

## Case Series

# Unusual etiology of stroke in young adults: think of Takayasu's arteritis

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## ABSTRACT

Takayasu arteritis is an uncommon inflammatory disease of vessels that preferentially affects the aorta and its major branches. It can be a potential cause of stroke in young adults. Current study included 7 patients aged between 18 to 48 years. Each patient had varying presentations of stroke with Takayasu's arteritis along with other neurological symptoms. Four of the 7 patients presented with ischemic strokes, one with hemorrhagic stroke, one with TIAs and one with syncopal attacks. All the patients had elevated erythrocyte sedimentation rates. Five of the seven patients were treated with steroids and methotrexate. Two were treated with azathioprine and steroids. Antiplatelets were given for those patients who had strokes and TIAs. Our cases demonstrate that Takayasu arteritis can present with varying presentations including stroke. Thus, it is important to consider Takayasu's arteritis as an unusual etiology of stroke especially in young adults.

**Keywords:** Takayasu's Arteritis, Stroke, Young stroke

## INTRODUCTION

Takayasu arteritis (TA) is an uncommon inflammatory disease of vessels that preferentially affects the aorta and its major branches. It can be a potential cause of stroke in young adults. The precise etiology of TA is unknown. An infectious process may act as a trigger. The inflammation is mediated by T cells, macrophages, and dendritic cells in the arterial wall. Elevated interleukin-6 and tissue necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels correlate with ongoing disease activity.<sup>1</sup>

An association with the HLA-B\*52 allele has been reported, which is more prevalent in Asian populations.<sup>1</sup> The primary sites of involvement include the aortic annulus and the origin of the great arteries from the aortic arch.<sup>2</sup> The inflammatory process, consisting of macrophages and giant cells, starts in the media and

adventitia of the vessel wall before becoming panarteritis.<sup>2</sup> This ultimately results in extensive fibrosis of the aorta and increases arterial wall thickness.<sup>3</sup> An aortic aneurysm, aortic valve disease, and extensive disease of the extracranial vasculature can develop as a complication. In comparison to Giant cell arteritis, which affects persons more than 60 years of age, few pathologic findings may overlap between the two diseases especially those with aortic involvement. In the following case series, we present seven patients of Takayasu's Arteritis with unique neurological presentations and stroke.

## CASE SERIES

### Case 1

An 18-year-old female presented with sudden onset left sided weakness. She had a past history of 3 episodes of

transient left sided weakness in the last 7 months, which improved within 1 hour each time. She also had sudden painless loss of vision in the right eye 5 months ago. Examination revealed absent pulses in both upper limbs. Right carotid bruit was present. Blood pressure in both lower limbs was 190/110 mmHg. Eye examination showed presence of RAPD in the right eye and pale disc on fundoscopy. There were signs of left hemiparesis. Laboratory investigations revealed an erythrocyte sedimentation rate of 70 mm at 1 hour. CRP was 8 mg%. ANA and APLA were negative. Renal function tests were normal. CT aortogram showed features suggestive of type I aortoarteritis. MRI brain showed infarct in the right MCA territory (Figure 1). Patient was started on antiplatelets, steroids and methotrexate. She made a good recovery.



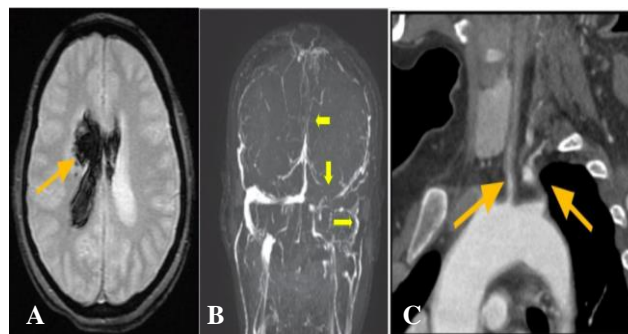
**Figure 1: CT aortogram depicting type I aortoarteritis.**

#### Case 2

A 27-year-old female presented with sudden onset right sided weakness. Examination revealed absent upper limb pulses. Right carotid was feeble. Blood pressure in lower limbs 150/100 mmHg. Signs of right hemiparesis were present. ESR was 82 mm at 1 hour. CRP was 6 mg % and ANA, APLA negative. Renal function tests were normal. CT aortogram confirmed Type I aortoarteritis. MRI brain showed a large infarct in the left fronto parietal region. Patient was treated with antiplatelets, steroids and methotrexate.

#### Case 3

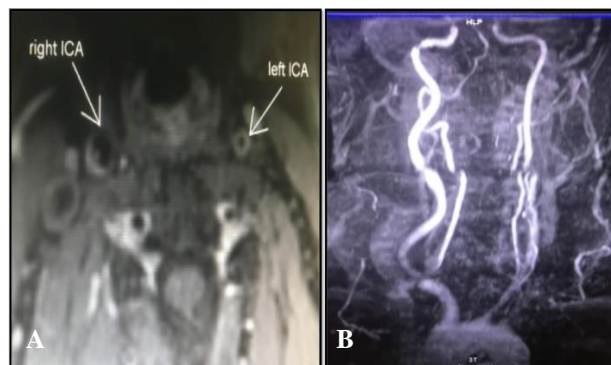
A 26 years old primigravida, previously healthy, presented at term with catastrophic headache, drowsiness and left sided weakness. On examination, the patient was drowsy but arousable. Blood pressure was not recordable in the upper extremities. In lower extremities, it was 220/110 mmHg. Laboratory investigations revealed ESR of 95 mm at 1 hour, CRP-12 mg% with ANA, APLA negative. CT aortogram confirmed type I aortoarteritis. MRI brain revealed right corona radiata bleed with intraventricular extension (Figure 2). Venography showed thrombosis of left internal jugular vein, transverse and sigmoid sinuses. She was treated with heparin, steroids and azathioprine.



**Figure 2: A) GRE images showing blooming; B) CT venogram is showing thrombosis of the SSS, left transverse sinus and left IJV; C) Type I aortoarteritis.**

#### Case 4

A 48 years old male patient presented with history of 3 strokes in the past year all presenting with right sided weakness. Examination revealed absent upper limb pulses and BP of 160/100 mmHg in both lower limbs. Patient had Broca's aphasia and signs of right hemiparesis. Investigations showed ESR of 52 mm at 1 hour, CRP 1.2 mg% and ANA, APLA, were negative. CT aortogram showed presence of type I aortoarteritis. MRI brain revealed chronic infarcts in the left cerebral hemisphere in left MCA territory (Figure 3). Vessel wall imaging revealed vasculitic involvement of left petrous ICA. He was treated with steroids, antiplatelets and methotrexate.



**Figure 3: A) On vessel wall imaging, left ICA showing circumferential thickening suggestive of vasculitis; B) CT aortogram showing type I aortoarteritis.**

#### Case 5

A 39-year-old female with past history of left sided Transient ischemic attacks, presented with left upper limb progressive weakness, wasting and paraesthesias over 2 months. Examination showed absent pulses in the left upper limb. Blood pressure was 180/90 mmHg in both lower limbs and 140/70 mmHg in the right upper limb. Weakness, wasting and sensory deficit were observed in distal left upper limb. Investigations showed ESR of 65 mm at 1 hour, CRP- 1.6 mg% and negative ANA, APLA.

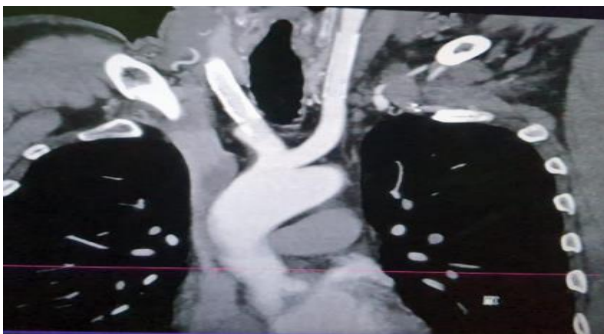
CT aortogram showed presence of type I aortoarteritis. MRI brain was normal. Nerve conduction studies revealed mononeuritis multiplex pattern involvement of the left upper limb. Patient was managed with steroids and azathioprine.

### Case 6

A 22 years female presented with a 3-month history of recurrent syncopal attacks. Examination revealed feeble upper limb pulses. Blood pressure was 150/90 mmHg in both lower limbs. A Subclavian bruit was present. There was no evidence of neurodeficit. Investigations showed ESR of 33 mm at 1 hour, CRP 6.8 mg% and negative ANA, APLA. CT aortogram showed type I aortoarteritis and normal MRI brain. She was treated with antiplatelets and methotrexate.

### Case 7

A 43-year-old male presented with sudden onset right hemiparesis. He had a history of recurrent TIA's of both sides in the past 5 years for which he had undergone angioplasty and stenting in both common carotid arteries and left subclavian artery. Examination revealed feeble upper limb pulses. Blood pressure in both lower limbs was 180/110 mmHg. There were signs of right hemiparesis. ESR was 16 mm at 1 hour, CRP was 2.2 mg%, ANA and APLA were negative. CT aortogram revealed type I aortoarteritis and MRI brain showed left MCA territory infarct (Figure 4). He was treated with steroids, antiplatelets and methotrexate.



**Figure 4: Type I aortoarteritis with multiple stents in situ.**

### Observations

Current study included 7 patients aged between 18 to 48 years. Of the 7 patients, 5 were female and 2 were male. All cases had varied neurologic presentations and associations. The first case had left hemiparesis and evidence of anterior ischemic optic neuropathy. Second case presented with right hemiparesis. Third case presented as a primigravida with intracerebral bleed and also had evidence of venous sinus thrombosis. The fourth patient was a 48-year-old male who presented with recurrent strokes and Broca's aphasia. The fifth patient

presented with recurrent TIA's and multiple mononeuropathy type involvement of the left upper limb. Sixth case presented with recurrent syncopal episodes due to subclavian steal phenomenon. The last case presented with recurrent strokes. All the patients in our series had elevated erythrocyte sedimentation rates. Five of the seven patients were treated with steroids and methotrexate. Two were treated with azathioprine and steroids. One patient was given heparin on account of cerebral venous sinus thrombosis. Antiplatelets were given for those patients who had strokes and TIAs.

### DISCUSSION

Takayasu's arteritis, which is a chronic inflammatory disease of the vessels, has unknown etiology. It is also known as pulseless disease. It usually affects the aorta and its main branches.<sup>2,4</sup> The first description of the disease was by Dr. Mikito Takayasu<sup>5</sup> a Japanese ophthalmologist, in 1905, where he described a young female with retinal arterio-venous anastomoses, syncope, and absent upper extremity pulses. Takayasu's arteritis is most commonly seen in females between the ages of 11 and 30 and is more common in Japan, Southeast Asia, India, and Mexico.<sup>6</sup> In India, few studies have reported a female to male ratio of 1.58:1 in Indian patients.<sup>7,8</sup> Indian male patients with TA have a higher frequency of hypertension and abdominal aorta involvement while female patients have a tendency towards involvement of aortic arch and its branches.<sup>9</sup> The average age of the Indian patient presentation is in the third decade.

The etiology of the disease is unknown, but an autoimmune process may be responsible, as it has associations with certain human leukocyte antigen (HLA) alleles and other autoimmune processes such as sarcoidosis and inflammatory bowel disease. Chronic infections such as tuberculosis may also have an association.<sup>10</sup>

With regards to the evolution of the disease, there may be two distinct phases of Takayasu arteritis (TA), active inflammatory phase and late chronic phase. The active phase, which is early, is characterised by symptoms such as malaise, fever, night sweats, arthralgias, headaches and rashes. During the chronic phase, which is late, vessel involvement is apparent. Those in the late chronic phase may have renovascular hypertension, acute mesenteric ischaemia, retinopathy, amaurosis fugax, transient ischaemic attacks and strokes.<sup>2</sup> As per studies, the incidence of stroke in patients of TA has been between 10% to 20%<sup>11</sup>. It is even rarer to have stroke as the initial manifestation of TA.<sup>12</sup> The various mechanisms of stroke in this setting include embolism from a proximal large vessel, occlusive lesions from stenosis, hypertension and cerebral hypoperfusion. The overall rarity of this condition is responsible for the delay in diagnosis especially when presenting with an ischemic stroke.<sup>13</sup> When patients have neurological deficits in the presence

of systemic symptoms, TA should be considered in the differential diagnoses.<sup>13</sup>

In 1990, the American college of rheumatology proposed a set of criteria which would help in the diagnosis of Takayasu arteritis.<sup>14</sup> The criteria include; age <40 years, claudication of an extremity, decreased brachial artery pulse, >10 mmHg difference in systolic blood pressure between arms, a bruit in subclavian arteries or aorta and angiography evidence of narrowing or occlusion of the aorta, its primary or proximal branches. Three of the six criteria need to be present for the diagnoses which have 90.5% sensitivity and 97.8% specificity. ESR and CRP are the markers that are commonly used to identify systemic inflammatory conditions. However, they are not reliable indicators and may underestimate disease activity as compared to arterial histopathology or angiography.<sup>15</sup> CT, doppler angiography and MRI/magnetic resonance angiography are the imaging techniques that help in diagnosis and can also be used to study disease progression and response to therapy. Based on changes of vascular lumen, including stenosis, occlusion, wall irregularity or aneurysm, an angiographic classification, has been proposed which classifies findings into four types; type I affects the aortic arch and its branches, type II involves the descending thoracic and abdominal aorta, type III is an extensive form affecting the arch and the thoracic and abdominal aorta and type IV involves pulmonary circulation in addition to findings of other types.<sup>16</sup>

The immediate aim of therapy is to treat acute vascular compromise through either medical treatment with thrombolytics or surgical or interventional revascularization. Long term therapy is aimed at reducing vessel wall inflammation and control of vascular disease and comorbid conditions. Glucocorticoids are the drugs which are commonly used to reduce inflammation. Other immunomodulators like methotrexate, cyclophosphamide and azathioprine can be used as steroid sparing therapies. Despite long term treatment with medical therapies, many patients will still have progressive vascular disease. As medical management does not reverse pre-existing vascular stenosis or occlusion, surgical or interventional revascularization may be needed if hemodynamic compromise is present.<sup>17,18</sup> As per studies, five-year survival is estimated to be 80% and depends on the clinical features of the disease and response to medical and surgical therapy.<sup>19</sup>

## CONCLUSION

Our cases demonstrate that Takayasu arteritis can present with varying presentations including stroke. In such patients, following assessments such as checking pulses in all limbs, measuring blood pressure in upper and lower limbs, measuring erythrocyte sedimentation rates, which aid in diagnosis as well as monitor disease activity and performing CT angiogram with CT aortogram upto diaphragm, may prove useful. Thus, it is important to

consider Takayasu's arteritis as an unusual etiology of stroke especially in young adults.

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