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Case Report

Recurrent stroke in Takayasu arteritis: a case report and review of literature

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ABSTRACT

Takayasu arteritis is a rare inflammatory vasculitis affecting medium to large blood vessels. Neurologic complications are seen in 10-20% of cases. A 28 year old female came in due to acute onset left sided weakness and numbness, with absent arterial pulses and blood pressure on the left extremities. She had a history of recurrent right-sided weakness and numbness. Imaging showed an infarct on the right thalamus and multiple chronic infarcts. CT aortogram was consistent with Takayasu arteritis type V. The patient was started dual antiplatelet consisting of aspirin and clopidogrel, and was started on Prednisone and Methotrexate with good clinical response.

Keywords: Takayasu arteritis, Ischemic stroke, Recurrent, Case report

INTRODUCTION

Stroke is the second leading cause of mortality worldwide, wherein 10-15% of these happen in individuals younger than 45 years of age.[1] Stroke in the young has a higher incidence in developing countries which can be attributed to poor health seeking behavior and differences in lifestyle. It is more economically debilitating when stroke affects younger individuals compared to older adults. Common causes of stroke include atherosclerosis and embolism. However, in stroke in the young, a wider range of conditions including systemic inflammatory or autoimmune diseases, hypercoagulable states, and vascular diseases such as dissection should be considered.[2]

Takayasu arteritis, also known as pulseless disease or occlusive thromboaortopathy, is a form of vasculitis of unknown cause that mainly involves the aorta and its major branches. It affects women eight times more frequently than men, and is more common in the young. The median age at onset is 25 years; however, approximately 25% of cases begin before age 20, and 10% to 20% after age 40 years.[3]

Neurological manifestations include lightheadedness, visual abnormalities, headache, transient ischemic attacks and stroke are seen among patients with Takayasu arteritis.[4] According to reports, 10-20% will suffer an ischemic stroke or Transient ischemic attack.[5]

CASE REPORT

A 28 years old, Filipino female, right-handed, was admitted for sudden onset of left sided body weakness and numbness. She initially presented with dizziness, limb claudication and pulselessness since 2014. She had recurrent episodes of cerebrovascular disease last April 2020 and April 2021 during which she presented with right sided body weakness and numbness lasting for 24 hours wherein she was given anti-coagulants. She was diagnosed with postpartum cardiomyopathy in 2020 and is taking the following medications: digoxin, carvedilol, enalapril, atorvastatin, dabigatran and folic acid with good compliance.

On admission, blood pressure measurements taken on the right upper and lower extremities were 140/90 and 130/80, respectively. BP was unappreciated on the left

extremities. Pulse rate was 80 beats per minute on the left carotid and right extremities. Pulses were not appreciated on left brachial, radial, popliteal, posterior tibial, and dorsalis pedis. On neurologic examination, the patient was awake, alert, able to follow commands. Cranial nerve examination was unremarkable. There was left-sided hemiparesis with 4/5 on manual muscle testing and 70% sensory deficit on her left sided extremities. She had hyperreflexia on the left biceps, triceps, brachioradialis, patella, and ankle. An extensor toe sign was seen on the left.

Review of her previous arterial ultrasonography from 2013 revealed left upper extremity arterial disease with total occlusion in the proximal segment of the subclavian artery with flow reconstitution via collateral in its mid segment and complete subclavian steal. CT aortogram done in this admission revealed multiple stenoses and fusiform dilatations throughout the course of the thoracic and abdominal aorta, as well as its arch and visceral branches; luminal narrowing were seen in both internal iliac arteries; tortuous right subclavian artery shows multiple moderate to severe stenoses and a fusiform aneurysm; a teat like projection representing the stenotic proximal left subclavian artery; several fusiform aneurysms are seen at the distal descending thoracic aorta the distal abdominal aorta; the bilateral internal iliac arteries are narrowed consistent with type V Takayasu arteritis. (Figure 1).

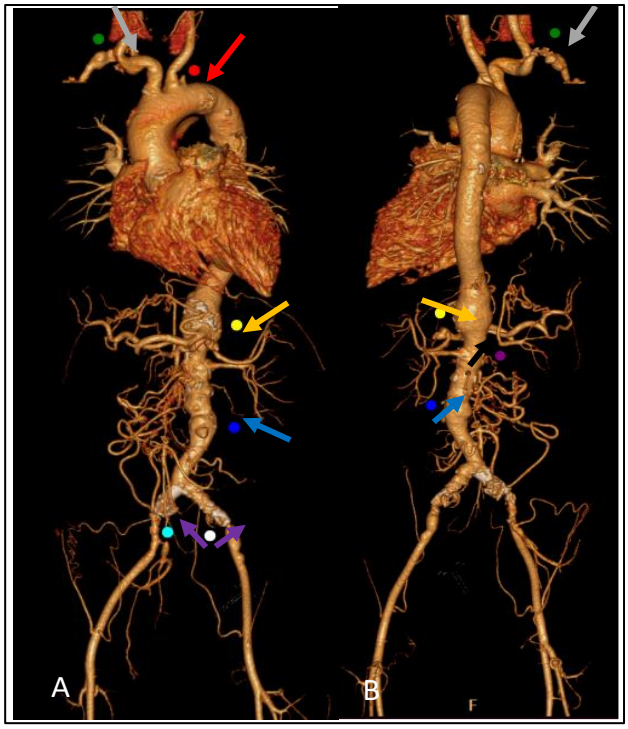

Figure 1 (A and B): CT aortogram 3D reconstruction in PA and AP views of the entire aorta.

There are multiple stenoses and fusiform dilatations throughout the course of the thoracic and abdominal aorta, as well as its arch and visceral branches. Luminal narrowings are seen in both internal iliac arteries. A tortuous right subclavian artery shows multiple moderate to severe stenoses and a fusiform aneurysm (green arrow). A teat like projection representing the stenotic proximal left subclavian artery (red arrow). Several fusiform aneurysms are seen at the distal descending thoracic aorta (yellow arrow) the distal abdominal aorta (blue arrow). The bilateral internal iliac arteries are narrowed (purple arrowheads).

Cranial MRI with IV contrast and MRA was done on day 19 post-ictus. It showed chronic slit-like hemorrhage in the left external capsule, multiple chronic infarcts in the lateral aspect of the right cerebellar lobe, right hemipons, and left caudate head with subacute infarct in the right thalamus. MRA revealed hypoplastic vertebral and basilar arteries and multiple segmental stenosis on bilateral internal carotid arteries and bilateral middle cerebral arteries. (Figure 2).

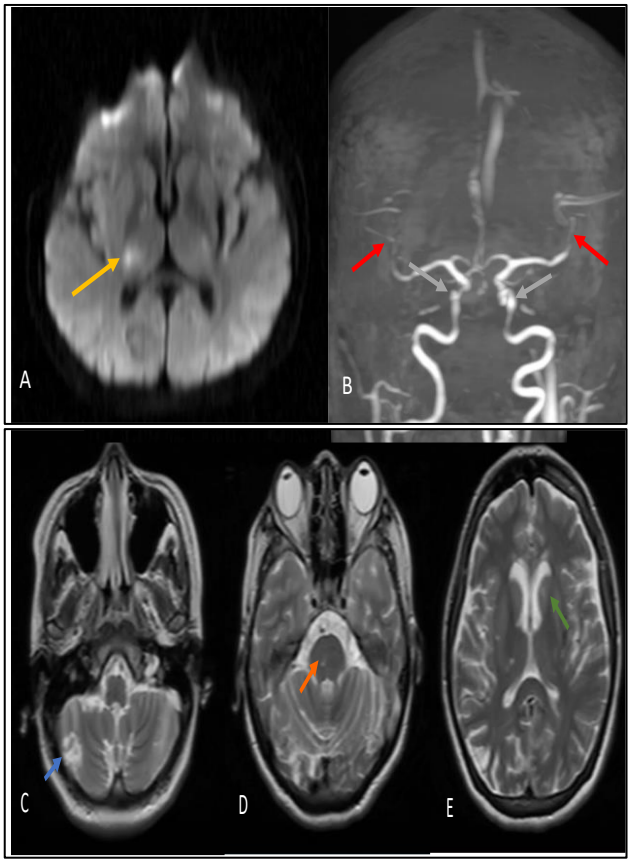

Figure 2 (A-E): Diffuse weighted magnetic resonance images revealed hyperintensity in the right thalamus (yellow arrow). Magnetic Resonance angiography revealed hypoplastic vertebral and basilar arteries and multiple segmental stenosis on bilateral internal carotid arteries (green arrow) and bilateral middle cerebral arteries (red arrow). T2 weighted images showing hyperintensities in right cerebellum (blue arrow), right hemipons (orange arrow) head of left caudate nucleus (pink arrow).

Echocardiogram showed concentric left ventricular hypertrophy with mitral, pulmonic, tricuspid regurgitation, global hypokinesia, and depressed systolic function with a reduced ejection fraction of 35 percentages. She had elevated erythrocyte sedimentation rate at 26 mm/hr.

She was discharged on the 20th hospital day improved. Home medications include dual antiplatelet therapy consisting of aspirin and clopidogrel, atorvastatin, carvedilol, digoxin, enalapril, prednisone at 1 mkd equivalent, calcium + vitamin D. Methotrexate was initiated with good clinical response and no recurrence of ischemic symptoms.

DISCUSSION

Takayasu arteritis is an idiopathic, chronic inflammatory arteriopathy that usually involves medium and large sized arteries with a strong predilection to aortic arch and its branches as well as the pulmonary arteries.[6] It commonly affects females between the age 11 to 30 and is more prevalent in Japan, Southeast Asia, India, and Mexico. The estimated annual incidence is 1.2-2.6 cases per million.[7] According to Abola, there are 61 reported cases of Takayasu arteritis in the Philippines.[8]

Patients would initially present with non-specific systemic inflammatory features such as fever, night sweats, weight loss, arthralgia, and body malaise. As the disease progresses, patients experience hypertension, limb claudication, peripheral cyanosis, light-headedness, and carotidynia as a result of narrowing, occlusion or dilation of arteries. Aortic regurgitation may result from dilation of the ascending aorta while cardiac ischemia and heart failure may be caused by aortic disease and hypertension.[2] Neurologic manifestations usually occur later in the disease course. Common neurologic manifestations include headache, dizziness, visual disturbances, seizures, transient ischemic attack, ischemic stroke and reversible posterior encephalopathy syndrome.[9]

Imaging of the arterial wall by MRA or CTA is used to evaluate the arterial lumen which may show smoothly tapered luminal narrowing or the occlusion that is sometimes accompanied by the thickening of the wall of the vessel. Positron Emission Tomography in combination with CT or MRI may also be used to evaluate for possible large vessel vasculitis seen as hot segments.[9] Erythrocyte Sedimentation Rate, the most commonly used serologic marker for inflammation, is nonspecific.[2]

There are several criteria used for the diagnosis of Takayasu arteritis. The Ishikawa criteria (Table 1) was proposed in 1988. In addition to the obligatory criterion, the presence of two major criteria; or one major and at least two minor criteria; or at least four minor criteria must be present. However, this only had a sensitivity of 60.4% and specificity of 95%.[10] A simpler but highly sensitive and specific criteria was proposed by the American college of rheumatology. The 1990 American college of rheumatology classification criteria (Table 2) consists of six criteria wherein the presence of three out if six fulfills the criteria for diagnosis of Takayasu arteritis. This has a sensitivity of 90.5% and a specificity of 97.8%.[6] The most recent criteria for the diagnosis of Takayasu arteritis is the 2022 American college of rheumatology classification for Takayasu arteritis (Table 3). A score of at least 5 points is needed for diagnosis of Takayasu arteritis. This has a sensitivity of 93.8% and a specificity of 99.2%.[11] Our patient fulfilled the obligatory criterion, two major criteria and four minor criteria of the Ishikawa's Criteria. There was 4 out of 6 criteria present in the 1990 American college of rheumatology classification for Takayasu arteritis, and has a score of 11 for the 2022 American college of rheumatology classification for Takayasu arteritis.

Stroke affects approximately 5% to 15% of people with Takayasu arteritis. Studies show that patients with Takayasu Arteritis usually suffer from ischemic stroke rather than its counterpart, hemorrhagic stroke. Variable patterns and locations of stroke occur in both the carotid and vertebrobasilar circulations and may be secondary to either intracranial or extracranial disease. The most common symptom is bilateral loss of vision, in which this involves the vertebral artery.[6] Stroke can be secondary to hypoperfusion as a result of hemodynamic compromise secondary to decreased cerebral blood flow from the occlusive or stenotic aortic arch and its main branches.[6,9] Systemic inflammatory response causes micro-embolic phenomenon and promotes premature atherosclerosis, which produces embolic or thromboembolic events as a result of artery-to-artery embolism or plaque rupture.[12,13]

Table 1: Ishikawa's criteria for diagnosis of Takayasu arteritis.

Obligatory criteria	
Age <40 (Years)	Age of 40 years at diagnosis or an onset of characteristic signs and symptoms of 1 month duration
Two major criteria	
Left mid subclavian artery	Most severe stenosis or occlusion present in the mid portion from the point 1 cm proximal to the left vertebral artery orifice to that 3 cm distal to the orifice determined by angiography.
Right mid subclavian artery	Most severe stenosis or occlusion present in the mid portion from the right vertebral artery orifice to the point 3 cm distal to the orifice determined by angiography.

Continued.

Obligatory criteria	
Nine minor criteria	
High ESR	Persistent ESR >20 mm/hour
Carotid artery tenderness	Unilateral or bilateral tenderness of common carotid arteries
Hypertension	Persistent BP >140/90 in brachial or >160/90 popliteal
Aortic regurgitation or annuloaortic ectasia	Done by auscultation, doppler echocardiography, two-dimensional echocardiography or angiography
Pulmonary artery lesion	Lobar or segmental arterial occlusion or equivalent determined by angiography or perfusion scintigraphy, or presence of stenosis, aneurysm, luminal irregularity or any combination in pulmonary trunk or in unilateral or bilateral pulmonary arteries determined by angiography
Left mid common carotid lesion	Presence of most severe stenosis or occlusion in the mid portion of 5 cm in the length from the point 2 cm distal to its orifice determined by angiography.
Distal brachiocephalic trunk lesion	Presence of most severe stenosis or occlusion in the distal third lesion determined by angiography
Descending thoracic aorta lesion	Narrowing, dilatation or aneurysm, luminal irregularity or any lesion combination determined by angiography; tortuosity alone is unacceptable.
Abdominal aorta lesion	Narrowing, dilatation or aneurysm, luminal irregularity or any combination and absence of lesion in aorto-iliac region consisting of 2 cm of terminal aorta and bilateral common iliac arteries determined by angiography; tortuosity alone is unacceptable

Table 2: 1990 American college of rheumatology classification criteria for Takayasu arteritis.

S. no.	Classification
1	Age of 40 years or younger at disease onset
2	Claudication of the extremities
3	Decreased pulsation of one or both brachial arteries
4	Difference of at least 10 mm Hg in systolic blood pressure between arms
5	Bruit over one or both subclavian arteries or the abdominal aorta
6	Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the upper or lower extremities that is not due to arteriosclerosis, fibromuscular dysplasia, or other causes

Table 3: 2022 American college of rheumatology classification criteria for Takayasu arteritis.

Criteria	Description	Score
Absolute requirements		
Age <60 years at time of diagnosis	-	-
Evidence of vasculitis on imaging	Evidence of vasculitis in the aorta or branch arteries must be confirmed by vascular imaging (e.g., computed tomographic/catheter-based/ magnetic resonance angiography/ultrasound/positron emission tomography)	
Additional clinical criteria		
Female sex	-	1
Angina or ischemic cardiac pain	-	2
Arm of leg claudication	-	2
Vascular bruit	Bruit detected by auscultation of a large artery including the aorta, carotid, subclavian, axillary, brachial, renal, or the iliofemoral arteries	2
Reduced pulse in upper extremity	Reduction or absence of pulse by physical examination of the axillary, brachial or radial arteries	2
Carotid artery abnormality	Reduction/absence of pulse of carotid artery/ tenderness of the carotid artery	2
Systolic blood pressure difference in arms >20 mmHg	-	1
Additional imaging criteria		
Number of affected arterial territories (select one):	Number of arterial territories with luminal damage (e.g., stenosis, occlusion or aneurysm) detected by angiography or ultrasonography form the following nine territories: thoracic aorta, abdominal aorta, mesenteric, left or right carotid, left or right subclavian, left or right renal arteries	
One arterial territory		1
Two arterial territories		2
Three or more arterial territories		3

Continued.

Criteria	Description	Score
Additional clinical criteria		
Symmetric involvement of paired arteries	Bilateral luminal damage (stenosis, occlusion or aneurysm) detected by angiography or ultrasonography in any of the following paired vascular territories: carotid, subclavian or renal arteries	1
Abdominal aorta involvement with renal or mesenteric involvement	luminal damage (stenosis, occlusion or aneurysm) detected by angiography or ultrasonography involving the abdominal aorta and either the renal or mesenteric arteries	3

Studies show that most strokes involve the anterior circulation, with a predilection to the perforating arteries, middle cerebral artery territories and internal/cortical borderzone area.[6,13] Brain imaging findings of small to medium-sized strokes in the cortex or subcortical structures in multiple vascular territories is suggestive of Takayasu arteritis.[9]

Current guidelines on anticoagulation with Takayasu Arteritis remain unclear.[7] Immediate treatment should address the acute vascular injury brought about by cerebral ischemia. Studies show that antiplatelet agents are useful where aspirin may be given as monotherapy or in combination with other antiplatelets.[9] Since the pathology of Takayasu arteritis is inflammation, long term treatment aim to decrease vessel inflammation and progression of vascular disease as well as control of comorbidities. Glucocorticoids remain to be mainstay anti-inflammatory treatment. Prednisone is given at 1 mg/kg/day for three to six months in tapering doses.[9] According to Adams et al, relapse may require higher dose of glucocorticoids are combination with immunomodulators such as methotrexate, cyclophosphamide, rituximab and azathioprine. These agents are shown to slow angiographic changes and lowers the glucocorticoid requirement. Studies show that a combination of immunomodulators and glucocorticoids have better outcomes and better event-free survival than those given glucocorticoids as monotherapy.[9]

Arterial complications include stroke, limb ischemia, hypertension, acute myocardial infarction, aortic aneurysm and aortic dissection. Studies show that the 15-year survival is 96% if complications were absent and 66% if present.[9]

CONCLUSION

Neurologic complications are usually seen in the chronic phase of the disease. Though rare, ischemic manifestations in the acute phase is a possibility wherein it may range from headache and dizziness to more drastic complications such as transient ischemic attack and ischemic strokes. Thus, Takayasu arteritis should be a consideration in stroke in the young. Multiple infarcts or infarcts of the middle cerebral artery, perforating branches and border zone infarcts are commonly seen in Takayasu arteritis. This may be secondary to an embolic or thromboembolic or may be due to hemodynamic compromise secondary to the stenotic vessel.

Our patient presented with recurrent stroke symptoms, in which only dabigatran was given as anticoagulant while glucocorticoids and immunomodulators were not initiated in her previous admissions. On this admission, however, the patient was treated as ischemic stroke as a complication of Takayasu arteritis. The patient was not only started on aspirin and clopidogrel, but glucocorticoids and methotrexate were initiated as well. Combination of these medications resulted to a good clinical response and no relapse has been reported.

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