Endovascular repair of a common iliac artery aneurysm with an iliac branch device in a patient with vascular Ehlers-Danlos syndrome due to a null *COL3A1* variant

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ABSTRACT

Endovascular repair is avoided in patients with connective tissues disorders due to concerns for stent graft migration and endoleaks. We describe a successful endovascular repair of a common iliac artery aneurysm with a bifurcated aortoiliac stent graft and iliac branch endoprosthesis in a patient with Vascular Ehlers-Danlos syndrome (VEDS) due to a null *COL3A1* variant. This case demonstrates that the VEDS genotype is associated with tissue integrity, specifically, individuals with VEDS due to null/haploinsufficiency variants, and adds to our understanding of endovascular repair in this population. (J Vasc Surg Cases Innov Tech 2023;9:1-5.)

Keywords: Connective tissue disorder; Endovascular aortic repair; Genetic aortopathy; Iliac artery aneurysm; Iliac branch endoprosthesis; Vascular Ehlers-Danlos syndrome

Iliac arteriopathy is reported in 17% to 37% of individuals with Vascular Ehlers-Danlos syndrome (VEDS).[1-3] Repair options include open surgical repair (aortobi-iliac or iliac bypass) or endovascular iliac stent graft placement with or without internal iliac artery (IIA) embolization.[1-3] We present the case of a patient with VEDS due to a null (also called haploinsufficiency) variant (*COL3A1*, c.555delT, p.Gly186ValfsTer36) with a common iliac artery (CIA) aneurysm treated with endovascular aortic aneurysm repair (EVAR) using a Gore Excluder (W.L. Gore & Associates) and an iliac branch endoprosthesis (IBE).[4] The patient provided written informed consent for the report of his case details and imaging studies via the prospective VEDS collaborative research study.[5]

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CASE REPORT

A 64-year-old male long-distance runner with VEDS presented with a 4-cm left CIA aneurysm extending into the takeoff of the IIA and a 2.9-cm distal infrarenal abdominal aorta dissection (Fig 1). He had no history of intestinal perforation, pneumothorax, or VEDS minor diagnostic criteria.[6] His family history is significant for a father who died at age 75 of an air embolism after open abdominal aortic aneurysm (AAA) repair, a sister who had undergone EVAR at age 59, and a niece who had developed internal carotid artery dissection at age 28. The niece was the proband and the cause for the family cascade genetic testing. The pathogenic *COL3A1* variant is a null (haploinsufficiency) variant due to a translational reading frameshift that results in a premature stop codon.

An open repair with an infrarenal aortobi-iliac graft and a jump bypass to the left IIA is high risk owing to VEDS-related significant bleeding and postoperative hernia risk.[7-10] The patient was also concerned about the possibility of intraoperative ligation of the left IIA as a bailout maneuver. This was an important quality-of-life issue related to the loss of antegrade perfusion and resultant buttock claudication should the IIA be ligated.[11] The patient's sister had already undergone successful percutaneous EVAR with a Gore Excluder 4 years earlier. She also enrolled in the VEDS collaborative research study and participated in the shared decision-making discussions. Her imaging studies demonstrated excellent AAA and CIA remodeling (Fig 2). Considering the molecular diagnosis of the *COL3A1* null variant and the excellent remodeling after EVAR in his sister, the shared decision was to proceed with EVAR with an IBE.

The patient was instructed to start taking vitamin C (1 g twice daily) to promote collagen production. This practice is based on our anecdotal experience with a reduction in bruising among patients with VEDS who start taking vitamin C. The operation was performed with the patient under general anesthesia. A radial arterial line was placed. Cell saver and massive transfusion blood products were available, and the team was prepared for the possibility of conversion to an open AAA repair. The EVAR

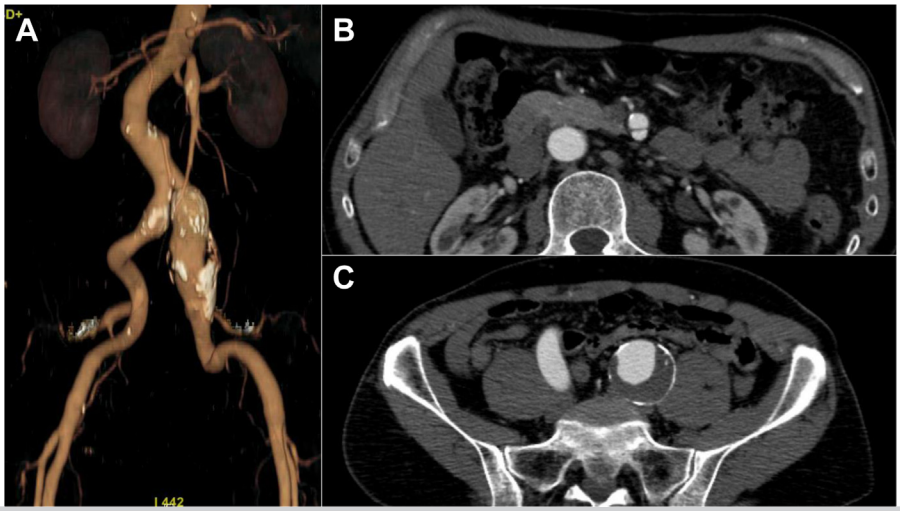

Fig 1. A, Postprocessing three-dimensional image of a computed tomography angiogram of a 62-year-old man with vascular Ehlers-Danlos syndrome (VEDS; *COL3A1*, c.555delT, p.Gly186ValfsTer36, null variant) demonstrating a 40-mm left common iliac artery aneurysm. **B,** Axial computed tomography image showing a superior mesenteric artery dissection. **C,** Axial computed tomography image showing a 40-mm common iliac artery (CIA) aneurysm.

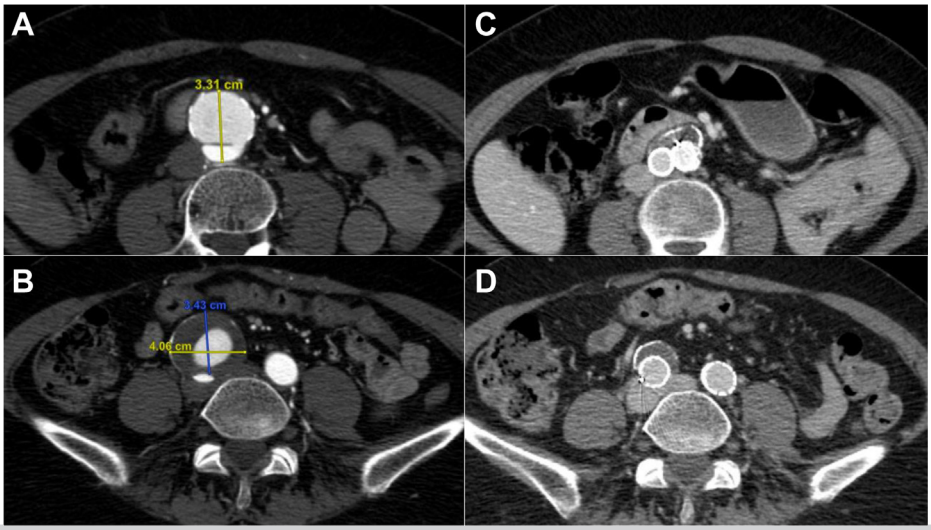

Fig 2. Axial views of computed tomography angiogram of a 59-year-old woman with vascular Ehlers-Danlos syndrome (VEDS; *COL3A1*, c.555delT, p.Gly186ValfsTer36, null variant) showing a 33-mm infrarenal abdominal aorta with dissection (**A**) and a 41-mm right common iliac artery aneurysm (**B**). Axial views of computed tomography angiogram 4 years later, showing the infrarenal abdominal aorta (**C**) and common iliac arteries (CIAs; **D**) with favorable remodeling.

device was minimally oversized to avoid the potential complication of proximal neck or distal iliac artery dissection or aneurysmal degeneration.

The bilateral common femoral arteries (CFAs) were exposed for direct access. After access and systemic heparinization, the sheaths were upsized over Amplatz superstiff wires to 16F and 12F on the right and left, respectively. A glide wire was snared from the right to the left to create a through-and-through wire. The aortic bifurcation was protected to avoid the risk of rupture using a Kumpe catheter over the wire and gentle advancement over the bifurcation. The 23-mm × 14.5-cm × 10-cm bifurcated iliac stent graft was advanced over the glide wire and Amplatz wire into the right CIA and deployed. The contralateral up and over 12F sheath was advanced into the device body, and the IIA was selected using a glide catheter and wire. The glide wire was exchanged for a Rosen wire (Fig 3). Next, an 8F sheath was advanced via the 12F sheath into the IIA, and an 8 × 59-mm VBX stent was deployed into the IIA. The IBE was gently ballooned into place (overinflation was avoided to minimize the risk of rupture or dissection). The 23-

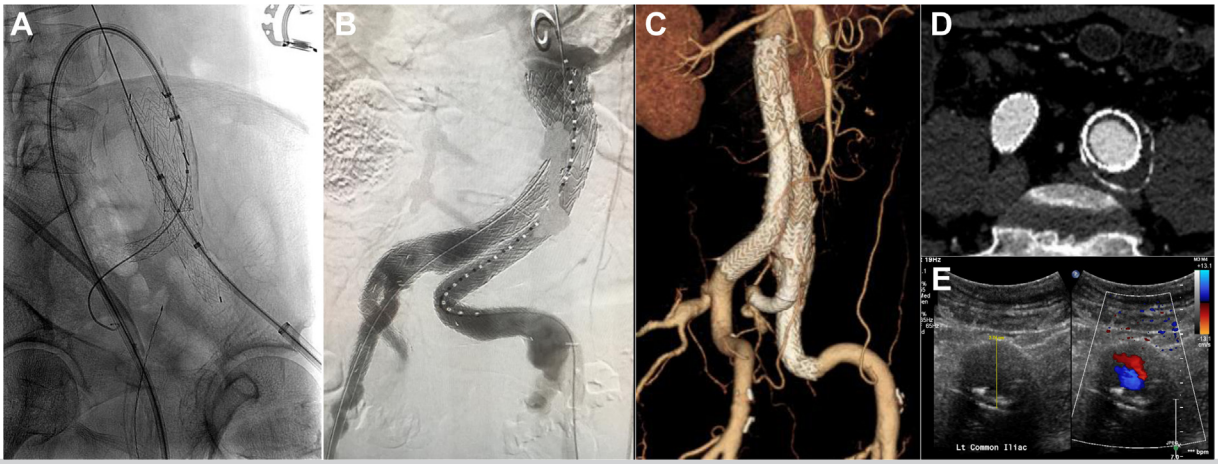

Fig 3. A, Intraoperative fluoroscopic image demonstrating deployment of the iliac branched device over a Rosen wire in a 62-year-old man with vascular Ehlers-Danlos syndrome (VEDS; *COL3A1,* c.555delT, p.Gly186-ValfsTer36, null variant). **B,** Intraoperative completion angiogram showing a satisfactory proximal seal and excellent blood flow into the preserved left internal iliac artery (IIA). **C,** Postprocessing three-dimensional image of a computed tomography angiogram 3 years postoperatively. **D,** Axial image of computed tomography angiogram demonstrating favorable common iliac artery (CIA) remodeling. **E,** Duplex ultrasound examination of the CIA 4 years postoperatively showing the same.

mm × 14.5-cm × 12-cm main body bifurcated endoprosthesis, a bridging 27-mm × 12-cm graft, and the ipsilateral 18-mm × 11.5-cm limb were sequentially deployed. The grafts were deployed over glide wires (Glidewire Hydrophilic Coated Guidewire; Terumo) to allow for the devices to take the tortuosity of the aorta and iliac arteries. A Coda balloon was then used to gently seal the graft in place with minimal ballooning at the neck (Fig 3). The CFAs were then clamped with padded clamps and repaired with interrupted 5-0 Prolene sutures with pledgets. The arteriotomy sites were circumferentially wrapped with 0.8 × 8-cm bovine pericardium to prevent pseudoaneurysm formation (Fig 4). A small area of adventitial hematoma at the site of one of the distal clamps was also circumferentially wrapped with bovine pericardium. The groin incisions were closed in layers and the skin with staples. The estimated blood loss was 200 mL.

Postoperative care included admission to the intensive care unit overnight, intravenous fluid resuscitation targeted to urine output of 0.5 mL/kg/h to avoid overresuscitation, maintenance of systolic blood pressure between 90 and 120 mm Hg, and continuation of vitamin C. The patient was discharged home on postoperative day 2.

The patient has had 3.5 years of follow-up, demonstrating excellent remodeling of the CIA aneurysm with no endoleak or graft migration (Fig 3). He has since undergone a valve-sparing aortic root replacement and ascending hemiarch for a 5.1-cm aortic root aneurysm and recovered well.

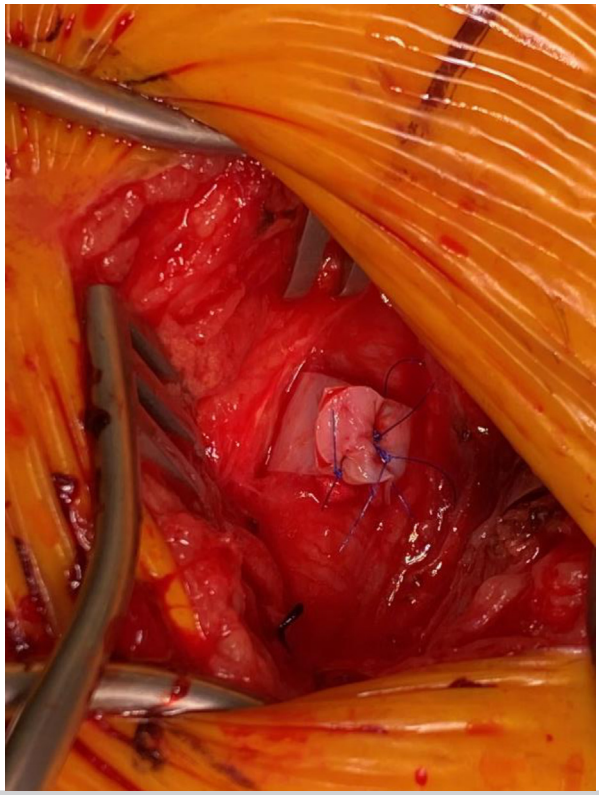

Fig 4. Intraoperative photograph of a common femoral artery (CFA) that was repaired with interrupted pledgeted 5-0 Prolene suture and wrapped with a 0.8-cm bovine pericardium patch.

DISCUSSION

Surgical repair in VEDS is complicated by a lack of tensile strength in the aortic and arterial walls and is associated with significant bleeding.[1,7,8,10,12] The use of endovascular aortic stent grafts in patients with connective tissue disorders is generally not recommended owing to the mismatch between the device radial force and the tensile strength of a diseased aorta.[13,14] The literature on EVAR for patients with VEDS is sparse and

comprises four case reports. One was of a 76-year-old man with VEDS and type Ia and Ib endoleaks 7 years after EVAR with suprarenal fixation for an infrarenal AAA. This was successfully treated with open AAA repair and explantation of the device.[15] We reported the case of a 45-year-old man with VEDS who underwent EVAR in our previous low frequency disease consortium study. That patient had 1 year of follow-up.[3] A more recent report described the use of thoracic EVAR and branched EVAR and fenestrated EVAR to treat dissection-related thoracoabdominal aortic aneurysm in two patients with VEDS (aged 56 and 47 years). The reported follow-up duration was 3.5 years and 1 year, respectively. Both patients survived acute type A aortic dissection repair before the endovascular repairs.[16] None of these patients had the genetic testing results reported; thus, the COL3A1 variant in these case reports is unknown.

Not knowing the *COL3A1* variant severely limits our understanding of the role of endovascular aortic repair in the heterogeneous VEDS population. The tissue quality in patients with VEDS is dependent on the *COL3A1* variant effect on type III collagen production.[2,17,18] Type III collagen is essential for the structural integrity of the arterial walls. In most patients, the variant *COL3A1* copy of the gene (allele) leads to the production of defective type III procollagen chain, which is incorporated into the type III procollagen trimer. Consequently, when the chains are incorporated, only one of eight trimers will have three normal chains. The effect on the secretion of the trimer and incorporation into fibrils outside the cell results in weakening most of the type III collagen produced.[19] In patients with a null/haploinsufficiency variant, the *COL3A1* gene is functionally silent; thus, the patient produces normal collagen but at 50% overall production.[2,17] Individuals with null variants account for 5% to 10% of the population with VEDS, have a milder clinical phenotype, and longer life expectancy compared with patients with VEDS due to other types of variants (eg, missense and exon skip).[18] Thus, we expect that the collagen in patients with VEDS due to null variants should have improved tensile strength compared with collagen produced in patients with VEDS caused by other variants. As our knowledge of VEDS continues to increase, it is important to include the results of genetic testing (*COL3A1* DNA and protein alteration) in case reports and series to better understand the implications of the genotype on operative repair outcomes (genotype—surgical phenotype correlation).

On a practical level, our understanding of the molecular biology and known favorable aortic remodeling after EVAR seen in our patient's sister helped guide the multidisciplinary decision toward an endovascular solution. Our patient's subsequent recovery after aortic root aneurysm repair reinforces the notion that the genotype predicts the tissue integrity (surgical phenotype). In consideration of the VEDS diagnosis, we oversized for <10% at the infrarenal neck proximal landing zone because of our concern for future neck expansion. The shared decision-making also included a clear understanding that lifelong follow-up is indicated because the long-term durability of the endovascular repair remains in question and delayed development of endoleaks at the fixation sites can occur, even among patients without VEDS.[4]

Finally, we performed open exposure and repair of the CFA, similar to that described by Brooke et al.[9] This was because of concerns for failure of a percutaneous approach in this patient population. The sister of our patient had undergone a successful percutaneous approach for large femoral sheath access. Additional work is needed in this area to determine the ideal femoral approach in patients with VEDS.

CONCLUSIONS

The genotype in VEDS is associated with tissue integrity and surgical phenotype. A role might exist for aortic endovascular repair for patients with VEDS due to null (haploinsufficiency) variants. However, larger studies are needed.

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