

CASE REPORT

Usefulness of ^{18}F -fluorodeoxyglucose positron emission tomography for diagnosis of asymptomatic giant cell arteritis in a patient with Alzheimer's disease

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It is often difficult to diagnose disease in elderly patients, in particular those with dementia, who do not present with typical symptoms. This report describes our experience of an elderly patient (an 83-year-old woman) who presented with a chief complaint of memory loss, showed a marked inflammatory response, and was diagnosed with large-vessel giant cell arteritis (GCA) on the basis of ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) findings. She had no symptoms typical of GCA including jaw claudication, visual field defect and heavy headed feeling. Corticosteroid therapy resulted in a trend toward improvement in the inflammatory response and then she first recognized that she might have experienced slight dull headache before treatment of GCA. This was probably because this patient had large-vessel GCA, which produces a few symptoms in the head and neck, and because she had Alzheimer's disease and could not accurately describe her symptoms. Our experience suggests the usefulness of FDG-PET for the diagnosis of GCA, particularly in elderly patients without typical symptoms. **Geriatr Gerontol Int 2011; 11: 114–118.**

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Introduction

In daily clinical practice, physicians sometimes encounter elderly patients who do not have typical symptoms of a disease as young patients do. Elderly patients with dementia cannot describe their symptoms accurately, which often makes diagnosis more difficult. Patients with giant cell arteritis (GCA) are characterized by jaw claudication, diplopia and headache,¹ but elderly patients often do not have these symptoms. It is reported that ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) is effective for the diagnosis of systemic inflammatory disease.^{2,3} Here, we report our

Table 1 Blood data on admission

Parameter	Value	Parameter	Value	Parameter	Value
WBC	5400/ μ L	γ -GTP	22 IU/L	Fe	13 μ g/dL
RBC	336 \times 10 ⁴ / μ L	CK	29 IU/L	UIBC	193 μ g/dL
Hb	8.7 g/dL	ChE	162 IU/L	Ferritin	107 ng/mL
Ht	28.0%	AMY	111 IU/L	IgG	2200 mg/dL
MCV	83 fL	Lipase	33 IU/L	IgA	382 mg/dL
MCH	25.9 pg	BUN	12 mg/dL	IgM	81 mg/dL
MCHC	31.1%	Cre	0.69 mg/dL	TSH	0.419 μ U/mL
Plt	53 \times 10 ⁴ / μ L	UA	4.3 mg/dL	fT3	2.2 pg/mL
Reticulocytes	0.7%	Na	139 mEq/L	fT4	1.27 ng/dL
PT%	76.5%	K	3.9 mEq/L	Vitamin B ₁	55 ng/mL
TP	7.5 g/dL	Cl	104 mEq/L	Vitamin B ₁₂	>1500 pg/mL
T-Bil	0.5 mg/dL	Ca	8.3 mg/dL	Folic acid	6.8 ng/mL
AST	15 IU/L	P	3.4 mg/dL	CRP	7.30 mg/dL
ALT	8 IU/L	Glu	170 mg/dL	ESR	>100 mm/h
ALP	255 IU/L	TG	47 mg/dL	HBsAg	(-)
LDH	139 IU/L	HDL-C	42 mg/dL	HCV-Ab	(-)
		LDL-C	56 mg/dL		

ALP, alkaline phosphatase; ALT, alanine transaminase; AMY, amylase; AST, aspartate transaminase; BUN, blood urea nitrogen; Ca, calcium; Cl, chloride; ChE, choline esterase; Cre, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Fe, iron; fT3, free triiodothyronine; fT4, free thyroxine; Glu, glucose; Hb, hemoglobin; HBsAg, hepatitis B surface antigen; HCV-Ab, hepatitis C virus antibody; HDL-C, high-density lipoprotein cholesterol; Ht, hematocrit; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; K, potassium; LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; MCHC, mean corpuscular hemoglobin concentration; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; P, phosphorus; Plt, platelet count; PT, prothrombin time; RBC, red blood cell count; γ -GTP, γ -glutamyl transpeptidase; T-Bil, total bilirubin; TG, triglyceride; TP, total protein; UA, uric acid; UIBC, unsaturated iron binding capacity; WBC, white blood cell count.

experience in a patient with GCA who showed a marked inflammatory response during tests for cognitive function, in whom the cause of inflammation was effectively diagnosed by FDG-PET.

Case report

An 83-year-old woman attended the outpatient department of our hospital with a chief complaint of memory loss. Her memory impairment had begun 1 year earlier and slowly progressed. From 4 months earlier, she had refused to take a bath occasionally. From 3 months earlier, she had begun to say or ask the same thing many times, and forgot appointments to meet her friends more frequently. She was aware of her memory loss. She could no longer manage money and began to dislike going shopping in the neighborhood. During the course of observation, she did not have such symptoms as jaw claudication, visual field defect, headache or numbness of the upper limbs. She had lost 3 kg in 1 month prior to admission, and was found to have a significant inflammatory response on blood tests, and was admitted to our department for further evaluation of cognitive impairment in June 2008.

She had no particular medical history. Her sister had a history of pituitary adenoma without neurological

disorder or dementia. She had no family history of collagen disease. She did not smoke, and drank alcohol only on social occasions. She had no history of allergy and had never been abroad. She had been educated for 8 years. She had worked as an accountant until the age of 60 years. She lived with her daughter's family.

She was 146.0 cm tall and weighed 39.8 kg, with a body mass index of 17.3 kg/m². Temperature was 37.1°C, and pulse was regular (89 b.p.m.). Blood pressure was 96/56 mmHg (left upper limb) and 108/56 mmHg (right upper limb). She had clear consciousness. No arterial bruit was heard in the carotid arteries. The temporal arteries were non-tender on palpation. The palpebral conjunctivae were pale, but the bulbar conjunctivae were not icteric. Funduscopic findings were normal. Superficial lymph nodes were not palpable and the thyroid gland was not enlarged. There were no abnormal findings in the thoracoabdominal region. Examination of the skin revealed no redness or rash. The limbs were not edematous. There was no arthralgia. Neurological findings were normal.

Blood data are presented in Table 1. Urine was negative for occult blood and protein, and many white cells were observed in the urinary sediment. Chest radiograph and electrocardiogram were normal.

Neuropsychological tests showed cognitive deterioration, with a Mini-Mental State Examination (MMSE) score of 20 points, and a revised Hasegawa Dementia Scale (HDS-R) score of 16 points. Specifically, she did not score high in delayed recall, calculation, orientation and verbal recall. The 10-word recall test and the Rey–Osterrieth complex figure test also indicated a significant decline in delayed recall. She was able to recall 5 digits in the same order as they had been presented and 3 digits in the reverse order. She took 210 s to finish the trail making test part A (mean: 151 s in healthy persons), and part B was discontinued because she did not understand the task. She was thus found to have reduced overall cognitive function with memory impairment and disturbance of attention.

Cranial magnetic resonance imaging (MRI) showed diffuse cerebral atrophy on T₁-weighted images; particularly, the Sylvian fissure and the inferior horns of the lateral ventricles were dilated, while there was marked atrophy in the medial parietal and temporal lobes. T₂-weighted images and fluid-attenuated inversion recovery images showed lesions deep in the white matter and a high-signal-intensity area in the paratemporal ventricles, appropriate for her age. Brain perfusion scintigraphy (¹²³I-iodoamphetamine single photon emission computed tomography) showed reduced blood flow in the medial temporal lobes, parietal-temporal association area and precuneus. Cerebrospinal fluid was colorless and transparent and showed a slightly increased protein level (65 mg/dL), with no increase in cell count (1/μL) and a normal glucose level (63 mg/dL) and blood glucose level (94 mg/dL). There was no obvious inflammatory response, with immunoglobulin (Ig)G index of 0.05 and negative test results for anti-herpes IgM and IgG antibodies. Phosphorylated tau protein level was 50.03 pg/mL (reference value: ≤31.3 pg/mL), and amyloid β₁₋₄₂ level was 254.31 pg/mL (reference value: ≥1005 pg/mL), supporting the diagnosis of Alzheimer's disease.

With regard to inflammatory responses, the patient had a persistent slight fever after admission, but did not experience any obvious symptoms including apparent appetite loss. She had lost approximately 3 kg during 1 month before admission. She had shown a prolonged inflammatory response since attendance at our outpatient department, and had normocytic normochromic anemia, decreased Fe, and increased ferritin, suggesting chronic inflammation. The patient also underwent investigation for systemic diseases, including infections, malignant diseases and collagen diseases.

Urinalysis on admission showed pyuria, and she was treated with 200 mg/day of levofloxacin under a diagnosis of urinary tract infection. The urinary findings improved, while the inflammatory response did not. Plain computed tomography (CT) of the chest and abdomen, upper and lower gastrointestinal endoscopy,

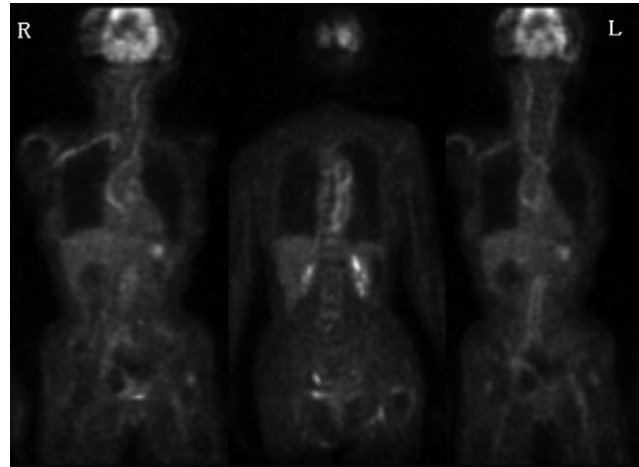


Figure 1 ¹⁸F-Fluorodeoxyglucose positron emission tomography (FDG-PET) demonstrated increased glucose uptake in the ascending aorta, both carotid arteries, both subclavian arteries, and from the descending aorta to both common iliac arteries.

and transthoracic echocardiography were performed to search for the site of inflammation, but failed to detect any obvious findings. Blood cultures were negative.

To search for collagen diseases, blood tests were performed and showed an elevated rheumatoid factor titer of 1:25 and an increased anti-cyclic citrullinated peptide antibody level of 277.0 U/mL. Early rheumatoid arthritis was suspected, but the patient did not have any joint symptoms, and radiography of the joints of the whole body did not show any findings suggestive of rheumatism.

Therefore, FDG-PET (Fig. 1) was performed to identify the site of inflammation. This examination showed increased glucose uptake in the ascending aorta, both carotid arteries, both subclavian arteries, and from the descending aorta to both common iliac arteries, raising the suspicion of aortitis syndrome. Contrast-enhanced CT of the chest and abdomen (Fig. 2) showed thickening of the wall of the thoracoabdominal aorta and delayed contrast enhancement of this part of the aorta. Ultrasonography of the superficial temporal arteries revealed a halo in both superficial temporal arteries and stenosis/occlusion of both frontal branches and both occipital branches. Biopsy of the left superficial temporal artery showed giant cell and lymphocytic infiltration of the arterial wall, leading to the diagnosis of GCA (Fig. 3).

Although the patient had extensive vasculitis, treatment was initiated with 20 mg of oral prednisolone because she did not have any lesions in the ocular fundi, and taking her age into consideration. Because she had a reduced bone mass (59% and 84% of that of the young adult mean measured in the forearm and a lumbar vertebra, respectively), oral bisphosphonate was also administered for the prevention of steroid-induced osteoporosis. Corticosteroid therapy resulted in a trend

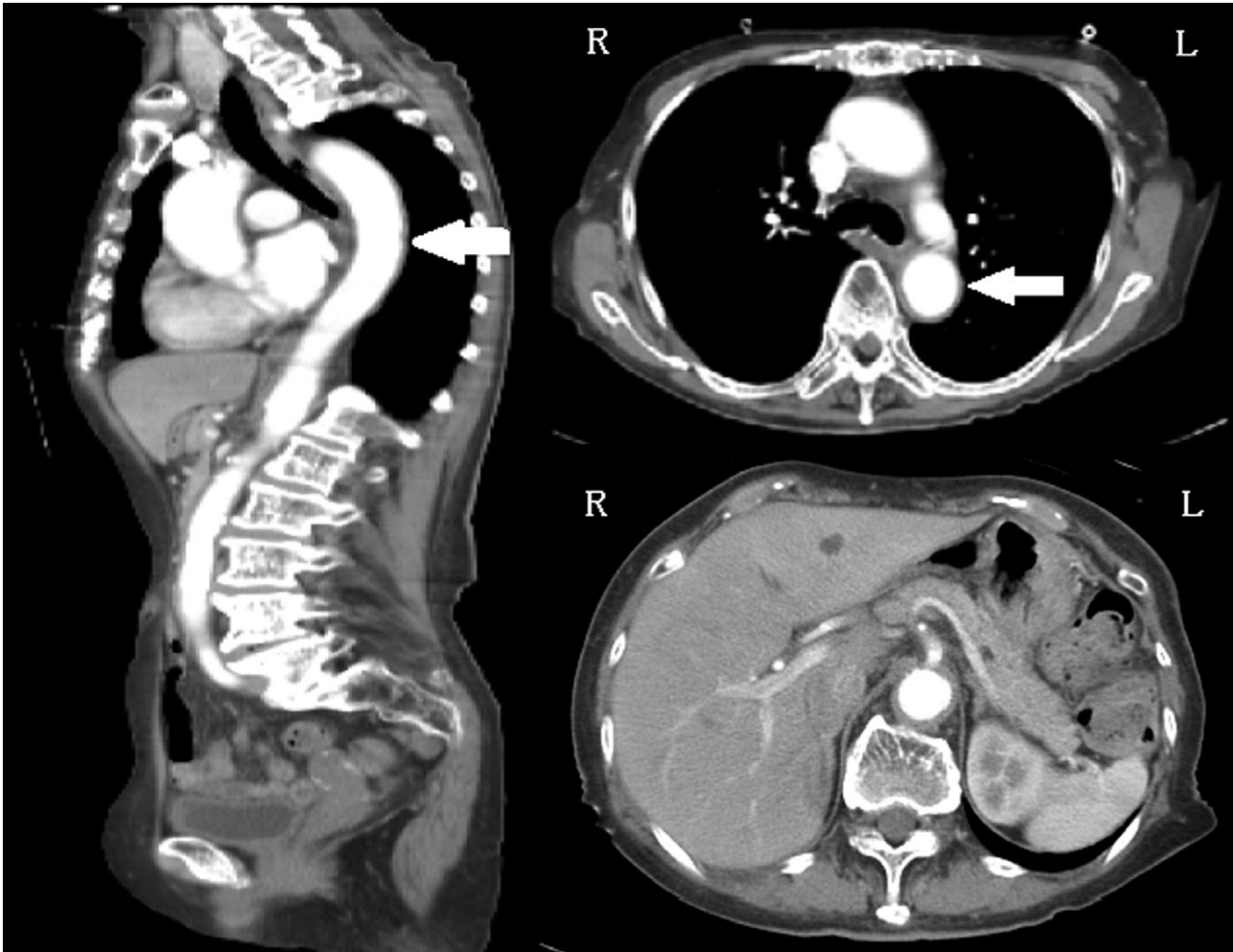


Figure 2 Contrast-enhanced computed tomography (CT) image. Contrast-enhanced CT of the chest and abdomen showed thickening of the wall of the thoracic descending aorta to the abdominal aorta and both common iliac arteries, and delayed contrast enhancement of these arteries. None of the aortic branches was stenosed.

toward improvement in the inflammatory response. The patient did not complain of her heavy headed feeling or any similar symptoms before treatment, but after successful treatment of GCA, she first recognized that she might have experienced slight dull headache. On day 29 of corticosteroid therapy, blood tests indicated improvement of the inflammatory response, with a negative result for C-reactive protein and an erythrocyte sedimentation rate of 21 mm after 30 min and 52 mm after 60 min. Accordingly, the dose of prednisolone was reduced to 18 mg. On day 32 of corticosteroid therapy, contrast-enhanced CT demonstrated reduced thickening of the aortic wall and reduced contrast enhancement. Neuropsychological tests were performed again on days 10 and 29 after initiation of oral corticosteroid therapy, but revealed no improvement (day 10: MMSE, 21 points; HDS-R, 13 points. Day 29: MMSE, 17 points; HDS-R, 12 points). The patient subsequently made favorable progress and was discharged.

Discussion

Giant cell arteritis normally occurs in patients aged 50 years or older. It is a granulomatous angiitis involving the aorta and its major branches. According to the classification proposed by the American College of Rheumatology,⁴ GCA should be diagnosed if at least three of the following five criteria are present: (i) age at disease onset of 50 years or more; (ii) new onset of localized headache; (iii) temporal artery tenderness to palpation or decreased pulsation; (iv) elevated erythrocyte sedimentation rate (≥ 50 mm/h); and (v) biopsy specimen with an artery showing necrotizing vasculitis characterized by a predominance of monocytes, or granulomatous change with multinucleated giant cells.

Because our patient did not complain of headache at first, FDG-PET, which was performed to identify the site of inflammation, played an important role in diagnosis.

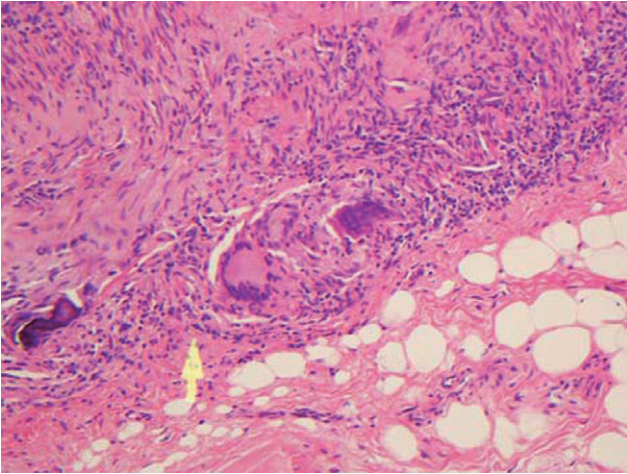


Figure 3 Histological findings of temporal artery. Biopsy of the left superficial temporal artery showed multinucleated giant cell and lymphocytic infiltration of the internal elastic lamina of the arterial wall (hematoxylin–eosin, original magnification $\times 200$).

Brack *et al.* reported that GCA can be divided into two groups: classic cranial GCA and large-vessel GCA. They mentioned that headache was the most frequent symptom for cranial GCA (42%), but not for large-vessel GCA.⁵ According to them, vasculitis is present around the aorta in large-vessel GCA. Temporal artery biopsy findings were negative in 42% of patients with large-vessel GCA, and many patients had ischemic disorders of the upper limbs (arterial bruit, 80%; pain on movement, 78%; difference in blood pressure measured in both arms, 58%) as initial symptoms, while only 10% of patients had headache as an initial symptom. They also reported that the time from disease onset to diagnosis was significantly longer in patients with vasculitis only involving the cranial arteries.⁵ Although there has been a report of a patient without headache in whom GCA was diagnosed on the basis of elevated glucose uptake in the aorta detected by FDG-PET, as was the case in our patient,⁶ thickening of the vessel wall shown by CT or MRI is also known to be a useful finding.^{7,8} The clinical course in our patient was consistent with that of large-vessel GCA, and she may have had fewer symptoms in the head and neck compared to those in the trunk and upper limbs. In addition, she may not have been able to accurately express her symptoms because of Alzheimer's disease.

Some patients with GCA also have cerebral infarction or transient cerebral ischemia resulting from vasculitis. In one study, 3% of patients with GCA had psychiatric symptoms, including depression,⁹ but it is not clear whether ischemia was involved in the mechanism. While there is a report of GCA in a patient with cognitive impairment that was improved by corticosteroid therapy,¹⁰ our patient did not show any change in cog-

nitive function after initiation of corticosteroid therapy, and thus there seems to be no relation between GCA and cognitive impairment. The decline of the score of MMSE was considered that it might be the effect of corticosteroids or hospitalization or progression of Alzheimer's disease. Our patient's course was also consistent with the diagnosis of Alzheimer's disease.

As detailed above, GCA should be positively differentiated when elderly patients have an inflammatory response, even if they do not have typical symptoms such as headache. In our patient, GCA was effectively diagnosed by evaluation of blood vessels by imaging, including FDG-PET and contrast-enhanced CT. Because of its high sensitivity in an active inflammatory state,² FDG-PET might become a powerful diagnostic tool in the management of large-vessel inflammation.

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