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Case Report

Rapid *de novo* Formation of a Large Aneurysm in a Patient with Fibromuscular Dysplasia

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Objective: The authors report the first case of intracranial fibromuscular dysplasia (FMD) presenting with rapid *de novo* formation of an unruptured large vertebral artery (VA) fusiform aneurysm.
Case Presentation: A 41-year-old man presented with left hemiparesis. He had a giant thrombosed aneurysm at the basilar artery-superior cerebellar artery (BA-SCA) junction and a left extracranial VA aneurysm. A *de novo* VA fusiform aneurysm developed during a 1-month interval following the first session of intravascular coil embolization for the BA-SCA aneurysm. Stress on the fragile artery due to FMD during micro-catheterization may have caused the *de novo* aneurysm. An anomalous aortic origin of the left VA may also have played a role in the formation of the large *de novo* aneurysm and extracranial VA aneurysm. We performed overlapping stent-assisted coil embolization for the VA fusiform aneurysm using an Enterprise VRDs, and coil embolization for the BA-SCA thrombosed aneurysm using the stent-assisted technique with an Enterprise stent. Both aneurysms remained occluded for 7 years.
Conclusion: We concluded micro-catheterization to be the cause of the large *de novo* aneurysm. This case emphasizes the importance of carefully performing intravascular interventional procedures for patients with FMD.

Keywords ▶ fibromuscular dysplasia, de novo aneurysm, partially thrombosed aneurysm, endovascular treatment

Introduction

Fibromuscular dysplasia (FMD) is a non-atherosclerotic arterial disease characterized by abnormal cellular proliferation of the vascular wall and irregular arterial lumen. It frequently develops in Caucasian females, and its incidence is low in Asians, including Japanese.[1)] Vascular fragility-related cerebral aneurysms and vascular dissection are common complications.[1,2)]

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In this study, we report a patient in whom a large aneurysm developed in a short period after endovascular treatment for multiple intra- and extracranial cerebral aneurysms with FMD of the intracranial vertebral artery (VA), and review the literature.

Case Presentation

Patient: A 41-year-old male.
Complaint: Left hemiparesis.
Family history/medical history: nothing particular.
Lifestyle: smoking (30 cigarettes /day), occasional alcohol consumption.
Present illness: In August 2011, he consulted our department for clumsiness of the left hand, which had persisted for 1 week.
Physical examination on admission: Consciousness was clear. Left hemiparesis (MMT 4/5) and incomplete paralysis of the right oculomotor nerve were observed.
Neuroradiological findings: Magnetic resonance imaging (MRI) revealed a giant thrombosed aneurysm involving the right midbrain to thalamus that measured 28 mm in maximum diameter (**Fig. 1A** and **1B**). On cerebral angiography, an aneurysm at the basilar artery-right superior

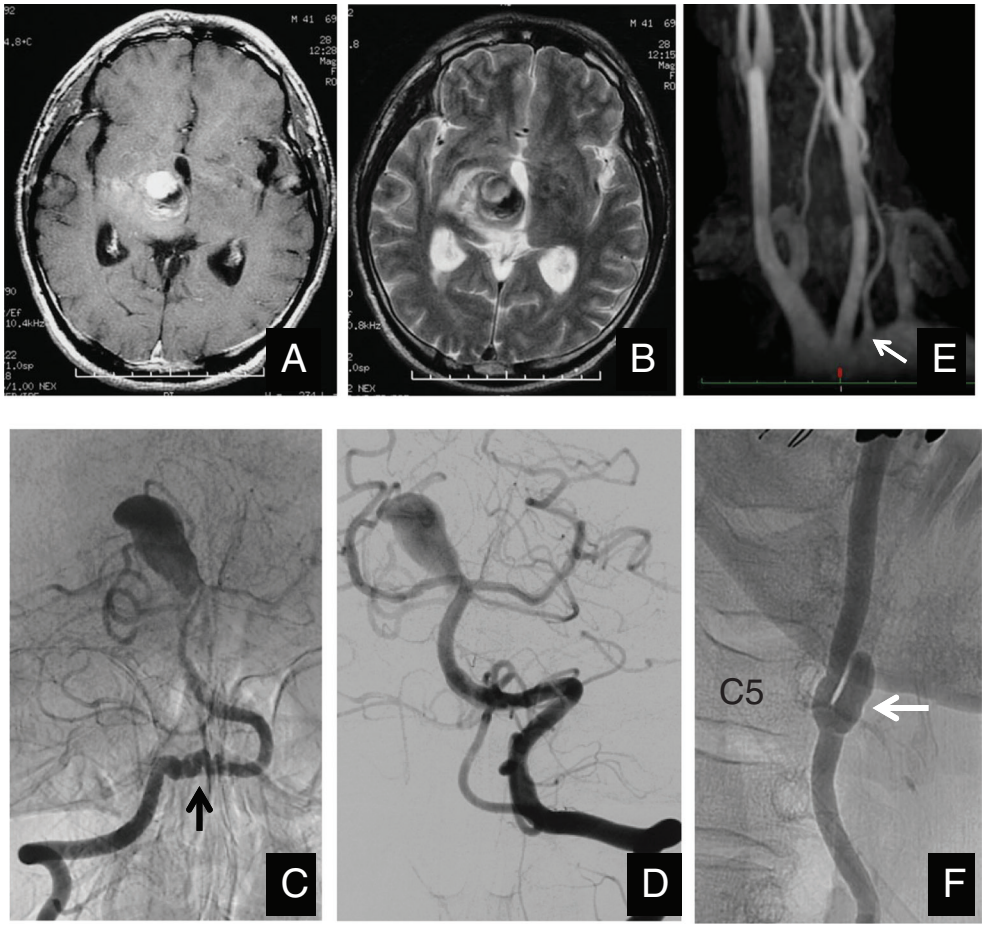

Fig. 1 (**A** and **B**) Enhanced T1 (**A**) and T2-weighted (**B**) MRI show a giant aneurysm with layering mural thrombus compressing the right midbrain and thalamus with perifocal edema. (**C** and **D**) Right (**C**) and left (**D**) vertebral angiogram shows a BA-SCA large aneurysm 22 × 12 mm in size concomitant with the "string of beads" sign in the right intracranial VA (arrow). (**E**) Extracranial MRA shows a bovine type aortic arch and left VA of aortic origin (arrow). (**F**) Left vertebral angiogram (right oblique view) shows the left VA entering the transverse foramen at the C-5 level, and a saccular left VA aneurysm originating just distal to the C-5 transverse foramen. BS-SCA: basilar artery-superior cerebellar artery; MRA: magnetic resonance imaging; VA: vertebral artery

cerebellar artery (BA-SCA) junction was visualized, with an aneurysmal lumen of 22 × 12 mm and neck of 6 mm (**Fig. 1C** and **1D**). Magnetic resonance angiography (MRA) demonstrated a bovine type aortic arch and the aortic origin of the left VA (**Fig. 1E**), and a saccular aneurysm measuring 12 × 4 mm at a level of the transverse foramen of the C5 cervical vertebra (**Fig. 1F**). The right intracranial VA showed the "string of beads" appearance (**Fig. 1C**). There were no abnormalities in other intra- or extracranial arteries or renal arteries.

Clinical course: Considering the risks/benefits of treatment methods, we selected endovascular treatment with Matrix 2 for the BA-SCA aneurysm as the initial treatment.

Neuroendovascular treatment

Initial treatment (October 2011): After administering 100 mg of aspirin and 75 mg of clopidogrel for 10 days prior to the endovascular procedure, the procedure was performed under general anesthesia. A 7Fr guiding catheter (GC) was inserted into the left VA for double-catheter embolization. A 5Fr GC was inserted into the right VA as for introducing a balloon catheter. Initially, a microcatheter (MC) ExcelsiorSL10 (SL10) (Stryker, Kalamazoo, MI, USA) was guided through the right VA. It was passed through the "string of beads" area without difficulty, but was unable to be guided into the right superior cerebellar artery, which branched like a hairpin. Therefore, the balloon-assisted method was abandoned. The SL10 was guided into the

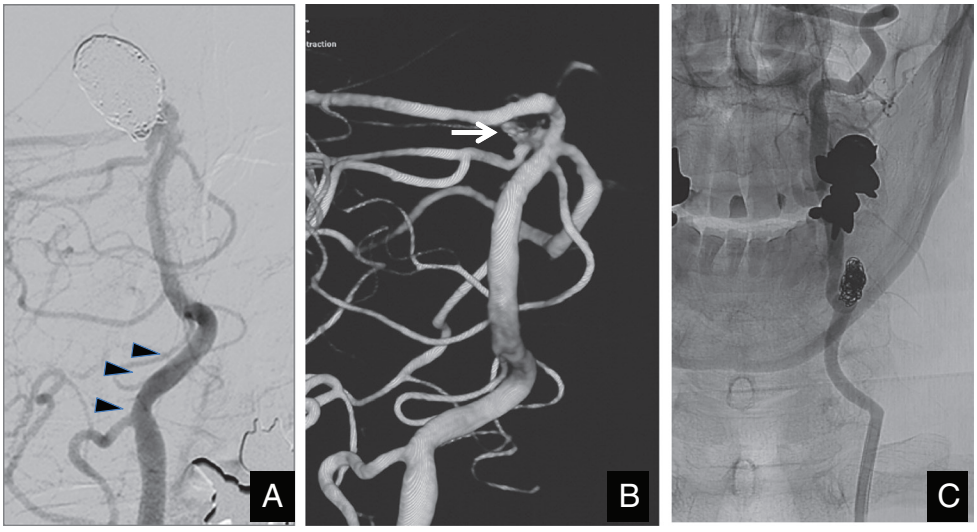

Fig. 2 (**A** and **B**) Left vertebral angiograms immediately after coil embolization demonstrate a small neck remnant (arrow). No vessel abnormality, such as dissection or vasospasm, was observed (arrow head). (**C**) Left vertebral angiogram immediately after coil embolization of the extracranial left VA aneurysm demonstrates complete occlusion of the aneurysm.

aneurysm for embolization. An Excelsior1018 (Ex1018) was guided into the aneurysm through the left VA, and coil embolization was performed using the double catheter technique. A framing was conducted using a GDC18 360 (Stryker, Fremont, CA, USA) 14 in diameter, 13 in diameter, and 12 mm in diameter (length of the each coil was 30 cm), and the inner area was filled with the Matrix2 (Stryker Neurovascular, Fremont, CA, USA) (total length of 360 cm). As the double catheter method with different arterial routes was adopted, one-by-one coil delivery and detachment were performed to avoid coil troubles. Although a small neck remnant remained, the procedure was completed after the disappearance of body filling, avoiding deterioration of mass effects (**Fig. 2A** and **2B**). The volume embolization rate was 31%, and a 75% of delivered coils was comprised of Matrix 2. An extracranial VA aneurysm was then embolized with the Matrix2 coils (total length of 63 cm) (**Fig. 2C**). The final angiography revealed no abnormalities such as occlusion, spasm, and arterial dissections of a major arteries (**Fig. 2A** and **2B**).

After the procedure, there was no new neurological deficit. During the follow-up period, left hemiparesis and diplopia disappeared. MRA 3 weeks after the initial procedure revealed a *de novo* left intracranial VA fusiform aneurysm.

Angiography (November 2011, 31 days after the initial treatment): A large, fusiform left VA aneurysm measuring 12 × 9 mm was noted distal to the left posterior inferior cerebellar artery (PICA) (**Fig. 3A**). As a "string of beads" sign in the contralateral right VA was observed, stent-assisted coil embolization with preserving the patency of the left VA was selected. According to the patient's request, treatment was scheduled 5 months later. There was no hemorrhage during the follow-up period.

Second session of the treatment (April 2012, 6 months after the initial treatment): The left VA aneurysm enlarged to a size of 18 × 14 mm, and it involved the origin of the PICA (**Fig. 3B**). After an Ex1018 was introduced into the aneurysm and it turned around the aneurysmal wall, another microcatheter was guided from the same axis distal to the union of the VAs. Through the latter catheter, an Enterprise VRD stent, 4.5 × 37 mm (Codman & Shurtleff, Raynham, MA, USA) was deployed from the VA union to the left VA to the aneurysm. An additional SL10 was guided into the aneurysm via a trans-cell route, and embolization was performed using the double catheter technique. A GDC18 360 12 mm × 30 cm was delivered as a flaming coil, and the inner area was filled with a coils (total coil length was 292 cm). The procedure was completed with some dome filling around the orifice of the PICA, for maintaining the patency of the PICA (**Fig. 3C**). Although the neck remnant of the BA-SCA aneurysm enlarged, we decided to continue follow-up. There were no complications, and the patient was discharged 10 days after the procedure without any neurological deficits.

The third session of treatment was performed on May 2012, 50 days after the second session of treatment. As the neck remnant of the BA-SCA aneurysm had further

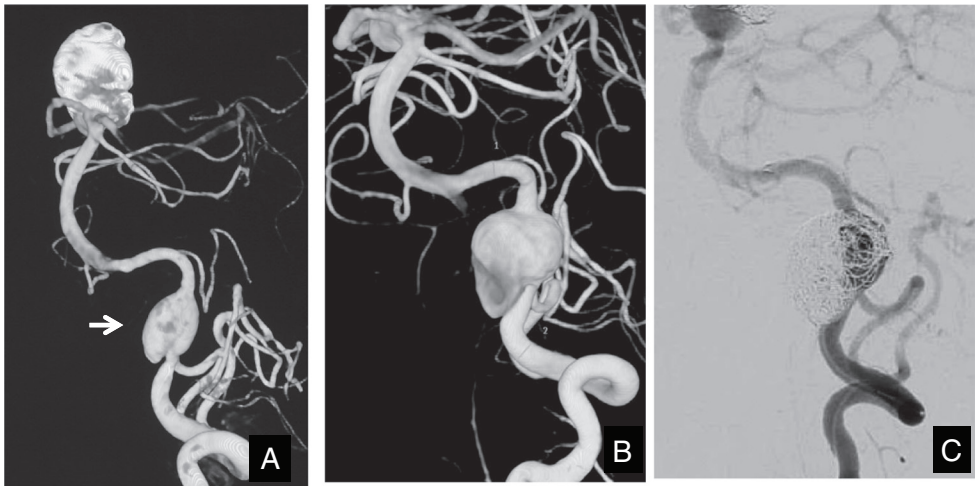

Fig. 3 (**A**) Left vertebral angiogram obtained 1 month after the coil embolization reveals a large *de novo* fusiform aneurysm of the left VA just distal to the PICA (arrow). (**B**) Left vertebral angiogram 5 months later reveals enlargement of the left vertebral aneurysm to 18 × 12 mm in size, which involved the PICA. (**C**) Left vertebral angiogram immediately after the stent-assisted coil embolization using the Enterprise VRD demonstrates dome filling with a patent PICA. PICA: posterior inferior cerebellar artery; VA: vertebral artery

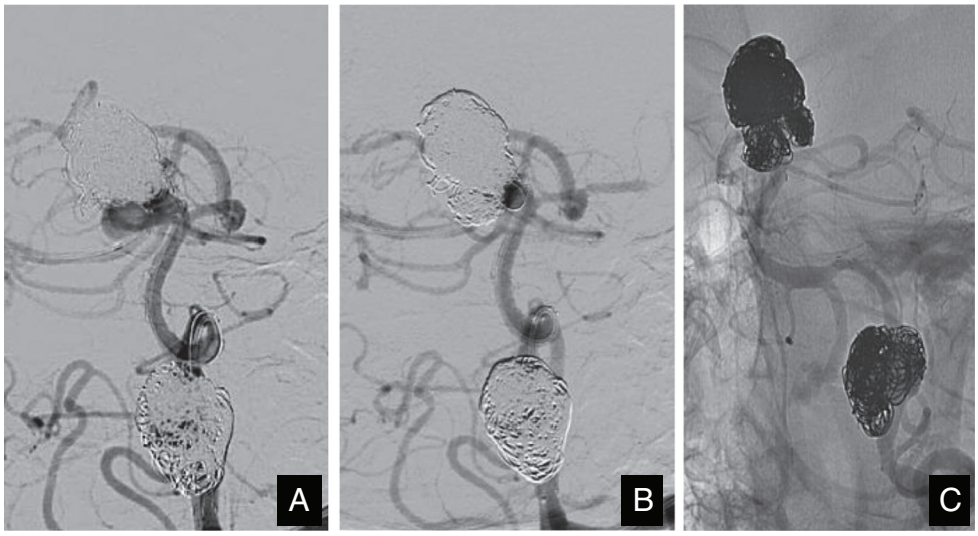

Fig. 4 (**A**) Left vertebral angiogram 50 days after the second endovascular procedure reveals major recanalization of the BA-SCA aneurysm and reduced opacification of the large left vertebral *de novo* aneurysm. (**B** and **C**) Left vertebral angiogram immediately after stent-assisted coil embolization of the BA-SCA aneurysm using the Enterprise VRD and additional deployment of the second Enterprise VRD in the large left vertebral *de novo* aneurysm. BS-SCA: basilar artery-superior cerebellar artery

enlargement, additional embolization was required (**Fig. 4A**). After delivering 90 cm of Target 360 coils, an Enterprise stent 4.5 × 28 mm was deployed from the right posterior cerebral artery to the basilar artery (**Fig. 4B**). Another Enterprise stent 4.5 × 37 mm was deployed across the left fusiform VA aneurysm using the stent-in-stent method for further flow-diverting effect. The opacification of the left VA fusiform aneurysm was delayed and decreased due to flow diverter effects related to additional stenting (**Fig. 4B** and **4C**).

Postoperative course: The patient was discharged after 7 days after the procedure without any neurological deficits (modified Rankin Scale score: 0). On angiography after 6 months, the aneurysms were not visualized on an angiography 6 months later. Dual antiplatelet therapy (DAPT) was then switched to clopidogrel alone, and it was withdrawn after 1 year. There were no neurological deficits. Follow-up examinations of 1, 4, and 7 years after the final treatment revealed no recurrence of aneurysms nor new vascular lesions in any other cerebral blood vessels (**Fig. 5A, 5B,** and **5C**).

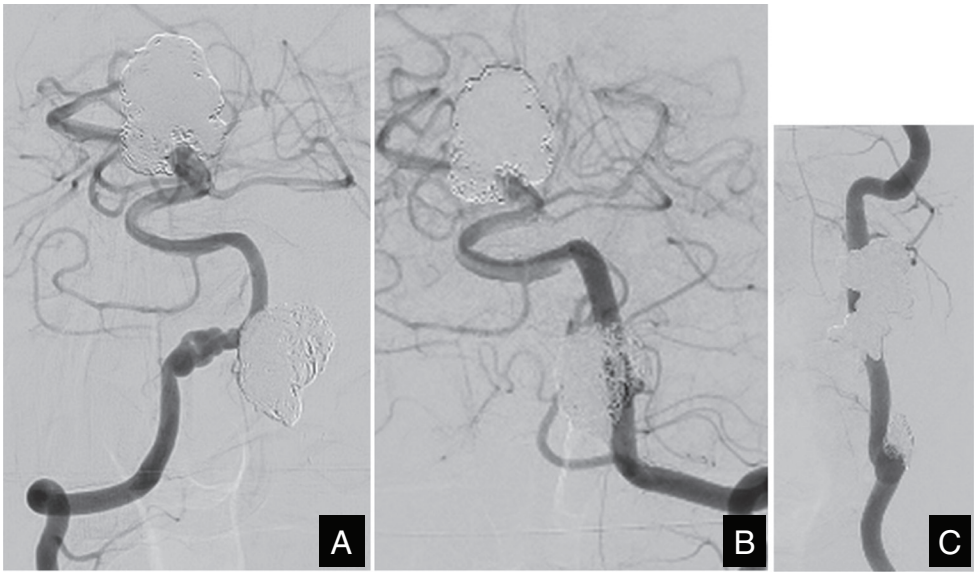

Fig. 5 (**A**) Right vertebral angiogram 7 year after the final endovascular procedure demonstrates complete occlusion of the BA-SCA giant aneurysm and unchanged "string of beads" appearance of the intracranial right VA. (**B**) Left vertebral angiogram demonstrates complete occlusion of the large left VA *de novo* aneurysm with a patent VA and PICA. (**C**) Left vertebral angiogram demonstrates complete occlusion of the extracranial left VA aneurysm. BS-SCA: basilar artery-superior cerebellar artery; PICA: posterior inferior cerebellar artery; VA: vertebral artery

Discussion

The first consensus regarding FMD[1] was published in 2019. According to this consensus, FMD is a non-atherosclerotic arterial disease characterized by abnormal cellular proliferation in arterial walls and irregular arterial lumen. FMD frequently involves the renal, extracranial carotid, and VAs. It has females dominancy account for 90% of patients, and it occurs frequently in Caucasians, but relatively rare in Asians including the Japanese. FMD is classified into two types: focal FMD, which is characterized by focal stenosis on angiography, and multifocal FMD, which is characterized by focal stenosis and dilatation, the so-called "string of beads" sign. A definitive diagnosis is made with former or latter or both findings. However, aneurysm, arterial dissection, or arterial tortuosity alone is insufficient to diagnose FMD. In the present case, a "string of beads" sign in the right intracranial VA was observed, suggesting multifocal FMD.

Among the three histological types of FMD, medial fibroplasia (medial type), which consists of thinning of the media, rupture of the internal elastic lamina, and hypertrophy of the media smooth muscle involving collagen fibers, accounts for 90%. This type of FMD demonstrates the "string of beads" sign on angiography,[3] and our patient was classified as medial FMD.

FMD induces cerebral aneurysms or arterial dissections related to the fragility of the arterial wall.[1] Among patients with FMD of the head and neck, cerebral aneurysms develop in 13–21% of patients. Of these, multiple aneurysms account for 33%.[2,4] Arterial dissections are observed in 26% of patients. Either or both of aneurysms and dissections are noted in 42% of patients.[2] According to the US registry, the incidence of large or giant aneurysms measuring ≥13 mm is less than 1% in patients with FMD,[4] but fusiform aneurysms are frequent.[5,6] There has been no report about the giant, saccular aneurysms with mass effects associated FMD, such as the giant thrombosed BA-SCA aneurysm in the present case. The previous studies also noted that aneurysms and arterial dissections were more frequent in male patients, leading to an aggressive course.[7]

Manlfe et al.[8] reported that pathological examination revealed characteristic finding of FMD in cerebral arteries, demonstrating normal on angiography. In several previous studies, biopsy of the superficial temporal artery without abnormalities on angiography suggested pathological findings characteristic of FMD.[5,9,10] We should aware of latent lesions of FMDs.

Endovascular treatment for cerebral aneurysms or arterial dissections in patients with FMD patients has been increasingly performed,[1,2,11] but few studies have reported procedure-related injury of the fragile vascular wall.[12,13]

Fuse et al.[12] reported a patient in whom FMD of the superficial temporal artery with only slight dissection had increased in size to a giant aneurysm measuring 3 cm during a 1-month period. They hypothesized that it was associated with frequent intra-arterial selective infusion of fasudil hydrochloride for treatment of cerebral vasospasm. In the present case, a large fusiform VA aneurysm was developed on an angiographically normal intracranial artery in a short period (3 weeks after treatment). To our knowledge, there has been no similar report. Although the catheterization distal to the PICA was uneventful, it could make stress on the arterial wall due to the steep vending of the VA proximal to the PICA. Therefore, we cannot exclude the possibility of vascular wall injury during catheterization. Although angiography was normal, fragile vascular wall of FMD with rupture or disappearance of the internal elastic lamina may have been present at the site of the lesion.

Bender et al.[13] performed 43 sessions of endovascular treatment (pipeline flow diversion: 29 sessions, coiling: 8, stent coiling: 5) for cerebral aneurysms in 31 patients with FMD, and reported no major complications or vascular dissection with a mean follow-up of 17 months, although FMD appearance with a "string of beads" sign were noted on access routes to the lesion in 27 of these sessions. They concluded that treatments of patients with FMD appearance on access routes were safe. In the present case, a microcatheter was guided through a morbid blood vessel with a "string of beads" sign, but there was no problem.

When reviewing the *de novo* aneurysm in the present case, the left VA originating from the aorta should also take into account. Komiyama et al.[14] reported that intracranial dissections of the VA originating from the aorta were more frequent than those originating from the subclavian artery. They suggested the following reasons: some kinds of defect of the vascular wall were frequent in the intracranial segment of VA (V4); direct blood flow from the aorta may cause hemodynamic alteration,[15] increasing shear stress to the vascular wall; and shear stress may further increase in case which VA enter high level of transverse foramen as demonstrated in the present case. In the present case, the aortic origin of the left VA may facilitate to develop the *de novo* aneurysm.

Conclusion

We reported a patient with intracranial FMD in whom a large VA aneurysm newly developed in a short period after endovascular treatment for a giant thrombosed aneurysm at the BA-SCA junction. When performing endovascular treatment, FMD-related vascular fragility must be considered.

Disclosure Statement

We declare no conflict of interest regarding this article.

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