

Giant cell arteritis with CD8+ instead of CD4+ T lymphocytes as the predominant infiltrating cells in a young woman

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Giant cell arteritis is rarely reported in people aged less than 50 years. We report a case of giant cell arteritis in a woman who developed symptoms of dizziness, headache, bilateral sensorineural hearing impairment, and had 1 episode of transient left hemiparesis before the age of 30. Carotid angiography showed multiple segmental narrowing in cranial vessels. Subsequently, at the age of 31, she had weight loss and developed a fever. Chest radiograph revealed mediastinal widening, and chest computed tomography revealed dilated pulmonary arteries and veins. Coronary angiography and aortography showed irregular narrowing of the descending aorta and multiple stenosis, with aneurysmal dilatation involving the proximal and distal coronary, pulmonary and mesenteric arteries. Multinucleated giant cells and predominant CD8+ T lymphocyte infiltration were noted in a left temporal artery biopsy specimen. The patient's age and the finding of dilated pulmonary veins and prominent CD8+ T lymphocytes in the biopsy specimen suggest that this case was a distinct form of systemic giant cell arteritis.

Key words: Aneurysm, CD8+ T-lymphocytes, giant cell arteritis, pulmonary veins, sensorineural hearing loss, Takayasu's arteritis

Giant cell arteritis occurs almost exclusively in persons aged 50 or older [1]. It is characterized by chronic granulomatous inflammation of large and medium-sized arteries. The process has a predilection for the extradural cranial arteries.

We report a case of giant cell arteritis in a young woman who presented with systemic vasculitis. Multinucleated giant cells and predominant CD8+ T lymphocyte infiltrates were found in the biopsy specimen from the temporal artery. The patient also had clinical manifestations of bilateral hearing impairment and unexplained dilations of pulmonary veins, which rarely occur in giant cell arteritis.

Case Report

A young woman suffered from tinnitus since 1997 (age 26) and bilateral hearing impairment since 1999 (age 28). She had 1 episode of left hemiparesis with slurred speech in February 2000 at the age of 29. Ischemic stroke was documented by brain computed

tomography. She had a satisfactory recovery from neurologic deficit. However, hearing impairment persisted and dull temporal and occipital headache developed in February 2001. Carotid angiography at that time revealed dolichoectatic change over branches of bilateral external and internal carotid arteries (Fig. 1). The left temporal artery was dilated and palpable without tenderness. A vessel biopsy was suggested; however, the patient refused this procedure.

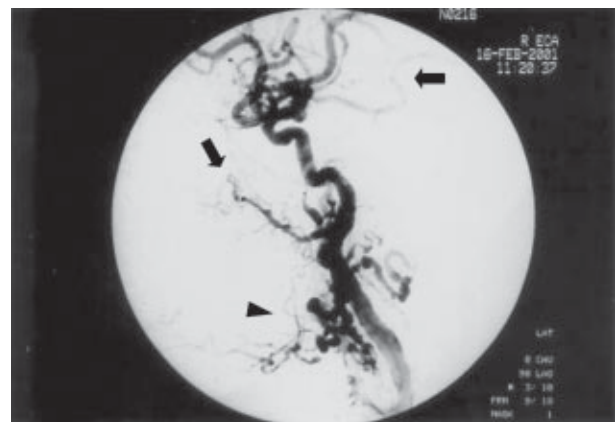


Fig. 1. Right carotid angiography showed multiple dolichoectatic change (arrowhead) and irregular narrowing (arrows) over branches of external and internal carotid arteries.

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Beginning in early 2002, the patient suffered from epigastralgia and poor appetite, with a resultant weight loss of 6 kg within 6 months. Panendoscopy conducted on admittance to National Taiwan University Hospital revealed esophagitis and gastritis. Following her discharge, she developed fever and chills with left flank pain in May 2002 leading to rehospitalization. On admission, physical examination revealed a chronically ill young woman with a body temperature of 38.8°C, heart rate of 84 beats/min, and blood pressure of 90/64 mm Hg (blood pressure in early 2002 was 100/60 mm Hg). A tortuous and dilated left temporal artery was noticed. Peripheral pulsation did not decrease in intensity. No bruit was audible at the carotid or subclavian areas. Blood pressure was checked at the 4 limbs and no obvious difference was evident between the 2 sides. There was no fragile skin, high palate arch or joint hypermobility. The patient also denied other manifestations such as oral ulcer, photophobia, floating body, red eyes and eye pain. Pathergy test was negative.

Laboratory testing revealed an initial white blood cell count of 3190/mm³, hemoglobin concentration of 11.7 g/dL, and a platelet count of 174,000/mm³. Serum C-reactive protein (CRP) level was 3.73 mg/dL (reference, <0.8 mg/dL). Erythrocyte sedimentation rate (ESR, determined by the Westergren method) was 10 mm in the first hour. Serological tests including hepatitis B, hepatitis C, Venereal Disease Research Laboratory slide test for syphilis, antineutrophil cytoplasmic antibody, and anticardiolipin antibody were negative.

Chest roentgenography showed a widened mediastinum, and computed tomography of the chest showed dilated pulmonary arteries and veins. Under suspicion of mycotic aneurysm or mediastinitis, empiric antibiotics (ceftriaxone and minocycline) were given. Fever subsided quickly after antibiotic administration. Blood cultures were negative and the antibiotics were discontinued.

Cardiac catheterization revealed normal hemodynamics and angiography showed irregular narrowing involving the thoracic and abdominal portions of the aorta. No valvular abnormality was found. Multiple stenoses with aneurysmal dilatation presenting a bead-like appearance were also noticed in branches of the coronary, mesenteric, and dilated pulmonary arteries. Pulmonary angiography in the venous phase showed marked dilatation of pulmonary veins at the junctions to the left atrium, which was compatible with the

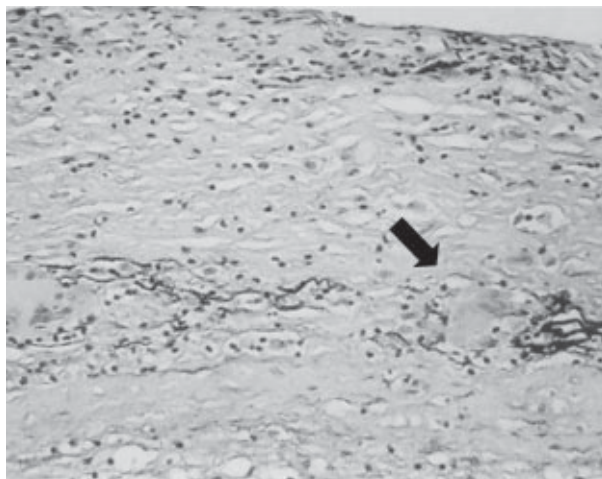


Fig. 2. Pathologic findings of left temporal artery biopsy included inflammatory infiltration with multinucleated giant cells, lymphocytes, eosinophils, plasma cells, and histiocytes. Two multinucleated giant cells show an intimate association with the internal elastic lamina, and the 1 indicated at the right of the micrograph (arrow) contains fragments of phagocytosed elastic fibers in the cytoplasm (elastic tissue stain, 66 × original magnification).

findings of chest computed tomography. Angiography found no evidence of systemic or pulmonary arteriovenous fistula.

A biopsy was done at the dilated and tortuous portion of the left temporal artery. Examination of the biopsy sample showed intimal thickening, subintimal fibrosis, and inflammatory infiltration with multinucleated giant cells, lymphocytes, eosinophils, plasma cells and histiocytes (Fig. 2). Some small nerve bundles were also enclosed in the inflammatory infiltration. Many of the multinucleated giant cells were close to the internal elastic lamina, and some contained fragments of phagocytosed elastica in their cytoplasm (Fig. 2). There was no fibrinoid necrosis of the blood vessels.

Immunohistochemical staining of the biopsy sample revealed a predominance of CD8+ T lymphocytes and an absence of CD4+ T lymphocytes. Neovascularization in the adventitia was demonstrated by CD31 immunohistochemical staining. Cytomegalovirus inclusion bodies were not evident in the vessel wall. Staining for Epstein-Barr virus was also negative.

The patient was treated with oral prednisolone at a reduced dose of 30 mg daily because of severe epigastralgia. CRP returned to normal levels after treatment. She was discharged 2 weeks after admission. The heavy sensation in her head improved and did not recur during 1 year of follow-up.

Discussion

This young patient initially presented with tinnitus, hearing impairment, headache, and stroke. The presence of headache, temporal artery abnormality, and abnormal temporal artery biopsy fulfill three of the five 1990 criteria of the American College of Rheumatology for giant cell arteritis [2]. Although the ESR in the first hour was not elevated as expected in this patient, only 86.5% of patients with giant cell arteritis have ESR ≥ 50 mm Hg [2].

The young age of this patient was unusual for giant cell arteritis, which typically occurs after age 50 [1] and is not frequently reported in young adults [3,4]. Hu et al reported temporal arteritis at a relatively young age in Chinese patients [5]. However, there was an unexplained male predominance of the arteritis and an absence of multinucleated giant cells in all 11 biopsy specimens of the temporal artery in their report, making the diagnoses inconclusive. In contrast, the detection of multinucleated giant cells in the temporal artery biopsy of the young woman of this report offers solid support for the diagnosis of giant cell arthritis.

The irregular narrowing of the thoracic and abdominal aorta and its branches is another concern in the differential diagnosis of giant cell arteritis. Although branches of the external carotid arteries are the most frequently involved vessels [6], large artery involvement can occur in 10-15% of patients [7]. Other causes of large vessel abnormality such as mycotic aneurysm, syphilis, Marfan's syndrome, polyarteritis nodosa, Behçet's disease, and Kawasaki disease can be excluded based on clinical criteria and appropriate laboratory, radiologic or pathologic studies.

Cogan's syndrome and Takayasu's arteritis can display aortitis and show some clinical features similar to those observed in our patient. Cogan's syndrome can manifest as inflammatory eye disease, vestibuloauditory dysfunction, and systemic vasculitis such as aortitis or systemic necrotizing vasculitis, and the presence of multinucleated giant cells in the aortic wall and large muscular arteries [8].

The diagnosis of Cogan's syndrome requires both ocular and audiovestibular manifestation. Cogan's syndrome is atypical if it is characterized by significant ocular inflammation apart from interstitial keratosis, iritis, or conjunctivitis or if more than 2 years have elapsed between the development of ocular and vestibuloauditory difficulties [9]. Our patient had no ocular manifestation even 5 years after the onset of

vestibuloauditory dysfunction. Furthermore, while hearing impairment has been reported in giant cell arteritis [10], the involvement of temporal artery has to our knowledge never been reported in Cogan's syndrome. Therefore, the diagnosis of giant cell arteritis rather than Cogan's syndrome seems to be indicated for this patient.

Concerning the possible diagnosis of Takayasu's arteritis, in this condition the involvement of aortic branches is usually limited to the proximal segments [11] and long segment stenotic lesions present in almost all patients [12]. These observations are strikingly different from the angiographic features noted in our patient. A form of disseminated visceral giant cell arteritis with diffuse involvement of coronary, renal and pulmonary arteries has been reported [13]. But, unlike our patient, all 4 reported cases occurred in men, and the cranial vessels were not involved.

Based on the pathologic evidence and location of lesions in large and medium-size vessels, systemic giant cell arteritis was diagnosed in our patient.

In giant cell arteritis, the vascular infiltrates contain multinucleated giant cells, histiocytes, plasma cells and lymphocytes. The lymphocytes are predominantly CD4+ helper T cells [14], which are critical in the disease process [15]. The temporal artery biopsy specimen of our patient showed multinucleated giant cells with typical distribution. However, the dominant lymphocytes were CD8+ T cells. The results of immunohistochemical study and the age of our patient were inconsistent with classical giant cell arteritis. Whether the atypical immunohistochemical staining was due to the timing of the biopsy or to a different pathogenesis is unknown. Although CD8+ T cells can outnumber CD4+ T cells or vice versa in lesions of Takayasu's arteritis [16], the radiologic findings in our patient excluded the diagnosis of Takayasu's arteritis.

One of the most striking features in this case was the finding of dilated pulmonary veins. To our knowledge, no similar finding has been reported in patients with giant cell arteritis or Takayasu's arteritis. Whether the dilated pulmonary veins and giant cell arteritis were caused by shared pathogenesis or were just a coincidental occurrence is unknown.

In summary, we report a case of giant cell arteritis with extended involvement of vessels. The age of the patient, the dilated pulmonary veins, and the predominant infiltration of CD8+ T lymphocytes in the biopsy specimen all support our contention that this case was a distinct form of systemic vasculitis with giant cell infiltration.

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