Recurrent symptomatic aortic aneurysm in a young girl with tuberous sclerosis complex and review of the literature

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ABSTRACT

An abdominal aortic aneurysm is a rare occurrence in pediatric populations. When present, it is usually associated with an underlying etiology such as a connective tissue disorder, inflammatory process, or noninflammatory medial degeneration. In the present report, we describe the case of a girl with tuberous sclerosis complex who underwent successful emergency open repair of a symptomatic infrarenal abdominal aortic aneurysm and recurrent type IV thoracoabdominal aortic aneurysm. (J Vasc Surg Cases Innov Tech 2023;9:101261.)

Keywords: Abdominal aortic aneurysm; Thoracoabdominal aortic aneurysm; Tuberous sclerosis complex

Aortic aneurysms occur rarely in the pediatric population and, when present, are usually related to an underlying condition, such as mycotic degeneration, vasculitis (eg, Kawasaki disease, Takayasu's arteritis, Behçet syndrome, Cogan syndrome, polyarteritis nodosa), or connective tissue disorders, and noninflammatory medial degeneration, such as cystinosis and tuberous sclerosis complex (TSC).[1-5] The incidence of aneurysm in patients with TSC is rare. In the present report, we describe the unique case of a girl with TSC who developed an infrarenal abdominal aortic aneurysm (AAA) and recurrent type IV thoracoabdominal aortic aneurysm (TAAA) requiring two open aortic repairs. The parent of the patient provided written informed consent for the report of the patient's case details and imaging studies.

CASE REPORT

We report the case of a 9-year-old girl with TSC diagnosed at 2 months of age by genetic testing (heterozygous in the TSC1 gene for a nonsense mutation [c.2689 C>T (p.Gln897Ter)] resulting in premature protein termination), complicated by epilepsy, rhabdomyoma of the heart, a brain mass requiring frontal lobotomy during infancy, and, ultimately, an AAA with eventual degeneration into a type IV TAAA. She initially presented at the age of 7 years with a 7.5-cm infrarenal AAA accompanied by fever, cough, severe abdominal pain, emesis, and bloody diarrhea. She underwent emergency transperitoneal open repair using a 12 × 6-mm expanded polytetrafluoroethylene graft with supraceliac aortic control via left medial visceral rotation (Fig 1).

The initial imaging surveillance study demonstrated a stable aorta; however, after 1 year, she was noted to have a 2.7-cm pararenal AAA. She was followed up with serial ultrasound scans every 6 months with a stable aneurysm size. At the age of 9 years, 31 months after the index operation, she presented with severe abdominal pain and upper respiratory infection symptoms. On computed tomography angiography, a 4.3-cm extent IV TAAA was noted (Fig 2). The patient underwent emergent TAAA repair through a ninth intercostal space thoraco-retroperitoneal incision with left heart bypass via femoral arterial—femoral venous bypass using a heart-lung machine. The diaphragm was partially incised and the left crus of the diaphragm divided to expose the distal thoracic aorta. The entire residual abdominal aorta, including the supraceliac segment, was aneurysmal. A 12-mm woven polyester graft with three separate 8-mm limbs was fabricated on the back table and used to effect TAAA repair, with each of the limbs sewn onto the orifices of the celiac axis and superior mesenteric artery as a Carrell patch owing to their proximity and right renal and left renal arteries with running 6-0 polypropylene suture (Fig 3). The proximal anastomosis was effected to the distal thoracic aorta with running 5-0 polypropylene suture and the distal anastomosis to the proximal segment of the antecedent expanded polytetrafluoroethylene graft.

Her postoperative course was complicated by perforated small bowel obstruction requiring small bowel resection on

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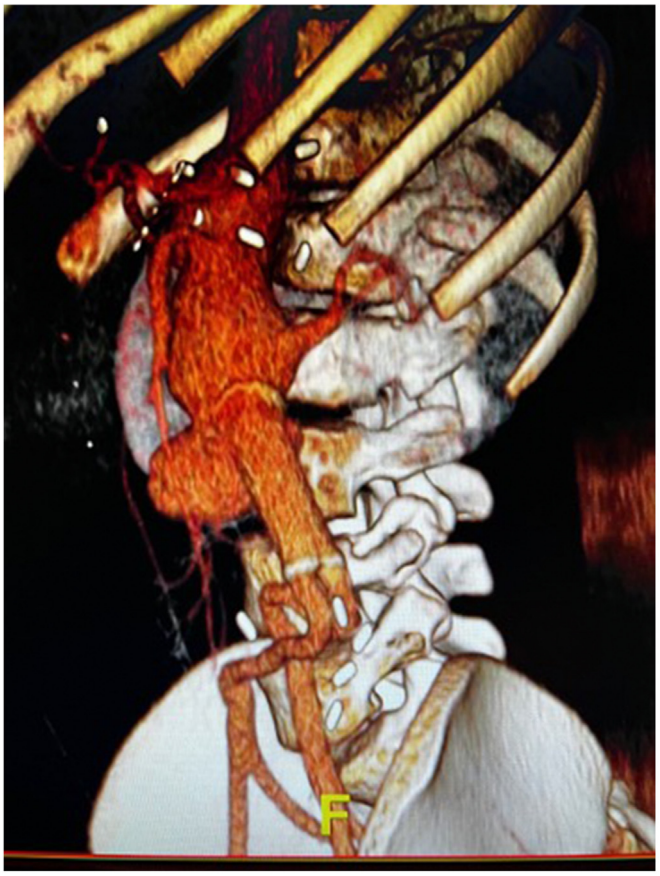

Fig 1. Three-dimensional rendition of computed tomography angiogram of aortic reconstruction after the index infrarenal abdominal aortic reconstruction.

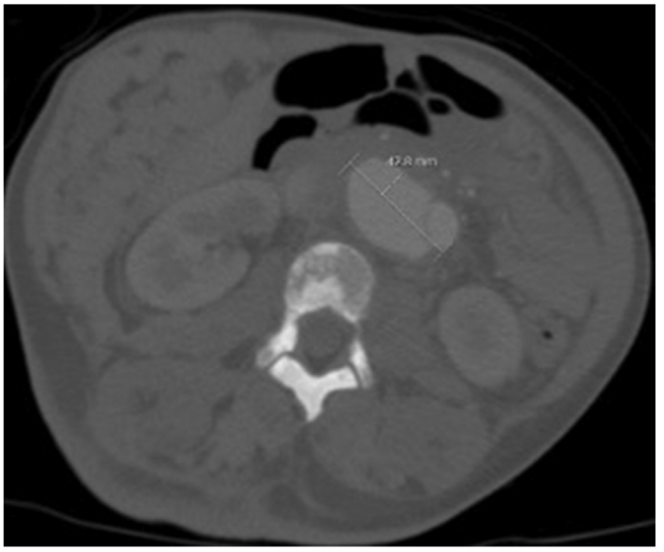

Fig 2. Computed tomography angiography demonstrating a 3.1-cm symptomatic type IV thoracoabdominal aortic aneurysm (TAAA).

postoperative day 5. She was ultimately discharged home on postoperative day 26. The pathology examination of the aortic wall revealed fibrosis with focal intimal fibrin deposition. A 3-month postoperative computed tomography angiogram showed no aneurysm recurrence with intact anastomoses. She was noted to be well at her 6-month follow-up visit.

DISCUSSION

Tuberous sclerosis, first reported by von Recklinghausen in 1862 and named by Bourneville in 1880, is one of the most common congenital disorders with autosomal dominant inheritance, occurring in ~1:6000 to 1:10,000 live births.[6] Its name is derived from the cortical tubers, the gross pathologic appearance of which is "potato-like."[6] The neurologic complications of TSC (ie, seizures, mental deficiency, behavioral abnormalities) are most common and, often, the most impairing. It is, however, a systemic disease with the development of hamartomas of all organs but primarily affecting the brain, heart, skin, eyes, kidneys, lungs, and liver. Neoplasms of the brain and kidney have also been reported.[2] Cardiovascular involvement includes vascular dysplasia, cardiac malformations, and rhabdomyomas.[2,7-9] To represent the multisystem involvement, it is now termed TSC.[3]

The pathogenesis of aneurysms in TSC relates to the loss of function mutation in one of two genes, TSC1 and TSC2, which encode hamartin and tuberin proteins, respectively.[10,11] This mutation, which affects the mTOR (mammalian target of rapamycin) pathway, a protein kinase pathway, leads to hyperplasia of smooth muscle cells without an increase in the contractile or synthetic function and, hence, not limiting, but actually contributing to, the development of aneurysms. These cells were found to have an increase in degradative protein expression, leading to medial degeneration within the blood vessels and possible formation of dissections and aneurysms.[11] Both aneurysmal and occlusive vascular manifestations, albeit rare, have been reported.[3,12] When presenting with occlusive disease, the aorta and renovisceral vessels are usually involved either in isolation or combined, contributing to mid-aortic syndrome.[3,7]

The most common site of aneurysm development in patients with TSC is the kidneys within angiomyolipomas (AMLs). AMLs can develop in ≤80% of this patient population, with a higher rate of aneurysm development with larger tumors.[13,14] AMLs can be found within the parenchyma or can be exophytic, making the origin of any aneurysm the small arteries. In contrast, the most common site of middle and large artery aneurysms in patients with TSC is intracranial, with approximately two thirds originating from the intracranial internal carotid artery.[15]

Although peripheral arterial aneurysms of the carotid, subclavian, axillary, renal, and popliteal arteries have

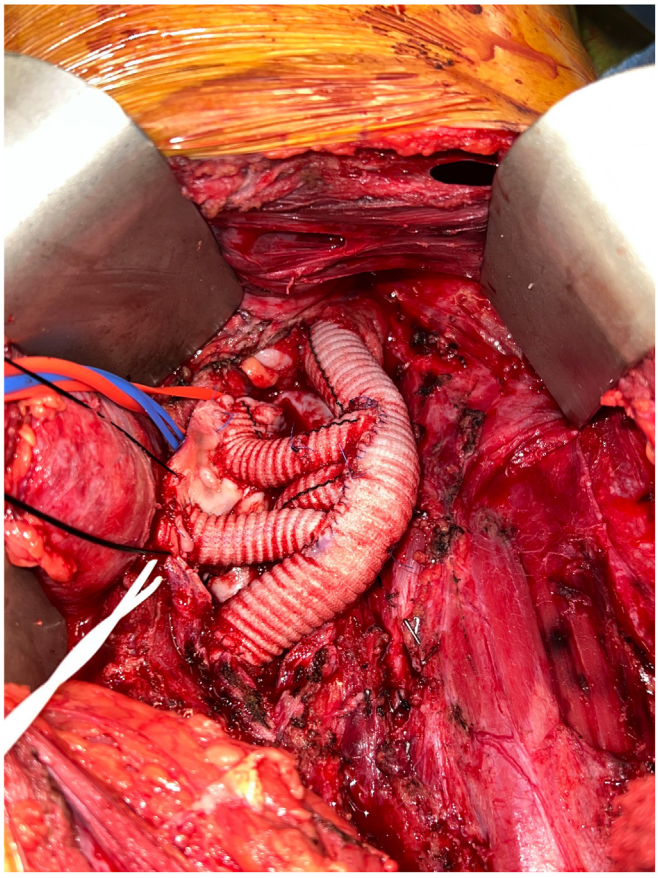

Fig 3. Intraoperative photograph demonstrating aortic reconstruction with individual bypass graft to the celiac axis, superior mesenteric artery, left renal artery, and right renal artery.

been reported,[16-18] the aorta appears to be the most common extracranial location. To date, 33 cases of aortic aneurysms in 28 patients with TSC have been reported in the English literature (Table), of whom 4 patients developed recurrences.[4,19,26,30] Most of these are reported in the pediatric population (25 of 28), of which 19 (76%) were in children aged ≤5 years, with the remainder aged 6 to 10 years. Only a few cases have been reported in young adults and in a middle-age man (age 41 years). The abdominal aorta is the most common location (n = 20) followed by the thoracic aorta (n = 7) and thoracoabdominal aorta (n = 6). Approximately one half of the cases were asymptomatic, with the aneurysms discovered incidentally by imaging studies (Table). Most of these cases were reported in 2000 and after, indicating increased detection with the increased use of imaging studies for these patients. Regarding the other cases, the most commonly reported signs or symptoms were a pulsatile mass or abdominal symptoms (n = 11) or hypertension (n = 5). Fever, respiratory distress, anorexia, and weight loss were rarely reported (only one case for each).

Once diagnosed, urgent repair is indicated, because the risk of rupture is high.[2] Aortic aneurysms accounted for 29% of deaths of patients with TSC in one study.[3] An open approach is the first line of therapy for the great majority of cases, given the small vessel size in this cohort. Only one case of successful endovascular repair of a descending thoracic aortic aneurysm in a pediatric patient has been reported.[5] The surgical techniques and the size of the graft must be chosen carefully to account for the potential growth of these patients. In the present case, a polyester graft was chosen to mitigate the risk of hygroma formation and bleeding through the needle holes, given the multitude of side branch grafts and full anticoagulation therapy during on-pump surgery.[31] A moderate degree of graft redundancy was allowed to accommodate the child's growth. The anastomoses, however, were effected with running sutures. Interrupted sutures were not thought to be necessary because (1) the aorta and renal or visceral vessels were large enough to accept adult-size grafts (12 mm and 8 mm, respectively); and (2) renal or visceral grafts were sewn onto the orifices at the aorta and not to the individual vessels. If, however, the aorta is of a smaller size, it should be beveled and sewn in with interrupted sutures to accommodate at least a 12-mm diameter graft. Similarly, when grafts are anastomosed to the individual branch vessels that are yet to grow, interrupted sutures would be recommended. In the present report, we describe the first case of aneurysm recurrence in a female patient, the first at age 7 years and the second at age 9 years, both of which were large enough to cause symptoms and required emergent repair in both cases, underlining the importance of surveillance to detect any recurrences.

A high degree of awareness and suspicion for a vascular manifestation is warranted in patients with TSC. Although aneurysmal complications of TSC can be detected during screening using magnetic resonance imaging for renal and brain manifestations per the current guidelines, whole body or targeted vascular imaging, as appropriate, should be performed for patients with TSC and signs and symptoms of aneurysm or occlusive arterial disease, such as renovascular hypertension.[4] The surgical therapeutic modality should be chosen according to the size of the patient and the patient's growth potential. Routine surveillance imaging, preferably with ultrasound or magnetic resonance imaging to minimize the radiation dose, every 1 to 3 years and counseling regarding the potential for future operations are warranted after vascular reconstruction in these patients.

Table. Summary of reported cases in English literature of aortic aneurysms in patients with tuberous sclerosis complex (TSC)

Investigator	Sex	Aneurysm location (age)	Recurrence	Presenting symptoms and signs related to aneurysm	Outcome or death related to aneurysm
Dutton et al,[19] 1975	Male	TAAA (6 months); AAA (2.5 years)	Yes	1: incidental finding on chest radiograph; 2: hypertension	Repaired; follow-up: thoracic aorta—infrarenal aorta bypass and right renal bypass grafting for graft calcification with hypertension at 12.5 years
Hagood et al,[5] 1976	Female	AAA (22 months)	No	Hypertension	Repaired; follow-up: no complications at 15 months
Rolfes et al,[7] 1985	Male	AAA (9 months)	No	Abdominal distension and vomiting	Repaired; follow-up: death at age 2 from hemorrhage due to dehiscence of proximal anastomosis site
Ng et al,[20] 1988	Male	AAA (24 years)	No	Pulsatile mass and hypertension	Repaired: perioperative death from bleeding from site of anastomosis
Shepherd et al,[9] 1988	Female	AsAA (3 years)	No	NA	Rupture and death
van Reedt et al,[21] 1991	Male	AAA (5 years)	No	1 Week history of fever, abdominal pain, and pulsating mass	Repaired; follow-up: no complications at 48 months
Tsukui et al,[22] 1995	Female	AAA (4 years)	No	Progressive abdominal distension	Repaired; follow-up: data NA
Tamisier et al,[2,5] 1997	Female	AAA (2.5 years)	No	Hypertension and pulsatile mass	Repaired; follow-up: no complications at 1 year
Baker et al,[3] 2000	Female	AAA (1 year)	No	Bowel obstruction	Repaired; follow-up: data NA
Jost et al,[2] 2001	Female	AAA (9 years)	No	Low back and abdominal pain	Repaired; follow-up: no complications at 7 years
Jost et al,[2] 2001	Male	DTA (41 years)	No	Asymptomatic; incidental finding	Repaired; follow-up: no complications at 8 years
Bavdekar et al,[5] 2000	Male	TAAA (6 years)	No	Respiratory distress and pulsatile mass	Death before surgical repair
Kimura et al,[3] 2005	Male	TAAA (2 years)	No	Asymptomatic; incidental finding on chest radiograph	Repaired; follow-up: data NA
Bahena et al,[5] 2005	Male	AAA (7 months)	No	Pulsatile mass	No repair: death from abdominal aortic dissection
Wong et al,[5] 2006	Female	AAA (9 months)	No	Hypertension	Repaired at 1 year; follow-up: hypertensive with loss of function of left kidney and right renal artery stenosis: hepatic—right renal bypass grafting performed at age 2 years; restenosis at proximal anastomosis and pseudoaneurysm at iliac bifurcation: iliac bifurcation pseudoaneurysm repair performed; autotransplantation of native kidney at age 5 years
Moon et al,[3] 2009	Female	AAA (8 months)	No	Asymptomatic; incidental finding on ultrasound	Repaired; follow-up: death 5 years later from uncontrolled seizures; no recurrent aneurysm or graft occlusion

Table. Continued.

Investigator	Sex	Aneurysm location (age)	Recurrence	Presenting symptoms and signs related to aneurysm	Outcome or death related to aneurysm
Salerno et al,[3] 2010	Female	AAA (14 months)	No	Asymptomatic; incidental finding on surveillance MRI	Repaired; follow-up: bowel resection at 2 months postoperatively for colonic obstruction due to segmental arterial thrombosis and ischemic colitis; no complications at 6 years
Ye et al,[5,23] 2012	Male	AAA (17 months)	No	NA	Repaired; follow-up: no complications at 34 months
Bailey et al,[24] 2013	Male	TAAA (3 years)	No	Anorexia, weight loss, and lethargy	Repaired; follow-up: no complications at 3 years
Sawan et al,[25] 2015	Male	TAAA (5 years)	No	Asymptomatic; incidental finding on ultrasound	Repaired; follow-up: no complications at 1 month
Eliason et al,[26] 2016	Male	AAA (5 years)	No	Asymptomatic; incidental finding on CTA	Repaired; follow-up: developed multiple small eccentric saccular DTA; no further operations at 4.8 years
Dueppers et al,[4] 2016	Male	AAA (2, 6.5, and 10 years)	Yes	Asymptomatic; incidental finding on CTA; recurrences detected on surveillance	Repaired × 3; follow-up: no complications at 8 months
Kwak et al,[27] 2019	Female	DTA (9.6 years)	No	NA	Repaired; follow-up: no complications at 1 month
Geiger et al,[28] 2019	Female	DTA (26 years)	No	Asymptomatic; incidental finding found on CTA	Repaired; follow-up: no complications at 6 months
Hedin et al,[29] 2021	Male	AAA (2 years)	No	Asymptomatic; incidental finding on MRI	Repaired; follow-up: no complications at 9 months
Byrne et al,[5] 2021	Female	DTA (8 years)	No	Asymptomatic; incidental finding on chest radiograph	Repaired; follow-up: data NA
Olvera et al,[30] 2022	Male	TAAA (4 years); DTA (5 years); TAAA (8 years)	Yes	Asymptomatic; recurrences detected on surveillance	Repaired × 3; follow-up: pseudoaneurysm at 10 years postoperatively in DTA: repaired
Gruhl et al,[23] 2022	Female	AAA (3 years, 8 months)	No	Painless pulsatile mass	Repaired; follow-up: no complications at 7 months
Present case	Female	AAA (7 years); TAAA (9 years)	Yes	1: fever, cough, abdominal pain, emesis, and bloody diarrhea; 2: abdominal pain and upper respiratory infection symptoms	Repaired; follow-up: bowel resection on POD 6 for perforated small bowel obstruction; no complications at 6 months

AAA, Abdominal aortic aneurysm; *AsAA*, ascending aortic aneurysm; *CTA*, computed tomography angiography; *DTA*, descending thoracic aortic aneurysm; *MRI*, magnetic resonance imaging; *NA*, not available; *POD*, postoperative day; *TAAA*, thoracoabdominal aortic aneurysm.

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