

SHORT REPORT

History of a Patient with Sack–Barabas Syndrome (Ehlers Danlos Type IV)—16 Years of Recurrent Life-extending Open and Endovascular Surgery

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The Sack–Barabas syndrome, the vascular type of Ehlers–Danlos syndrome type IV, is considered the most serious form of Ehlers–Danlos syndrome as the vascular system is prone to aneurysmatic degeneration and rupture without preference of anatomic regions. We report a patient with Sack–Barabas syndrome who was treated by one vascular surgeon for 16 years, from the first of many operations until death at the age of 27.

Keywords: Ehlers–Danlos syndrome type IV; Sack–Barabas syndrome; Aneurysms.

Introduction

The German physician Georg Sack and the British surgeon A. P. Barabas first described the syndrome in the 20th century.^{1,2} Ehlers–Danlos syndrome is a group of inherited disorders affecting the connective tissue.^{3–5} The vascular type is considered one of the most serious forms of Ehlers–Danlos syndrome because blood vessels and organs are prone to rupture. This condition was formerly called type IV Ehlers–Danlos syndrome, and is now known as Sack–Barabas syndrome (SBS). Patients with this disorder have thin, fragile skin that bruises easily. Hands and feet may have an aged appearance. Unlike patients with other forms of Ehlers–Danlos syndrome, patients with the vascular type have skin that is soft but not overly stretchy. Facial features are often distinctive, including protruding eyes, a thin nose and lips, sunken cheeks, and a small chin. Other signs of the disorder include hypermobility of joints, tearing of tendons and muscles, painfully swollen veins in the legs, lung collapse, and slow wound healing following injury or

surgery. Infants with the condition may be born with hip dislocations and clubfeet. Unpredictable ruptures of arteries and organs are serious complications of SBS syndrome.^{6,7,8} Ruptured arteries, causing internal bleeding, stroke, or shock, are the most common cause of death in patients with SBS. Rupture of the intestine is seen in 25–30% of affected individuals and tearing of the uterus during pregnancy affects 2–3% of women.^{9,10} Although these symptoms are rare in childhood, more than 80% of patients experience severe complications by the age of 40. Teenage boys are at high risk for arterial rupture, often fatal. Herein, we report the case of a patient initially presenting at the age of 11 with an iliac aneurysm rupture and life long follow-up and interventions.

Case Report

The first presentation of the patient to a vascular surgeon was in 1988. The vascular surgeon on call (GWH) was called to assess an 11 years old boy with a painful pulsatile mass in his left groin. CT-scan and angiography (Fig. 1) showed bilateral iliac artery aneurysms, with a rupture on the left. In addition,

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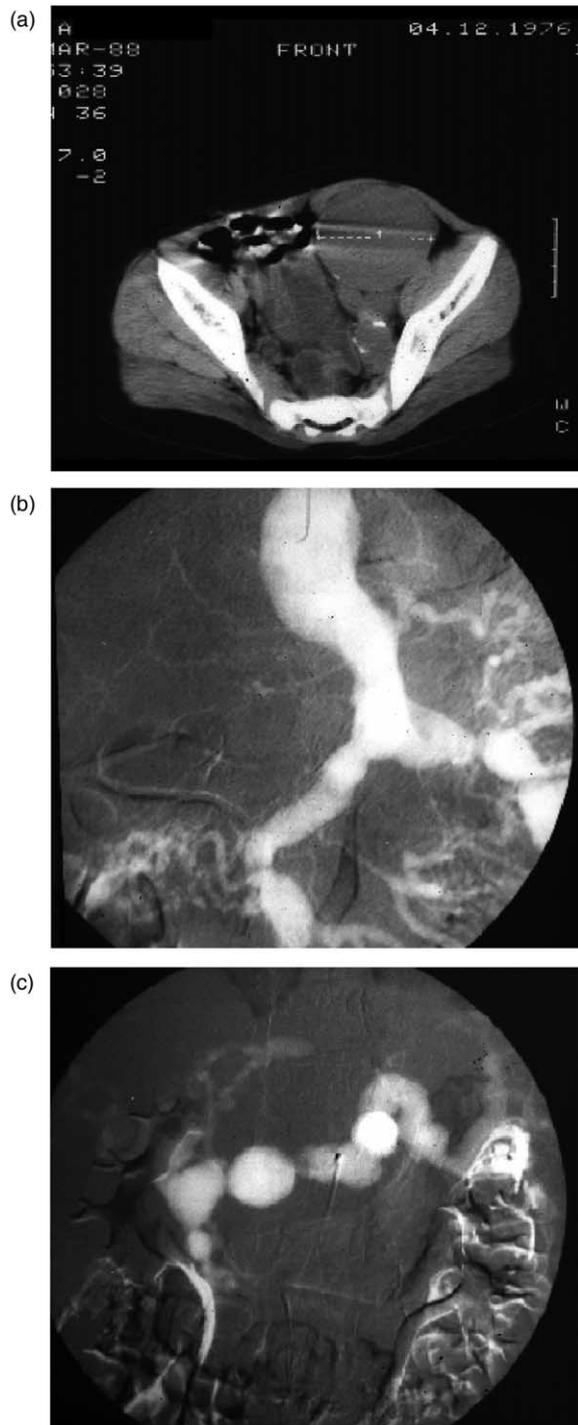


Fig. 1. (a) Abdominal CT: iliac aneurysm in rupture. (b) Selective angiography: diffuse SMA-aneurysm. (c) Lienal artery aneurysms.

multiple asymptomatic aneurysms of the superior mesenteric, the common hepatic and both renal arteries were found. The ruptured iliac artery was repaired with an emergency aorto-bifemoral bypass graft. After a recovery period of 3 months the intestinal

aneurysms were treated by resection and PTFE graft interposition of the superior mesenteric, the common hepatic and the right renal artery. The aneurysmatic splenic artery was ligated, no splenectomy was necessary. The resected aneurysm walls were histologically analysed and SBS was verified. Our patient was a sporadic case of SBS, caused by new mutations in one copy of the COL3A1 gene as described by Hassan *et al.*⁶ Screening of all family members was negative.

The right renal artery and celiac axis interposition grafts occluded after 2 weeks. Right nephrectomy was necessary due to major renal necrosis. The blocked celiac axis graft was managed conservatively in the absence of major liver ischaemia. The patient recovered and was discharged home on anti-hypertensive therapy.

In 1990 the patient suffered synchronous pulsating neck- and headaches. Bilateral diffuse extracranial vertebral aneurysms were found and were treated by carotid vertebral C1-bypasses and ligation of the aneurysm (Fig. 2).

In 1997 a Hemobahn stentgraft[®] (W. L. Gore Flagstaff, USA) was implanted in a left brachial artery aneurysm. The cubital artery on the same side needed to be bridged with a PTFE-graft because of a large aneurysm causing severe discomfort. The following year the patient developed left leg claudication, caused by a superficial femoral artery aneurysm. This was treated with a Hemobahn stentgraft[®], implanted by a cut down incision into the common femoral artery.

In 1999 the patient returned with therapy-resistant pulsating left sided headache, caused by a symptomatic aneurysm of the left intrasphenoidal internal carotid artery. Exclusion with a Hemobahn stentgraft[®] through the common carotid artery was attempted unsuccessfully. The aneurysm had to be excluded by coil embolisation and the internal carotid artery was ligated. The patient suffered from a transient aphasia lasting 24 h. In the same year claudication of the right leg required a Hemobahn stentgraft[®] to be implanted in an aneurysmatic right common and superficial femoral artery. The claudication was caused by thromboembolic events originating from in the femoral aneurysms.

The last interventions were in 2001. Motor and sensory dysfunction of the left arm required a left brachial artery redo—PTFE-graft. Large right subclavian and brachial artery aneurysms (Fig. 3) were stented with a Hemobahn[®] prosthesis due to impending rupture.

In 2004, the patient was 27 years old. He suffered from claudication (50 m walking distance) since 1998,

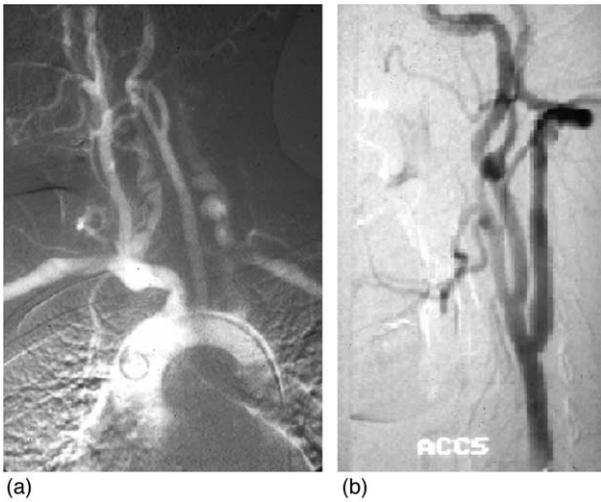


Fig. 2. (a) Bilateral vertebral artery aneurysms. (b) Common carotid vertebral bypass left side (C1-bypass).

without the possibility of revascularisation. However, he was content with his quality of life and working regularly. Except aspirin, he was on no medication. Angiography of the visceral arteries and the extremities performed in July 2004 did not show any vascular abnormalities requiring surgery (Fig. 4).



Fig. 3. Hemobahn stentgrafts of the right subclavian-axillary and brachial arteries.

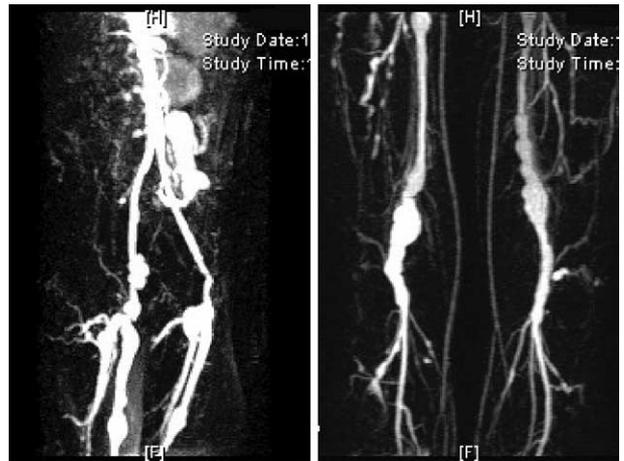


Fig. 4. Aneurysms of the lower extremities: common femoral, superficial femoral, profund femoral and popliteal arteries.

In August 2004 the patient was admitted with severe epigastric pain, hypotension and collapse. An abdominal CT (Fig. 5) showed free fluid in the left upper abdomen and calcified aneurysms of the upper mesenteric artery and celiac axis. The patient was immediately transferred to theatre for emergency surgery of a suspected rupture of the splenic artery aneurysm ligated in 1988. The patient died on the way to theatre, 16 years after his first operation. All surgical interventions over this period were performed by one vascular surgeon (Fig. 6).

Discussion

Sack–Barabas syndrome, the vascular manifestation of



Fig. 5. Native abdominal CT: calcified upper intestinal aneurysms, suspicious enhanced free liquid between them (ruptured aneurysm of the lienal artery).



Fig. 6. Native abdominal CT: calcified upper intestinal aneurysms, suspicious enhanced free liquid between them (ruptured aneurysm of the lienal artery).

Ehlers–Danlos syndrome is rare and has an estimated prevalence of one in 100,000–200,000 and is caused by mutations in the COL3A1 gene.

The protein determined by the COL3A1 gene is used to assemble larger type III collagen molecules. Collagens provide structure and strength to connective tissue throughout the body. Type III collagen is mostly found in skin, blood vessels, and internal organs. If the structure or production of type III collagen is altered by a mutation in the COL3A1 gene, collagen fibrils cannot be assembled properly in these tissues, and the symptoms of Ehlers–Danlos syndrome result.^{3–5}

The condition is inherited in an autosomal dominant pattern, which means only one copy of an altered gene is needed to cause the disorder. About half of all cases are inherited from a parent who has the condition. The other half of cases occurs in patients whose families have no history of the disorder. These sporadic cases are caused by new mutations in one copy of the COL3A1 gene.

The tests to verify the disease are biochemical samples such as collagen typing (performed on a skin biopsy sample) or collagen gene mutation testing.

There is no cure for Ehlers–Danlos syndrome, so individual problems and symptoms must be evaluated and treated accordingly. The initial clinical manifestation of vascular problems in patients with

SBS is early, about 25% have their first presentation at age 20 and more than 80% of patients in a large cohort have had at least one complication by the age of 40. The median survival of the entire cohort was only 48 years.³

Genetic counselling is recommended for prospective parents with a family history of Ehlers–Danlos syndrome. Recognition of this syndrome is necessary because of increased risk of premature death due to rupture of arteries, bowel or uterine rupture in pregnant women with a reported mortality rate of 50%.³

The key for managing these patients is to be aware of their disease and escort them through complications, plan surgical procedures and pregnancy in affected women. As the reported case demonstrates, close follow-up and planning of interventions can significantly prolong and maintain the quality of life of a patient with this disease.

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