Int J Clin Exp Med 2019;12(1):1107-1112
www.ijcem.com /ISSN:1940-5901/IJCEM0078159

Case Report

Giant cell arteritis involving the aorta and its major branches: a case report and literature review

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Received October 25, 2017; Accepted October 9, 2018; Epub January 15, 2019; Published January 30, 2019

Abstract: Giant cell arteritis (GCA) is an inflammatory vasculopathy involving large and mid-sized vessels that commonly occurs in elderly people. GCA mainly affects cranial arteries derived from carotid artery, and only 10-15% cases involve the aorta and its major branches. Herein, we described a 78-year-old female patient who initially presented with mild headache, followed by pain in the limbs and pulselessness. Vascular ultrasound and computed tomography angiography showed multiple arterial stenosis, sclerosis, and occlusions. The temporal artery biopsy confirmed the presence of GCA. After therapy with methylprednisolone and cyclophosphamide, the pain in the limbs had disappeared, and the fingers had obviously improved. We also conducted a systematic review of 11 previously reported cases of GCA with pulselessness.

Keywords: Giant cell arteritis, pulselessness

Introduction

Giant cell arteritis (GCA) is a type of granulomatous arteritis involving large and mid-sized arteries, which mainly influences the extra cranial branches of the internal and external carotid arteries, particularly the temporal artery. GCA occurs predominantly in females, with a mean age at diagnosis of 79 years (range, 50-90 years) [1, 2]. Typical symptoms include headache, loss of vision, jaw claudication and polymyalgia. However, atypical symptoms may appear as initial manifestations, which delay the diagnosis and treatment. Herein, we described a case of GCA in an elderly female with complaints of pulselessness and headache, and also conducted a systematic review of 11 previously reported cases.

Case presentation

A 78-year-old female was admitted to our department with headache, pain in the limbs and pulselessness. She reported that the headache appeared five months ago with no obvious trigger, especially the bilateral temporal, accompanied by excessive bilateral temporal artery filling. The headache was relieved after 20 days. Four months ago, she experienced pain in the upper limbs and her fingers were white and cold. Two months later, the pain extended to her lower limbs, and the radial artery and dorsalis pedis artery pulses disappeared. The patient did not have any typical risk factors for arteriosclerosis such as smoking, hypertension, diabetes, and hyperlipidemia. She had a history of tuberculosis and hysterectomy. There were no other positive findings on physical examination. Initial laboratory investigation indicated mild anemia and significantly elevated inflammatory markers (erythrocyte sedimentation rate 110.0 mm/h, C-reactive protein 24.7 mg/L). The renal and liver function tests were normal. Assessments for infectious and autoimmune diseases were negative. Vascular ultrasound and computed tomography angiography showed multiple arterial stenosis, sclerosis, and occlusion, which included carotid artery, vertebral artery, supraclavicular artery and subclavian artery, bilateral upper limb artery and bilateral popliteal artery (**Figures 1** and **2**). Computed tomography showed changes in the temporomandibular joint. Hence, a left temporal artery biopsy was performed that

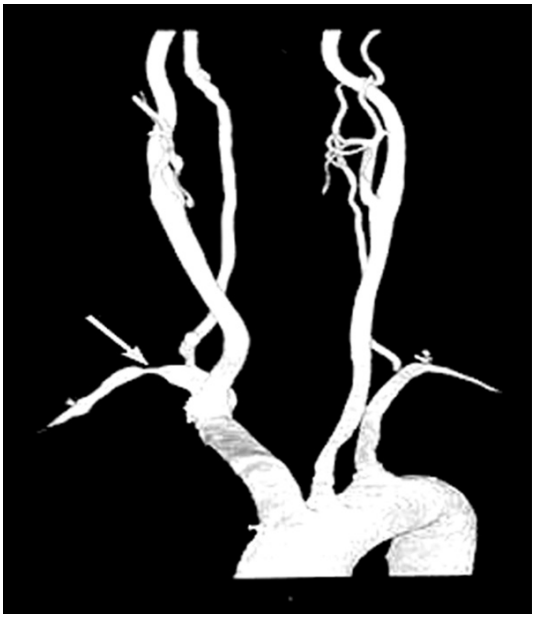

Figure 1. Head and neck computed tomography angiography showed right subclavian artery proximal stenosis, with narrowing of about 70%.

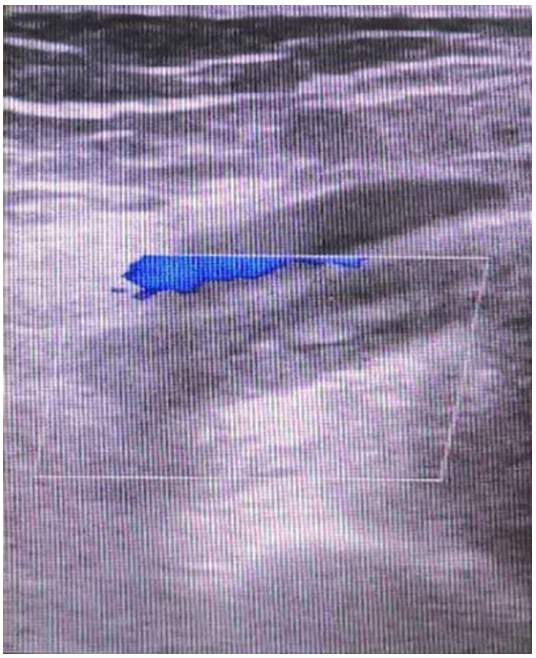

Figure 2. Vascular ultrasound showed popliteal artery occlusion.

showed the vascular wall was thickened, the lumen was narrow, and there were numerous inflammatory cells, epithelioid cells and individual multinucleated giant cells infiltrating into the blood vessel wall (**Figure 3**). At the same time, the patient was older than 50 years old and developed a new headache, temporal artery abnormalities, the erythrocyte sedimentation was larger than 50 mm/h. According to the American College of Rheumatology 1990 GCA classification criteria, the diagnosis of giant cell arteritis can be obtained. The patient was immediately administered methylprednisolone (40 mg intravenous) and cyclophosphamide (0.2 g, once daily for two days), supplemented by low molecular weight heparin (3200 U, once daily) and clopidogrel (50 mg, once daily). The patient presented a significant clinical and laboratory response. One month later, her inflammatory markers returned to normal (erythrocyte sedimentation rate 23.0 mm/h, C-reactive protein 1.04 mg/L). Subsequently, methylprednisolone dose was gradually reduced. At the three-month follow-up, the pain in the patient's limbs had gradually disappeared and her fingers felt normal. However, she had no palpable radial artery and dorsalis pedis artery pulses. The erythrocyte sedimentation rate and C-reactive protein were within normal range. The present study was approved by the ethics committee of Xiangya Hospital. Written informed consent was obtained from the patient prior to enrollment in the study. All specimens were anonymously handled in accordance with the Declaration of Helsinki and legal standards.

Literature review

A literature search of PubMed was conducted for all case reports of patients presenting with pulselessness as a clinical manifestation of GCA. Nine articles published between January 1996 and July 2017 were identified, which reported 11 cases (**Table 1**). All the patients were elderly females, >50 years. The main manifestations included pain in the limbs and claudication. Digital necrosis occurred in the severely affected individuals. Only one case experienced headache. No typical clinical features such as jaw claudication, visual impairment and polymyalgia rheumatism were observed. These findings confirmed that large arterial lesions were often unaccompanied by headaches or other typical GCA symptoms. In most cases, the upper limbs were involved, with only one case involving the lower extremity arteries. All patients had a significant increase in erythrocyte sedimentation rate and C-reactive protein, and imaging examinations showed arterial stenosis or occlusion. All patients were treated with high doses of corticosteroids at the time of diagnosis of GCA.

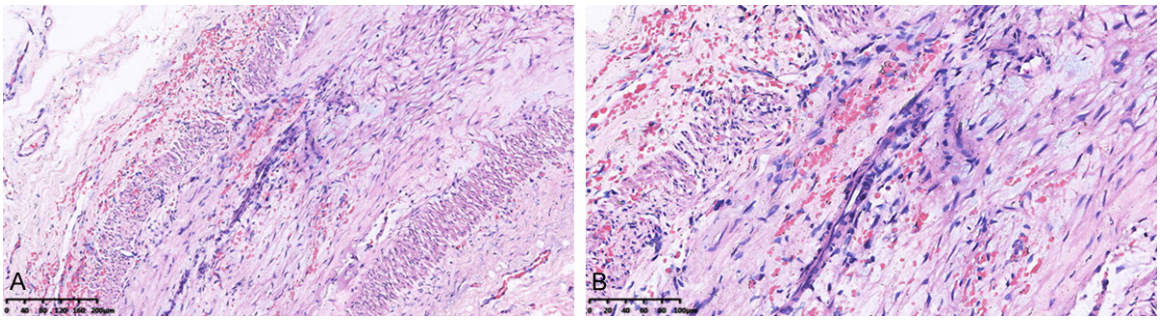

Figure 3. Temporal artery biopsy showed the vascular wall was thickened, the lumen was narrow, and there were numerous inflammatory cells, epithelioid cells and individual multinucleated giant cells infiltrating into the blood vessel wall.

Most patients had satisfactory responses to corticosteroids. However, four patients progressed rapidly and required surgical treatments.

Discussion

The typical manifestations of GCA include headache in 90% of cases, polymyalgia rheumatism (34%), jaw claudication (50%), amaurosis fugax, and blurred vision (40%) [3]. However, approximately 40% of the patients experience atypical symptoms [4, 5]. Within this group, clinical involvement of the aorta and its major branches is initially found in 10-15% of the patients, which eventually increases to 27% [6]. Often early lesions are arterial stenosis, leading to intermittent dyskinesia; carotid artery, subclavian artery, brachial artery and brachial artery murmur; weakened or no pulse in neck or limbs and Renault phenomenon. Late lesions are mainly aneurysms. A study of 41 patients who developed a trend toward advanced aneurysms showed that the average time from diagnosis of GCA to the onset of these complications was seven years [7]. Patients with large vessels stenosis generally have fewer cranial symptoms and changes in the temporal arteries on biopsies as well as a less pronounced increase in acute-phase reactants [6]. The patient in the present case report had headache and aortic stenosis. Her erythrocyte sedimentation rate and C-reactive protein were significantly increased, and temporal artery biopsy was positive. The diagnosis was in line with the 1990 American College of Rheumatology (ACR) classification criteria for GCA [8].

Similar to GCA, Takayasu arteritis (TA) is also a granulomatous vasculitis that predominantly affects large and medium-sized vessels [9]. Both diseases predominantly occur in women. However, TA is typically seen in younger individuals, <40 years. It mostly involves the aorta and its major branches, whereas GCA is predominant in people >50 years, and mainly affects branches of the external carotid artery. The clinical manifestations of TA can vary depending on the arteries involved. Patients can be asymptomatic or have sporadic findings that may lead to diagnosis (eg, decreased peripheral artery pulses, blood pressure difference between arms and legs, bruits and hypertension) or present dramatic symptoms/signs (eg, congestive heart failure, cerebrovascular event, or aortic aneurysm disruption) [10-13]. Our patient was initially hospitalized in the medicine department of our hospital because of pain in the limbs and pulselessness, which were consistent with the typical clinical manifestations of TA. Since the patient was 78 years old, we asked the detailed history again. One month before the onset of pain in the limbs, the patient had a headache, the bilateral temporal arteries were obvious and overfilled. So we suspected GCA and performed the temporal artery biopsy, which confirmed GCA. Thus, it is occasionally difficult to distinguish between GCA and TA due to similar clinical, radiographic and histologic features. It has been proposed that GCA and TA are different phenotypes of a single disease spectrum [14-16]. Hence, the therapeutic approach to GCA and TA is generally similar.

Corticosteroids remain the cornerstone of therapy for GCA because of their rapid action and suppression of inflammatory symptoms, and the ability to prevent GCA-related ischemic events. Nevertheless, there is limited evidence supporting this strategy for GCA patients with

Table 1. Literature review of reports on giant cell arteritis patients with pulselessness

Author	Reference	Pulseless arteries	Age/Gender	Associated symptoms	ESR/CRP	Treatment
Almeida-Morais L (2016)	[22]	Bilateral radial or cubital arteries	80/Female	Bilateral arm claudication, severe pain with restricted mobility, cold extremities and digital necrosis	120/123	Prednisolone(1 mg/kg/d) Surgery: A bilateral cartoid-humeral bypass
Shibutani S (2011)	[23]	Right distal artery	75/Female	Right arm claudication, weight loss	108/2.5	Prednisolone 50 mg/d Surgery: The stenotic segment of the right brachial artery was resected and restored blood flow by the interposition graft with autologous saphenousvein
Stephen Bagg (2006) case1	[24]	Left ulnar and radial arteries	79/Female	Sudden onset left arm pain	112/4.3	Prednisolone 60 mg/d
Stephen Bagg (2006) case2	[24]	Arteries of both upper extremitis	75/Female	Bilateral arm pain and cramping with activity, jaw claudication	-	-
Cohen HE (2003)	[25]	Right radial and brachial arteries	69/Female	Acute ischaemic right arm	26/-	Intravenous methyl-prednisolone convert to oral prednisolone (60 mg) Surgery: Right arm embolectomy and above-elbow amputation
De Bruyne L (2001)	[26]	Arteries of left upper extremitis	66/Female	Anorexia, nausea, epigastric discomfort, weight loss, left arm pain	142/16.1	Methylprednisolone (32 mg)
Le Hello C (2001) case 1	[27]	Bilateral radial and brachial arteries	57/Female	Headache, temporal artery abnormality, arm claudication	88/-	Prednisolone (1 mg/kg/d)
Le Hello C (2001) case 2	[27]	Bilateral radial and brachial arteries	60/Female	Arm claudication	140/-	Prednisolone (1 mg/kg/d), Surgery: M-1: bilateral femoropopliteal bapasses M0: unilateral amputation
Kelly J (2001)	[28]	Bilateral radial and brachial arteries	72/Female	Malaise, lethargy, cold hands, arm weakness	80/107	Prednisolone
García Vázquez JM (1999)	[29]	Bilateral pedial or tibial pulse, left popliteal pulse	52/Female	Weight loss, asthenia,ischaemia in both lower limbs and left upper limb	121/154	Prednisolone 40 mg/d
Hatzis GS (1996)	[30]	Left radial and brachial arteries were absent, right branchial artery was faint	53/Female	Fainting	44/88	Prednisolone 40 mg/d

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

involvement of limbs and arteries. For most patients, an initial dose of 40-60 mg/day prednisolone appears to be adequate. GCA combined with impending visual loss may require higher doses of intravenous methylprednisolone (1 g daily for three days) followed by oral prednisolone [17]. Withdrawal of corticosteroids can be attempted after four weeks by closely monitoring the clinical symptoms, and erythrocyte sedimentation rate and C-reactive protein levels [17]. Even if the dose of prednisone is gradually reduced, >50% of patients show recurrence in the first year [18]. Patients at highest risk of recurrence are those with initial strong systemic inflammatory response [19] or pre-existing complications such as diabetes and hypertension [20]. Usually, prednisone 10 mg is given based on the last dose used for disease control, which can control the relapse. However, the incidence of glucocorticoid-related adverse events in GCA is very high, with up to 86% patients experiencing these events at 10 years [21]. Adding immunizing agents such as methotrexate, azathioprine, cyclophosphamide, or reducing the levels of hormones can prevent disease recurrence. IL-6 blockade is also beneficial in GCA. The current findings indicate that a single targeted treatment may be inadequate, and combined therapy may be the best option for the future. Patients with severe ischemic symptoms, who are unresponsive to corticosteroids, may require arterial surgeries. The indication for surgical treatment should be based on the severity of the clinical symptoms of upper/lower limbs associated with GCA in order to avoid unnecessary morbidity during interventional therapy. In the present case, the patient's symptoms were significantly relieved after initiation of corticosteroid therapy. Though pulselessness persisted, the patient did not feel particularly uncomfortable, so surgical treatment was not considered.

Conclusion

Pulselessness in elderly should serve as a warning for GCA, although it is rarely an initial presentation. The physician should be aware of this atypical symptom, and strive for early diagnosis and treatment in order to delay the progression of the disease. Patients at highest risk of relapse are those with strong initial systemic inflammatory response or pre-existing comorbidities, such as diabetes and hypertension.

Acknowledgements

The patient agreed to the publication of this report.

Disclosure of conflict of interest

None.

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