

Early Diagnosis in an Unusual Presentation of Takayasu's Arteritis

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Takayasu's arteritis (TA) is a relatively rare form of large vessel vasculitis that primarily involves the aorta and its main branches. It usually affects young women of Asian descent, but it has been reported in all ethnicities with varying incidence [1]. The disease often presents in two stages: acute and chronic. In the first phase, symptoms are mostly constitutional, including malaise, fever, fatigue and arthralgia. As the disease progresses, narrowing and stenosis of major blood vessels affect regional circulation and organ functioning. The clinical presentation at that stage differs according to the vessels involved. Lesions of the aortic arch and its branches can cause neck and chest pain; numbness of arms; reduced, absent or asymmetric pulses in the extremities; and neurologic complaints such as headaches and visual disturbance. Involvement of pulmonary arteries could cause chest pain and dyspnea. Lesions in the abdominal aorta cause hypertension, intermittent claudication, and abdominal and lower back pain [1,2].

As TA early symptoms are similar to other systemic conditions, diagnosis is difficult and often overlooked. We report

here the case of a young man admitted with temporal tenderness that proved to be a first presentation of TA. A high level of suspicion led to comprehensive assessment, early diagnosis and prompt treatment.

PATIENT DESCRIPTION

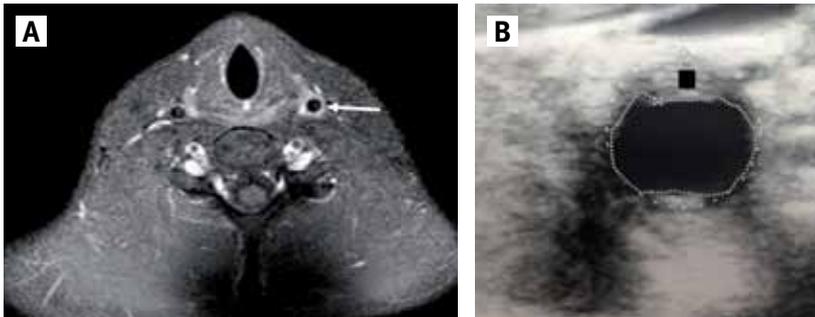
A 20 year old Caucasian Sephardic Jewish man presented to the emergency department with a 1 month history of worsening headache over the left temple together with lower back pain. The pain was constant throughout the day, awakening him from sleep, and was relieved with analgesics. During the previous week he also had fever reaching 38.5°C. He mentioned subjective loss of weight during the past month. He did not have chills, sweating, arthralgia, blurred vision or neurological symptoms. His past medical history included mild non-active bronchial asthma. He denied the use of alcohol, tobacco products or recreational drugs, and had not experienced a traumatic event.

On examination, temperature was 37.2°C, blood pressure 103/50 mmHg in the left arm and 118/57 in the right, pulse 76 beats per minute, and room air saturation 97%. There was severe tenderness over the area of the left temporal artery. A weak left temporal pulse was noted. Radial and dorsalis pedis artery pulses were equal and palpable bilaterally. Cardiac auscultation revealed normal sounds. No cardiac, carotid, subclavian or abdominal bruits were present. The rest of his physical and neurologic examinations were unremarkable. Fundoscopy of both eyes was normal.

Laboratory tests showed mild normocytic anemia (hemoglobin 12.3 g/dl, hematocrit 37.5%, mean cell volume 88.9 fl, mean cell hemoglobin 29.1 pg), mild hypoalbuminemia (3.10 g/dl), and elevated inflammatory biomarkers, namely erythrocyte sedimentation rate (ESR) 70 mm/hr and C-reactive protein (CRP) 129.02 mg/L. White blood cell count and differential; platelet count; levels of electrolytes; and renal, liver and thyroid function tests were normal. A possibility of TA was considered and the patient was admitted to the internal medicine ward for further evaluation.

Upon hospitalization, thoracic and abdominal computed tomography angiography (CTA) demonstrated concentric thickening of the left common carotid artery (CCA) and the diaphragmatic segment of the aorta. The walls of the superior mesenteric artery (SMA) and the origin of the celiac trunk were also thickened with mild narrowing of the lumen, with no decrease in blood flow. The pulmonary trunk and arteries were normal. No regional lymph node enlargement, pleural or pericardial effusion were seen. Magnetic resonance angiography (MRA) of the neck using gadolinium contrast media exhibited enhancement of the left CCA in a segment 4 cm long [Figure 1A]. A Doppler sonogram of the vessels in the neck showed segmental wall thickening of the left CCA [Figure 1B]. Transthoracic echocardiogram was within normal limits, exhibiting normal coronary arteries without aneurysms, no pericardial effusion and an estimated pulmonary pressure of 25 mmHg. A sonogram of the temporal arteries was normal.

Figure 1. [A] Magnetic resonance angiography (MRA) image showing enhancement of the left common carotid artery wall (white arrow). **[B]** Pre-treatment left carotid sonography showing soft tissue thickening in the wall causing luminal narrowing of 35% (black square)



For this reason, biopsy of the temporal artery was not performed.

Other conditions in the differential diagnosis were investigated. A serologic evaluation, including rheumatoid factor, antinuclear antibody, anti-double stranded DNA, antiphospholipid antibodies, anti-cardiolipin antibodies, and antineutrophil cytoplasmic antibodies, was unremarkable. Immunoglobulin level and serum protein electrophoresis were normal. Hepatitis panel test was negative. Epstein-Barr virus and cytomegalovirus serologic tests showed no evidence of active disease. Urine and blood cultures were negative. Urinalysis was normal. A test for *Treponema pallidum* was not performed since the patient's history and clinical signs were not compatible with syphilis.

Treatment with prednisolone 60 mg/day (1 mg/kg) was initiated with a rapid amelioration of the patient's symptoms and improvement in laboratory parameters (raised hemoglobin level of 15.00 g/dl and reduction in CRP 19.48 mg/L).

Two weeks after discharge the patient complained of minimal occasional headaches only. His inflammatory markers were further reduced (ESR 24 mm/hr and CRP 3.84 mg/L). Follow-up using carotid Doppler sonography demonstrated a decrease in the wall thickening of the left CCA. Treatment with oral methotrexate 12.5 mg/week and folic acid 5 mg/week was initiated, and tapering down of prednisolone was planned. Appointments for continuous monitoring in our clinic were scheduled.

COMMENT

We describe a young Caucasian man presenting with non-specific symptoms of systemic inflammation. Tenderness and diminished pulse in the left temporal area, headache, low back pain and elevated CRP and ESR were a clue for the diagnosis of large vessel vasculitis. This clinical picture resembled temporal arteritis. However, due to his young age, TA, another form of large vessels vasculitis, had already been suggested in the emergency department.

The incidence of TA is estimated to range from 0.4 to 2.6 cases/million. It is more common in young females under 40 years old [2]. Nearly equal representation in men and women has been reported in Israel, with a female to male ratio of 1.7:1 [3]. The average time from disease onset to diagnosis reported in the literature is months to years [2,4]. If diagnosis is delayed, TA can cause significant morbidity and compromised daily living function, and can even be life-threatening [5]. However, early diagnosis remains a challenge due to a wide range of clinical presenting symptoms.

There is no confirmatory blood test for TA. Laboratory signs of inflammation such as anemia, elevated CRP and ESR may be present, but these are not specific. Recent studies have investigated different biomarkers as potential diagnostic tools in TA: matrix metalloproteinases, interleukin (IL)-6, IL-18, soluble receptor for advanced glycation end-products, serum amyloid A, and others. However, none has

been found sufficient for diagnosis and for monitoring disease activity [1].

Imaging studies are essential for the diagnosis of TA. Radiographic angiography is considered the gold standard diagnostic modality. It enables visualizing the lumen of involved arteries. However, it does not assess arterial wall thickening and thus lacks sensitivity in early stages [1]. Recent advances in imaging allow early diagnosis and follow-up evaluation of TA with non-invasive tools. Positron emission tomography (PET) is a functional imaging modality that enables detection of active inflammation via increased uptake of radiolabeled glucose. PET is especially useful in the early inflammatory stage of TA. On the other hand, PET cannot delineate luminal patency and structure. CTA, MRA and color-Doppler sonography can outline luminal changes as well as provide information about the vessel wall. Therefore, they can point to early inflammatory signs such as wall thickening and edema, and later complications such as vascular narrowing, stenosis and aneurysms [1]. MRA and sonography are preferable modalities in serial imaging due to the lack of exposure to radiation [1]. Radiation exposure is of course a matter of concern, especially in this population of young patients.

In our case, CTA, MRI and carotid sonography studies were performed, confirming the diagnosis of TA. Carotid sonography also assisted in our primary follow-up. As the patient presented early in the course of the disease, he did not exhibit stenotic lesions on CTA and MRA. The American College of Rheumatology (ACR) 1990 criteria for the classification of TA [2,4] rely solely on the gold standard angiography studies and do not include current imaging modalities. In addition, the majority of criteria address the late stenotic phase of TA. Our patient was under age 40 when admitted, had more than 10 mmHg difference in systolic blood pressure in his arms, but showed no arteriographic signs of narrowing or stenosis; he therefore did not meet the ACR 1990 criteria for TA. However, he did meet Ishikawa's proposed criteria for the clinical diagnosis of TA [2]

with high probability, the major criteria being age under 40, duration of symptoms (headache, backache, fever) for more than one month, and minor criteria comprising involvement of mid-common carotid artery, involvement of abdominal aorta, and elevated ESR. We believe that the ACR 1990 criteria should be reconsidered to include newly developed imaging modalities (CTA, MRA, Doppler sonography and PET) in order to allow diagnosis of TA in the early stage of the disease before development of arterial structural damage. Early diagnosed disease could be controlled with

the standard therapies, and irreversible complications prevented [5].

This case report highlights the importance of modern-day imaging in the diagnosis of TA. Using the latest technology, we established the diagnosis of TA one month after the appearance of initial clinical symptoms. To our knowledge, it is the first reported case of TA diagnosis at such an early phase of the disease.

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