Common Iliac Artery Aneurysm and Spontaneous Dissection with Contralateral Iatrogenic Common Iliac Artery Dissection in Classic Ehlers–Danlos Syndrome

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Abstract

Keywords

- Ehlers–Danlos syndrome
- iliac artery aneurysm
- spontaneous arterial dissection

We describe a 43-year-old man who developed a spontaneous dissection of a right iliac artery aneurysm after performing vigorous physical exercise. Additionally, during peripheral intervention, the patient developed iatrogenic dissection of the left iliac artery. The patient had the characteristic physical findings of Ehlers–Danlos syndrome (EDS), classic type. Genetic testing revealed a mutation in the *COL5A1* gene associated with EDS, classic type. Vascular aneurysms and dissections are characteristics of EDS vascular type, but not the classic type. Only one previous case with EDS, classic type with spontaneous iliac artery dissection has been described.

Ehlers–Danlos syndrome (EDS) is a constellation of connective tissue disorders,¹ caused by a mutation in genes that encode fibrillar collagens or collagen-modifying enzymes.² Affected individuals display hypermobility, hyperextensibility, tissue fragility, and vascular complications.^{2,3}

Type IV, or vascular type EDS (mutations in *COL3A1*), is relatively rare. The prevalence is 1 in 250,000 individuals.⁴ It is associated with life-threatening arterial, intestinal, and organ ruptures.^{5–7} While aneurysms and dissections are more commonly associated with vascular EDS, it is rarely seen in EDS, classic type.⁸ Here, we describe a patient with classic EDS (mutations in *COL5A1*) who developed a spontaneous dissection of a peripheral artery aneurysm as well as an iatrogenic dissection of the contralateral artery during stenting procedure of the dissection.

Case Report

A 43-year-old Caucasian man with a past medical history of well-controlled essential hypertension presented to the emergency department with abdominal pain.

Before the onset of his symptoms, the patient was performing intense anaerobic physical exercise including resistance training.

The past history was remarkable for recurrent skin tears, joint laxity, tendon rupture, and knee and elbow operations as a child. He denied complaints of fatigue, dental abnormalities, problems with wound healing, myalgias, and arthralgias. Family history was significant for two children with joint laxity, atrophic scars, and skin hyperextensibility (►Fig. 1). Furthermore, his wife also had two spontaneous early miscarriages. A similar history of symptoms in the patient's siblings was negative. There was no reported consanguinity. He was clinically diagnosed with EDS, 5 years earlier. At that time, molecular testing for only *COL3A1* (associated with EDS, vascular type) was clinically available and was performed to rule out vascular EDS, which was negative. When testing for *COL5A1* (associated with EDS, classic type) on peripheral blood sample became available, his daughter was tested and was found to have a heterozygous (single) frameshift mutation in exon 23 (c.2185C > T; Gln729Term).

A computed tomography (CT) scan showed a right iliac artery aneurysm with dissection (►Fig. 2). A decision was

Fig. 1 Pedigree of patient demonstrating only three members with EDS symptoms and signs. Crossed line-deceased *3 - three children. EDS, Ehlers-Danlos syndrome.

made to stent the dissection. Access was achieved via the left common femoral artery via a standard Cook (Bloomington, IN) needle. After inserting a 5-French sheath, a guidewire was advanced to the level of the abdominal aorta and a contra catheter was positioned in the abdominal aorta. An angiogram revealed normal renal arteries and abdominal aorta. Consistent with the CT findings, the angiogram revealed a right common iliac aneurysm with dissection. Next, access was achieved in the right common femoral artery via a standard Cook needle and a guidewire was advanced toward the aorta (►Fig. 3a). After sizing the vessel, a stent was advanced over the wire in an attempt to cover the dissection. The stent was positioned and deployed; however, it became evident that the stent had been deployed in the aneurysmal segment of the artery rather than the dissection, without being not opposed to the vessel wall. A decision was made to stent the dissection coming from the left side rather than the right side. Using the left common femoral sheath, a 10 cm × 38 mm noncovered stent was advanced over the guidewire and deployed successfully. The balloon from this stent was used to fully expand the stent that was previously deployed in the aneurysmal segment of the right iliac artery. The next angiogram showed good stent apposition of both

stents. However, it appeared that there was now a dissection in the left common iliac artery (►Fig. 3b). A 11 mm × 5 cm Viabahn (Flagstaff, AZ) Gore-Tex-covered stent graft was deployed in the left common iliac artery to cover this iatrogenic dissection. Repeat angiogram showed successful results (►Fig. 3c). Both sheaths were removed and the patient was sent to the recovery unit. On follow-up at 8 months, the patient was doing well without complaints.

After the dissection and hospital events as described above, the patient underwent genetic counseling. Physical examination revealed a well-nourished male with no evidence of bruising. The skin was remarkably hyperextensible with a widened atrophic-healed surgical scar over the right elbow from open reduction of a fracture that he incurred in the past. There were no other appreciable cutaneous findings. Additional genetic testing for the mutation that had been found in his daughter was found to be positive. This genetic testing confirmed his diagnosis of EDS, classic type.

Discussion

EDS is a connective tissue disorder with several subtypes. Given that collagen is a substrate in joints, skin, tissue, and the vascular matrix, it is common for affected individuals to display hypermobility, hyperextensibility, tissue fragility, and vascular complications.^{2,3}

Previously, 10 distinct phenotypes of EDS were described. While there is frequent phenotypic overlap amongst all groups, six main types have now emerged to be clinically significant.⁹ These include classic type, hypermobility type, vascular type, kyphoscoliosis type, arthrochalasia type, and dermatosparaxis type. Type IV, or vascular type EDS, caused by mutations in *COL3A1*, is associated with life-threatening arterial, intestinal, and organ ruptures.⁵⁻⁷ Affected patients are cautioned against contact sports and intense weight-bearing exercises and invasive procedure in these patients must be performed with extreme caution given the potential of rupture from the underlying weakened collagen matrix.¹⁰ Arterial ruptures in association with mutations in *COL1A1* genes have also been previously reported.^{11,12} While glycine substitutions in *COL1A1* lead to osteogenesis imperfecta, it is

Fig. 2 CT scan of the pelvis. Arterial phase of contrast-enhanced CT scan of the right common iliac artery demonstrates aneurysm and dissection. (A) CT without contrast-black arrow: dissection flap in an aneurysmal right common iliac artery. (B) CT with contrast-delayed phase of contrast-enhanced CT scan demonstrates a false lumen significant for arterial dissection (white arrow). No hematoma is seen. CT, computed tomography.

Fig. 3 (a) An angiogram showing a right common iliac artery aneurysm with distal dissection and a catheter that was advanced from the left femoral artery to the aorta. (b) Stents were deployed into the right common iliac artery, but a new dissection is seen in the proximal part of the left common iliac artery. (c.) Final angiogram showing that all dissections are well covered by the stents.

now believed that nonglycine substitutions may result in a variable phenotype that includes EDS, classic type with propensity for arterial rupture. However, arterial aneurysms and dissections are not commonly seen in classic EDS associated with mutations in *COL5A1*.⁸ The patient discussed had a molecularly confirmed diagnosis of EDS, classic type.

Similar to the case described by Borck et al,⁸ our patient suffered from well-controlled essential hypertension. Furthermore, he had an intense exercise regimen. His arterial aneurysm and dissection may have been from a “triple hit” comprised of underlying weakened collagen matrix from EDS, chronic hypertension, and elevated vascular stress from resistance training.

This case, along with the previous reported cases, suggests that EDS, classic type may rarely predispose individuals for arterial complications. As more cases of arterial ruptures in patients with EDS, classic type are established, it may become necessary to explore whether there are specific genetic mutations that may be associated with higher risk for vascular complications. Moreover, it may be needed to recommend aggressive treatment modalities including tight blood pressure control in these patients. Guidelines for behavioral modifications including avoidance of contact sports and intense resistance training will need to be formalized. Additionally, invasive procedures should be performed with care to avoid potential devastating complications.

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