Utility of FDG-PET/CT in the diagnosis of IgG4-related diseases

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Abstract

Objective

The purpose of this work is to evaluate the usefulness of ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging in management of IgG4-related disease (IgG4-RD) by retrospective analysis of PET/CT results in IgG4-RD patients.

Methods

Twenty-six patients diagnosed with IgG4-RD according to Japanese diagnostic criteria who underwent ^{18}F-FDG-PET/CT scans in the PLA General Hospital from January 2010 to May 2015 were enrolled in the study. Their clinical presentations and ^{18}F-FDG-PET/CT findings were analysed.

Results

A total of 26 patients (20 men; 6 women) with a mean age of 53.8 years (range 35–71 years) and mean treatment course of 7.1 months (range 0.33–72 months) who underwent ^{18}F-FDG-PET/CT scans were analysed. CRP was relatively low in all patients (mean 0.79 mg/dl). ^{18}F-FDG-PET/CT images confirmed that two or more organs were involved in all patients, and average SUV values for involved organs was 4.14 (range 0.30–8.78). Eleven patients were misdiagnosed with submandibular tumours, pancreatic cancer, pancreatitis, pulmonary interstitial fibrosis, retroperitoneal fibrosis or systemic vasculitis prior to ^{18}F-FDG-PET/CT imaging.

Conclusion

^{18}F-FDG-PET/CT imaging is a useful tool for the differential diagnosis of IgG4-RD, and for mapping involved organs, guiding biopsy, and monitoring treatment response.

Key words

FDG-PET/CT, IgG4-related disease, autoimmune pancreatitis, diagnosis, standardised uptake value

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Received on March 22, 2015; accepted in revised form on September 9, 2015.

Competing interests: none declared.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognised relapsing-remitting immune-mediated fibro-inflammatory disease comprised of a collection of disorders. Commonly shared features include enlargement or nodular hyperplasia in involved organs due to IgG4-positive lymphoplasmacytic infiltration and variable degrees of fibrosis. The pathogenesis of IgG4-RD is poorly understood. Various organs known to be affected include pancreas, lacrimal/salivary glands, retroperitoneum, biliary tract, kidneys, thyroid gland, and pituitary gland, and vascular and chronic inflammation are documented to occur in certain tissues (1, 2). Clinical symptoms are heterogeneous, which can easily lead to misdiagnosis or missed diagnosis.

Several imaging modalities can provide complementary data to address specific clinical concerns associated with IgG4-RD. These include contrast-enhanced computed tomography (CT) and magnetic resonance (MR) imaging for pancreatic parenchymal lesion localisation and characterisation, endoscopic retrograde and magnetic resonance cholangiopancreatography (ERCP and MRCP) to assess ductal involvement, and more recently, positron emission tomography (PET) imaging to assess extra-pancreatic sites of involvement. Although CT and MR imaging play an important role in diagnosing IgG4-RD, their imaging findings are usually nonspecific. At CT, involved organs may be enlarged or less attenuated; with T2-weighted MR imaging, organs may have relatively low signal intensity due to increased cellularity and fibrosis (3, 4). In addition, imaging modalities provide limited evaluation of the whole body as imaging is often targeted to a local lesion, especially MRI (5). Therefore, the usefulness of imaging for identifying involved organs that are distributed throughout the body is quite limited.

Whole-body ^{18}F-FDG-PET/CT is an imaging technique commonly used in clinical oncology (6, 7) and it is gaining attention as a useful tool for evaluating the activity of several inflammatory diseases such as sarcoidosis, atherosclerosis, Takayasu's disease, inflammatory bowel disease and rheumatoid arthritis (8). ^{18}F-FDG-PET/CT has been used for assessing inflammation of the head and neck glands (5, 9), prostate (10), and retroperitoneal fibrosis (11) in patients diagnosed with IgG4-RD. ^{18}F-FDG-PET/CT can be used to differentiate benign from malignant findings and to determine optimal biopsy site diagnosis, as well as to monitor response to steroid therapy (12-16). Here we describe a retrospective analysis for evaluating the utility of ^{18}F-FDG-PET/CT for IgG4-RD management by analysing ^{18}F-FDG-PET/CT findings in patients with IgG4-RD.

Methods

Patients

All patients diagnosed with IgG4-RD in our hospital according to Japanese comprehensive diagnostic criteria for IgG4-RD (17) from January 2010 to February 2014 were retrospectively reviewed. Only patients who underwent ^{18}F-FDG-PET/CT imaging (n=26) were included in this study.

^{18}F-FDG-PET/CT imaging

A Siemens Biograph 64 PET/CT (52 LSO crystal and 64-layer spiral CT) was used for imaging. ^{18}F-FDG (radiochemical purity >95%) was provided by PET Centre of PLA General Hospital. Subjects were instructed to fast for more than 6 h, and 3.70–5.55 MBq/kg of ^{18}F-FDG was injected intravenously. Participants were allowed to rest in a quiet and warm lobby for 45–60 min. CT was acquired to perform transmission correction for PET at 120 kV and 170 mA with a scan time of 18.67–21.93 s and a slice thickness of 3 mm. After CT scanning, whole-body PET scan was performed at 2.5 min per bed position. CT images were reconstructed using the conventional filtered back projection method. PET image reconstruction was performed using the TureD workstation for post-processing, and images in the axial, coronal, or sagittal planes and three-dimensional projection images were formed.

This retrospective study did not include patient intervention. Thus, no human subject approval was required from the Institutional Review Board Committee.

Table I. Clinical characteristics of 26 patients with IgG4-RD.

Patient ID#	Disease course (month)	Serological tests						Involved organs										
		Syndrome	Misdiagnosis	IgG4 (mg/dl)	IgG (mg/dl)	CRP (mg/dl)	ANA	Pancreas	Parotid gland	Sub-mandi-bular gland	Lymph node	RPF	IP	Biliary duct	Liver	Artery	Orbit	Acces-sory nasal sinuses
1	2	Right submandibular swelling	Submandibular tumour	441	2270	1.6	—	—	—	+	+	—	+	—	—	—	—	—
2	1	Abdominal pain, jaundice	N/A	1180	1190	0.1	—	+	—	—	+	—	—	—	—	—	—	—
3	1	Abdominal pain, jaundice	N/A	2811	3950	1.38	—	+	—	—	+	—	—	—	—	+	—	—
4	12	Abdominal pain	N/A	1410	3724	0.36	—	+	—	—	—	—	—	—	—	+	—	—
5	1	Abdominal pain, jaundice	Pancreatic cancer	868	1420	1.8	—	+	—	—	+	—	—	+	+	—	—	—
6	1	Fever, rash	Interstitial pneumonia	363	907	0.82	—	—	—	—	+	—	+	—	—	—	—	—
7	2	Abdominal pain	N/A	489	1120	1.5	—	+	—	—	—	+	—	—	—	+	—	—
8	24	Abdominal pain	N/A	1020	2860	0.1	—	+	—	+	+	—	—	—	—	—	—	—
9	3	Fever	N/A	2130	3150	1.6	—	—	—	—	+	—	+	—	—	—	—	—
10	0.75	Abdominal pain, jaundice	Retroperitoneal fibrosis	254	1460	0.42	1:160	—	—	—	+	+	—	—	—	+	—	—
11	1	Fever	N/A	370	1600	1.32	1:160	—	—	—	+	—	+	—	—	—	—	—
12	12	Abdominal pain, jaundice	Pancreatitis	271	2320	0.1	—	+	—	—	+	—	—	—	—	—	—	—
13	12	Abdominal pain	Retroperitoneal fibrosis	243	980	0.74	—	—	—	—	+	+	—	—	—	—	—	—
14	48	Fever	Interstitial pneumonia	1420	1520	0.1	1:320	—	+	—	—	—	+	—	—	—	—	—
15	1	Abdominal pain, jaundice	Pancreatitis	352	1770	0.1	—	+	—	—	+	—	—	—	—	—	—	—
16	4	Abdominal pain	N/A	256	1510	0.62	—	—	+	—	—	+	+	—	—	+	—	—
17	2	Skin, sclera yellow	Pancreatic cancer	374	1110	0.35	—	+	—	—	+	—	—	—	+	—	—	—
18	1	Bulging eyes	N/A	929	1190	0.34	—	—	—	+	+	—	—	—	—	—	+	+
19	7	Swelling of the eyelids	Systemic vasculitis	2570	3160	0.35	—	—	—	—	+	—	+	—	—	—	—	+
20	3	Abdominal pain, jaundice	Pancreatitis	1180	2130	0.3	—	+	—	+	—	—	—	+	—	—	—	—
21	12	Abdominal pain	N/A	//	//	0.2	—	+	—	—	—	+	—	+	—	—	—	—
22	1	Abdominal pain	N/A	//	//	0.1	—	+	—	—	+	—	—		—	—	—	—
23	1	Abdominal pain	N/A	3770	3890	0.35	—	+	—	—	—	—	—	+	—	—	—	—
24	1	Abdominal pain	N/A	367	1460	0.4	—	+	—	—	+	—	—	—	—	—	—	—
25	0.33	Abdominal pain	N/A	//	//	0.3	—	+	—	—	+	—	—	+	—	—	—	—
26	72	Abdominal pain, jaundice	N/A	3220	4360	3.34	—	+	+	+	+	—	—	—	—	—	—	—

Table II-1. The SUVmax values of the involved organs in the IgG4-RD patients with pancreatic involvement.

	SUVmax of involved organs																		
											Lymph nodes								
Patient ID#	Pancreas	Parotid gland	Submandibular gland	Biliary duct	Liver	RPF	IP	Artery	Orbit	Accessory nasal sinuses	Neck	Axillary	Submandibular	Hilar and Mediastinal	Parasternal	Retroperitoneum	Inguinal	Mesenteric
2	3.43	—	—	—	—	—	—	—	—	—	—		2.1	2.3	—	—	—	—
3	3.82	—	—	—	—	—	—	+	—	—	—	1.84		6.35	—	2.48	—	—
4	4.33	—	—	—	—	—	—	+	—	—	—	—	—	—	—	—	—	—
5	5.6	—	—	5.6	—	—	—	—	—	—	3.8			3.1	4.0	—	—	—
7	4.8	—	—	—	—	6.0	—	3.2	—	—	—	—	—	—	—	—	—	—
8	5.5	—	+	—	—	—	—	—	—	—	—	3.5	—	—	—	—	—	—
12	3.7	—	—	—	—	—	—	—	—	—	—	—	—		—	—	4.4	—
15	3.0	—	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—
17	3.6	—	—	—	2.91	—	—	—	—	—	—	—	—	4.1	—	—	—	—
20	8.87	—	—	+														
21	2.46	—	—			1.2												
22	5.7	—	—	+							+							
23	2.9	—	—															
24	4.6	—	—	+										6.4				2
25	5.18	—	—											2.46				
26	6.4	9.1	9.1								3	4.3				5.7	3.5	
Mean	4.62	9.1	9.1	5.6	2.91	3.60		3.2			3.63							
SD	1.61	—	—	—	—	3.39		—			1.42							

Table II-2. The SUVmax values of the involved organs in the IgG4-RD patients without pancreatic involvement.

	SUVmax of involved organs																		
											Lymph nodes								
Patient ID#	Pancreas	Parotid gland	Submandibular gland	Biliary duct	Liver	RPF	IP	Artery	Orbit	Accessory nasal sinuses	Neck	Axillary	Submandibular	Hilar and Mediastinal	Parasternal	Retroperitoneum	Inguinal	Mesenteric
1	—	—	5.58	—	—	—	4.4	—	—	—	—	—	—	—	—	5.76	—	—
6	—	—	—	—	—	—	1.88	—	—	—	—	—	—	—	—	—	—	3.6
9	—	—	—	—	—	—	1.83	—	—	—	—	—	—	2.49	—	—	—	—
10	—	—	—	—	—	4.89	—	+	—	—	—	—	—	1.98	—	—	—	—
11	—	—	—	—	—	—	8.2	—	—	—	—	—	—	3.7	—	—	—	—
13	—	—	—	—	—	4.87	—	—	—	—	1.98	—	—	4.3	—	—	—	—
14	—	3.0	—	—	—	—	0.9	—	—	—	—	—	—	—	—	—	—	—
16	—	+	—	—		5.5	2.4	+	—	—	—	—	—	—	—	—	—	—
18	—	—	+	—	—	—	—	—	4.3	5.2	2.3	—	1.2	—	—	—	—	—
19	—	—	—	—	—	—	0.3	—	4.9	6.5	5.4	—	—	7.9	—	—	—	—
Mean	—	3.0	5.58	—	—	5.09	2.84	—	4.60	5.85					3.69			
SD	—	—	—	—	—	0.36	2.69	—	0.42	0.92					2.02			

Statistical analysis

Baseline characteristics of patients are summarised in Table I with mean values for continuous variables. A student's *t*-test was used to analyse gender, age, duration of disease, and SUV_{max}.

Results

Patients' characteristics

Patient characteristics are shown in Table I. Our study consisted of 26 patients (20 men, 6 women) with a mean age of 53.8 years (range 35–71 years) and a mean course of disease 7.1 months (range 0.33–72 month). Eleven patients had been misdiagnosed prior to ^{18}F-FDG-PET/CT examination. Histopathological examinations were performed to confirm the diagnosis of IgG4-RD in 21 patients, but not performed in the remaining 5 patients either because the patients declined the assessment or because the involved organs were difficult to biopsy.

PET/CT finding in previously misdiagnosed IgG4-RD patients

Ten patients had been misdiagnosed prior to ^{18}F-FDG-PET/CT examination (Table I). ^{18}F-FDG-PET/CT imaging identified two or more involved organs in these patients. The mean maximum standard uptake value (SUV_{max}) of the

involved organs was 4.14 (range 0.30–8.78). After serum IgG4 testing and histopathological examination, these patients were diagnosed with IgG4-RD.

Serological testing

For all 26 patients, IgG and IgG4 values were 1,958.47±964.65 mg/dl and 934.26±807.66 mg/dl (mean ± SD), respectively. The ratio of IgG4/IgG was 46.1±28.1%. CRP was 0.79±0.64 mg/dl (mean ± SD). Thirteen patients had normal CRP values.

Imaging evaluation on organ involvement

Abnormal ^{18}F-FDG uptake was observed in the pancreas (autoimmune pancreatitis, n=16), salivary gland (2 parotid and 2 submandibular), lymph node (n=18), retroperitoneal fibrosis (n=5), pulmonary interstitial fibrosis (n=7), biliary tract (n=8), and arteries (n=5). Two patients had four organs involved; 7 patients had 3 organs involved; and 9 patients had 2 organs involved. SUV_{max} values of each involved organ are listed in Tables II-1, II-2.

Some lesions did not have high ^{18}F-FDG uptake on PET/CT images and were detected by either ultrasound imaging (patients 8 and 16 with submandibular involvement, and patients 3, 4, 10, and 16 with arterial involvement) or pulmonary CT imaging (patient 15 with mediastinal lymph node involvement).

IgG4-related pancreatic lesions

Sixteen patients had autoimmune pancreatitis (AIP, IgG4-related pancreatitis). Diffusely elevated ^{18}F-FDG uptake was observed in the pancreas (Fig. 1), with an average SUV_{max} of 4.62 (range 2.48–8.87). Most of these patients had abdominal pain. Then, we selected 19 patients with pancreatic cancer who also had abdominal pain. ^{18}-FDG uptake in patients with pancreatic cancer was focal (Fig. 2), and SUV_{max} values were 5.84 (3.1–17.4), which were significantly higher than in patients with AIP (p<0.05; Table III). A receiver operating characteristic (ROC) analysis indicated that the ^{18}FDG-PET scan had a diagnostic sensitivity of 73.7%, a specificity of 64.7%, and an area under the curve of 0.72 (CI: 0.549~0.892) for IgG4-related pancreatic lesions when the SUV_{max} was 4.9 (Fig. 3).

Fig. 1. Diffusively elevated ^{18}F-FDG uptake in pancreas of patient 8.

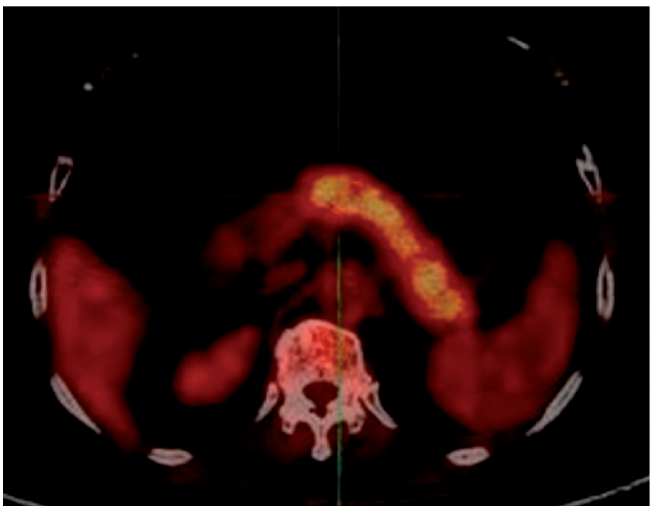

Fig. 2. Focally elevated 18-FDG uptake in pancreatic cancer

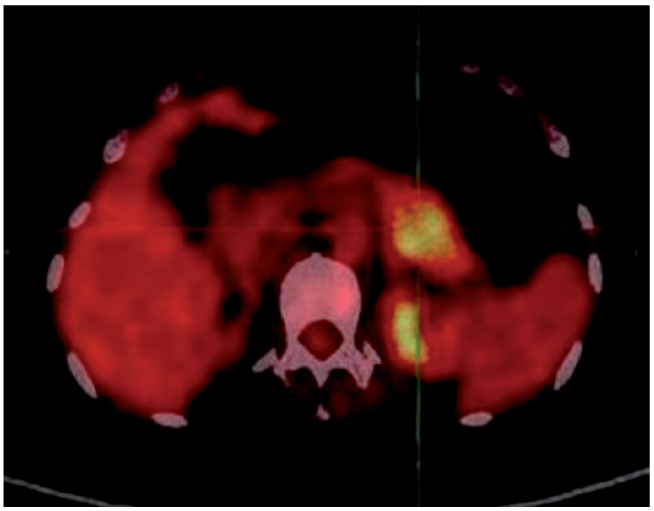

Table III. IgG4-RD of autoimmune pancreatitis compared to patients with pancreatic cancer.

	Gender (Male/Female)	Age (years)	Duration of disease (months)	SUVmax
Autoimmune pancreatitis	15/1	54.69 ± 11.63	6.22 ± 8.12	4.20± 0.92
Pancreatic cancer	13/6	58.17 ± 12.98	3.00 ± 2.45	6.14± 1.75
p-value		0.788	0.211	0.035

IgG4-related extra-pancreatic lesions

In addition to ^{18}F-FDG-avid lesions related to pancreatic disease, various extra-pancreatic lesions were observed in parotid (n=3) and submandibular glands (n=4), liver (n=1), biliary tract (n=8), arteries (n=5) and lymph nodes (n=18), as well as retroperitoneal fibrosis (n=5), pulmonary interstitial fibrosis (n=7). SUV_{max} values of each involved organ are provided in Table II-2 and these data are not significantly different among involved organs. However, among patients with submandibular and arterial involvement, three (6, 16, and 18) and four patients (3, 4, 10, and 16) did not have elevated ^{18}F-FDG uptake. In summary, ^{18}F-FDG-PET/CT can detect multiple abnormal lymph nodes throughout the body which can facilitate a diagnosis of IgG4 RD.

Discussion

IgG4-RDs are diseases with multiple organ involvement characterised by elevation of serum IgG4, IgG4-positive plasmacyte infiltration and fibrosis in

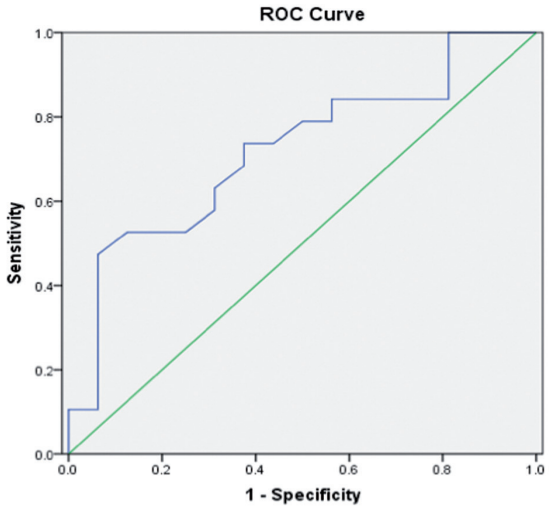

Fig. 3. ROC curve for SUV_{max}.

involved organs. Due to fibrosis and chronic inflammation, organs become hyperplastic and swollen, and this leads to compression, obstruction or dysfunction of surrounding organs. IgG4-RD can affect multiple organs and tissues, so the clinical picture is highly heterogeneous. In 2011, a Japanese group proposed diagnostic criteria and a consensus was reached to use these criteria for diagnosis of IgG4-RD: (1) Physical examinations indicated diffusive or focal enlargement and lumps in one or more organs; (2) elevated serum IgG4 (>1,350 mg/L); (3) histopathological features including (a) typical tissue fibrosis or sclerosis; (b) lymphocyte infiltration; and significant IgG4-positive plasmacyte infiltration (the ratio of IgG4-positive plasmacytes >40% and more than 10 IgG4-positive plasma cell/HPFs). When criteria 1–3 are met, the diagnosis of IgG4-RD is definite when criteria 1 and 3 are met IgG4 is possible and when criteria 1 and 2 are met the diagnosis is probable. Sometimes a single organ is involved and the abovementioned criteria do not justify a diagnosis. Then, diagnostic criteria for organ-specific IgG4-RD manifestation should be considered. IgG4-RD is a systemic disorder associated with characteristic lesions with mass-forming involvement in multiple organs. Resulting lesion configurations in different organs complicate the diagnosis because they mimic malignancy.

^{18}F-FDG-PET/CT is a whole-body functional imaging modality which reveals lesion distribution and quantitates FDG accumulation in target lesions. Generally, at an inflammatory site, blood flow increases with capillary dilatation, rupture, angiogenesis, and transudation of blood constituents, along with inflammatory cell (granulocytes, lymphocytes, macrophages, etc.) infiltration, leading to fibroblast proliferation and collagen production with consequent fibrosis. During this process, FDG is likely to accumulate in activated lymphocytes, macrophages, and granulocytes which utilise anaerobic glycolysis as a source of energy. FDG eventually accumulates at the site of inflammation where carbohydrate metabolism is enhanced. The pathological features of IgG4-RD include the presence of marked lymphocyte and plasma cell infiltration and fibrosis, with IgG4-positive plasma cell infiltration. Although we lack direct evidence about where FDG molecules accumulate in involved organs, accumulation of FDG in lesions may be caused by local inflammation. This information is helpful for differentiating IgG4-RD from other inflammatory and malignant diseases. IgG4-RD has specific organ involvement such as the pancreas (AIP), parotid and submandibular glands, and can cause retroperitoneal fibrosis, interstitial pneumonitis, and lymphadenopathy (18-27).

Although ^{18}F-FDG-PET/CT greatly facilitates the diagnosis of IgG4-RD, distinguishing IgG4-RD from other inflammation or malignancies with SUV alone is difficult. A biopsy is needed for final diagnosis. Our results indicate that SUV_{max} values of AIP patients are significantly lower than for patients with pancreatic cancer and that the FDG/PET scan was sufficiently sensitive and specific with SUV_{max} values were 4.9. Still, our small number of cases suggests that the SUV_{max} cut-off value has not been validated. Uptake of ^{18}FDG has been reported to be lower with chronic pancreatitis, but it can increase significantly in patients with AIP, a special type of chronic pancreatitis (28, 29). Similar results have been reported for IgG4-related disease with inflammation of head and neck glands (5).

FDG accumulation patterns in involved organ may also facilitate a diagnosis of IgG4-RD. For example, pancreatic cancer typically has focal ^{18}FDG accumulation, whereas AIP has a more diffuse pattern. Ozaki's group reported that ^{18}F-FDG uptake by the mediastinal lymph node was significantly higher in AIP compared to pancreatic cancer, and uptake by the parotid gland, biliary duct, and retroperitoneum occurred only in AIP (30). In our study, 16 patients had AIP and 8 had lymph node involvement. Of these, five had mediastinal lymph node involvement. Other lymph nodes involved included axillary, retroperitoneal, parasternal, and inguinal lymph nodes. ^{18}F-FDG-PET/CT showed retroperitoneal fibrosis and arterial involvement. Among patients with lymph node involvement, two patients (patient 5 and 25) also had biliary duct involvement; five patients (3, 4, 7, 10 and 16) had arterial involvement; and one patient (patient 17) had liver involvement. Thus analysis of PET images for the distribution of ^{18}FDG in organs can improve diagnostic accuracy18.

In addition to pancreatic involvement, imaging testing also indicated a variety of extra pancreatic involvement although SUV values were not significantly different among these lesions. The average CRP for all 26 patients was 0.79 mg/dl (±0.64) and 19 patients were normal for CRP. Thus, IgG4-RD is not necessarily accompanied by elevated inflammation. When inflammation is not apparent, ^{18}F-FDG-PET/CT often shows elevated ^{18}F-FDG uptake in two or more than two characteristic organs, so there is a high probability of a IgG4-RD diagnosis.

Because we do not fully understand mechanisms behind IgG4-RD and the

variety of disease clinical presentations, rates of misdiagnosis and missed diagnosis are high. Patients may have non-specific symptoms (fever and abdominal pain). Here, 11 patients were misdiagnosed, including 1 submandibular tumour, 2 cases of pancreatic cancer, 3 pancreatitis, 2 interstitial pneumonia, 2 retroperitoneal fibrosis, and 1 systemic vasculitis. Serum IgG4 was elevated for some patients diagnosed with systemic lupus erythematosus or another connective tissue disease, likely due to autoimmune activity. Elevated IgG4 alone cannot be used to diagnose IgG4-RD, but if ^{18}F-FDG uptake was confirmed in two or more than two characteristic organs, a diagnosis would be suspected or a minimally invasive biopsy could be performed to support a diagnosis. In the current study, two patients (9 and 11) presented with fever and elevated CRP (1.60/1.32 mg/dl). Also, antibiotic treatments were ineffective and serum IgG4 was elevated, but no organs were involved. PET/CT revealed retroperitoneal fibrosis and involvement in hilar and mediastinal lymph nodes. These patients were thus diagnosed after biopsy.

Lymphoplasmacytic arteritis and inflammatory aneurysm are the most common cardiovascular disorders in IgG4-RD. In the current study, five patients had arterial involvements characterised by lesions of adventitia. These lesions were considered to be associated with IgG4-RD. However, in four of five patients, peri-arterial lesions were detected during vascular ultrasonography and did not show increased ^{18}F-FDG uptake on PET/CT images. Only one patient (patient 7) had elevated ^{18}F-FDG uptake (SUV_{max} = 3.2) and focally thickened aortic arch walls. Thus, ^{18}F-FDG-PET/CT may not be a sensitive method for detecting arterial involvement in IgG4-RD because ^{18}F-FDG-PET/CT is more sensitive to abnormal cellular metabolism and is not specific to vascular lesions. Therefore if a pulsatile mass is palpable upon physical examination, vascular ultrasonography should be recommended first for detailed examination of a vessel even after negative PET/CT imaging.

^{18}F-FDG PET/CT is not a routine workup of clinical examination. However, ^{18}F-FDG uptake in pancreatic and/or extra-pancreatic lesions has been documented to occur in IgG4-related disease (28, 29). Nakamoto's group (29) initially described two cases of AIP with diffusely and focally intense pancreatic uptake, and this resolved after steroid therapy. Kajiwara and co-workers (28) described two cases with multifocal ^{18}F-FDG uptake of the pancreas, corresponding to focal pancreatic masses of AIP. Additional reports indicate extra-pancreatic findings in cases of AIP associated with sclerosing cholangitis, sialadenitis, and lymphadenopathy (18, 19). Recently, ^{18}FDG PET/CT has confirmed to be effective for assessing the location of extra-lacrimal or salivary glands lesions in patients with IgG4-RD with lacrimal or salivary glands inflammation (5), as well as other cardiovascular disorders (1, 2, 13, 16).

Here, we retrospectively analysed ^{18}FDG/PET in 26 patients with or without pancreatic involvement. SUV_{max} values for differentiating AIP from malignant tissue were proposed and FDG accumulation patterns in extra-pancreatic lesions were analysed. We conclude that there is a high probability of IgG4-RD when inflammatory reactions are not observed and ^{18}F-FDG-PET/CT shows elevated ^{18}F-FDG uptake in multiple organs commonly involved in IgG4-RD. In addition, ^{18}F-FDG-PET/CT can help to identify disease distribution and can guide minimally invasive biopsy and support a diagnosis. ^{18}F-FDG-PET/CT generally reflects glucose metabolism and thereby disease activity. As a result, ^{18}F-FDG-PET/CT can highlight specific conditions for which steroid therapy is indicated and can be used to monitor therapeutic response. However, the diagnostic sensitivity of ^{18}F-FDG-PET/CT is not the same for all the involved organs; specifically it is less sensitive than vascular ultrasonography for detecting IgG4-RD arteritis. Thus, to make a definite diagnosis of IgG4-RD, characteristic clinical manifestations of each patient must be weighed to justify different imaging modalities.

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