Value of Carotid Artery Tenderness for the Early Diagnosis of Takayasu Arteritis

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Abstract

The early diagnosis and treatment of Takayasu arteritis (TA) is crucial to prevent the devastating complications of vascular insufficiency. This report describes a patient with a persistent fever in whom carotid artery tenderness led to a diagnosis of TA. This case suggests that carotid artery tenderness is a useful physical finding that warrants 2-deoxy-2-[Fluorine-18] fluoro-D-glucose positron emission tomography/computed tomography to confirm a diagnosis of early TA.

Key words: Takayasu arteritis, carotid artery tenderness, positron emission tomography

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Introduction

Takayasu arteritis (TA), also called aortitis syndrome, is an autoimmune vasculitis of the aorta and its first branches. Stenosis gradually develops at the vessel wall over a long period of active inflammation, and the clinical symptoms of vascular insufficiency to end organs eventually become apparent. Because of the progressive nature of the disease, early diagnosis and treatment is critical to prevent the occurrence of end organ dysfunction which significantly exacerbates the patient outcomes. However, patients with TA often present with fever and inflammation of unknown origin that spontaneously resolves and relapses, thus making early diagnosis both difficult and challenging.

Carotid artery tenderness (carotidynia) refers to pain of the anterior neck induced by palpation of the carotid arteries. It occurs in about 30% of patients during the course of TA (1) and suggests inflammatory processes in large arteries.

Several recent studies suggest that TA may be diagnosed and followed up based on 2-deoxy-2-[Fluorine-18] fluoro-D-glucose (FDG) accumulation in affected vessels using positron emission tomography combined with computed tomography (PET/CT) (2-4). This modality might also benefit patients with fever of unknown origin by directly visualizing the foci of active inflammation based on elevated glucose metabolism in inflammatory tissue (5, 6).

Here, we describe a 65-year-old Japanese woman who presented with fever that had persisted for five months. There was no evidence of vascular insufficiency, but left common carotid artery tenderness suggested the possibility of TA, which was confirmed by FDG PET/CT. The patient was successfully treated without developing severe complications of TA. Carotid artery tenderness is an apparently useful physical finding indicating TA that justifies the use of FDG PET/CT for examining patients with chronic fever and/or inflammation.

Case Report

A 65-year-old Japanese woman developed a low-grade remittent fever that reached 37.5°C and which had persisted for five months, when she was referred to our department. She had undergone orthodontic surgery three months before referral, based on a preoperative diagnosis of osteomyelitis of the jaw. Calcification was identified in the resected specimen, but no osteomyelitis was evident. The fever worsened to 37.9°C around the time of the surgery and thereafter. She was examined at another institution two months before her referral, where contrast-enhanced CT of the trunk and ultrasonography of the abdomen were reportedly normal. Results

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of repeated laboratory tests revealed that C-reactive protein (CRP) had increased to around 4 mg/dL. She was referred to our department for further investigation.

Her medical history included type 2 diabetes mellitus and gastric infection with Helicobacter pylori. She was medicated with Loxoprofen, Rebamipide and Nateglinide. She had not traveled abroad recently. She had experienced pain in the posterior and left anterior sides of the neck during the fever, and she had lost 2.5 kg within three months. She had no headache, visual disturbance, facial tenderness, cough, anorexia, jaw claudication, shoulder and pelvic girdle muscle pain, morning stiffness, upper arm tenderness, back pain, abdominal pain, dizziness or any changes in her urinary habits.

A physical examination revealed slight fatigue, blood pressure of 140/82 mmHg with no significant difference between the two arms and otherwise normal vital signs. Her conjunctivae were not anemic and no petechiae were observed. There were no visual field deficits. Both temporal arteries were normal without tenderness on palpation. She reported moderate tenderness on palpation of the left common carotid artery. There was no skin injection or swelling. The cervical lymph nodes were not swollen and the thyroid glands felt normal without tenderness. Chest auscultation revealed a Levine 1° systolic murmur at the left and right second sternal borders. Abdominal findings and those of the extremities were normal.

Laboratory results were: erythrocyte sedimentation rate 101 mm/h, white blood cells 7,640/mm³, Hb 12.3 g/dL, platelets 29.3x10⁹/mm³, Hb A1c 7.7% and CRP 3.65 mg/dL. Urinalysis showed mild leukocyturia (10 to 19 per high power field) without casts, bacteria or fungi. Blood, urine and urine acid-fast cultures were negative, as were the results of tests for rapid plasma regain, Treponema pallidum latex agglutination, serum procalcitonin and the QuantiFERON-TB test. Electrocardiographic findings were within normal limits and transthoracic echocardiography revealed no evidence of vegetation. Magnetic resonance imaging and magnetic resonance angiographic images of the head were reportedly normal.

Since the persistent fever and left common carotid artery tenderness led us to a suspected diagnosis of large vessel vasculitis, FDG PET/CT imaging was performed with the patient’s consent. Imaging one hour after the injection of 5 MBq/Kg of FDG, using a PET/CT scanner (Siemens, biograph 16) revealed high FDG accumulation at the aorta, bilateral carotid arteries (left side dominant), subclavian arteries, common iliac arteries, and femoral arteries. No abnormality was seen in the temporal artery or pulmonary artery (Figs. 1, 2). Slight and nonspecific FDG accumulation was seen in bilateral shoulder joints and spinous processes of several vertebrae suggesting mild inflammatory changes. There were no other abnormalities suggesting malignancy or active inflammation. These FDG PET/CT findings were consistent with those of TA.

She was diagnosed with TA based on the systemic inflammation, carotid artery tenderness. FDG PET/CT results, negative history and physical findings for giant cell arteritis, and negative test results for systemic bacterial or fungal infection. No temporal artery biopsy was performed. Treatment with 20 mg/day prednisolone caused the rapid disappearance of the symptoms and the CRP level returned to the
normal range after two weeks. Prednisolone was slowly tapered with no clinical relapse of the disease.

Discussion

A patient with prolonged fever was diagnosed with TA before the onset of symptoms of vascular insufficiency and successfully treated with prednisolone. Carotid artery tenderness and FDG PET/CT images significantly facilitated an early diagnosis.

Giant cell arteritis is another cause of large vessel vasculitis (7) and is an alternative differential diagnosis for this patient because she is relatively old, but we believe that TA is a more likely diagnosis than giant cell arteritis for three reasons. First, there were no clinical symptoms and signs of polymyalgia rheumatica and/or giant cell arteritis, such as visual disturbance, jaw claudication, temporal artery tenderness and pulse deficit, shoulder and pelvic girdle muscle pain, morning stiffness, or upper arm tenderness. Giant cell arteritis presents with some localized symptoms more often than TA. Second, TA is more common than giant cell arteritis in Japan. This is in contrast to the U.S. and Europe where giant cell arteritis is the most prevalent large vessel vasculitis. Third, a nationwide cohort study in Japan has shown that TA can occur in patients in their 60’s (8). The possibility of giant cell arteritis still remains, since neither ultrasonography nor a biopsy of the temporal arteries was performed on this patient. However, the reasons listed above indicate that TA is a more likely diagnosis for this patient.

TA is an autoimmune disease that causes devastating disabilities if left uncontrolled for long periods (9, 10). The prevalence and the involved vessels vary across ethnicities. TA is the most common large vessel vasculitis in Asian countries, and tends to affect vessels in the thorax rather than in the abdomen (8, 11, 12). TA is a large vessel vasculitis characterized by activated cytotoxic T lymphocyte infiltration of the media and adventitia of the aorta and its primary branches (13-15). There is a period of inflammation, followed by either destruction of the media or scarring from the adventitia that leads to aneurysmal dilation or stenosis of the vascular lumen, respectively. Intimal proliferation and thickening secondary to inflammation might also contribute to the latter pathology (16). The typical signs and symptoms of TA such as claudication of the extremities, syncope, decreased brachial artery pressure, blood pressure difference, bruit over the subclavian arteries or aorta and arteriographic abnormalities only develop after stenotic lesions become prominent (9, 17). Patients diagnosed with these late complications often require surgical intervention and their outcomes are poorer than those diagnosed without complications. Indeed, complications are associated with a poor prognosis and decreased quality of life (18). Therefore, TA should be diagnosed before the onset of ischemic clinical symptoms and complications.

However, an early diagnosis of TA is notoriously difficult. Patients commonly present with fatigue, weight loss and low-grade fever, and laboratory data indicate chronic inflammation. Specific laboratory tests such as those using anti-endothelial cell antibodies (19, 20) are currently unavailable in clinical practice and the findings of imaging modalities such as contrast enhanced CT may be unremarkable during the early phase of the disease.

Several imaging modalities have been investigated in early TA. FDG PET/CT imaging is an emerging diagnostic tool that can be applied to a variety of inflammatory or infectious diseases. FDG PET/CT images of TA have been extensively studied, and they are now regarded as almost diagnostic because they can reveal diffuse inflammation and increased metabolism in the affected arteries (21, 22). Although other imaging modalities used in large vessel vasculitis such as ultrasonography of the carotid and subclavian arteries can also be beneficial in diagnosing TA (23), FDG PET/CT is superior to ultrasonography in detecting the complete distribution of the involved vessels. In addition, some reports indicate that FDG PET/CT is useful for monitoring TA disease activity (24-26) and for diagnosing fever of unknown origin (5, 6). However, FDG PET/CT is expensive and currently available at only a limited number of medical centers, thus its cost-effectiveness as a general diagnostic tool for inflammatory or pyretic conditions remains unclear (27). Therefore, careful assessment of the pre-test probability of the suspected diagnosis is important to avoid unnecessary imaging procedures.

Carotid artery tenderness is a physical finding that reflects inflammation of the carotid arteries and is found in 29% of patients with TA (1). The left subclavian artery and left common carotid artery are frequently (60% and 40%, respectively) involved in Japanese patients with TA (8). In contrast to the established ischemic signs of TA, carotid artery tenderness may occur before stenosis develops, since it is not a result of arterial stenosis but rather indicates that the carotid arteries are involved in an inflammatory process (16). Tenderness in the carotid arteries (especially the left common carotid artery) might be the only significant physical finding in a patient presenting with inflammation of unknown origin, as it suggests that the large arteries have inflammation. Thus, a diagnosis of large vessel vasculitis such as TA is indicated.

In conclusion, we suggest that if carotid artery tenderness, especially in the left side, is positive in patients presenting with persistent fever, clinicians should consider TA as a differential diagnosis even in the absence of symptoms or signs of vascular insufficiency. This clinical approach may allow early diagnosis, as well as treatment options for some patients with TA that otherwise would be misdiagnosed for years and would develop ischemic symptoms and complications.

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References