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CASE REPORT

Metachronous Bilateral Posterior Tibial Artery Aneurysms in Ehlers-Danlos Syndrome Type IV

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Abstract Ehlers-Danlos syndrome type IV is a life-threatening genetic connective tissue disorder. We report a 24-year-old woman with EDS-IV who presented with metachronous bilateral aneurysms/pseudoaneurysms of the posterior tibial arteries 15 months apart. Both were treated successfully with transarterial coil embolization from a distal posterior tibial approach.

Keywords Ehlers Danlos syndrome type IV · Posterior tibial artery · Aneurysm · Pseudoaneurysm · Embolization

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Introduction

Ehlers-Danlos syndrome (EDS) type IV is the predominantly vascular type of EDS [1]. EDS-IV is a rare condition [1]. The presentation of EDS-IV does not always involve a family history (although it is typically inherited in an autosomal dominant pattern) because many of these cases occur spontaneously [2]. EDS-IV comprises only 4% of all patients with any type of EDS [1]. EDS-IV involves a specific mutation of the COL3A1 gene. This results in abnormal synthesis of type III procollagen and dramatically fragile tissues [2].

The average age of the first clinical presentation for EDS-IV patients is 24.6 years [2]. EDS-IV commonly presents with arterial rupture. Other clinical features include easy bruisability, translucent skin, characteristic facial features (thin face with minimal subcutaneous fat, large eyes, thin nose and hair, and lobeless ears), and uterine or gastrointestinal rupture [1]. This hereditary connective tissue disorder bears a risk of vascular complications throughout the life of the patient [3]. The prognosis of EDS-IV patients is poor, and most die from vascular complications by age 40 years [2]. Arterial rupture, aneurysm, and pseudoaneurysm formation and arteriovenous fistula formation can affect any artery in the body [2, 4–8]. The spectrum of vascular complications is broad, and they have been located in many arterial territories [4, 6, 9–16]. Treatment often poses a dilemma both with regard to timing and type of procedure. This is mainly due to the high rate of complications associated with the repair of the manifestations of EDS-IV. Newer endovascular techniques allow treatment of many vascular complications with acceptable risk, at least in patients who elect such treatment [17]. We report a young woman with EDS-IV who underwent transcatheter embolization of

metachronous posterior tibial artery aneurysms using the novel distal arterial access initially developed for retrograde subintimal recanalization [17].

Case Report

A 24-year-old white woman presented to the emergency department with left calf pain. The symptoms began abruptly 10 h earlier and had gradually worsened to the point where she had difficulty ambulating. She denied precipitating symptoms or traumatic events. The calf was tight and sensitive to touch with normal palpable femoral, popliteal, dorsalis pedis, and posterior tibial pulses. An ultrasound examination of the left lower extremity identified occlusive thrombus within the left peroneal and posterior tibial veins without other anomalies. The patient was admitted for management of her deep vein thrombosis with enoxaparin followed by warfarin. Her pain continued despite administration of significant amounts of narcotics. Therefore, ultrasound examination was repeated, which showed a $7 \times 2 \times 2$ cm mass in the posterior compartment of the mid-calf immediately adjacent to an abnormal area of the posterior tibial artery. Doppler ultrasound imaging demonstrated turbulent blood flow within the mass indicative of a pseudoaneurysm, and diagnosis was confirmed by computed tomography angiogram (CTA) (Fig. 1). A decision was made to proceed with transarterial embolization of the pseudoaneurysm. Abdominal computed axial tomography scan 4 years before the current admission had shown an enlarged infrarenal aorta; therefore, an underlying connective tissue disorder was considered. Due to our concern for arterial injury at the puncture site through the standard transfemoral approach [18], we elected to obtain retrograde access to the pseudoaneurysm by way of the distal posterior tibial artery at the ankle. Using ultrasound guidance, the puncture was made with a 21-gauge micropuncture needle. A 4F hydrodrophilic catheter was advanced proximal to the lesion, and coil embolization of the posterior tibial artery was performed proximal and distal to the pseudoaneurysm using 3- and 5-mm Gianturco and Tornado coils (Cook Medical, Bloomington, IN) (Fig. 1). Repeat arteriogram demonstrated complete obliteration of the pseudoaneurysm; the catheter was withdrawn; and hemostasis was obtained with manual compression. Further vascular imaging demonstrated also aneurysms of the extracranial and abdominal arterial circulation. Skin fibroblast analysis confirmed the suspected diagnosis of EDS-IV.

Fifteen months later the patient presented with pain in the other calf. CTA showed a new large fusiform aneurysm of the mid/distal posterior tibial artery measuring approximately 2.9×1.8 cm in diameter (Fig. 2). This new pathology was again successfully managed with transcatheter embolization using the identical technique (4- and 6-mm coils) (Fig. 2). CTA showed persistent occlusion of the left posterior tibial artery aneurysm and no puncture-related complication in the distal posterial tibial artery caused to the access procedure 15 months earlier. The patient was seen 3 months later without evidence of

Fig. 1 Computed tomography angiography (CTA) of the calves shows the left posterior tibial artery pseudoaneurysm (*left panel*). The middle panel shows a digital catheter angiogram of the pseudoaneurysm. The catheter was advanced from the distal punture site with its tip proximal to the aneurysm. The right panel shows the completion angiogram following proximal and distal coil embolization

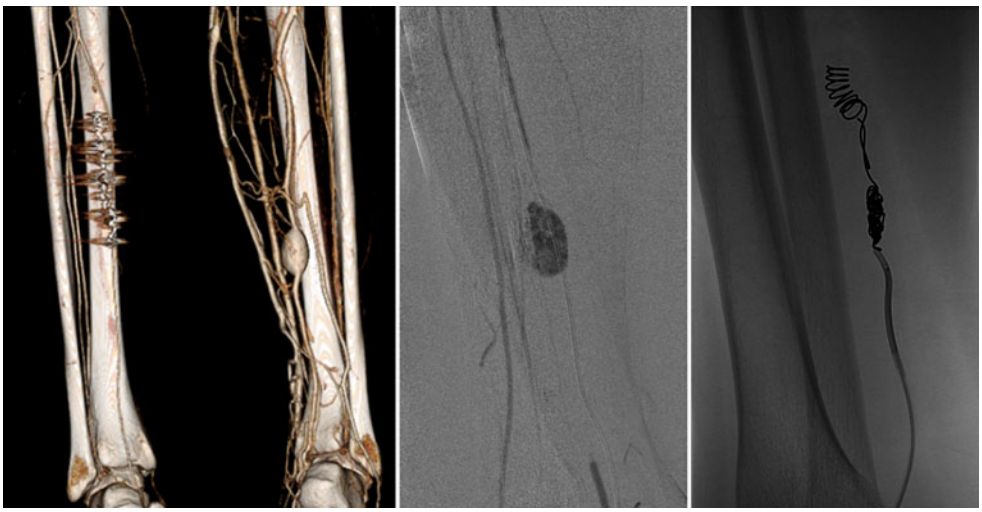

Fig. 2 CTA of the calves shows the right posterior tibial artery aneurysm and the coils in the left posterior tibial artery (*left panel*). The middle panel shows a digital subtraction angiogram of the aneurysm using carbon dioxide as contrast agent. The right panel shows the coils during the embolization procedure

access-site complications on clinical examination and is alive 7 months after the procedure.

Discussion

A number of therapeutic strategies exist for patients with aneurysms or pseudoaneurysms in the setting of EDS-IV. In our case, open surgery would have consisted of aneurysm neck ligation and repair of the arterial injury or arterial ligation, which in EDS-IV patients is associated with a high risk. The mortality rate of vascular surgery in patients with EDS has been reported to be between 19 and 47% and is highest in emergency cases mainly due to the friability of the arterial wall [2, 19–21]. Therefore, it has been suggested that EDS-IV patients should preferably be treated in dedicated centers using induced hypotension during vessel clamping, wide vascular exposure to avoid reclamping the same area, and circumferential felt reinforcement [22]. A recent article reported a relatively low mortality of 11% in nine patients undergoing surgical procedures for vascular EDS using such adjunctive techniques [22]. In addition, performing the procedures electively rather than on an emergent basis has a significant impact on outcomes [21, 22].

Because of their less-invasive nature, endovascular procedures are generally preferred in EDS patients [20, 22]. However, complications are still not infrequent. The incidence of complications resulting from common femoral arterial puncture and diagnostic angiography alone was reported to be as high as 67% in patients with EDS-IV [21]. The mortality rates reported in these series were between 6 and 19% [18, 19, 23]. Although these high complication rates are partially explained by the larger size of access devices in these older case series, local vascular complications remain a problem, and thus angiography is generally not used for diagnostic purposes in EDS patients.

Transcatheter embolization and endograft placement are the main endovascular procedures used in EDS patients. The use of endografts remains controversial, mainly because (1) limited experience exists and (2) there is concern about the durability of the procedure in arteries without a healthy graft-fixation zone [22, 24, 25]. A recent consensus document advised against the use of stent grafts in patients with connective tissue disorders [26]. Nevertheless, there is anecdotal evidence for good results with covered stents in selected patients [20].

No controversy exists regarding the use of embolotherapy, if feasible. Our review of the English literature produced 20 patients with vascular extracranial complications of EDS who underwent endovascular therapy [4, 10–15, 20, 21, 24, 27–33]. Thirteen underwent embolotherapy, and the remainder underwent stent graft placement (Table 1). In these 13 patients, the investigators attempted to treat 15 aneurysms/pseudoaneurysms. The procedure was technically successful in 14 of 15 aneurysms. In all cases, coils were the primary embolic agent, whereas in two cases polyvinylalcohol particles or *N*-butyl cyanoacrylate (NBCA) were also used. The only patient in whom embolization was initially unsuccessful was a 43-year-old woman presenting with melena and multiple fusiform jejunal aneurysms. Coil embolization of the jejunal aneurysms was successful, but new extravasation from branches distal to the embolized segment occurred

Table 1 Summary of reported cases in which endovascular therapy was used to treat extracranial arterial complications of EDS

Investigator	Year	Age	Sex	No. of patients	No. of complications	Vascular complication	Therapeutic modality	Technical success
Nosher	1986	24	M	1	1	Hepatic arterial aneurysm	Coil embolization	Yes
Sherry	1992	16	M	1	1	Hepatoportal fistula	Coil embolization	Yes
Bloch	2001	43	F	1	2	Jejunal fusiform aneurysm and GI bleed; 3rd right lumbar artery aneurysm	Coil embo/PVA & coil embo	No/Yes
Maltz	2001	28	M	1	1	Rupture of subcostal and intercostal arteries	Coil embolization	Yes
Kurata	2003	44	M	1	1	Left common carotid dissecting aneurysm	Stent graft	Yes
Casana	2004	26	F	1	1	Hepatic artery aneurysm	Coil embolization	Yes
Sugawara	2004	27	F	1	1	Spontaneous iliac arterial rupture	Coil embolization	Yes
Oderich	2005	33	F	1	2	Ruptured splenic vein aneurysm; ruptured inferior epigastric artery	Both coil embolization	Yes
Uchiyama	2006	37	M	1	1	Post-tibial A pseudoaneurysm (L)	Coil embo	Yes
Bade	2007	67	M	1	1	Abdominal aortic aneurysm	EVAR	Yes
Naidu	2007	37	M	1	1	Lumbar pseudoaneurysm	Percutaneous coil embolization	Yes
Tonnessen	2007	57	M	1	1	Iliac artery aneurysm	EVAR	Yes
Geibüsch	2008	41	M	2	1	Type A chronic expanded aortic dissection	TEVAR	Yes
Geibüsch	2008	65	M	2	1	Thoracic aortic aneurysm	TEVAR	Yes
Lim	2008	26	F	1	1	Carotid dissecting pseudoaneurysm	Covered Stent	Dead
Mandeville	2008	28	F	1	1	Pseudoaneurym peroneal artery	Coil embolization	Survived
Calvo	2009	28	F	1	1	Splenic artery aneurysm	Coil embolization	Yes
Iida	2009	20	M	1	1	Spontaneous subclavian arterial rupture	Coil embolization	Yes
Khalique	2009	61	M	1	1	Type B dissection	Stent graft	Survived
Matsushima	2009	27	F	1	1	Spontaneous rupture posterior tibial artery	Coil embo & NBCA	Survived

EVAR endovascular aneurysm repair, *TEVAR* thoracic endovascular aneurysm repair

afterward. Intra-arterial vasopressin infusion ultimately led to cessation of bleeding and recovery of the patient [4]. Endovascular therapies and coil embolization in particular benefit from the availability of increasingly smaller access devices, which appear to result in fewer access complications as reported in the newer literature [4]. Smaller access devices and choice of the access vessel are key to minimizing access-related complications. We considered distal puncture of the posterior tibial artery the best approach in this regard. Puncture of the small, distal lower extremity arteries has been described previously in the treatment of occlusive peripheral arterial disease at our institution [17]. Selection of this method of arterial access for embolization of the pseudoaneurysm allowed us to perform the procedure without accessing the common femoral artery and to place the site of arterial injury distal to the embolized site, resulting in decreased arterial pressure [18]. Although not without risk, loss of the posterior tibial artery is better tolerable than loss of the common femoral artery because three runoff vessels still exist. Other techniques to minimize access-site complications exist. Brooke et al. recommend surgical cutdown to the access vessel and placement of a "U" stitch pledgett buttress-reinforced monofilament suture before needle entry and sheath placement. After sheath removal, the suture is tied down, and a circumferential felt reinforcement is approximated to decrease systolic pressure [22]. Three of the published embolization procedures were performed for aneurysms or pseudoaneurysms of the runoff vessels (two posterior tibial arteries and one peroneal artery [13, 14, 34]). In all three cases, coils were used, and in one case the aneurysm was also filled with NBCA [14].

Metachronous occurrence of vascular complications in EDS treated with endovascular techniques has to the best of our knowledge not previously been described in the extracranial circulation. However, there is one published case of a bilateral carotid cavernous fistula (CCF). Spontaneous direct CCFs are the most common neurovascular complication in EDS-IV cases [28]. In that patient, a right CCF was diagnosed and successfully treated with detachable coil embolization when the patient was 40 years old [35]. Eight years later she presented with a left CCF, which was treated with transarterial coil embolization, which was complicated by a fatal left intracranial hemorrhage [36]. This demonstrates the need for lifelong surveillance of EDS patients, both to monitor previous access sites as well as to watch for new aneurysms.

In summary, we present the case of a 24-year-old woman with EDS-IV who presented with metachronous bilateral aneurysms/pseudoaneurysms of the posterior tibial arteries 15 months apart. Both were successfully treated with transarterial coil embolization from a distal posterior tibial approach.

Conflict of interest statement The authors declare that they have no conflict of interest.

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