Aortic aneurysms in children and young adults with tuberous sclerosis: Report of two cases and review of the literature

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Abdominal aortic aneurysms (AAAs) in children and young adults are rare; some have been observed in patients with tuberous sclerosis (TS). We report two cases and review the literature. A 9-year-old girl with TS was diagnosed with a 3-cm calcified AAA, and a 41-year-old man with TS was diagnosed with a 7.5-cm thoracic aortic aneurysm (TAA). Both patients underwent open repair with a tube polyester graft without complication. They are both doing well at 7 and 8 years after surgery. Pathologic evaluation revealed medial atrophy and focal medial disruption in the aortic wall in both patients. With our two cases, 15 patients with TS and aneurysms have been reported; 12 had AAA, and four had TAA (one patient had both). Three AAAs and two TAAs ruptured. Six patients died because of aneurysmal disease. There is an association between TS and aortic aneurysms. Patients should be screened for aortic aneurysms at the time TS is diagnosed and annually thereafter. Because of the high risk of rupture, early elective repair is suggested. New aortic aneurysms after repair may also develop. (J Vasc Surg 2001;33:639-42.)

Aortic aneurysms rarely occur in children or young adults. Little information is available on their pathogenesis and clinical outcomes.[1-3] Reported causes include atherosclerosis, infection, vasculitis (Takayasu's, Kawasaki's, Cogan's, and Behçet's), inherited disorders of connective tissue (Marfan's and Ehlers-Danlos syndromes), and tuberous sclerosis (TS).[3]

TS is an autosomal dominant complex that was first described by von Recklinghausen in 1862 and named by Bourneville in 1880.[4] The classic triad includes epilepsy, mental retardation, and facial angiofibroma (adenoma sebaceum); however, the full complex is only exhibited in a few affected individuals. The proper terminology is "tuberous sclerosis complex," with the primary pathologic process involving the development of hamartomas of almost every organ system, and the occasional development of neoplasms of the brain and kidney.[4] Reports of vascular dysplasia,[5] cardiac malformations,[6] rhabdomyomas (present in 49% of patients),[7] and aneurysms have also been noted.[5,8] Aortic aneurysms in patients with TS have been reported presenting from infancy to 24 years of age.[9] Peripheral arterial aneurysms of the carotid, axillary, and renal arteries have also been noted.[10-13] We report on two patients with TS who were diagnosed with aortic aneurysms that developed at an early age and required surgical treatment. We also review the world literature on TS associated with aortic aneurysms.[7,14-24]

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CASE REPORTS

Case 1. A 9-year-old girl was admitted with 2 weeks' duration of low back pain and 1 year duration of abdominal pain. Her medical history was significant for seizures with onset at 4 months of age, at which time she was diagnosed with TS. At age 7 she underwent resection of an astrocytoma and had development of secondary hydrocephalus, which was managed with a ventriculoperitoneal shunt. Her medications included phenobarbital and valproic acid. She had a learning disability with inability to read at age 9 and was integrated into a second grade classroom. She had no cardiovascular risk factors. On physical examination she had red raised fibrous papules across her nose (facial angiofibromata), and connective tissue plaques of the skin (Shagreen's patch) on her right forehead. In the left lumbosacral region, there was a hypopigmented macule (ash-leaf spot). The aortic pulse was prominent, without tenderness. Abdominal sonography and computed tomography (CT) revealed an intact 3-cm calcified infrarenal AAA (Fig 1). Aortography confirmed an aortic aneurysm (Fig 2).[25] At operation a calcified infrarenal aortic aneurysm was noted, with a proximal aortic stenosis immediately distal to the renal arteries. The aneurysm was repaired by

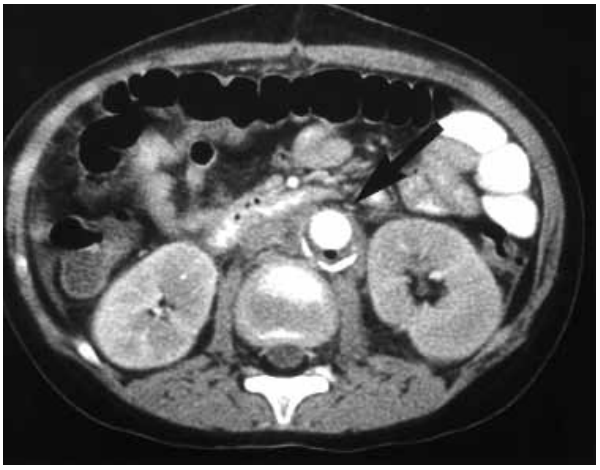

Fig 1. CT scan of 9-year-old female demonstrates 3-cm calcified AAA.

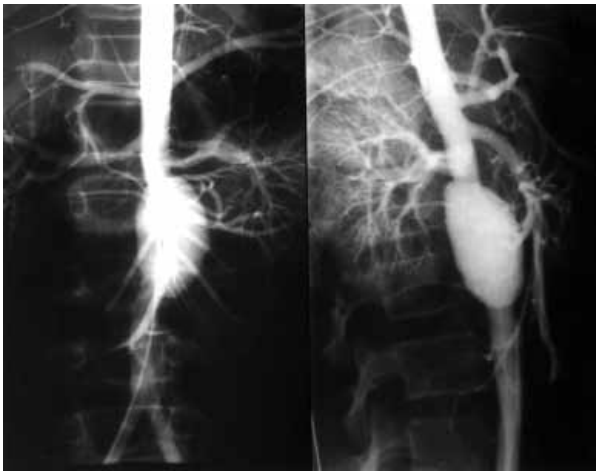

Fig 2. Transfemoral aortogram from case 1: anterior to posterior view. Used with permission from Rooke T, Joyce JW. Uncommon arteriopathies. Rutherford RB, editor. Vascular surgery. 5th ed. Philadelphia: WB Saunders; 2000. p. 418-34.

Fifteen reported cases of TS and aortic aneurysm

Author	*Age at diagnosis*	*Location of AA*	*Outcome*
Freycon et al[9]	8.5 mo	Abdominal	Rupture-death
Larbre et al[8]	31 mo	Thoracic	Rupture-death
Dutton et al[24]	6 mo/2.5 y	Thoracic and abdominal	Repaired
Hagood et al[23]	22 mo	Abdominal	Repaired
Roulfes et al[5]	9 mo	Abdominal	Repaired/death*
Ng et al[21]	24 y	Abdominal	Repaired/death*
Shepherd et al[7]	3 y	Thoracic	Rupture-death
Van Reedt et al[19]	5 y	Abdominal	Repaired
Occhionorelli[18]	19 y	Abdominal	Repaired
Lavocat et al[16]	4.5 mo	Abdominal	Rupture-death
Tsukui et al[15]	4 y	Abdominal	Repaired
Paraf et al[17]	2.5 y	Abdominal	Repaired
Tamisier et al[14]	30 mo	Abdominal	Repaired
Jost et al	9 y	Abdominal	Repaired
Jost et al	41 y	Thoracic	Repaired

*Death at 2 years because of rupture of a new aneurysm proximal to graft.

use of a suprarenal aortic clamp for the proximal anastomosis, correcting the aortic stenosis with a high, juxtarenal proximal anastomosis. A 12-mm collagen-coated polyester tube graft was inserted. Histologic evaluation revealed a true aneurysm with medial dysplasia, disruption of the normal layers of the aortic wall, and atrophy. Secondary intimal fibrosis was far more prominent than adventitial fibrosis, and there was intimal hyperplasia with calcification (Fig 3). The patient's postoperative course was uneventful, and she was discharged on postoperative day 6. Seven years later the patient is well with a patent graft and no new aneurysms as confirmed by CT scanning (Fig 4). She continues to have psychosocial impairment, and her seizures are controlled by medications. She is under observation for a heterogenous renal mass.

Case 2. A 41-year-old man with TS was admitted because of an abnormal chest radiograph. At age 18 TS was diagnosed after the patient had development of a seizure disorder, cerebral calcifications, and facial angiofibromata. He did not have significant mental retardation. He had no risk factors of atherosclerosis. A chest radiograph revealed a wide mediastinum. CT scanning confirmed a thoracic aortic aneurysm (TAA) distal to the left subclavian extending to the diaphragmatic crura. CT scanning performed 1 year later documented interval enlargement of the aneurysm. The calcified 7.5-cm distal TAA was reconstructed with a 22-mm knitted polyester tube graft by use of a "clamp-and-sew" technique, without complications. Microscopy revealed intimal and medial dysplasia. The patient was doing well 8 years later, and his chest radiograph was normal.

LITERATURE REVIEW

A MEDLINE search from 1966 to 1999 identified 13 reports of aortic aneurysms associated with TS (Table).[5,7-9,14-24] With our two patients, 15 cases have been reported with TS and aortic aneurysms. Twelve patients had abdominal aortic aneurysms (AAAs), and four had TAAs (1 patient had both). The mean age at diagno-

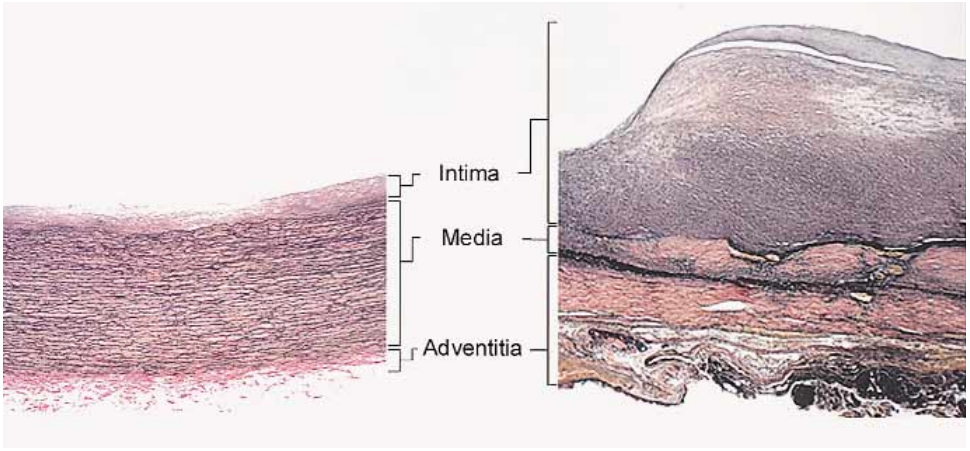

Fig 3. Photomicrographs of normal abdominal aortic wall (*left*) and of aneurysm wall with TS—case 1 (*right*) shows all three arterial layers (Verhoff-van Gieson stain; original magnification × 10). Diseased aorta exhibits dysplastic features, marked medial atrophy, fibrosis with focal disruption, prominent intimal hyperplasia, and moderate adventitial fibrosis.

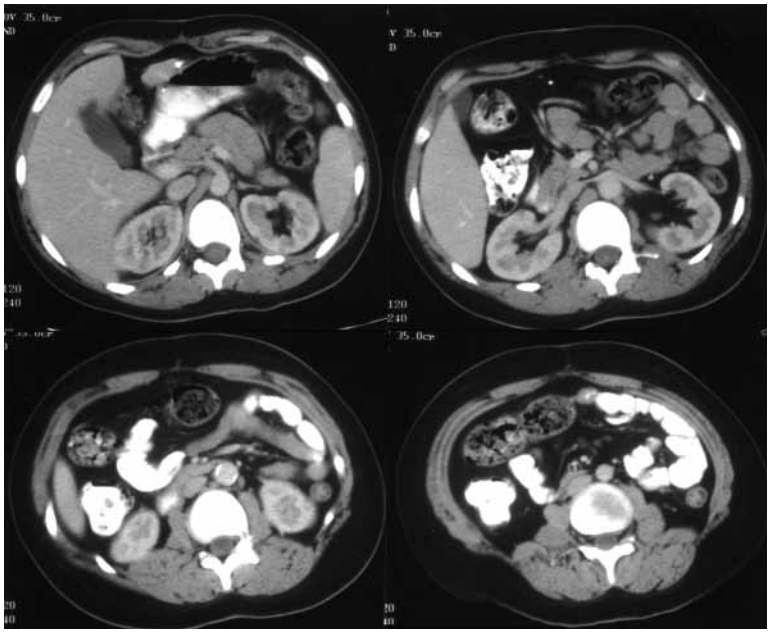

Fig 4. CT scan with intravenous contrast 7 years after AAA repair (case 1) shows normal aorta and patent aortic graft. Note calcification of aortic wall around graft.

sis of AAA was 5 years (0.5 months to 24 years), and the mean age at diagnosis of TAA was 11.7 years (6 months to 41 years). Gender was reported in 11 patients, (7 males, 4 females). The diameter of AAAs at presentation averaged 5.4 cm (range, 3-9 cm; n = 7), and the diameter of TAAs averaged 6 cm (range, 4.5-7.5; n = 2).

Three AAAs and two TAAs ruptured. Ten AAAs were repaired on an elective basis, with an early mortality rate of 10% (1 of 10). One additional patient died because of rupture of an aneurysm that developed proximal to the graft at 2 years. Two other patients who were admitted with ruptured AAA died, one after attempted repair. Of the four patients with TAA, two underwent successful elective repair, and two died after aneurysm rupture. Six of the 15 patients (40%) died because of aneurysmal disease.

DISCUSSION

The association of TS with aortic aneurysms has been previously recognized.[9] Aneurysms can develop in patients with TS at a very early age; the youngest patient reported with aneurysm in our review was 4.5 months old. The size of the reported aneurysms was large, and rapid progression has been observed. Mean AAA size was 5.4 cm, and mean TAA diameter was 6 cm. The risk of rupture is high; one third of the aneurysms presented had ruptured.

The pathogenesis of aortic aneurysms in TS is not well

known, but they are likely caused by disorders of the connective tissue.[3,14,15,19] Loss of elastin fibers similar to those noted in Marfan's syndrome has been described.[19] Hagood et al[23] noted iliac artery occlusive disease and medial fibromuscular hyperplasia. Rolfes et al[5] noted an association with fibromuscular disease and suggested that the vascular dysplasia/hyperplasia might be a manifestation of hamartomatous formation of the vasculature. Dysplastic features were identified in our cases, in addition to medial atrophy and focal medial disruption. Secondary intimal fibroplasia was more prominent than adventitial fibrosis, and intimal calcification occurred in both patients. Intimal fibroplasia was present and caused stenosis of the juxtarenal aorta in one of our patient. Dysplasia and medial atrophy contributes to the loss of aortic wall strength and aneurysm formation.

Aortic aneurysms in patients with TS are frequently missed, and diagnosis is first made after aneurysm rupture. We recommend that patients with TS undergo abdominal ultrasound scanning and chest radiography at the time TS is diagnosed to exclude TAA or AAA. If no aneurysm is found, surveillance for aneurysmal disease should be similar to surveillance of renal neoplasms in patients with TS: ultrasound scanning every 2 to 3 years before puberty and yearly thereafter.[26] Because of the increased risk of rupture, elective repair is justified when an aortic aneurysm is identified in a patient with TS. Open repair with the largest possible polyester graft is recommended to compensate for the growth of the aorta in children and young adults. Because of the long life expectancy of these patients, it is difficult to recommend endovascular repair. A much more important contraindication is, however, the increasing aortic size: growth of the aorta would likely result in proximal endoleak after endovascular repair.

In conclusion, this study supports previous observations that TS in children and young adults is associated with the development of aortic aneurysms. Therefore patients should be screened for aortic aneurysms at the time TS is diagnosed and at regular intervals thereafter. Because of the high risk of rupture, early elective open surgical repair is recommended. New aortic aneurysms after repair may also develop; therefore, patients with TS need lifelong follow-up to prevent death because of rupture of an aortic aneurysm.

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