Klippel-Trénaunay-Weber syndrome associated with abdominal aortic aneurysm in childhood

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Klippel-Trénaunay-Weber syndrome (KTWS), also known as angioosteohypertrophy syndrome, is a rare congenital malformation with unknown etiology characterized by the combination of capillary malformations (port-wine strain), venous varicosities, and a soft tissue or bony hypertrophy of the affected limb. It is known to be rarely associated with abdominal aortic aneurysm (AAA) in adults. We report the first published case of KTWS and a rapidly progressing symptomatic AAA undergoing open repair in a child. This underlines the importance of AAA screening and treatment rather than surveillance in patients with KTWS. (J Vasc Surg Cases 2015;1:174-6.)

Klippel-Trénaunay-Weber syndrome (KTWS), or angioosteohypertrophy syndrome, is a rare congenital malformation syndrome with unknown etiology.[1] It is characterized by the combination of capillary malformations (port-wine strain), venous varicosities, and a soft tissue or bony hypertrophy of the affected limb.[2,3] One hypothesis is that KTWS is a generalized mesodermal abnormality during fetal development.[4] Recent discoveries show that mutations of the *RASA1* gene, which interacts with the Rap1a protein, a member of the Ras family, is involved in the pathogenesis of cavernous angiomas.[5]

Reviews of large patient series of KTWS show a remarkable difference in the incidence and frequency of clinical symptoms.[6] The prevalence of KTWS in children is 1/20,000 to 40,000, with a male-to-female ratio of 1:1.

KTWS in adults has been reported in association with arterial aneurysms, mostly in cerebral, renal, and popliteal arteries.[7-10] To our knowledge this is the first reported case of KTWS associated with an abdominal aortic aneurysm (AAA) repair in a child. The patient gave consent for publication.

CASE REPORT

A 15-year-old female patient was admitted to our clinic after incidental ultrasound imaging found an asymptomatic abdominal aortic ectasia during a cardiac workup due to nonspecific cardiac pain. KTWS was diagnosed at the age of 3. The clinical examination revealed an asymptomatic AAA associated with limb shortening, circumference discrepancy, and varicosis of the lower right extremity (Fig 1, *A*). Magnetic resonance angiography (MRA) detected a 46-mm AAA and an ectasia of the right popliteal artery to 13 mm. No signs of deep venous thrombosis or arteriovenous fistulas were found on ultrasound imaging or on MRA.

The risk assessment for prophylactic repair was borderline and evaluated individually with the patient and her parents. A "watchful waiting strategy" was considered for the AAA even being within a treatment threshold of 50 mm. MRA follow-up 4 months later showed an asymptomatic progression to 53 mm. Careful patient reassessment was performed based on the recent previous cardiac and respiratory workup. Elective operative treatment was indicated and scheduled in 4 weeks' time. Endovascular repair was not considered as an option due to her age, the AAA morphology, and etiology.

The patient was readmitted 2 weeks later with abdominal pain. Computed tomography angiography revealed the AAA had rapidly increased in size, with maximum diameter of 57 mm, without signs of rupture (Fig 1, *B*). Open repair with an aortobiiliac Gelsoft surgical graft (Vascutek, Bad Soden, Germany) was performed without any intraoperative problems (Fig 2). The integrity of the aortic wall during suturing was inconspicuous.

The patient's postoperative course was uneventful, and she was discharged on day 7 after surgery. Clinical and ultrasound examination after 6 months showed no abnormality. Histologic analysis showed loss of elastic fibers, microcystic mucoid degenerations of the tunica media, and fibrosis of the tunica intima. Evidence of Marfan or Ehlers-Danlos syndrome was excluded from electron microscopy (Fig 3).

DISCUSSION

This is the first case describing a symptomatic, large AAA associated with KTWS in a child. AAAs are extremely rare in children. A MEDLINE database search from 1975 to 2008 found only 41 cases of AAAs in children.[11] Causes included mycotic aneurysms, vasculitides (Takayasu arteritis), connective tissue diseases (Marfan syndrome, Ehlers-Danlos syndrome, tuberous sclerosis), and traumatic false aneurysms.[12] Because AAAs in children are rare, the

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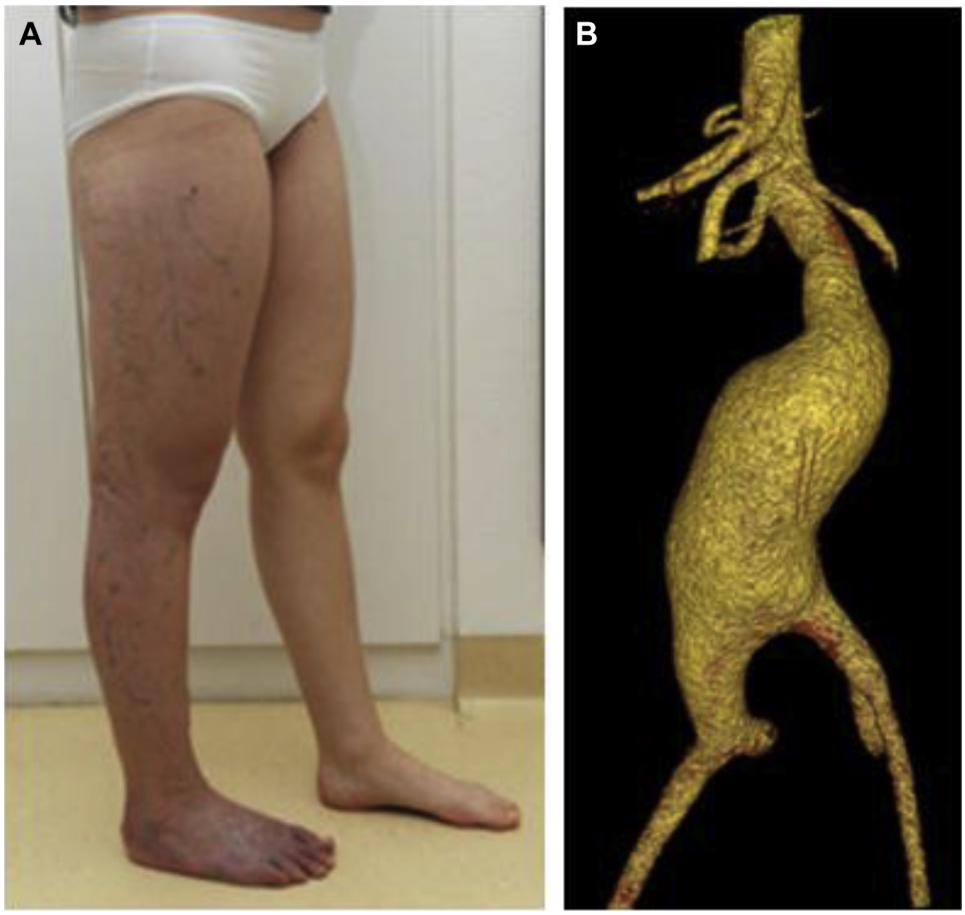

Fig 1. Clinical presentation of Klippel-Trenaunay-Weber syndrome (KTWS) with **(A)** gigantism of the right lower extremity and **(B)** computed tomography angiography finding of the associated symptomatic abdominal aortic aneurysm (AAA).

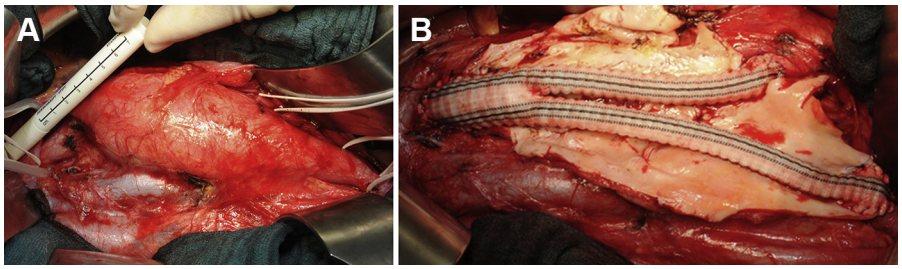

Fig 2. Intraoperative view **(A)** before and **(B)** after surgical bypass.

etiology, natural progression, and prognosis remain mostly unknown.[12] In this patient, rapid progression and development of symptoms were observed.

KTWS is a combination of cutaneous angiomatosis, varicose veins, and enlargement of soft tissue first described in 1900. The KTWS occurs mostly sporadically, affecting males and females in equal numbers in about 1/100,000 people.[10] KTWS has been reported to be associated with cerebral, aortic, renal, and popliteal aneurysms in only 12 adult patients.[4-7] Further, cerebral and retinal vascular anomalies, for example, choroidal hemangioma and spinal cord arteriovenous, malformations rarely are described.

KTWS is associated with mutations of the *RASA1* gene, which belongs to the SH2 domain-containing family of genes. *RASA1*-related disorders are characterized by the presence of multiple, small (1-2 cm in diameter) capillary

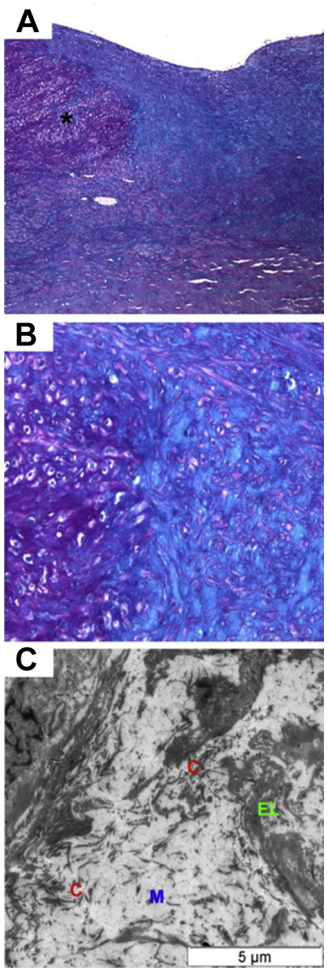

Fig 3. Histologic findings of the abdominal aortic aneurysm (AAA) wall. Alcian-blue/periodic acid Schiff-stained sections of the tunica media at **(A)** original magnification ×4 and **(B)** original magnification ×200 demonstrate loss of elastic fibers and microcystic mucoid degeneration. Remnants of normal tunica media are marked by an *asterisk*. Electron microscopic image **(C)** shows mucoid material (*M*), rarefaction of collagen fibers, and degenerated elastic fibers (*EL*).

malformations mostly localized on the face and limbs. *RASA1* gene mutations also have been identified in patients with Parkes Weber syndrome and with basal cell carcinoma.[16]

Open surgical repair should be considered even in adolescents to prevent AAA rupture using a tensile polyester graft prosthesis to compensate for the process of growth. In young patients, the endovascular approach with short-term follow-up results and relevance of X-ray surveillance and reinterventions is not recommended. Neuraxial anesthesia should only be performed after excluding the presence of vascular malformations of the spine.[12-15] In addition, aortic growth would likely result in migration and secondary endoleaks after endovascular therapy. If managed conservatively, close monitoring of aneurysms using MRA and ultrasound imaging is essential.[6]

CONCLUSIONS

AAAs can be a concomitant disease in patients with KTWS, even in children and adolescents. Therefore, abdominal ultrasound screening should be performed in these patients regardless of age. Open surgery is the first choice treatment in young patients.

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