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Letter to the Editor

Vascular Ehlers-Danlos syndrome, a therapeutic challenge

Síndrome de Ehlers-Danlos tipo vascular: un reto terapéutico

Dear Editor,

Vascular Ehlers-Danlos syndrome (vEDS) is an autosomal dominant inherited connective tissue disorder with an estimated prevalence of 1/150,000. It is caused by mutations in the III (COL3A1) collagen alpha 1 chain gene, which encodes a fibrillar protein expressed mainly in the walls of blood vessels and hollow organs. The resulting tissue fragility increases the risk of arterial rupture, dissection and development of aneurysms, as well as perforation of the bowel and gravid uterus. The 2017 international classification of Ehlers-Danlos syndromes lists major and minor criteria that are suggestive of vEDS.[1] However, the diagnosis of vEDS is confirmed when a pathogenic variant is found on one allele of the COL3A1 gene.

A 19-year-old man, carrier of a pathogenic variant of the COL3A1 gene, was admitted to our intensive care unit with a type B aortic dissection at 6 cm from the origin of the left subclavian artery to both common iliac arteries. An emergency endovascular repair was performed by placing 2 overlapping stents from the proximal descending aorta to the origin of the celiac trunk. Another bifurcated stent was placed in the abdominal portion of the aorta, extending from the origin of the superior mesenteric artery to the distal portion of the common iliac arteries. Eight days later, a type I endoleak developed in the anterior and superior part of the aortoiliac stent, leaving the celiac trunk and superior mesenteric artery patent (Fig. 1). Another emergency endovascular repair was performed by placing a fenestrated stent, excluding the ruptured aortic segment, and a stent in the superior mesenteric artery, excluding the celiac trunk and both renal arteries. After 8 months of hospitalisation and multiple complications (ischaemic spinal cord injury, compartment syndrome of both lower limbs, nosocomial infections, ischaemic cholangitis, renal failure on haemodialysis, gastrointestinal intolerance, etc.), the patient died.

There are still no treatment guidelines for vEDS. In 2010, the *Beta Blocker in Ehlers-Danlos Syndrome Trial* (BBEST) demonstrated a 64% reduction in the risk of arterial rupture or dissection in patients treated with celiprolol compared to controls.[2] Similarly, in the study by Bowen et al. 5-year survival was 96.53% for those taking any cardiovascular medication (including beta-blockers and angiotensin receptor blockers) and 42.69% for patients in the control group.[3]

The high clinical variability of vEDS presentation means that the surgical strategy, both open and endovascular, must be personalised for each patient based on clinical condition, comorbidities and associated risks. Due to vessel tortuosity and the congenital tendency of aneurysms to dilate, endovascular treatment is not the first choice because of the high risk of endoleaks and reinterventions. However, as this is a percutaneous treatment, the associated risks are considerably lower than with the open technique. Endovascular repair therefore finds its greatest application in emergency cases and where immediate treatment with a low complication rate must be guaranteed.[4]

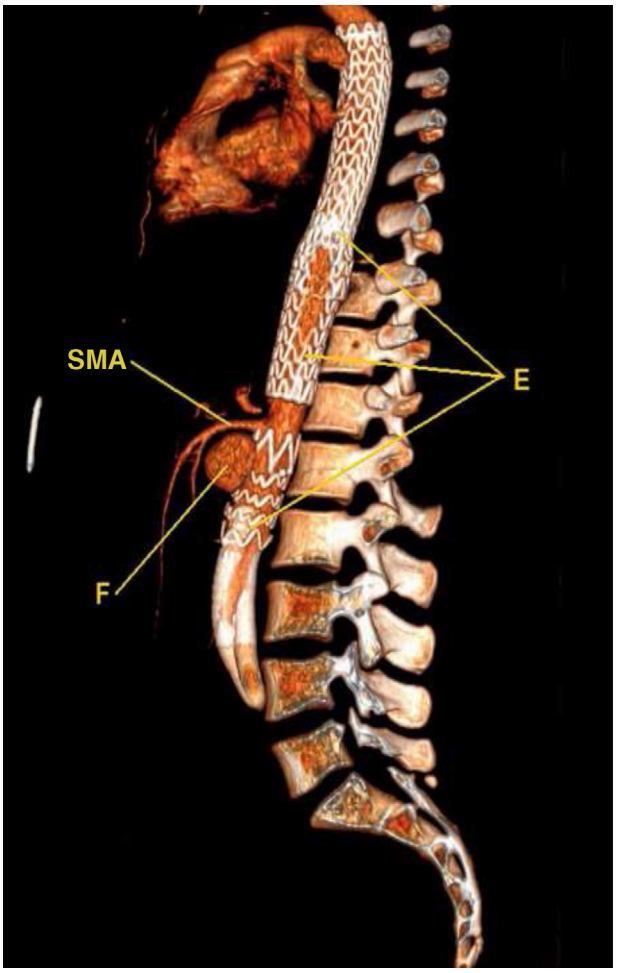

Figure 1. 3D reconstruction of a CT angiogram showing 2 overlapping stents (E) in the proximal descending aorta and another bifurcated stent in the abdominal portion of the aorta. Immediately caudal to the origin of the superior mesenteric artery (SMA), a type I endoleak is observed (F).

In terms of prognosis, the study *Genetically Triggered Thoracic Aortic Aneurysm and Cardiovascular Conditions* (GenTAC) shows that mortality from cardiovascular causes is higher in these patients than in other connective tissue diseases, probably due to the greater severity of the disease.[5] However, this prognosis seems to have improved significantly over the last 20 years due to several factors: firstly, a better preventive strategy in affected patients, with a

multidisciplinary approach in reference centres, where adequate long-term care and follow-up is ensured (blood pressure monitoring, transthoracic echocardiography, as well as whole body vascular imaging with computed tomography or magnetic resonance angiography) and, in addition, pharmacological treatment with beta-blockers and/or inhibitors of the renin-angiotensin-aldosterone system, which may also play a key role in the treatment of the disease.

In summary, vEDS is an ominous disease, even in young individuals, although outcomes have improved significantly in recent years. The best therapeutic strategy is the prevention of cardiovascular complications, such as aortic dissections, which most negatively affect prognosis. Beta-blockers and angiotensin receptor blockers have shown some benefit. However, more studies are needed in this population to help us determine the best therapeutic options and to rule out those that are futile when complications arise.

CRediT authorship contribution statement

All authors have contributed equally to the conception, drafting and final approval of the scientific communication.

Ethical considerations

Instructions to authors and ethical responsibilities have been taken into account. In addition, the hospital's protocols and procedures related to the publication of patient data and the privacy of the subject have been followed.

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Declaration of competing interest

None.

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