Extracranial carotid artery aneurysms in two of three monozygotic triplets with tuberous sclerosis complex

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Tuberous sclerosis complex (TSC) is an autosomal dominant disorder with multisystem clinical manifestations. Dysplastic proliferations of small blood vessels including hemangiomas are common; however, anomalies of medium- and large-size vessels are rare. The only extracranial carotid artery aneurysm in a patient with TSC was reported in 1998. Since then, 19 cases have documented intracranial aneurysms in patients with TSC. The case of two of three identical triplet sisters with TSC who were treated for extracranial carotid artery aneurysms is presented. To the authors’ knowledge, this is the first reported case of monozygotic siblings who both manifested this rare expression of TSC.

CASE REPORT

Triplet A is a 32-year-old woman in whom TSC was diagnosed at age 5 years. She is a monozygotic triplet, and all three siblings are affected with the disease. The triplets’ maternal grandmother had TSC and died of a ruptured intracranial aneurysm before their birth. Their mother is still alive with TSC but does not have any known carotid or intracranial aneurysms.

Triplet A has severe seizures, multiple intraventricular tumors, and classic skin lesions (adenoma sebaceum). Her history includes bilateral partial nephrectomies for renal cell carcinoma and for angiomylipomas and several pulmonary resections for tumors. She presented to our institution with a pulsatile right-sided neck mass and was found to have a large carotid artery aneurysm. The aneurysm was 2.2 cm in maximum diameter, was lined with mural thrombus, and extended 6.2 cm from the carotid bifurcation into the distal internal carotid artery to the level of C2 (Fig 1). She was asymptomatic and denied stroke, transient ischemic attack, or cranial nerve dysfunction.

The repair required subluxation of the mandible for appropriate exposure. After appropriate identification of the hypoglossal and vagus nerves, the common carotid, external carotid, superior thyroid artery, and distal internal carotid artery were isolated in the standard fashion (Fig 2). A 3-cm segment of great saphenous vein was harvested from the right thigh, and valves were lysed with a valvulotome. The aneurysm was opened, and all thrombus was removed. The vein graft was placed over an 8F Argyle shunt (Covi-dien, Mansfield, Mass) and anastomosed as an interposition between the common carotid and internal carotid arteries, preserving the external carotid branch. Before completion of the proximal anastomoses, the shunt was removed, and all vessels were back bled and flushed in the standard fashion (Fig 3). Twin A did well with no complications and was discharged postoperatively day 2.

In Triplet B, TSC was diagnosed in childhood. She also had severe seizures and multiple intraventricular tumors and underwent bilateral nephrectomies because of renal cell carcinoma. Triplet B noted a pulsatile neck mass 2 years before Triplet A’s presentation, and a carotid artery aneurysm was diagnosed at a hospital in Florida. She underwent successful excision with interposition vein graft. After recovery, Triplet B received a renal transplant. However, non-Hodgkin lymphoma developed as a result of chronic immunosuppression, and Twin B died of overwhelming pneumonia.

Triplet C also received a diagnosis of TSC in childhood and was recently screened at our request at an outside institution. Computed tomography angiography of the head and neck confirmed no intracranial or extracranial carotid aneurysms.
DISCUSSION

Tuberous sclerosis was first described by Bourneville in 1880 as a triad of seizures, mental retardation, and facial adenoma sebaceum⁷; it has since been expanded to include the full clinical spectrum of multiorgan involvement. TSC includes cortical and subcortical hamartomas, hypopigmented macules, facial angiofibromas, cardiac rhabdomyomas, retinal hamartomas, renal angiomylipomas, cystic lung disease, and sclerotic bone islands in the vertebrae or long bones.⁸ Vascular manifestations of TSC are rare, and only case reports document aneurysmal or occlusive disease in these patients. The abdominal aorta is most commonly affected with 21 cases of aortic aneurysm and TSC reported to date.⁹ Less frequently, peripheral aneurysms in the axillary, subclavian, and iliofemoral arteries have been cited.stitial⁴ Stenotic disease, reports of which are even more rare than reports of aneurysms, also usually involve the abdominal aorta, manifesting as aortic coarctation and renal artery stenosis either alone or in association with each other as components of the middle aortic syndrome.⁹

There have been 19 cases of intracranial aneurysms reported in patients with TSC ranging in age from 5 months to 53 years. The most commonly affected vessel is the internal carotid artery; the anterior cerebral artery, middle cerebral artery, and vertebral artery are affected in decreasing frequency.²⁴ Infants have been documented with single or multiple intracranial aneurysms⁵ causing cavernous sinus syndrome and cranial nerve deficits.⁴ The first and only reported case of an extracranial carotid artery aneurysm in a patient with TSC was in an 8-year-old child who presented with a pulsatile right neck mass that had been enlarging for 4 years.³ The present report represents the second and third cases of this unique presentation of extracranial carotid artery aneurysm in TSC and the first presentation affecting monozygotic twins.

Studies detailing the development and clinical manifestations of TSC in monozygotic twins show that outcomes are quite variable,⁶ and having mildly affected and severely affected patients within the same family is a normal occurrence.¹⁴ Two twin sisters developing the same distinctive presentation speaks to the need for vascular screening in
patients with a strong family history of vascular involvement and TSC. It has been proposed that intracranial aneurysm be added to the other nonprimary diagnostic criteria of TSC. However, it has not been established whether vascular screening should be employed in all patients with the disease. Sources agree that whole-body or targeted vascular screening should be obtained in patients with TSC and palpable vascular masses, hypertension, abdominal pain, or other symptoms concerning for aneurysmal or stenotic occlusive disease, with duplex ultrasound being the initial diagnostic modality of choice. We propose that asymptomatic patients with TSC and a strong family history of vascular involvement be included in screening efforts. The screening study in these cases should be based on the family history and the clinical presentation. Routine vascular screening in asymptomatic patients with TSC without a known family history is not recommended because these conditions are infrequent in these patients.

Although the genetics of the disorder do not explain the fact that one of the monozygotic triplets did not have an aneurysm, we believe that the family history of aneurysm disease over two generations highlights the important association between family history and vascular involvement in this rare autosomal dominant disorder.

REFERENCES


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