

Transvenous Embolization for Carotid-Cavernous Fistula in a Patient with Vascular Type of Ehlers-Danlos Syndrome—Direct Superior Ophthalmic Vein Approach: Case Report

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Abstract

The vascular type of Ehlers-Danlos syndrome (vEDS) is an autosomal dominant hereditary disease characterized by connective tissue fragility throughout the body, including the arteries, viscera, and gastrointestinal tract. We report a case in which we performed transvenous embolization (TVE) via direct superior ophthalmic vein (SOV) approach to treat a direct carotid-cavernous fistula (CCF) in a patient with Ehlers-Danlos syndrome (EDS). The patient was a 37-year-old woman who developed tinnitus in her left ear and a headache during examination in the outpatient clinic of another hospital in order to make a definitive diagnosis of vEDS, and she was referred to our hospital and examined. Based on the results of all of the studies she was diagnosed with a CCF. Conservative treatment was attempted, but was not very effective. Because of progressing aphasia, TVE was performed via the SOV direct cut. There were no intraoperative or postoperative complications. It has been reported that cerebral angiography is generally contraindicated in vEDS and that the morbimortality associated with endovascular treatment is very high. When performing treatment it is necessary to be sufficiently aware of the risks it entails.

Key words: carotid-cavernous fistula, Ehlers-Danlos syndrome, vascular type, embolization

Introduction

Ehlers-Danlos syndrome (EDS) is known to be an autosomal dominant hereditary disease that is characterized by connective tissue fragility throughout the body, including the arteries, viscera, and gastrointestinal tract, and its manifestations are widely known to include thin, transparent skin, a bleeding diathesis, and hypermobile joints. The first report of EDS is thought to have been made by a Dutch surgeon in 1668,¹⁾ and the descriptions by Ehlers²⁾ and Danlos³⁾ were made in the early 1900s.

EDS has been classified into approximately 10 subtypes, and type IV is also called the vascular type of Ehlers-Danlos syndrome (vEDS). In 1967, the classification was modified by Barabas,⁴⁾ and the vEDS was found to be attributable to a genetic abnormality of type III collagen (COL3A1) and to be the most pernicious and highly life-threatening type, with ruptures and dissection of blood vessels and arterial aneurysm formation being more common than in the other types.^{5–7)}

While making the diagnosis, there is a strong likeli-

hood of vEDS if any two of the following four criteria are met: (1) arterial rupture, (2) intestinal rupture, (3) uterine rupture during pregnancy, and (4) family history of vEDS. A definitive diagnosis can be made on the basis of biochemistry tests and genetic testing.

We performed transvenous embolization (TVE) via the superior ophthalmic vein (SOV) to treat a carotid-cavernous fistula (CCF) in patients with vEDS and were able to achieve a favorable therapeutic outcome. There have been occasional reports of TVE in the literature that we were able to collect in the past,⁸⁾ but there have been no reports of treatment via the SOV, making this the first such case. We report this case based on the pitfalls and aspects that require caution when this treatment is selected.

Case Report

I. History of the present illness

The patient was a 37-year-old woman with a history of intestinal perforation, but no history of cranial or orbital trauma recently.

While undergoing genetic diagnosis of vEDS in the outpatient clinic of another hospital, the patient experienced

a sudden onset of a vascular murmur in the vicinity of the left ear, tinnitus, and a headache. The tinnitus disappeared when the left carotid artery was compressed, and a bruit was heard over the left eyeball. No clear abnormal findings were detected by computed tomography (CT) of the head, but magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the head revealed a CCF, and the patient was referred to our hospital and examined.

The patient's consciousness level was clear on arrival at our hospital. Ophthalmological examination indicated corrected visual acuity of 1.0/1.0. Bilateral Amsler grid testing indicated no abnormalities at any point in either visual field. The left eye was markedly red with dilated irregular conjunctival and subconjunctival vessels. Hess chart testing indicated abducens nerve paralysis. Based on the patient's family history, past medical history, and the imaging findings, there was a strong possibility of a CCF complicating EDS, and because of the possibility that angiography would cause vascular injury, the preoperative evaluation was performed by 3D CTA.

II. Family history

Elder brother: Dissection of the thoracic aorta
 Father's family: Rupture of the abdominal aorta, sudden death

III. Course after admission

Although the symptoms temporarily improved in response to intermittent manual compression of the carotid artery, they became more severe again (Fig. 1). Because of the development of higher function disorders, including aphasia and agnosia, associated with marked cortical reflux within the cranium, endovascular treatment (TVE) was performed under general anesthesia.

A direct CCF from the vicinity of the left internal carotid artery (ICA) at the C3–4 level was confirmed by digital subtraction angiography (DSA). Marked retrograde flow into the intracranial veins was observed, and treatment was performed as described below (Fig. 2).

IV. Treatment

General anesthesia: No heparinization
 Micro catheter: Excelsior 45° (Boston Scientific, Natick, Massachusetts, USA)
 SL-10 45° (Boston Scientific, Natick, Massachusetts, USA)
 Micro guidewire: GT-0.016W.90° × 2 (Terumo, Tokyo)
 Synchro14S (Boston Scientific, West Valley, Utah, USA)

Diagnostic catheter: An incision was made in the skin of the right inguinal area, and after directly puncturing the femoral artery with an 18G needle under direct vision, a 0.035 GW was inserted. A 4Fr diagnostic catheter (Berenstein type; Terumo Cinical Supply Co., Ltd., Gifu) was then directly inserted into the artery and gently advanced to the left ICA.

Treatment catheter: A transverse incision was made in the left superciliary area, and the SOV was exposed based on Doppler ultrasonography and the markers placed in advance when 3D CTA was performed. Since the tissue was fragile, with postoperative hemostatic maneuvers in mind, after lifting the SOV with 3-0 silk, we punctured it with a 20G needle, and inserted the Excelsior 45° inside to the cavernous sinus (CS), guiding the TERUMO GT0.016.

Coil embolization was started at the left superficial sylvian vein, where retrograde intracranial flow had been observed, and elimination of the intracranial retrograde flow was confirmed. We changed the working angle frequently to prevent the coil from migrating to the internal carotid artery. After embolizing the CS, we continued

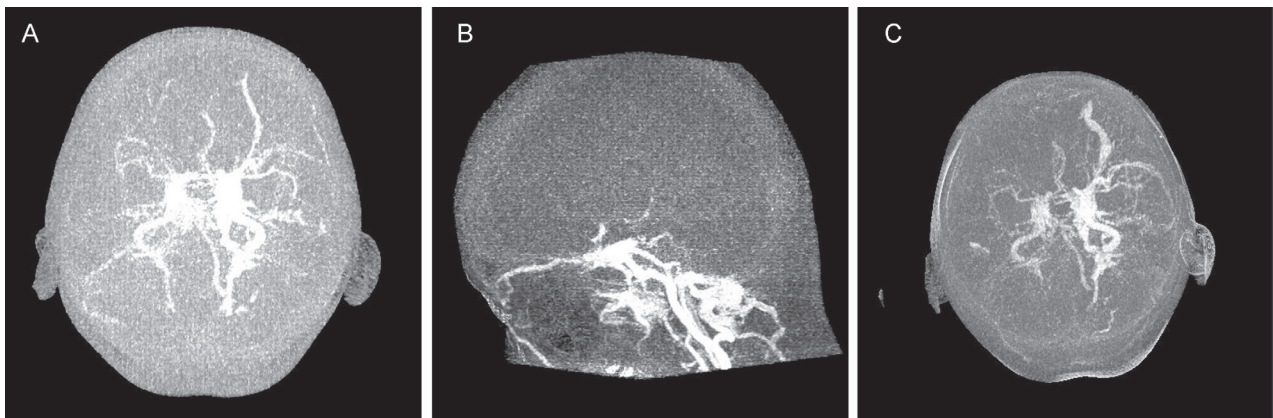


Fig. 1 Dynamic CTA (preop: axial lateral). A: Dynamic CTA shows dilatation of the left SOV and insufficient intracranial circulation. B: Dynamic CTA shows aggravation of CCF. An increase in the dilatation of the left SOV can be observed in addition to intracranial cortical vein reflux. C: Dilatation of the left SOV and marked retrograde flow in the left intracranial veins can be seen. CCF: carotid-cavernous fistula, CTA: computed tomography angiography, SOV: superior ophthalmic vein.

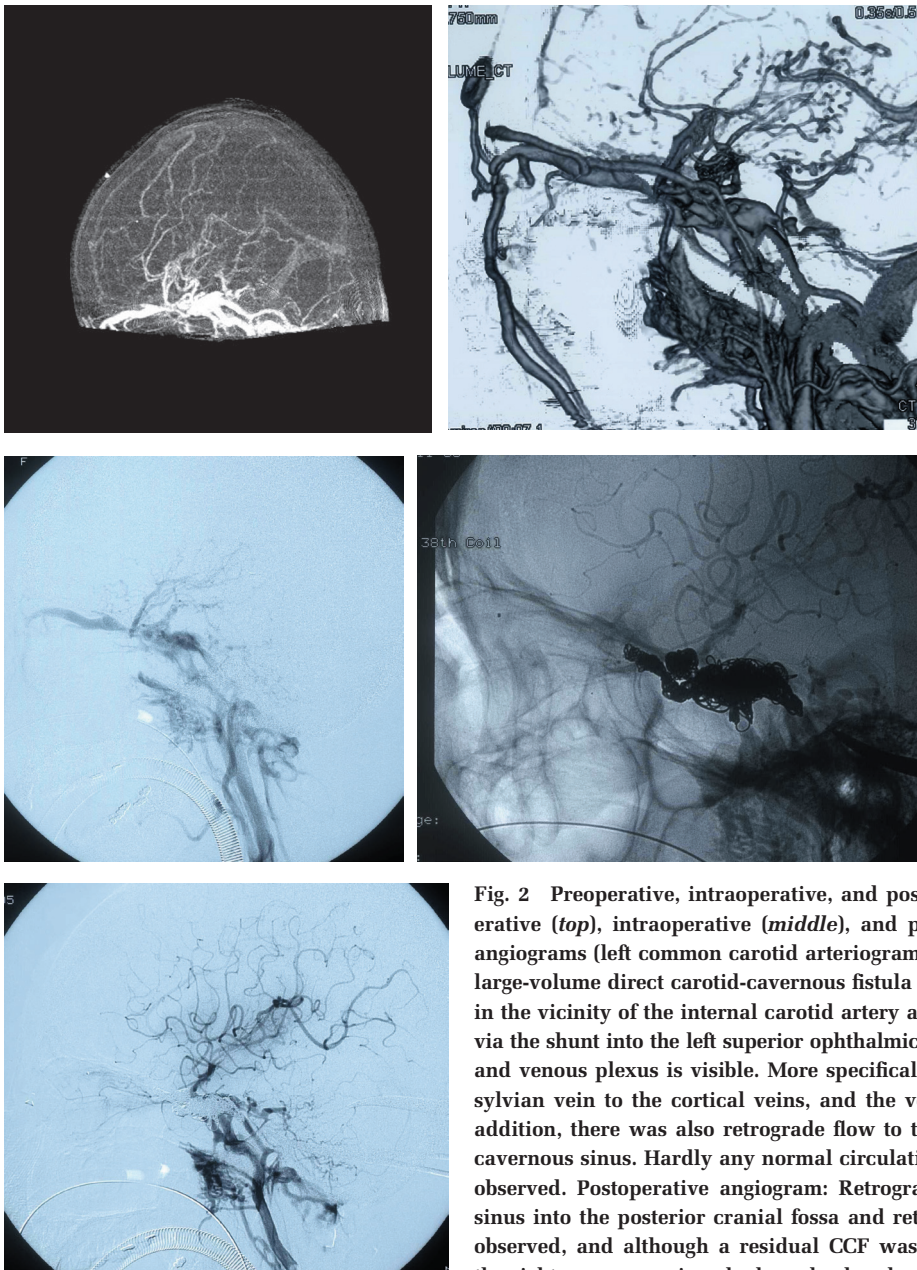


Fig. 2 Preoperative, intraoperative, and postoperative DSA, DA (lateral view). Preoperative (top), intraoperative (middle), and postoperative (bottom). Digital subtraction angiograms (left common carotid arteriogram, lateral view). Preoperative angiogram: A large-volume direct carotid-cavernous fistula (CCF) shunt into the jugular vein is visible in the vicinity of the internal carotid artery at C3–4 in the early arterial phase. Outflow via the shunt into the left superior ophthalmic vein, left sylvian vein, left pterygoid sinus, and venous plexus is visible. More specifically, there was retrograde flow from the left sylvian vein to the cortical veins, and the veins had become dilated and tortuous. In addition, there was also retrograde flow to the right superior ophthalmic vein via the cavernous sinus. Hardly any normal circulation from the arteries into the cranium was observed. Postoperative angiogram: Retrograde flow from posterior to the cavernous sinus into the posterior cranial fossa and retrograde flow into the venous plexus was observed, and although a residual CCF was visible, because the retrograde flow into the right cavernous sinus had resolved and sufficient normal circulation had developed.

the embolization as we returned to the SOV. Although a residual CCF was observed, it had been possible to sufficiently reduce it, and since normal circulation had been adequately restored and the retrograde flow into the right CS had also stopped. After removing the femoral catheter, we manually compressed the puncture site with fibrin glue and polyglycolic acid (PGA). We observed the puncture site under direct vision and confirmed hemostasis, following which we concluded the operation.

V. Postoperative course

The patient's intraoperative and postoperative course was uneventful. The higher function disorders, including

the aphasia, resolved and the tinnitus had completely disappeared by about 2 weeks postoperatively. The patient was discharged in a state of mRS 0. Because of the problems created by the coil artifacts, the postoperative evaluation was performed by MRDSA, but no deterioration was observed as of the 18-month follow-up examination (Fig. 3).

Discussion

I. Summary

EDS is an autosomal dominant hereditary disease that has been classified into approximately 10 subtypes.

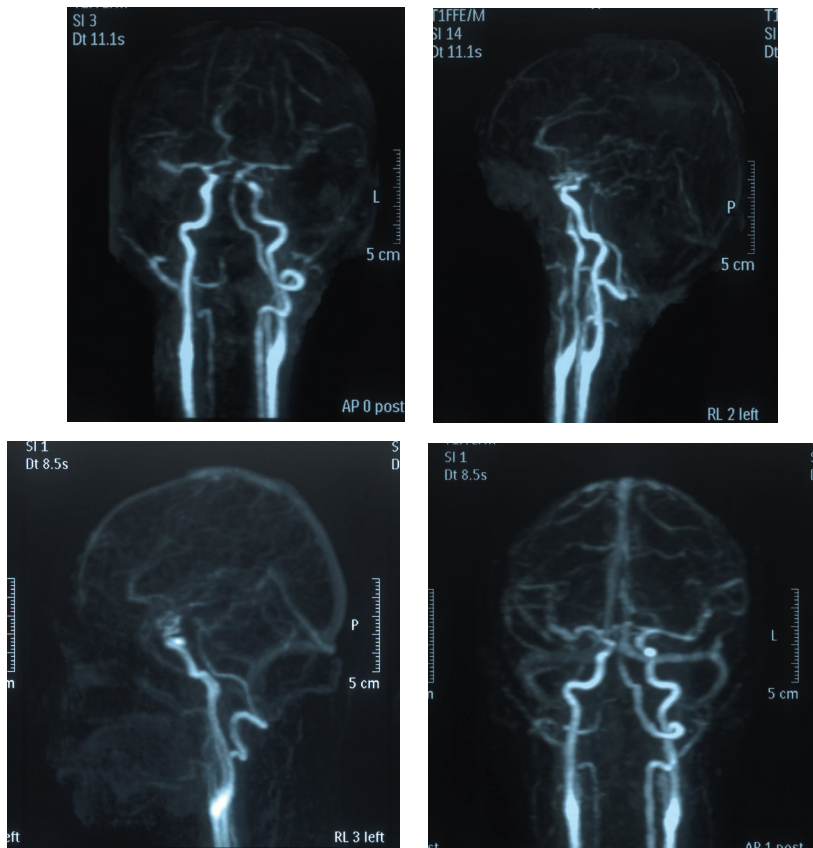


Fig. 3 Postoperative follow-up MRDSA. *Upper panel:* One week postoperatively. *Lower panel:* 18 months postoperatively. No clear shunts were visible in either study, and no recurrence of the carotid-cavernous fistula was detected.

Type IV is also called the “vascular type” and accounts for approximately 4% of all cases. vEDS is a connective tissue disease with a very poor prognosis and is often the cause of sudden death in young people. It is characterized by a tendency for viscera and blood vessels to rupture idiopathically. The early mortality rate is high, and arterial and cardiac rupture, aortic dissection, and gastrointestinal rupture tend to occur, and recovery from the tissue fragility is difficult.^{9–11} Boutouyrie et al.¹² conducted a study of the carotid arteries in vEDS cases and reported findings that wall stress was 22% to 43% higher and intima-media thickness 32% thinner than in a normal group. Because stress on vessel walls increases as a result of the reduced thickness of the intima and media, the risk of arterial dissection and vascular rupture is said to be higher, and fistulas, aneurysms, and dissections are cited as complications in the neuroendo vascular area.

II. Angiography

Freeman et al.¹³ reported a high major complication rate (22%) and mortality rate (5.6%) in 18 vEDS patients examined by cerebral angiography, and Schievink et al. reported a morbidity rate of 35% and mortality rate of 12% in a report on 25 cases,⁸ and thus both morbimortality rates were very high. Their causes have been reported to be not only bleeding at the puncture site and arterial dissection and retroperitoneal bleeding along the catheter

access route, but vascular damage completely unrelated to the catheter maneuvers as well.^{14,15} Whenever possible, it is necessary to refrain from puncturing blood vessels, especially arteries, in vEDS, and we consider casual angiography to be contraindicated. If preoperative evaluation is possible, noninvasive CT and MRI (MRA) are useful, and in our patient we conducted the preoperative evaluation by three-dimensional computed tomography angiography (3D CTA) and the postoperative evaluation by magnetic resonance digital subtraction angiography (MR DSA).

III. Endovascular treatment (Table 1)

The risk of angiography in relation to the treatment of direct CCF is even greater, and there is even a report in the literature of a 50% major morbidity rate and 25% mortality rate.¹⁶ Actually, there is also apprehension in the literature about postoperative intracranial hematomas,¹⁷ asphyxiation as a result of hematomas caused by direct punctures of the neck,⁵ the development of secondary arterial aneurysms as a result of hemodynamic changes associated with ligation, and recurrences of the CCF.¹⁸ The transvenous approach appears useful from the standpoint of avoiding invasion of the artery, but there is also a problem, for example postoperative massive intraperitoneal and retroperitoneal bleeding because of tissue fragility in relation to veins as well,^{19,20} we made the approach via direct SOV approach in our patient to

Table 1 Literature review table

Author (yr)	Age	Sex	Fistula side/type	Complications of angiography	Treatment	Outcomes
Halbach et al. (1990) ¹⁶⁾	19 y/o	N/A	(-)/direct	(Cerebral angiography) Transfemoral→unsuccessful (excessive tortuous) Carotid puncture→massive hematoma	Direct surgical ligation	Good (spontaneously closed)
	22 y/o	F	Lt/direct	(Cerebral angiography) Transfemoral→massive external hemorrhage (puncture site)	1st TVE (silicon balloon)	Improve
	24 y/o	N/A	Rt/direct	(Cerebral angiography) Transfemoral→iliac artery dissection→graft repair	Direct surgical repair	Dead (POD4) fatal pontine hemorrhage
	39 y/o	F	Lt/direct	(Cerebral angiography) N/A	1st TAE	Visual loss, ophthalmoplegia
	49 y/o	F	Rt/direct	(Cerebral angiography) N/A	2nd TAE 3rd TAE (liquid) TAE	Initial improvement (recurrence) Unsuccessful Good Good (asymptomatic iliac dissection)
Schievink et al. (1991) ⁸⁾	17 y/o	F	Lt/direct	(Cerebral angiography) Direct carotid puncture→large hematoma	ICA ligation	Good
	20 y/o	N/A	Rt/direct	(Cerebral angiography) Transfemoral→large hematoma (puncture site)	Rt ICA embolization	Fail (tortuous)
					Rt carotid puncture	Bleeding→CPA (common carotid clamp)
Debrun et al. (1995) ¹⁸⁾	39 y/o	F	Rt/direct	(Cerebral angiography) N/A	TAE (balloon)	Recurrence (ICO)
	39 y/o	F	Lt/direct	(Cerebral angiography) N/A	TAE (balloon)	Good
Bashir et al. (1999) ²³⁾	53 y/o	F	Lt/direct	(Cerebral angiography) N/A	TVE (coil)	Dead (haemothorax, abdominal aortic rupture)
Chuman et al. (2002) ²⁴⁾	57 y/o	M	Lt/direct	(Cerebral angiography) Multiple AN (abdomen-pelvis)→dissection, groin hematoma	TVE	Good (POD3 colon rupture→colostomy)
Mitsuhashi et al. (2004) ¹⁴⁾	30 y/o	F	Rt/direct	(Cerebral angiography) Rt femoral artery rupture→retroperitoneal bleeding	Extracranial ligation	Good (watershed infarction)
Desal et al. (2005) ¹⁷⁾	48 y/o	F	Lt/direct	(Cerebral angiography) N/A	TAE (balloon×→coil)	Dead (POD7) lt frontal hematoma

CPA: cardio pulmonary arrest, F: female, ICA: internal carotid artery, ICO: internal carotid artery occlusion, M: male, N/A: not available, POD: postoperative day, TAE: transarterial embolization, TVE: transvenous embolization, y/o: years old.

avoid contact with the vessel as much as possible. We made a direct skin incision for intraoperative diagnostic cerebral angiography and punctured the femoral artery under direct vision. These enabled us to perform reliable hemostasis under direct vision. The reason we placed a direct catheter without placing a sheath is that we chose a method of treatment that avoided vascular stress as much as possible. In addition, the contrast injection must be performed manually and gently in order to avoid detachment of the vascular endothelium.

Because the diagnosis of EDS had already been made before treatment in this case, we conducted the perioperative management cautiously, and favorable results of treatment were achieved. However, the diagnosis of EDS often may not have been made before the diagnostic studies or when the treatment is performed. While performing treatment in cases in which the diagnosis has already been made, it is important to determine in advance, before surgery, whether an aneurysm or dissection of the thoracoabdominal aorta or its major branches is present

by multi detector-row computed tomography (MD-CT), etc.^{21,22)} Moreover, quite a few complications of angiography and endovascular treatment are often recognized after treatment, for example arterial bleeding, abdominal organ rupture, vessel rupture, remote and delayed arterial rupture etc. So a careful postoperative monitoring of the patient's course is also necessary.¹⁴⁾ It is also necessary to take the possibility of EDS into consideration as a cause when complications develop that cannot be explained by routine clinical tests or treatment. Cerebral angiography is generally considered to be contraindicated in vEDS, and very high morbimortality has been reported in association with interventional radiology. The risk must be sufficiently borne in mind when performing treatment.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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