Glue embolus complicating endovascular treatment of a patient with Loeys-Dietz syndrome

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A 43-year-old woman was diagnosed with Loeys-Dietz Syndrome. Five months later, the patient presented with a symptomatic 2.6 cm subclavian pseudoaneurysm. Staged endovascular treatment was initiated with left vertebral artery embolization, followed by sac ablation and stent graft exclusion. The pseudoaneurysm cavity was filled with N-butylcyanoacrylate ("glue") via a microcatheter. Despite balloon occlusion of the pseudoaneurysm orifice, a small amount of glue debris embolized to the brachial artery, necessitating a vein bypass. In this case, distal embolization of glue may have been avoided by leaving a microcatheter in the aneurysm sac for glue injection after first deploying the stent graft. (J Vasc Surg 2010;■■:■■■.)

A 43-year-old woman with mild hypertension on no medications presented acutely with a right Horner's syndrome in 2008. A right internal carotid artery (ICA) dissection was diagnosed with sequela of a right eye ptosis. Six months later, similar symptoms occurred on the left side. A magnetic resonance angiography (MRA) indicated left ICA and left subclavian artery (LSA) dissections. She was referred for evaluation and was diagnosed with Loeys-Dietz Syndrome (LDS). Her exam was relevant for a unified but hooked uvula, joint hypermobility, easy bruising, mild hypertelorism, mild pectus carinatum, and scoliosis. Genetic testing confirmed a TGFBR 2 mutation (c.1512G>C; Trp504 Cys). Imaging studies revealed ascending aortic ectasia (3.6 cm) and bilateral ICA tortuosity. The patient underwent genetic counseling, was started on atenolol and losartan, and restrictions were instituted regarding contact sports and stimulant use.

Five months following diagnosis of the left ICA and LSA dissections, the patient complained of left supraclavicular pain and a pulsing sound in her left ear. Computed tomography angiography (Fig 1) revealed a 2.6 cm proximal LSA pseudoaneurysm and a new 1.4 cm distal left ICA dilation. Both of these aneurysms were in previously dissected areas and thus were classified as pseudoaneurysms. Given the symptomatic nature of the LSA aneurysm, a staged endovascular treatment was proposed to the patient. First, carotid and vertebral angiography (Fig 2) was followed by a left vertebral temporary balloon occlusion test. The patient exhibited no new neurological findings and successfully underwent left vertebral artery embolization using platinum electrolytically-detachable coils (Micrus Endovascular, San Jose, CA). Two days later, the patient underwent embolization and stent graft therapy of the LSA pseudoaneurysm using a combined brachial and femoral approach. A small incision was made in the arm to isolate the brachial artery for possible stent graft delivery from the arm. Aortography confirmed adequate exclusion of left vertebral artery. Coil embolization of the left internal mammary artery (micro-detachable coils, 2 mm), thyrocervical trunk branches and the aneurysm sac (12 mm Nester coils, Cook, Inc., Bloomington, IN) was performed (Fig 3). An 8 mm × 4 cm balloon angioplasty catheter (Opta, Boston Scientific, Natick, MA) was placed via the femoral approach and inflated to cover the mouth of the aneurysm during N-butylcyanoacrylate (n-BCA, "glue," TRUFILL, Cordis Inc., Bridgewater, NJ) embolization. The glue was diluted 1:1 and instilled via a coaxial 3 Fr microcatheter within a 5 Fr glide catheter from a brachial approach. A total of 1.5 mL was instilled. During deflation of the angioplasty balloon, a small amount of glue debris was noticed going down the subclavian artery to the brachial artery. Immediately, the brachial artery was clamped with sheath removal. Following this, a long 12 Fr sheath was promptly placed via the femoral approach, and a 10 mm × 5 cm stent graft (Viabahn, Gore Inc., Flagstaff, AZ) was deployed excluding the LSA pseudoaneurysm (Fig 4), with no evidence of antegrade flow into the aneurysm or endoleak from LSA branches. After a failed attempt of glue debris removal using Fogarty thrombo-embolectomy balloons (Fig 5), a brachial-to-brachial reversed vein bypass was successfully performed. The patient was discharged on postoperative day 5, asymptomatic with a palpable left radial pulse. At 1 year follow up, she is doing well without evidence of subclavian aneurysm recurrence. Her left ICA pseudoaneurysm is stable and is being followed.

DISCUSSION

LDS is a recently characterized connective tissue disorder associated with mutations of transforming growth factor (TGF)-beta receptors I and II, and is inherited in an autosomal dominant pattern.[1] In this case, the patient presented with bilateral ICA and LSA dissections, with the

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Fig 1. Computed tomography angiography reveals a new 2.6 cm proximal LSA pseudaneurysm (short arrow) and a new 1.4 cm distal left ICA dilation at the bottom of a complete coil (long arrow) in a patient with LDS.

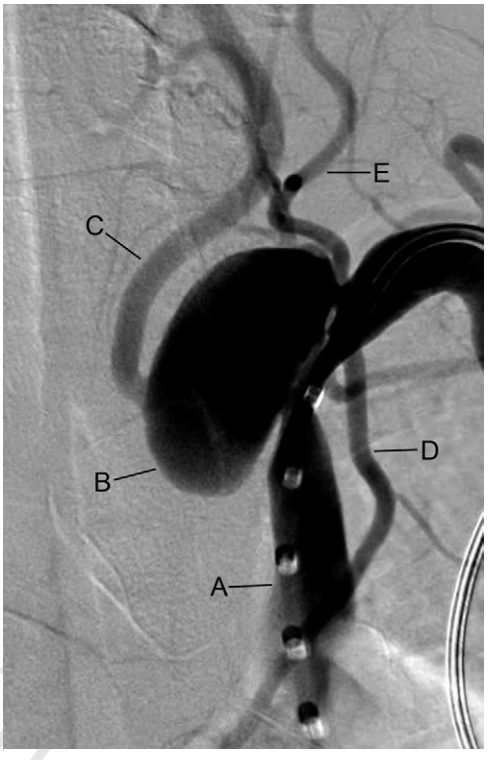

Fig 2. Marker catheter angiography via the left subclavian artery **(A)** documents a large pseudoaneurysm **(B)** with the vertebral **(C)**, internal mammary arteries **(D)**, and thyrocervical trunk **(E)** in close proximity.

left ICA and LSA degenerating into pseudoaneurysms. Traumatic lesions secondary to venous access attempts are the main cause of subclavian artery pseudoaneurysms, occurring in 0.1% to 0.4% of central venous punctures.[2] Isolated true aneurysms of the subclavian artery are among the rarest of all peripheral aneurysms. Atherosclerotic degeneration is the most common etiology for true aneurysms; non-atherosclerotic subclavian aneurysms are even more rare,[3] and usually due to connective tissue disorders (eg, Marfan's syndrome, Ehlers-Danlos syndrome, LDS), vasculitis (eg, giant cell arteritis, Takayasu's arteritis), or arterial thoracic outlet syndrome.

LDS has a wide spectrum of phenotypic presentations including cardiovascular, skeletal, and craniofacial abnormalities.[1] Skeletal features may include long fingers, pectus abnormalities, scoliosis, cervical instability, and joint laxity. Craniofacial findings may include wide-spaced eyes, cleft palate, bifid or wide uvula, and early fusion of skull bones (craniosynostosis). Cardiovascular findings may include aortic and other aneurysms, dissections, tortuous vessels, and congenital heart defects. These abnormalities may be clinically asymptomatic. Alternatively, patients may present acutely with chest pain, compressive symptoms (dysphagia, neuropathy), hemoptysis, ischemia, or aneurysm complications. Severe cardiovascular abnormalities can found even at an early age.[4,5] Median survival is 37 years; the main cause of death being dissection of the thoracic aorta (67%), dissection of the abdominal aorta (22%), and intracranial bleeding (7%).[6]

Abdominal aortic aneurysmal disease in LDS has been identified in 10% of the cases and branch vessel disease in 7% (superior mesenteric, iliac, femoral run-off arteries, etc). There is a 33% to 47% risk of multiple location aneurysms.[7-9] Arterial aneurysms in LDS are more aggressive than in other connective disorders, with more frequent complications (dissection, rupture)[1,6] in patients at younger ages and at smaller diameters.[10] Therefore, complete imaging of the aorta and its branches should be done usually with computed tomography angiography or MRA. Imaging of the cerebrovasculature, including the intracranial vessels, is recommended. Recently published multispecialty consensus guidelines have recommended yearly cerebrovascular to pelvis MRA imaging for patients with LDS.[11] Surgical repair should be considered in symptomatic patients or in cases of rapid aneurysm expansion. Prophylactic repair may be considered in aneurysms at smaller diameters than traditional aneurysms because of the aggressive natural history of aneurysmal disease in LDS.[11] Open operative repair often requires extensive incisions and dissection to get to large aneurysms. In this case, we believed the patient had a LSA pseudoaneurysm since recent previous imaging had shown a dissection flap, and the artery expanded rapidly. Most reports on LDS indicate aneurysm,

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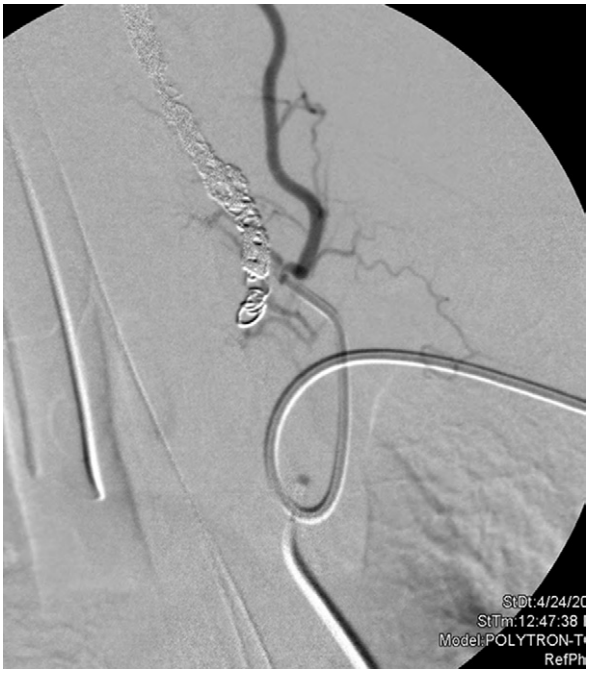

Fig 3. Embolization and stent-graft therapy of the LSA pseudoaneurysm using a combined brachial and femoral approach. Multiple coils have been already placed into the vertebral artery in this staged procedure. The brachial glide catheter (left) is used to select a thyrocervical branch for embolization. The femoral angled catheter (bottom) allows contrast injections and eventual guidewire and stent graft placement.

Fig 4. Completion imaging after stent graft deployment showing an excluded LSA pseudoaneurysm with no evidence of antegrade flow into the aneurysm, or endoleak from LSA branches. The coil and glue mass in the LSA pseudoaneurysm is seen.

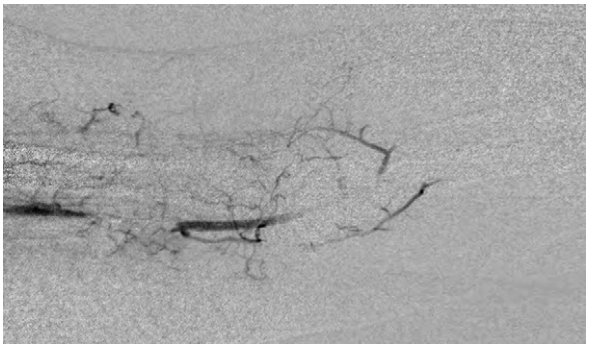

Fig 5. Glue embolus to the mid brachial artery complicating this endovascular case. Late images (not shown) revealed a patent distal brachial artery allowing a brachial to brachial reversed vein bypass.

rather than pseudoaneurysm morphology, but pseudoaneurysms may be underappreciated. In our case, we considered other operative options. Sternotomy or thoracotomy and a supraclavicular incision would have been required for proximal, distal, and control of arterial branches. Alternatively, control of the arterial inflow may have been accomplished using a balloon catheter or arterial plug device. Resection of the pseudoaneurysm coupled with restoration of continuity of flow through a graft interposition or a subclavian-to-carotid artery transposition were entertained. Given the rapidity of pseudoaneurysm growth, we were concerned about the fragility of the subclavian artery and opted for endoluminal ablation and stent grafting. In retrospect, the lack of fragility in the brachial vessels may indicate that either our concerns were unwarranted, or that arterial regions are variably affected by LDS.

Endovascular treatment is a minimally invasive alternative in patients with favorable anatomy with adequate attachment areas for stents. It consists of exclusion of dilated area with a covered stent.[12,13] First reported by MacSweeney in 1996,[14] new generations of endografts are smaller and more flexible. In this particular patient with LDS, extensive, staged embolization of proximal left subclavian branches was required to insure pseudoaneurysm enlargement and/or rupture secondary to a type II endoleak. This was done with coil embolization of the vertebral, internal mammary, and thyrocervical trunk arteries. In concordance with our experience treating visceral artery aneurysms,[15] catheter-directed n-butyl cyanoacrylate sac embolization was done for complete ablation of the pseudoaneurysm sac and any remnant small branches. The unexpected distal migration of part of this glue and the further need of bypass surgery could have been avoided if this catheter-directed sac injection had been done after the Viabahn deployment. This technical tip could have been accomplished by leaving

a microcatheter in the pseudoaneurysm sac via a brachial approach as the stent graft was deployed from the femoral approach. The n-butyl cyanoacrylate could then be injected at an appropriate dilution and rate to allow complete ablation of the sac with subsequent microcatheter removal.

This patient will need rigorous surveillance to follow the treated LSA pseudoaneurysm and the currently small ICA pseudoaneurysm. All patients with LDS need tightly controlled blood pressure, typically with beta blockade and/or angiotensin receptor blockade, activity restrictions, and surveillance imaging to identify new aneurysms or complications related to this virulent disease process. Genetic counseling and screening of selected family members is also recommended.

AUTHOR CONTRIBUTIONS

Conception and design: LM, VK
Analysis and interpretation: RG, HG
Data collection: LM
Writing the article: LM, VK
Critical revision of the article: RG, HG, VK
Final approval of the article: LM, RG, HG, VK
Statistical analysis: N/A
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Overall responsibility: VK

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