Arterial Tortuosity Syndrome With Multiple Intracranial Aneurysms

A Case Report

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Objective: To report a new manifestation of the rare connective tissue disorder arterial tortuosity syndrome in the absence of skin and soft-tissue abnormalities and with bilateral, giant fusiform intracranial aneurysms.

Design: Case report.

Setting: University teaching hospital.

Patient: A 67-year-old man with a history of hypertension presented to medical attention after a syncopal episode. Imaging revealed incidental, bilateral, giant fusiform intracranial aneurysms of the internal carotid artery at their junction of the circle of Willis. There was also aneurysmal dilatation of the left main coronary artery ectasia and aneurysmal dilation of the aorta and bilateral iliac arteries, suggestive of arterial tortuosity syndrome.

Results: The patient's syncope was attributed to transient complete heart block for which a permanent pacemaker was placed. The patient started taking aspirin for stroke prevention and losartan potassium for blood pressure control.

Conclusions: To our knowledge, we present the first case of arterial tortuosity syndrome with marked bilateral intracranial artery dilation in the absence of concurrent skin and soft tissue abnormalities. Workup may include systemic vascular imaging to characterize the extent of disease. Antiplatelet therapy can be used for stroke prevention by reducing the risk of clot formation in ectatic vessels with altered hemodynamics and subsequent embolism. Losartan is known to inhibit transforming growth factor β signaling and may be a specific modulator of disease expression in this syndrome.

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ARTERIAL TORTUOSITY SYNDROME (ATS) is a rare connective tissue disorder characterized by tortuosity, dilation, stenosis, and aneurysms of large and mid-size arteries. We report a new manifestation of this rare clinical syndrome in the absence of skin and soft tissue abnormalities and with bilateral, giant fusiform intracranial aneurysms.

A REPORT OF A CASE

A 67-year-old man with a history of hypertension presented to the Massachusetts General Hospital after a syncopal episode. He recalled 1 previous presyncopal event while exercising 2 years prior. The patient reported a history of rheumatic fever at age 6 years, bilateral ophthalmic artery aneurysms, and asymptomatic aortic root dilation diagnosed more than 20 years earlier. A review of systems was negative for chest pain and palpitations. There was no family history of arrhythmia, structural heart disease, or vasculopathy. On examination, the patient had no neurological deficits. Auscultation of the heart was unremarkable.

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A chest radiograph obtained on hospital admission demonstrated a tortuous aorta measuring 4.8 cm in diameter at the level of the aortic arch. A noncontrast head computed tomographic scan done at the referring hospital demonstrated an abnormality. Computed tomography angiography of the head and neck vessels identified diffuse abnormalities of the intracranial arteries: dolichoectasia with eccentric fusiform aneurysmal dilation of both intracranial internal carotid arteries; dilation of the bilateral M1, A1, and posterior communicating arteries; and ectasia and tortuosity of the vertebral and basilar arteries (Figure 1). Given the patient's history and computed
tomography findings, further systemic vascular imaging was performed. Computed tomography angiography of the chest and abdomen (Figure 2) revealed aneurysmal dilatation of the left main coronary artery, aorta (the aortic root was dilated at 48 mm, the ascending aorta was 42 mm, and the descending aorta was 34 mm), and bilateral iliac arteries. These findings were suggestive of ATS.

The patient’s syncope workup was significant for an electrocardiogram identifying first-degree atrioventricular block and right bundle branch block along with clear Mobitz II heart block. Given these findings, the patient underwent left cephalic vein placement of a St Jude cardiac pacemaker. An echocardiogram demonstrated mild to moderate aortic insufficiency as well as a patent foramen ovale. The patient was prescribed losartan potassium to augment his blood pressure control and aspirin was added for stroke prevention. Since his hospital discharge, the patient has not had additional syncopal events and remains neurologically intact.

**COMMENT**

Arterial tortuosity syndrome is a rare connective tissue disorder characterized by cardiovascular anomalies, including tortuosity, dilation, lengthening, stenosis, and aneurysms of large and mid-size arteries. Fewer than 50 cases of ATS have been previously described; most consist of pediatric patients. Vessels commonly involved are the aorta and coronary and pulmonary arteries; however, mesenteric and peripheral arteries can also be affected. Although rare, aneurysmal dilation of the intracranial arteries has been described in ATS, but not in the absence of concurrent skin and soft tissue abnormalities such as stretchable skin, joint laxity, arachnodactyly, and characteristic facial features (high arched palate, beaked nose). Arterial tortuosity syndrome often has a similar presentation as other connective tissue disorders, such as Ehlers-Danlos and Marfan syndrome; severe tortuosity favors ATS.

Recent genetic studies of ATS have identified a characteristic genetic mutation in SLC2A10 (chromosome 20q13), encoding glucose transporter GLUT-10, a mutation that likely leads to upregulation of transforming growth factor β (TGF-β). As an autosomal recessive mutation, it is characterized disproportionately in cases of consanguinity. Two closely related syndromes, Loeys-Dietz syndrome and Marfan syndrome, have also been shown to be due to dysregulation of the TGF-β cytokine cascade.

The patient in this report started taking losartan, a TGF-β signaling inhibitor, to augment his blood pressure control. Transgenic mouse models suggest that using the angiotensin receptor blocker losartan, which is known to inhibit TGF-β, reduces aortic aneurysm progression. In addition to blood pressure control, losartan may modulate the expression of his syndrome.

Syndromes associated with widespread arterial tortuosity are more common in the pediatric population, likely because of characteristic findings of connective tissue disease (including joint laxity and characteristic facial features), severity of early symptoms, and a high mortality rate. While the patient was found to have aortic arch dilation in his fourth decade of life, it was not until 30
years later when ATS was suspected as a result of an incidental workup for syncope. He started antithrombotic therapy for stroke prevention to reduce clot formation and possible embolic phenomenon.

Follow-up for this patient will include serial imaging to better delineate any changes in vessel morphology that would indicate progression/regression of expression of his syndrome. Additionally, he will undergo genetic testing. While the results of genetic analysis will not likely have a major impact on his individual treatment plan, the results may be significant for other members in his family. Information gained may also be useful in gene-dependent therapies that may arise in the future.

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REFERENCES


Correction

Error in Byline. In the Observation titled “Reversible Extralimbic Paraneoplastic Encephalopathies With Large Abnormalities on Magnetic Resonance Images” by McKeon et al, published in the February 2009 issue of the Archives (2009;66[2]:268-271), an author’s name included an incorrect middle initial in the byline on page 268. The third author’s name should have appeared as “Jeffrey W. Britton, MD.” This article was corrected online.