induced rapid improvement of clinical symptoms. Two months later, the laboratory data had returned to normal levels.

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The subjects have signed a written informed consent.

JW and XL are contributed equally to this article and should be considered co-first authors.

The authors declare that they have no conflict of interest.

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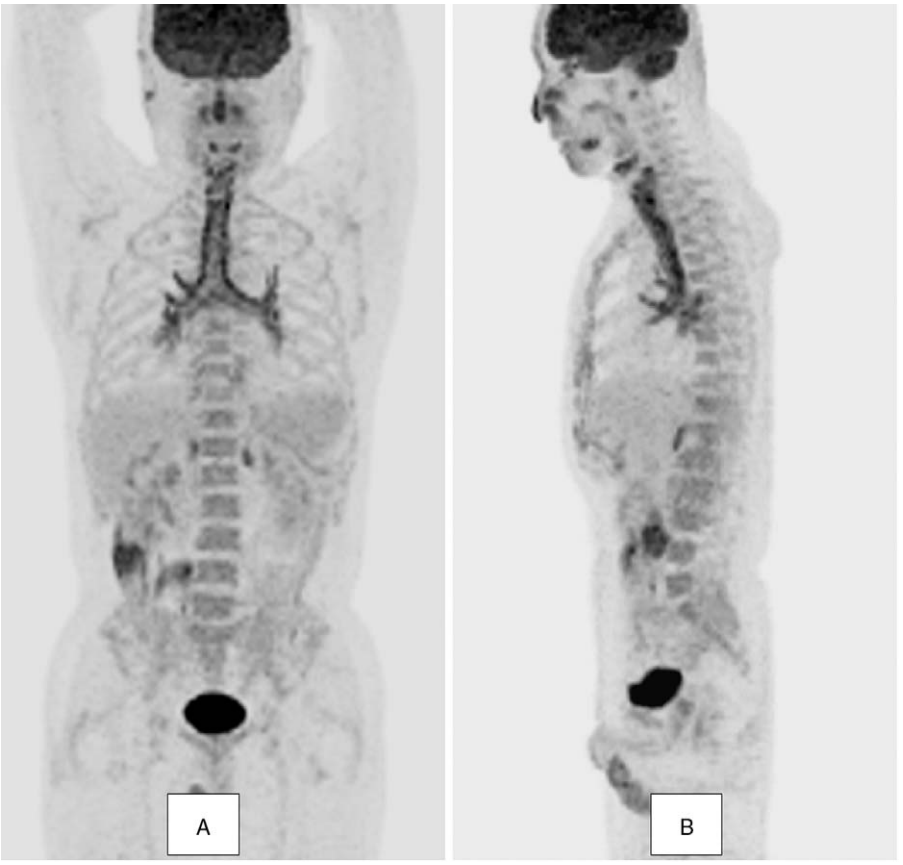

Figure 1. Maximum intensity projection (MIP) images of FDG PET showed intense FDG accumulation in the nasal cartilages, laryngeal, tracheobronchial tree, and right auricle (A, B). FDG was also accumulated in all intercostal cartilages (B). FDG PET = fluorodeoxyglucose positron emission tomography.

The present study was approved by the Ethics Committee of our hospital, and the patient information was anonymized and de-identified prior to analysis. It was not necessary that the patient must signed a consent form for this retrospective and anonymous research in our institute (Figure 3).

3. Discussion

RP is a rare autoimmune disease of unknown etiology with multiple system involvement. The typical pathological manifestations of RP are cartilage degeneration, necrosis, lysis, and inflammatory responses. The first symptom had no specific characteristics but did show complex clinical manifestations, such as fever, local pain during activity, fatigue, and loss of appetite, with possible additional organ-specific signs and symptoms, which poses a challenge to routine diagnosis.

Diagnostic criteria for RP were first proposed by McAdam et al in 1976.[1] In 1979, Damiani and Levine[2] extended and modified these diagnostic criteria. The current diagnostic criteria, which have been used extensively, are a modified version of the diagnostic criteria posted by McAdam et al in 1989.[3] The clinical manifestations of RP are related to the localization and severity of cartilage involvement. Respiratory involvement, usually the first symptom to emerge, has been rarely reported, included in approximately 18% of all reports. However, the ultimate respiratory involvement is as high as 50% or more.[4] Before the introduction of FDG PET/CT in the most recent years as the diagnostic reference criteria, the lack of specific-serum markers and characteristic imaging findings rendered early diagnosis of RP extremely challenging.

Because fluorodeoxyglucose (^{18}F-FDG) can be taken up by malignant tumor cells and inflammatory cells, Whole body ^{18}F-FDG PET/CT can be used in the imaging of inflammation and infected lesions. The hidden parts of inflamed tissue and infected lesions are detected during the early stages of disease by increasing the FDG uptake of the inflammatory lesions.[5] The patient in this study was misdiagnosed with pulmonary infection and received anti-infective treatment before admission to our hospital, without response to the treatment. Interferon-gamma Release Assay (IGRA) for tuberculosis showed both the tuberculosis-specific antigens were positive. Self-antibody spectrum was a negative. After autoimmune disease and typical acute infection were ruled out, it was posited that the patient's condition might be associated with a previous tuberculosis infection. However, the chest CT of the patient showed no clear tuberculosis lesions in both lungs, only tracheal and bronchial wall thickening and luminal patency. FDG PET/CT demonstrated intense symmetric FDG uptake in tracheobronchial tree, auricle, larynx, and all intercostal cartilages. Given the patient's medical history, the inflammation of the cartilaginous tissue was considered accordingly.

The pathological mechanisms underlying RP-induced airway disease include a high degree of inflammatory swelling of the cartilage and submucosal tissue during physical activity, causing airway stenosis. This inflammation causes both exudate retention and functional damage to the cilia that ordinarily remove bacteria from the airway, which exacerbate the severity of airway obstruction. Scar contracture during the late stage causes

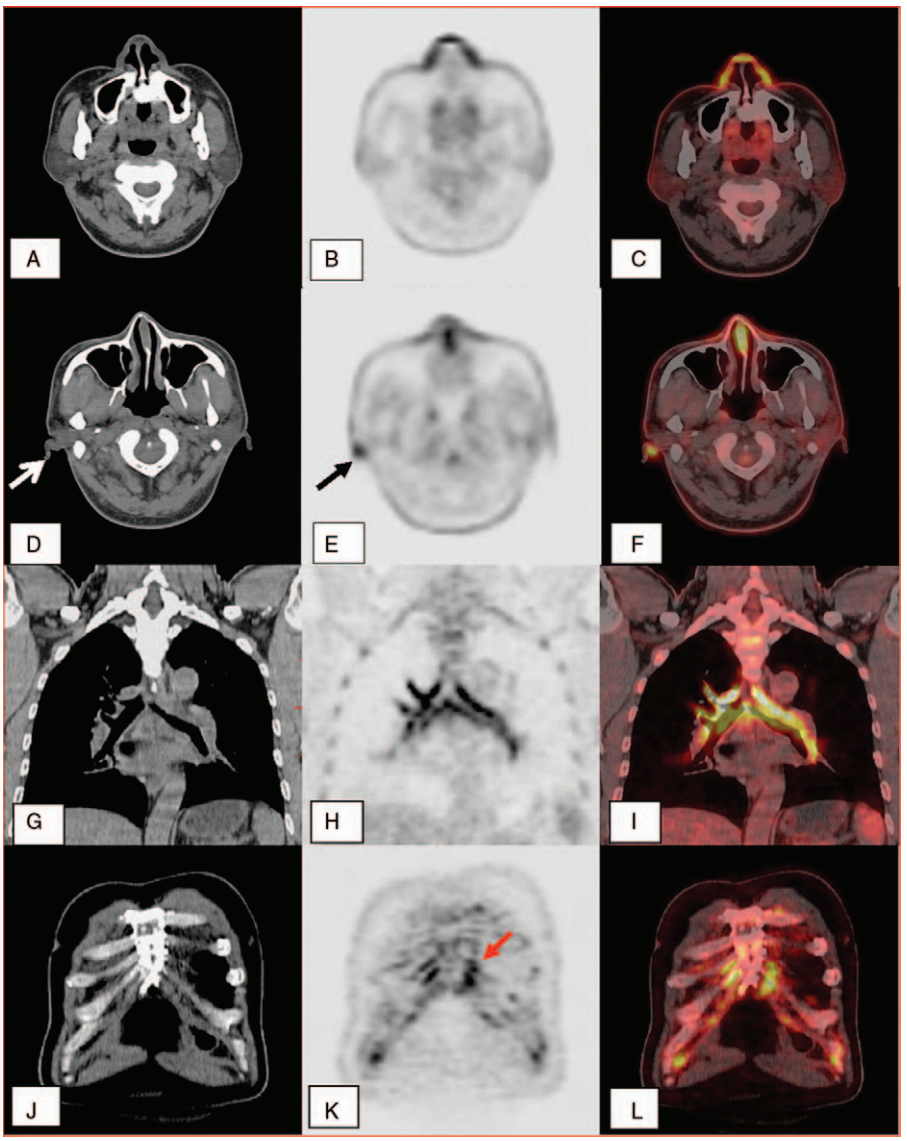

Figure 2. Unenhanced CT images (left column), PET images (middle column), and the PET/CT fusion images (right column) showed increased FDG uptake in the nasal cartilage (B, C), right auricular cartilage (E, black arrow), left and right main bronchi (H, I), and bilateral intercostal cartilges (K, red arrow, fusion image in L). Axial CT image also showed thickening of right auricular cartilage tissue (D, white arrow). CT = computed tomography, FDG = fluorodeoxyglucose, PET = positron emission tomography.

narrowing of the airway or lysis of the tracheal rings, resulting in tracheomalacia. Because of inflammatory cell infiltration into the cartilage, FDG PET/CT imaging can be used to discover systemically distributed cartilage inflammation in the early stage. Studies have shown that CT mainly demonstrates diffused thickening of the airway wall accompanied by stenosis. Calcification of tracheal cartilage is believed to be common feature of RP. It was visible on CT imaging and did not involve the membranous posterior wall of the trachea, which strongly suggests a clinical diagnosis of RP.

However, these require ruling out other diseases with similar manifestations, because diffuse increased FDG accummulation along the trachea and bronchi can also resulted from other etiology, including bronchial tuberculosis, acute bronchitis, tracheobronchial amyloidosis.[6] Therefore, the differential diagnosis is necessary when giving the final diagnosis of RP was made on the basis of FDG PET/CT findings.

Multidetector CT can clearly define the location and extent of the fixed airway narrowing and wall thickening. Tc-99m methylene diphosphonate (MDP) bone scintigraphy has also been used to assess RP. And, some case reported that MDP bone scintigraphy may be a valuable tool in the follow-up of RP. In addition, using F18 sodium flouride PET/CT in the evaluation of RP is also effective.[7] FDG PET/CT enables higher spatial resolution than do conventional nuclear medicine imaging techniques. Previously, only several limited studies have reported clinical value of FDG PET/CT imaging for the diagnosis of RP.[8,9] Most of the them well depicted tracheobronchial tree and intercostal cartilages involvement, but the nasal and larynx cartilages were not involved. More recently, many case reports showed that relapsing polychondritis were involved with multiple organs throughout body beside the tracheobronchial tree,[10,11] as was noted in our cases. Patients with RP who was associated with positive of tuberculosis-specific antigens by IGRA test were

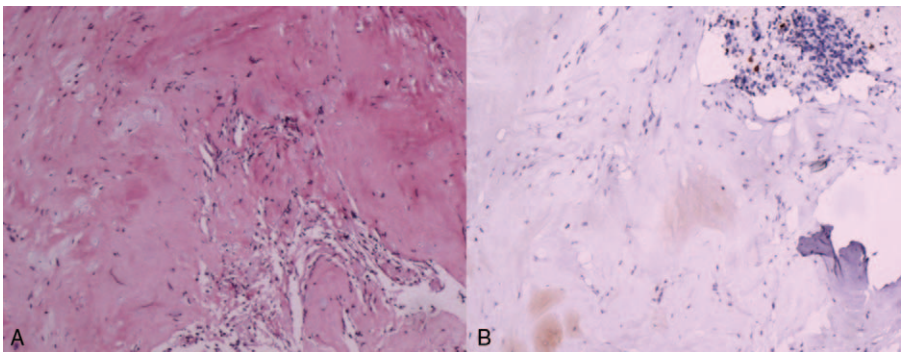

Figure 3. Routine HE staining in picture A (×100), and histopathology showed a few lymphocytic cell infiltration and degeneration of cartilaginous tissue. Immunohistochemical observation showed several CD3 positive cells in cartilage tissue. (See picture B, ×100).

rarely mentioned previously, as was noted in our case, which maybe mislead the clinician.

Our case demonstrates that FDG PET/CT has been proven to be a useful radiological tool to accurately determine the extent of inflammation throughout the body, especially the tracheobronchial tree involvement. Identification of airway involvement in the initial stages of RP is very important on FDG PET/CT, because early aggressive treatment may prevent irreversible cartilaginous destruction, it has considerable significance in the improvement of patient prognosis. Moreover, FDG PET/CT is very useful for providing a possibility for a suitable choice of biopsy sites, by localizing the sites of active inflammation.

In conclusion, although the diagnosis of RP is mainly established clinically, our case shows that FDG PET/CT imaging is a useful radiological tool to accurately determine the extent of inflammation throughout the body and to guiding the selection of a biopsy site. It may be of great value in improvement of patient's prognosis.

Acknowledgments

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