Endovascular repair of a dissecting pararenal abdominal aortic aneurysm in a patient with type III Loeys-Dietz syndrome

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ABSTRACT

Loeys-Dietz syndrome (LDS) type 3 results from a SMAD3 mutation and is a phenotypically milder variant of LDS with frequent aortic, visceral, and cerebral vascular pathologies and osteoarthritis. Historically, endovascular treatment (endovascular aortic repair [EVAR]) of LDS-related aortic aneurysmal disease with traditional modular bifurcated devices has been limited owing to concerns regarding continued aortic dilation at proximal fixation sites. Furthermore, associated dissection pathology has also precluded traditional modular bifurcated EVAR owing to inadequate proximal infrarenal necks and narrow distal aortic domains leading to compromised contralateral gate opening and cannulation as well as limb flow compromise. To address these barriers to EVAR, we present our approach for the endovascular treatment of a dissecting pararenal abdominal aortic aneurysm using an anatomically fixated, bifurcated, unibody aortic stent graft in a patient with LDS-3. (J Vasc Surg Cases and Innovative Techniques 2021;7:10-5.)

Keywords: EVAR; Loeys-Dietz; Infrarenal aortic dissection; smad3; Mutation

Loeys-Dietz syndrome (LDS) represents a set of connective tissue disorders classically associated with transforming growth factor (TGF)βR1 or TGFβR2 mutations, leading to deficient TGF-beta signaling, less synthesis and secretion of matrix components, and weakened vessels.[1] Discovered in 2011, SMAD3 mutations causing aneurysm-osteoarthritis syndrome are the third type of LDS (LDS-3).[2] LDS-3 can present with early-onset aneurysms of the aortic root, abdominal aorta, visceral arteries, and osteoarthritis.[2] Owing to concerns about high radial force stent graft placement within weakened aortic wall, endovascular repair has not been widely used in LDS-related aortic pathologies, unless these high radial force proximal and distal fixation sites are anchored in synthetic grafts from prior open surgery.[3]

There is scarce literature available on endovascular aortic repair (EVAR) for dissecting aortic pathology in LDS.[4] In and of itself, dissecting abdominal aortic pathology—regardless of association with underlying connective tissue disorders—presents unique technical challenges and considerations that render traditional modular bifurcated EVAR an unsuitable approach. These include, but are not limited to, reliance on high radial force direct infrarenal proximal fixation and concerns for continued proximal seal degeneration; lack of an adequate proximal infrarenal neck to accommodate proper device deployment; narrow true lumen and/or distal aortic domain compromising contralateral gate opening and cannulation; and limb flow competition caused by limb compression in a narrow bifurcation and leading to poor flow and thrombosis.[4] We describe our technique for overcoming these historical barriers to EVAR by using an anatomically fixated, bifurcated, unibody aortic stent graft in a patient with LDS-3-related dissecting pararenal abdominal aortic aneurysm (AAA).

Consent from the patient was obtained to publish this report.

CASE REPORT

A 60-year-old woman was referred for management of mild to moderate abdominal pain of several weeks duration in association with recently discovered aneurysmal degeneration of an abdominal aortic dissection (type B aortic dissection [TBAD] 8,10). History was notable for LDS-3, attributed to autosomal-dominant SMAD3 p.Arg287Trp point mutations found in her son. Both had procoagulant diathesis attributed to point mutations in the FT (pR287W) and MPL genes (pW474X) and frameshift mutation in STAB2. Her son presented with a ruptured hepatic artery aneurysm resulting in acute liver failure; the patient was a living hepatic donor to the son. Surgical history was also remarkable for cholecystectomy, and medical history was notable for incidentally discovered intracranial venous malformation of the right frontal lobe.

On examination, her abdomen was minimally tender to deep palpation of a pulsatile, left periumbilical mass.

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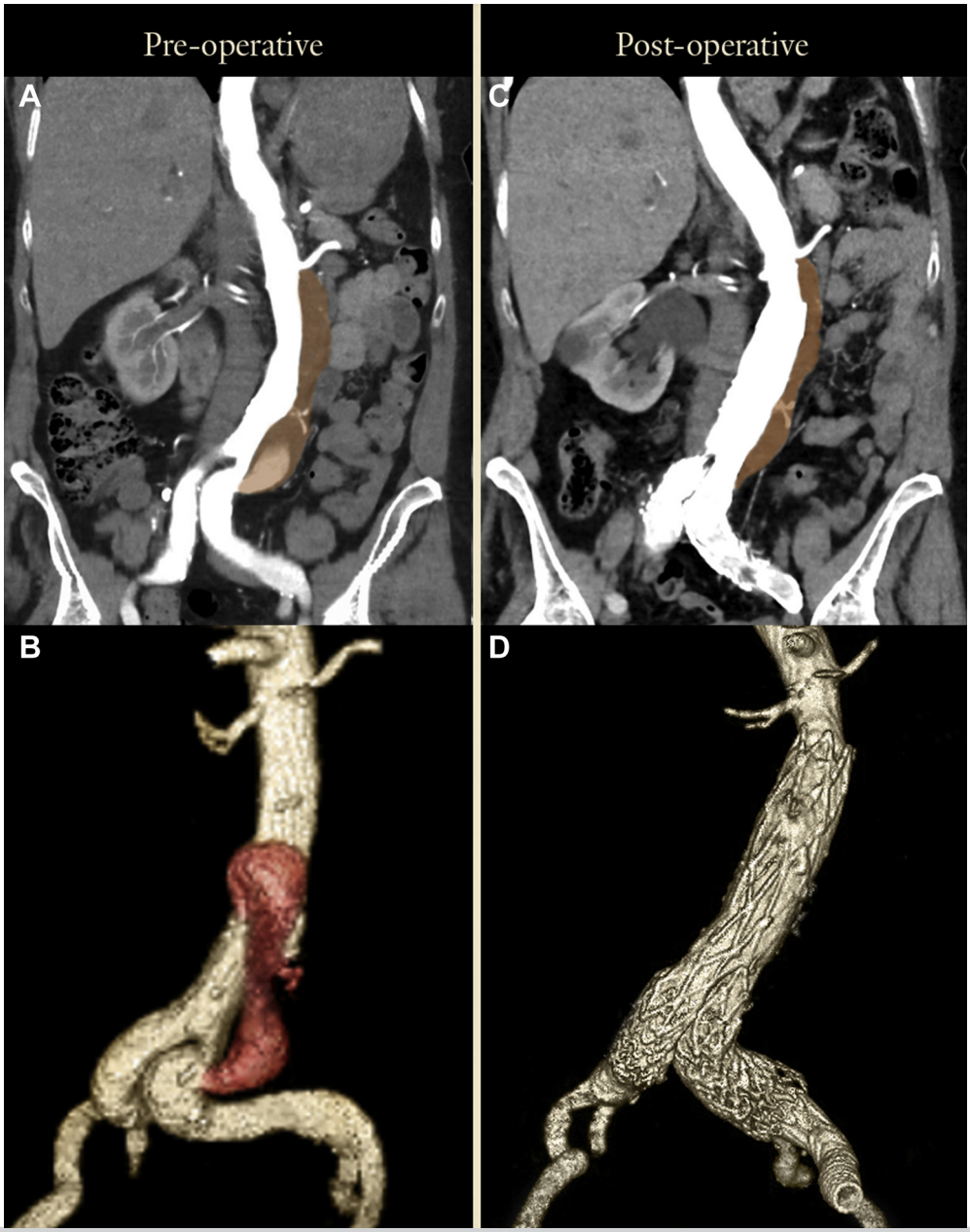

Fig 1. A, Preoperative computed tomography scan with extent of false lumen to zone 8 proximally and zone 10 distally highlighted. **B,** Three-dimensional reconstruction of preoperative computerized tomography, demonstrating extravasation of contrast from the true lumen (*white*) into the false lumen (*red*) through fenestrations in zones 9 and 10. **C,** Postoperative computed tomography scan showing significant shrinkage of the false lumen, highlighted. **D,** Postoperative three-dimensional reconstruction demonstrating cessation of false lumen flow.

Distal pulses were intact. Computed tomography angiography demonstrated a TBAD with aneurysmal degeneration to 4.7 cm (Fig 1). Multiple large fenestrations feeding the false lumen were identified in mid to distal zone 9, and proximal zone 10 on the left. There was aneurysmal degeneration of bilateral common iliac arteries to 2.0 cm (right) and 2.4 cm (left). There was a 1-cm splenic artery aneurysm. Ascending aorta was non-aneurysmal. No prior CT scans were available for review.

Given these findings, the patient's desire for the least-invasive therapeutic option, and a history of multiple prior intra-abdominal pathologies and surgeries, we opted for an endovascular approach for repair of her TBAD and AAA.

SURGICAL TECHNIQUE

Following percutaneous bilateral common femoral artery access and preclosure via suture-mediated

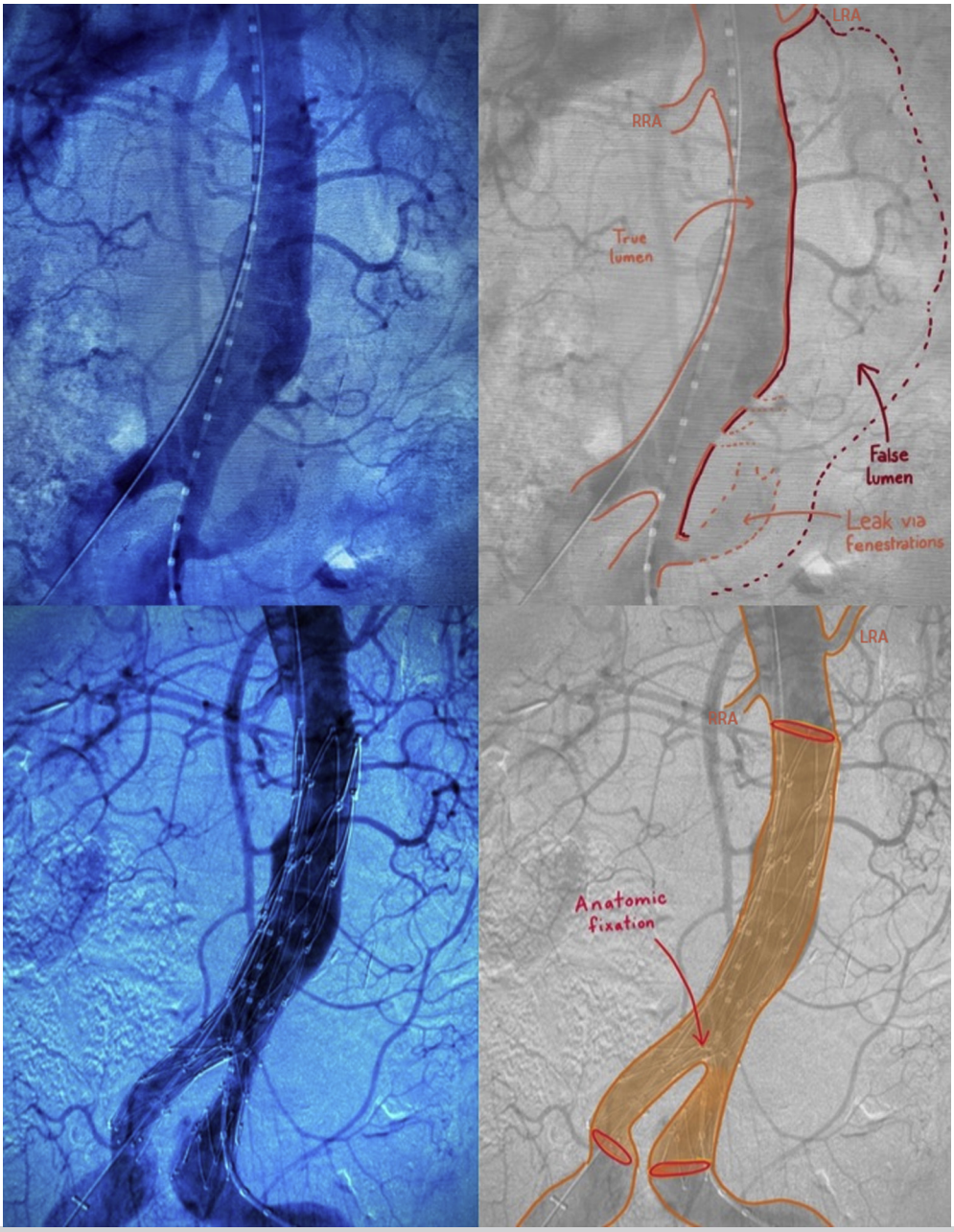

Fig 2. Angiography before and during endovascular aortic repair (EVAR) deployment. (*Top*) Intraoperative flush aortography, demonstrating multiple zones 9 and 10 fenestrations leaking blood into the false lumen. (*Bottom*) Flush aortography after deployment of endograft, demonstrating anatomic fixation and complete cessation of false lumen flow without endoleak. *LRA*, Left renal artery; *RRA*, right renal artery.

Proglide closure devices (Abbott, Abbott Park, Ill), flush abdominal aortography with bilateral iliofemoral runoff confirmed presence of multiple zones 9 and 10 fenestrations feeding the false lumen of a TBAD, the largest of which was located in the left zone 10, 1.5 cm distal to the aortic bifurcation. The false lumen extended proximally to include zone 8 (Fig 2, *top*) obviating the possibility of deploying a proximally fixated modular bifurcated device and obtaining adequate proximal seal. To avoid reliance on high radial force fixation at a compromised, dissected proximal neck, we opted to cover all zones 9 and 10 fenestrations by using a 28 mm-100 mm-20 mm-40 mm AFX aortic endograft (Endologix, Inc, Irvine, Calif). Via a right transfemoral approach, the device was introduced, advanced, snared, saddled, and deployed per the usual standard

Table. Summary of clinical characteristic of Loeys-Dietz syndrome (LDS)

Type	Mutation	Clinical features[1,5-8]
1	TGFβR1	Arterial aneurysms, aortic root dilation, early aortic dissection, and vascular tortuosity with facial dysmorphic features (hypertelorism, bifid uvula, cleft palate)
2	TGFβR2	Arterial aneurysms, aortic root dilation, early aortic dissection, and vascular tortuosity with cutaneous features (atrophic scarring, visible veins, poor wound healing)
3	SMAD3	Arterial aneurysms, aortic root dilation, and vascular tortuosity with bone and sometimes joint pathology (osteoarthritis, osteochondritis dessicans)
4	TGFβ2	Arterial aneurysms, aortic root dilation, and vascular tortuosity with tall stature, hernias. Markedly less severe phenotype than TGFβR1/2 mutations.
5	TGFβ3	Late (>50 years) aortic and cerebral arterial dissection, lack of arterial tortuosity, tall/short stature, wide phenotypic range. Less well-characterized.[9,10]
6	SMAD2	Arterial tortuosity, aortic/coronary/carotid dissections, arthritis. Similar to type 3, less well-characterized (~15 patients total).[11-13]

instructions for use at the aortic bifurcation with full, uncompromised expansion into the aortoiliac true lumen (Fig 2, *bottom*). To avoid chronic strain in the immediate infrarenal region, proximal extension with a cuff was not performed.

We then performed bilateral iliac limb extensions to the iliac bifurcation using 3 Ovation limbs (Endologix, Inc) measuring 28 × 45 mm on the left and 22 × 45 mm on the right. Finally, we performed postdeployment kissing balloon angioplasty of the aortic bifurcation and iliac limb overlap sites. Completion aortogram demonstrated complete exclusion of the false lumen with unimpeded brisk true lumen flow through zones 9, 10, and 11. The patient was discharged on postoperative day 1, recovered uneventfully, and is maintained on aspirin monotherapy. She experienced immediate postoperative resolution of presenting abdominal pain. Follow-up imaging at 3 and 6 months have demonstrated widely patent and augmented true lumen flow, complete thrombosis of the false lumen, and overall decrease in aneurysm sac to 4.3 cm. At the time of writing, she has 7 months of clinical follow-up with no recurrence of abdominal or back pain and has not had any access related complications. She has a normal, active lifestyle without restrictions. She is currently scheduled to undergo annual aortoiliac duplex ultrasound examination computed tomography angiography for on-going surveillance.

DISCUSSION

LDS is a connective tissue disorder associated with heterozygous mutations of TGFβR1/2, SMAD2/3, and TGFβ2/3 (Table).[1,14,15] Patients with LDS present with more aggressive vascular phenotypes than Marfan's syndrome because the TGF-β pathway has many pleotropic functions, unlike single-molecule mutations in Marfan syndrome.[5,6]

The SMAD3 mutation causes LDS-3 and was first described as aneurysm-osteoarthritis syndrome in 2011.[2] LDS-3 is less severe than LDS-1 or LDS-2 owing to the preservation of non-SMAD pathways for TGF-β signal transduction.[16] Sudden death occurs at 35 to 69 years, vs 26 years in LDS-1 or LDS-2.[2] Aortic root aneurysms are found in 71% of patients, other aneurysms in 33%, and cerebrovascular anomalies in 56%.[17] Radiologic evidence of arthritis is found in 96%; symptoms are only reported in 30%.[18,19] Our patient's mutation and presentation of splenic and aortic aneurysms and cerebrovascular malformation without symptomatic arthritis is consistent with LDS3.[20]

Isolated infrarenal aortic dissections are generally rare and pose a number of technical challenges regardless of associations with connective tissue disorders.[21] Proximal juxtarenal, pararenal, or suprarenal extension of the false lumen eliminates the possibility of a safe and effective proximal infrarenal seal, particularly when relying on high radial force traditional EVAR platforms. Any compromise in the true lumen diameter can complicate contralateral gate deployment and cannulation and can cause limb flow compromise distally. The use of anatomically fixated, bifurcated unibody endografts obviates the issue of friable proximal seal zone by relying on aortic bifurcation to anchor the graft.[22]

In the setting of a dissecting aneurysm with distal zones 9 and 10 fenestrations, this device represents an ideal platform to cover fenestrations and promote false lumen thrombosis without excessive strain on a friable, dissected proximal neck. We purposefully avoided more proximal extension of the endograft via cuff placement to the immediate infrarenal level to avoid chronic strain at that location. The ability to reconstruct the aortoiliac anatomy caudal to rostral via an anatomically fixated platform not relying on radial force for seal is an important added benefit of this approach and allows the surgeon the option of foregoing extensive proximal extension. Furthermore, these endografts have performed well in narrow aortoiliac domains and have become the endograft platform of choice for many vascular surgeons in patients with concomitant aortoiliac occlusive disease, so much so that we and others have deployed these in occlusive disease without concomitant degenerative pathology.[23] Other considerable benefits of an anatomically fixated endograft include preservation of "up-and-over" femoral access to

contralateral iliacs in the future.[7,24] Noncovered endovascular dissection stents have been described to address infrarenal dissection but would have been inadequate in this patient owing to the zone 9 and 10 fenestrations necessitating a covered stent.[25]

Further support for the more liberal use of endovascular platforms in patients with LDS-3-related vascular pathology was provided by Van der Linde et al,[26] who described 6 patients with LDS-3 who underwent visceral and iliac procedures, noting that "tissue handling felt the same as in patients without a connective tissue disorder; thus, elective interventions seem to be feasible and safe in aneurysm-osteoarthritis syndrome patients so far." They encouraged visceral stenting in LDS-3. Although the use of a traditional modular bifurcated EVAR would be unsuitable in LDS owing to the proximal seal required, the longer seal zone and anatomic fixation of the graft used in this case allowed for the avoidance of the highly morbid supraceliac clamping that would have been required in open repair of this zones 8 to 10 dissection. The long-term durability remains to be seen and continued proximal degeneration may be possible, but this technique provides a stable platform for future proximal endovascular options.

Although endovascular treatment has historically not been the treatment of choice in LDS owing to weakened aortic walls, in appropriately selected patients with suitable anatomy, anatomically fixated, bifurcated, unibody endografts make EVAR a technically feasible, safe, effective, and minimally invasive alternative therapeutic option for isolated dissecting AAAs in patients with LDS-3.

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