

## Usefulness of F-18 FDG PET/CT in a Case of Relapsing Polychondritis

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We report a case of relapsing polychondritis who underwent F-18 fluorodeoxyglucose (FDG) positron-emission tomography/computed tomography (PET/CT), and the F-18 FDG uptake in the larynx, central airway and rim cartilages was observed. After corticosteroid and immunosuppressant drug therapy, clinical findings were improved and F-18 FDG uptake almost disappeared. F-18 FDG PET/CT is a useful tool in the diagnosis of relapsing polychondritis and the follow-up after therapy. *Shinshu Med J 64 : 349—355, 2016*

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### I Introduction

Relapsing polychondritis is a rare autoimmune disease, characterized by multisystemic inflammatory lesions of cartilaginous tissues, such as the external ear, nose, larynx and tracheobronchial tree<sup>1)</sup>. The first diagnostic criteria for relapsing polychondritis, including auricular, nasal, and respiratory tract chondritis and so on, were proposed by McAdam et al.<sup>2)</sup>. The clinical symptoms caused by auricular chondritis are the most frequent, appearing in 80 % of patients with relapsing polychondritis. Laryngotracheobronchial and cardiovascular manifestations are life-threatening symptoms, for example, obstruction of the airway and ruptured aortic aneurysm<sup>1)</sup>. These various clinical findings are caused by polychondritis, so systemic evaluation is necessary in the diagnosis of relapsing polychondritis and the assessment of its severity.

We report a case of relapsing polychondritis in

which F-18 fluorodeoxyglucose (FDG) positron-emission tomography/computed tomography (PET/CT) demonstrated systemic cartilaginous inflammation, and report on the therapeutic responses to corticosteroid administration.

### II Case Report

A 47-year-old woman presented with a persistent cough with no response to antibacterial therapy for six months before admission to our hospital. Additionally, she had nasal redness and swelling for two months before admission, but this symptom had disappeared when she was admitted. She complained of severe cough, shortness of breath and stridor. She was a smoker, with a 25-year history.

Her height was 157 cm and weight was 55.7 kg. Blood pressure was 105/80 mmHg, pulse was 82/min, respiratory rate was 16/min, body temperature was 36.1 °C, and oxygen saturation (SpO<sub>2</sub>) was 96 % (room air). Both auricles were normal. She had a finger tremor and proximal interphalangeal joint tenderness. The physical examination revealed wheezes in the lung. Her physiological and blood examinations are shown in **Table 1**. The erythrocyte sedimentation rate (ESR) was 116 mm/hr and the C-

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Table 1 Laboratory examinations

TP	7.6 g/dl	Na	139 mmol/l	WBC	5800/ $\mu$ l	RF	negative
ALB	3.3 g/dl	K	4.0 mmol/l	NEU	67 %	ANA	negative
UA	18.8 mg/dl	Cl	103 mmol/l	LYM	24.0 %	ACPA	negative
CRE	0.87 mg	cCa	10.0 mg/dl	MON	7.1 %	MMP-3	70.5 ng/ml
AST	24 IU/l	KL-6	250 U/ml	EOS	0 %	AJo-1A	negative
ALT	12 IU/l	IgM	94 mg/dl	RBC	$3.53 \times 10^6/\mu$ l	PR3-ANCA	negative
$\gamma$ -GT	15 IU/l	IgG	2004 mg/dl	Hb	10.6 g/dl	MPO-ANCA	negative
T-Bil	0.54 mg/dl	IgE	265 IU/ml	HCT	31.6 %	AFP	3.1 ng/ml
ALP	321 IU/l	ESR	116 mm/1hr	PLT	$39.7 \times 10^4/\mu$ l	CEA	1.2 ng/ml
LDH	186 IU/l	CRP	9.27 mg/dl	sIL-2R	489 U/ml	SCC	0.8 ng/ml
AMY	75 IU/l	BNP	5.7 pg/ml			PIVKA-II	15 mAU/ml

TP Total protein ; ALB Albumin ; UA uric acid ; CRE creatinine ; AST aspartate aminotransferase ; ALT alanine aminotransferase ;  $\gamma$ -GT gamma guanosine triphosphate ; T-Bil total bilirubin ; ALP alkaline phosphatase ; LDH lactate dehydrogenase ; AMY amylase ; Na serum sodium ; K serum potassium ; Cl serum chloride ; cCa corrected serum calcium ; KL-6 sialylated carbohydrate antigen KL-6 ; IgM Immunoglobulin M ; IgG immunoglobulin G ; IgE immunoglobulin E ; ESR erythrocyte sedimentation rate ; CRP C-reactive protein ; BNP brain natriuretic peptide ; WBC white blood-cell ; NEU neutrophil ; LYM lymphocyte ; MON monocyte ; EOS eosinophil ; RBC red blood cell ; Hb hemoglobin ; HCT hematocrit ; PLT blood platelet ; sIL-2R soluble interleukin-2 receptor ; RF rheumatoid factor ; ANA antinuclear antibody ; ACPA anti-cyclic citrullinated peptide antibody ; MMP-3 matrix metalloproteinase-3 ; AJo-1A anti Jo-1 antibody ; PR3-ANCA proteinase-3 anti-neutrophil cytoplasmic antibody ; MPO-ANCA myeloperoxidase anti-neutrophil cytoplasmic antibody ; sIL-2R soluble interleukin-2 receptor ; AFP  $\alpha$ -fetoprotein ; CEA carcinoembryonic antigen ; SCC squamous cell carcinoma antigen ; PIVKA-II protein induced by vitamin K antagonist-II

Table 2 Pulmonary function tests

FVC	2.22 l	FEV <sub>1</sub> /FVC	55.9 %	FRC	2.48 l (138.5%)
%FVC	81.0 %	PEFR	1.99 l/s (34.4%)	RV	1.68 l (119.1%)
FEV <sub>1</sub>	1.24 l	V50	0.85 l/s (24.3%)	TLC	4.21 l (106.9%)
%FEV <sub>1</sub>	53.4 %	V25	0.56 l/s (38.9%)	DLco	17.25 ml/min/mmHg
				%DLco	80.0 %

FVC forced vital capacity ; %FVC % forced vital capacity ; FEV<sub>1</sub> forced expiratory volume in 1 second ; % FEV<sub>1</sub> % predictive forced expiratory volume in 1 second ; PEFR peak expiratory flow rate ; V50 expiratory flow rate at 50 % lung volume position ; V25 expiratory flow rate at 25 % lung volume position ; FRC functional residual capacity ; RV respiratory volume ; TLC total lung capacity ; DLco diffusing capacity for carbon monoxide ; %DLco % predictive diffusing capacity for carbon monoxide

reactive protein (CRP) level was 9.27 mg/dl (normal level < 0.1). The white blood-cell count was 5800/ $\mu$ l. Antinuclear factor was normal and matrix metalloproteinase-3 (MMP-3) was also normal (70.5 ng/ml). Pulmonary function tests showed a low FEV<sub>1</sub>/FVC value (55.9 %, **Table 2**). The flow-volume curve (**Fig. 1**) revealed prominently decreased peak flow. These results were compatible with obstructive pulmonary dysfunction due to central airway stenosis.

After admission she underwent a chest X-ray examination, which revealed stenosis of the trachea and bilateral main bronchi. Neck and chest CT showed calcifications in the bilateral ear canals, abnormal tissue around thyroid cartilage, swelling of costal cartilages, and thickening of bronchial cartilage. We considered the differential diagnosis, such as relapsing polychondritis, granulomatous polyangiitis, tracheal tumor, and bronchial asthma, and performed a biopsy on the lesions in the bron-

Fig. 1 The flow-volume curve revealed central airway stenosis.

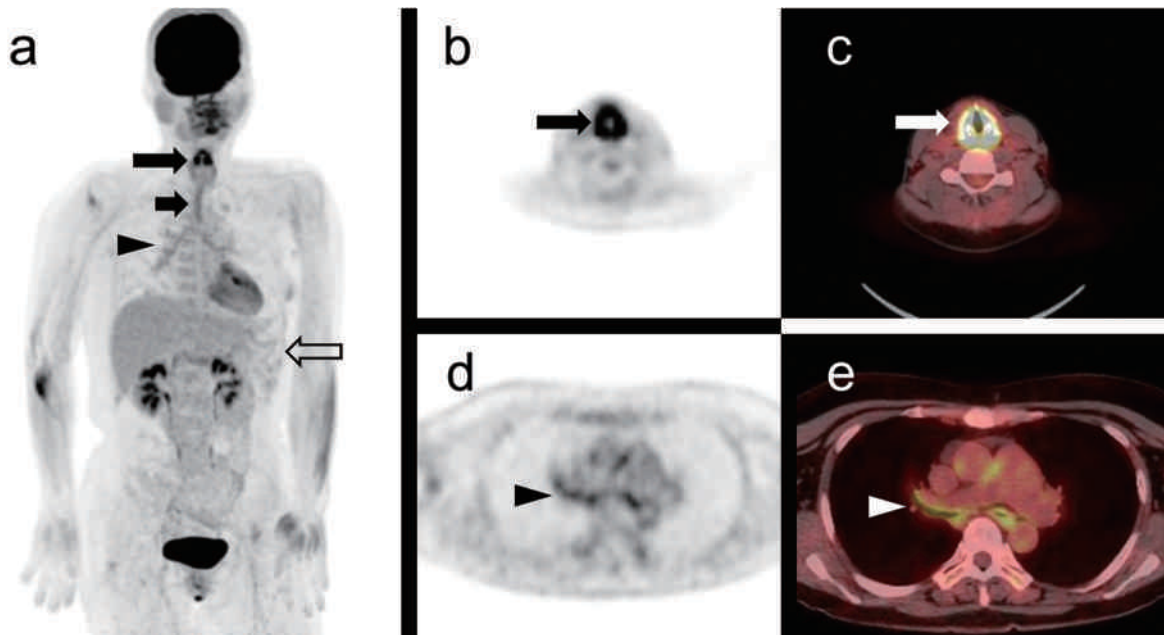
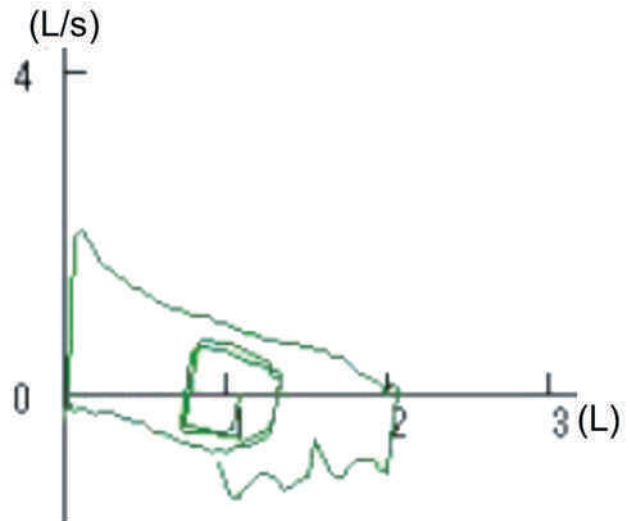


Fig. 2 Maximum intensity projection (MIP) image of FDG PET in the supine position showed FDG uptake in the larynx (long arrow), trachea (short arrow), main bronchi (arrowhead) and rim cartilages (open arrow) (a). Axial PET (b) and fusion images (c) showed high FDG uptake in the larynx (arrows). Axial PET (d) and fusion images (e) showed moderate FDG uptake in the main bronchi (arrowheads).

chial wall by bronchoscopy, however, the specimen did not show inflammation of bronchial cartilage. Next, FDG PET/CT was performed to exclude malignant lesions such as tracheal neoplasms and to attempt to find the extent of other inflammatory lesions in order to determine for the focus of the biopsy site. She fasted for 15 hours before receiving an intravenous injection of 190 MBq F-18 FDG.

Then, 60 min after injection, attenuation correction CT (AC-CT) and emission scans were obtained from the upper thigh to the head using a PET/CT scanner (Biograph mCT-S(40) 4R, Siemens, Germany). Maximum intensity projection (MIP) images of FDG PET showed increased FDG accumulation in the larynx, trachea, main bronchi, and some rim cartilages (**Fig. 2**). The maximum standard uptake

value ( $SUV_{max}$ ) of the larynx at 60 min was 12.6. In addition, we performed bone scintigraphy with technetium-99m hydroxymethylene diphosphonate to evaluate for cartilaginous inflammation, which showed no abnormal accumulation (Fig. 3). As a result, we identified the inflammation in the bronchial cartilage by FDG PET/CT and decided to perform a biopsy again from the bronchial wall by bronchoscopy. We obtained cartilage from the bronchial wall and this time the pathological examination revealed inflammatory cell accumulation in the cartilage. We referred to the diagnostic criteria of relapsing polychondritis proposed by Damiani et al.<sup>3)</sup>. The criteria included clinical findings (bilateral auricular chondritis, nasal cartilage inflammation, respiratory tract chondritis, non-erosive sero-negative polyarthritits, ocular inflammation, and audiovestibular involvement), histologic confirmation, and positive response to corticosteroids or dapson. The diagnosis of relapsing polychondritis was based either on three clinical findings or at least one clinical finding and a positive histological confirmation, or two clinical findings and a positive response to corticosteroids or dapson. In



Fig. 3 Planar image of bone scintigram using technetium-99m hydroxymethylene diphosphonate showed no abnormal accumulation in the larynx, trachea, main bronchi and rim cartilages.

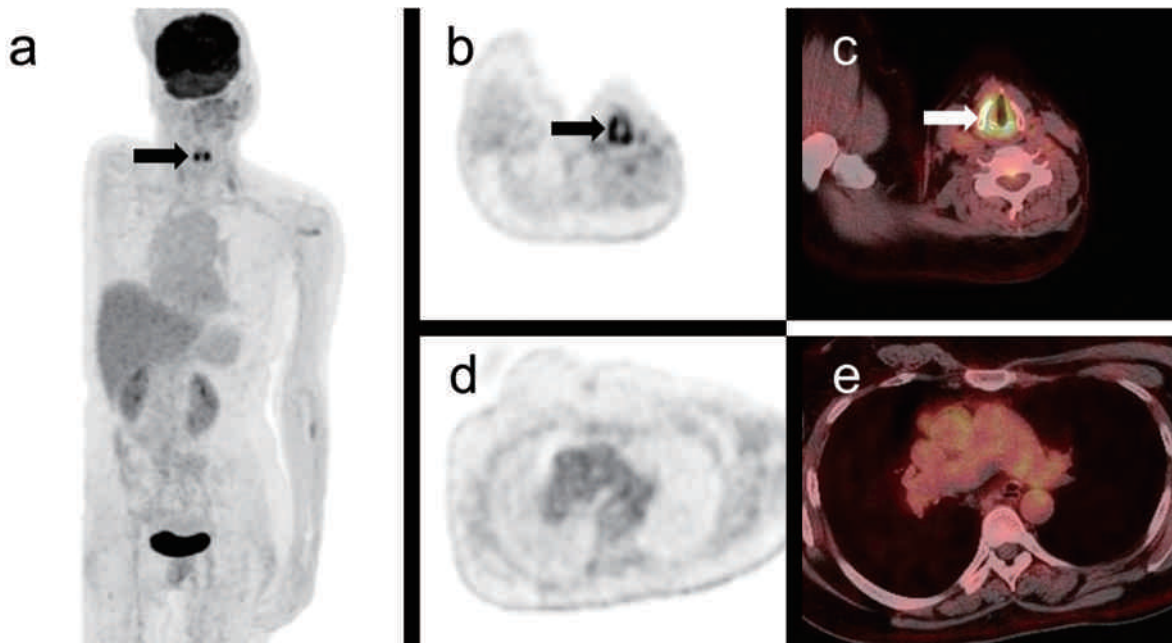


Fig. 4 Maximum intensity projection (MIP) image of FDG PET in the right lateral decubitus position showed decreased FDG uptake in the larynx (arrow), trachea, main bronchi and rim cartilages (a). Axial PET (b) and fusion images (c) showed moderate FDG uptake in the larynx (arrows). Axial PET (d) and fusion images (e) showed disappearance of FDG uptake in the main bronchi.



this case, the patient was compatible with these criteria because she had one clinical finding (respiratory tract chondritis) and histologic confirmation.

After diagnosis, she received corticosteroid and immunosuppressant therapy. Her persistent cough gradually improved with the therapy. The ESR decreased to 29 mm/hr and the CRP level decreased to 0.01 mg/dl. Five months after the therapy, the second FDG PET/CT showed that the FDG accumulations in the cartilaginous tissues had almost disappeared (**Fig. 4**). Additionally, the CT images showed that the thicknesses of the airway wall and rim cartilages were improved. Accordingly, the doses of corticosteroid and immunosuppressant were gradually tapered.

### III Discussion

Relapsing polychondritis is an uncommon disorder that mainly involves systemic cartilaginous tissues. In particular, auricular chondritis and polyarthritis are found in 80 % of patients with this disease<sup>1</sup>. Laryngotracheobronchial involvement is life-threatening due to obstruction of the airway, so assessment of the involvement of respiratory organs is important for patients<sup>1</sup>. In relapsing polychondritis, there are no specific laboratory data for diagnosis. Laboratory data for inflammatory activity, such as CRP and ESR, are frequently used for the evaluation of disease activity, however, elevation of these factors may be caused by nonspecific inflammatory lesions.

High-resolution CT is useful for evaluation of the respiratory tract, such as the thickness of bronchial cartilage, airway stenosis, and calcification of cartilaginous tissues<sup>4</sup>. In addition, Lee et al. suggested that the important findings in diagnosing relapsing polychondritis were tracheomalacia and air trapping with dynamic expiratory CT<sup>5</sup>. However, this method alone does not enable evaluation of inflammatory activity throughout the body. In the patient we needed to perform a systemic evaluation of active inflammation in order to determine the biopsy site, so CT was inadequate for our purpose.

Magnetic resonance imaging (MRI) is used for the

evaluation of focal inflammation of cartilage and arthritis, particularly in detecting perichondrial and chondroepiphyseal inflammation in the early stages of the disease process<sup>6</sup>. However, this method requires quite a long examination time, and as our patient was unable to maintain the supine position for long because of dyspnea, we were unable to perform the necessary MRI examination in the present case.

In contrast, radionuclide imaging is used for detection of chondritis, not only for focal lesions but also for systemic inflammation in relapsing polychondritis. Bone scintigraphy with technetium-99m methylene diphosphonate shows increased accumulation in cartilaginous inflammation<sup>7,8</sup>. Borg et al. suggested that bone scintigraphy showed high accumulations such as extensive calcifications of rim cartilages, and was useful for selecting the site of biopsy<sup>7</sup>. However, the accumulation of radioisotope tracer depends on bone metabolism and amounts of calcification. Our case showed no abnormal uptake at calcifications of the bilateral ear canals because of the slight amounts present. In addition, bone scintigraphy might not properly depict the sites of cartilaginous inflammation. Gallium scintigraphy is useful in determining inflammatory lesions in relapsing polychondritis<sup>9</sup>. Okuyama et al. reported gallium scintigraphy was valuable for evaluating inflammatory sites such as subglottic lesions<sup>10</sup>. They also reported that gallium scintigraphy might be superior to bone scintigraphy in examining for lesions unrelated to bone. However, this method has a lower spatial resolution than FDG PET/CT. Therefore, the accumulation at small inflammatory lesions, such as in the larynx and bronchial cartilage, might not be seen with this method.

FDG PET/CT, which is mainly used in the diagnosis of malignant lesions, was reported to be useful in the evaluation of inflammatory tissues<sup>11,12</sup>. Nishiyama et al. reported the first case of relapsing polychondritis with FDG PET examination<sup>13</sup>. They suggested that FDG PET might be a more powerful tool than conventional radionuclide imaging such as gallium scintigraphy in the diagnosis of relapsing

polychondritis because of its higher spatial resolution. In addition, some reports assessed the usefulness of FDG PET/CT in the diagnosis of relapsing polychondritis and monitoring the therapeutic response<sup>14)15)</sup>. Unfortunately, the health insurance system in Japan does not yet support the use of FDG PET/CT in the diagnosis of inflammatory diseases. In addition, evidence from FDG PET/CT is not necessarily required in the diagnostic criteria of relapsing polychondritis. However, FDG PET/CT is well known to be useful in the diagnosis of inflammatory lesions<sup>11)12)</sup>. In particular, it is a powerful tool for detecting active inflammatory lesions and for determining the site of biopsy for diagnosis.

FDG PET/CT clearly showed systemic inflammatory lesions, such as in the larynx, bronchi and rim cartilages in the present case, which were not detected by bone scintigraphy. In addition, this method helped to determine the site of biopsy in this case. The change in the accumulation of FDG furthermore helped in the evaluation of the therapeutic effectiveness of corticosteroid administration.

In conclusion, FDG PET/CT was a useful radiological tool for the diagnosis of relapsing polychondritis and the evaluation of the therapeutic response in the present case.

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