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Takayasu arteritis presenting with fever of unknown origin and bilateral carotid artery tenderness: A case report

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Abstract

A 51-year-old otherwise healthy woman was referred to our hospital with a fever of unknown origin, liver dysfunction, and anemia. One month prior, she had persistent and spontaneous anterior neck pain, with no exacerbation during swallowing or neck movements. Physical examination revealed no pharyngeal or tonsillar abnormalities, heart murmur, arthritis, skin rash, or lymphadenopathy, except for mild bilateral common carotid artery tenderness at the level of the thyroid cartilage. Blood tests showed nonspecific chronic inflammatory findings, anemia, and liver damage, whereas blood cultures, viral antibodies, interferon-γ release assay, and antibodies specific for any collagen disease showed negative results. Echocardiography and computed tomography without contrast of the neck, chest, abdomen, and pelvis showed no apparent abnormalities. She was subsequently diagnosed with Takayasu arteritis using positron emission tomography. Identifying a characteristic history of bilateral carotid artery tenderness and subsequent positron emission tomography can be useful for diagnosing Takayasu arteritis.

Keywords

Carotidynia, fever of unknown origin, neck pain, positron emission tomography, Takayasu arteritis, vasculitis

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Introduction

Takayasu arteritis (TA) is a systemic large-vessel arteritis of an unknown etiology, with approximately 300 new cases diagnosed annually in Japan, and more than 6000 cases currently registered as incurable.[1] However, several cases remain undiagnosed[1] due to a variety of initial symptoms, along with nonspecific findings[2] and asymptomatic presentation.[3]

Systemic manifestations of fever (34.7%) and malaise (12.1%) are the most common initial symptoms, followed by neck pain (9.7%).[2] However, neck pain as the first symptom can be misdiagnosed as carotidynia, temporomandibular joint disorder, dental pulpitis, or subacute thyroiditis.[4,5] Neck and throat symptoms are frequently seen by primary care physicians,[6] and a detailed analysis of neck pain can be the first step in diagnosing TA, which is a relatively rare disease.

No specific hematologic or biochemical tests to diagnose TA exist.[1] Findings such as anemia, elevated erythrocyte sedimentation rate, increased C-reactive protein levels, and leukocytosis can aid in the diagnosis, but are not considered major criteria.[1] Although liver injury is generally considered rare in TA,[7] blood tests may reflect a variety of organ dysfunctions due to the heterogeneity of the affected vessels.[3]

We report the case of a patient with TA, where a history of anterior neck pain, findings of bilateral carotid artery tenderness, and subsequent positron emission tomography (PET) findings were key to the diagnosis.

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Table 1. Hematological and biochemical investigation results.

Variable	Reference range	Upon presentation	9 Days after naproxen administration	4 Weeks after prednisolone administration
White blood cell count (/μL)	3300–8600	6000	7240	9220
Red blood cell count ($\times 10^4$/μL)	386–492	327	299	387
Reticulocyte (%)	0.8–2.2	1.2	1.5	
Hemoglobin (g/dL)	11.6–14.8	9.2	8.2	10.8
Mean corpuscular volume (fL)	83.6–98.2	90.5	89.3	89.7
Mean corpuscular hemoglobin (pg)	27.5–33.2	28.1	27.4	27.9
Platelet (/μL)	158,000–348,000	703,000	655,000	378,000
Erythrocyte sedimentation rate (1 h/2 h) (mm)	3–15 (1 h)	90/96	100/105	16/36
Albumin (g/dL)	4.1–5.1	2.7	2.8	3.8
Blood urea nitrogen (mg/dL)	8–20	11	15	14
Creatinine (mg/dL)	0.46–0.79	0.44	0.41	0.52
Aspartate aminotransferase (U/L)	13–30	36	27	12
Alanine aminotransferase (U/L)	7–23	56	21	13
Alkaline phosphatase (U/L)	38–113	319	209	88
Lactate dehydrogenase (U/L)	124–222	259	301	141
Total bilirubin (mg/dL)	0.4–1.5	0.4	0.4	0.7
Gamma-glutamyl transferase (U/L)	9–32	133	67	27
C-reactive protein (mg/dL)	0–0.14	16.19	13.36	0.16
Ferritin (ng/mL)	12–60	418	347	
Hepatitis B surface antigen	Negative	Negative		
Hepatitis C antibodies	Negative	Negative		
Proteinase-3-antineutrophil cytoplasmic antibody	Negative	Negative		
Myeloperoxidase-antineutrophil cytoplasmic antibody	Negative	Negative		
Antinuclear antibody	<40	160		
Anti-double stranded DNA antibody	Negative	Negative		
Anti-SSA/Ro antibody	Negative	Negative		
Anti-SSB/La antibody	Negative	Negative		
Interferon-γ release assay	Negative	Negative		

Anti-SSA, Anti–Sjögren's-syndrome-related antigen A; Anti-SSB, Anti-SSB, Anti–Sjögren's-syndrome-related antigen B

Case

A 51-year-old otherwise healthy female patient was referred to our hospital presenting with fever of unknown origin, liver dysfunction, and anemia. One month prior to her visit, she developed a fever of 38°C and anterior neck pain. No upper or lower respiratory symptoms, abdominal symptoms, skin rash, or arthralgia were present. The neck pain was persistent and spontaneous, with no exacerbation during swallowing or neck movements. Three weeks prior, she visited a community clinic where she was prescribed acetaminophen for symptomatic treatment after a negative coronavirus disease antigen test. A week later, her neck pain gradually improved but her fever persisted, and blood tests at the clinic indicated liver damage and anemia. Empirical treatment with levofloxacin was ineffective, and the patient was referred to another community hospital. Despite detailed blood tests, the underlying cause remained unknown, and she was referred to our hospital.

At the time of presentation to our hospital, no apparent vital sign abnormalities other than sinus tachycardia were observed (blood pressure, 137/68 mmHg; pulse rate, 106 beats per minute; axillary body temperature, 36.4°C). Physical examination revealed no pharyngeal or tonsillar abnormalities, heart murmur, arthritis, skin rash, or lymphadenopathy, except for mild tenderness above the bilateral common carotid artery at the level of the thyroid cartilage. Her weight was 46.6 kg with no change over the past year. She was able to perform everyday activities when the antipyretic medication was effective and did not miss work. Blood tests showed nonspecific chronic inflammatory findings, anemia, and liver damage, whereas blood cultures, viral antibodies (cytomegalovirus, Epstein–Barr virus, parvovirus), interferon-γ release assay, and antibodies specific for any collagen disease showed negative results (Table 1). Echocardiography and cervical computed tomography (CT) without contrast of the neck, chest, abdomen, and pelvis showed no apparent abnormalities. Her fever had resolved with naproxen 200 mg twice daily; however, the inflammatory findings did not improve for 9 days (Table 1). Considering the possibility of malignant lymphoma or vasculitis, we performed ^{18}F-fluorodeoxyglucose PET. We found abnormal accumulation uptake in the aorta, bilateral

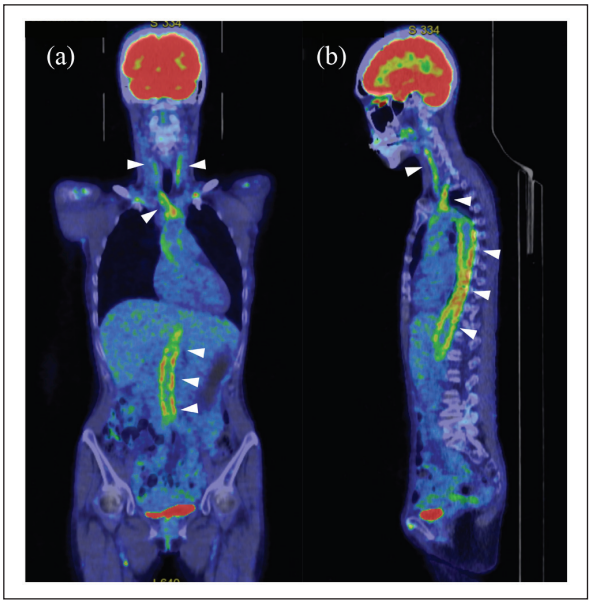

Figure 1. (a) Coronal and (b) sagittal views of ^{18}F-fluorodeoxyglucose positron emission tomography. Intense uptake of ^{18}F-fluorodeoxyglucose (white arrowhead) was observed in the aorta, bilateral common carotid arteries, brachiocephalic artery, and left subclavian artery.

common carotid arteries, brachiocephalic artery, and left subclavian artery, and a diagnosis of TA type V was made (Figure 1). In accordance with Japanese guidelines,[1] prednisolone 30 mg once daily was started; subsequently, the fever, liver damage, and inflammatory findings promptly improved (Table 1). Approximately 5 months after treatment initiation, a follow-up contrast-enhanced CT was conducted, which revealed no evidence of vascular stenosis. At the time of writing this report, prednisolone has been tapered down to a daily dose of 12 mg, without any symptoms reappearing, and the C-reactive protein levels remain negative.

Discussion

Our case revealed that anterior neck pain with fever and chronic inflammatory findings could be a specific history of TA, especially if the pain is isolated bilaterally. Primary care physicians should check for tenderness and classify the patient's complaint of a sore throat as neck pain originating from the carotid artery, thyroid gland, muscles, or lymph nodes, rather than simply assuming pharyngeal soreness, even if the symptoms are masked by acetaminophen or nonsteroidal anti-inflammatory drugs. Carotidynia can also cause bilateral anterior neck pain, however, it usually presents unilaterally and improves within 2 weeks, without elevation of C-reactive protein levels or the erythrocyte sedimentation rate.[8] Our patient responded favorably to naproxen, with resolution of the fever and neck tenderness. While naproxen can be used in the diagnosis of tumor fever, its resolution does not necessarily suggest malignancy or rule out collagen disease.[9] Since Takayasu vasculitis can progress chronically and result in irreversible vascular complications such as valvular disease, ischemic heart disease, and aortic aneurysms,[1] early detection by primary care physicians is crucial.

Furthermore, CT is not sensitive enough to exclude a TA diagnosis. In a report evaluating the diagnostic accuracy of contrast-enhanced CT for large-vessel vasculitis using three criteria (visualization of circumferential thickening of the aortic wall, contrast enhancement in the aortic wall, and inflammatory changes in the periaortic tissue), the diagnostic accuracy was reported to have 60.9% sensitivity and 97.2% specificity.[10] In our patient, a contrast-enhanced CT was performed after the diagnosis was confirmed, and only slight circumferential wall thickening of the aorta was observed with contrast enhancement (Supplemental Figure S1). Therefore, primary care physicians should be cautious about ruling out TA on CT if vasculitis is suspected, especially in the early stages of the disease. PET is increasingly used to evaluate the possibility of large-vessel vasculitis. ^{18}F-fluorodeoxyglucose accumulation in sites of active inflammation is a valuable finding for the diagnosis of TA, and the degree of such accumulation also correlates with clinical disease activity.[1] PET should be considered in cases in which clinical symptoms are inconsistent with laboratory and CT findings.

Conclusion

When suspecting TA, it is important to focus on neck pain and carotid artery tenderness, rather than rely on less sensitive imaging methods such as CT or nonspecific laboratory findings such as liver dysfunction or anemia. Additionally, PET should be considered in cases in which the clinical symptoms are inconsistent with laboratory and CT findings.

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Author contributions

H.M. conceived the idea and wrote the original draft of the article. T.K. and T.A. developed the theory of this study. All authors discussed the case and commented on the article. H.M., T.K., and T.A. revised and edited the article. All authors gave final approval before submission of the article.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declaration of conflicting interests

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Informed consent

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Supplemental material

Supplemental material for this article is available online.

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