Continued growth of and increased symptoms from a thrombosed giant aneurysm of the vertebral artery after complete endovascular occlusion and trapping: the role of vasa vasorum

Case report

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A 58-year-old woman harboring a partially thrombosed giant aneurysm of the vertebral artery (VA) presented with lower cranial nerve palsies and cerebellar ataxia. The authors initially attempted to reduce the mass effect by obliterating the lumen of the aneurysm as well as by trapping of the parent artery with coils. Although there was no angiographically demonstrated evidence of filling, the aneurysm continued to enlarge. Magnetic resonance imaging revealed a marked enhancement around the packed coils close to the neck of the aneurysm. Aneurysmectomy and removal of the coils were performed and resulted in an almost complete cure of the patient’s symptoms. Interestingly, at the time of resection, a marked development of vasa vasorum on the occluded VA and the neck of the aneurysm was noted. When the occluded VA was cut, there was blood oozing through the coils packed within its lumen on the side where the aneurysm lay. Histological examination showed the presence of inflammatory cells and neovascularization of a partially organized thrombus around the packed coils in both the aneurysm and occluded VA. The proliferation of vasa vasorum was also recognized histologically. This unique case provides insight into the growth mechanisms of a partially thrombosed giant aneurysm after an apparently complete occlusion by endovascular treatment, especially the role of vasa vasorum on the occluded parent artery in the dynamic process of neovascularization in the incomplete organization of thrombus around the packed coils.

Key Words • giant aneurysm • vertebral artery • coil embolization
pitfalls of endovascular trapping and endosaccular coil embolization for the treatment of partially thrombosed giant aneurysms.

Case Report

History. This 58-year-old woman was referred to our tertiary care neurovascular center with a 6-month history of progressive swallowing disturbance and dysarthria. Truncal ataxia had developed 1 month before the woman was admitted to our facility.

Examination. A neurological examination performed on admission revealed dysarthric speech, absence of the gag reflex, and an impaired tandem gait. Computerized tomography scans displayed a large, partially thrombosed right VA–PICA aneurysm, 2 cm in diameter, with a small area of calcification at its neck. A T1-weighted MR image demonstrated a large thrombosed aneurysm compressing the brainstem, with a hyperintense area indicating the presence of a subacute clot within the aneurysm (Fig. 1a).

On a FLAIR image, extensive edema was apparent in the brainstem, with a hyperintense area indicating the presence of a subacute clot at the fundic side of the aneurysm (arrows). b: A FLAIR MR image demonstrating marked edema in the brainstem surrounding the aneurysm. c: A coronal Gd-enhanced T1-weighted image visualizing the small patent portion of the thrombosed aneurysm (arrows). The hyperintense rim on the image is located mainly on the side contralateral to the patent lumen. d: Right VA three-dimensional digital angiogram revealing a patent portion of the aneurysm that projects superiorly at the VA–PICA junction. Note the stenosis on the parent artery just distal to the VA–PICA junction and the right AICA, which sweeps around the neck of the aneurysm.

First Embolization Procedure. While implementing systemic heparinization, embolization of the aneurysm was performed using GDCs (Boston Scientific/Target, Natick, MA), as was endovascular trapping of the adjacent short segment of the right VA immediately distal to the origin of the PICA (Fig. 2a). At the end of the procedure, VA angiograms demonstrated that the aneurysm was not filled from either side.

Clinical Course After the First Embolization. The patient experienced moderate improvement in her ability to swallow after the intervention, despite the fact that there was no decrease in brainstem edema exhibited on MR images. There was no marked effect on her gait disturbance. She was discharged home and appeared well for 3 months until her swallowing and gait deteriorated again, coinciding with an increase in brainstem edema on MR images. She was readmitted to our institution for further intervention. On the second admission, she demonstrated marked deterioration in her ability to swallow and truncal ataxia. In addition, she complained of general fatigue, sensation of cold on her tongue, numbness in her left fingers, and paresis of her left arm. The VA angiograms obtained on both sides revealed no recanalization of the parent artery or aneurysm. An MR image demonstrated a slight enlargement of the aneurysm, with persistent brainstem edema. At the first intervention, only a short segment of the parent artery had been occluded with coils to spare the origin of the PICA. This factor suggested that a possible connection between the unorganized thrombus in the aneurysm and the more proximal parent artery or the proximal segment of the PICA may have prevented the dissolution of the clot in the aneurysm, possibly by producing minor hemorrhages. Therefore, we decided to obliterate the more proximal segment of the right VA involving the origin of the PICA to ensure sequestration of the thrombosed aneurysm from the circulation.

Second Embolization Procedure. At the second intervention, a balloon test occlusion was performed using a temporary-occlusion silicone balloon catheter placed at the right VA just proximal to the occluded segment. After the patient tolerated a 15-minute test occlusion with angiographic demonstration of the right PICA territory supplied by the posterior meningeal artery, the more proximal segment of the right VA was occluded with GDCs and fiber coils (Fig. 2b).

Clinical Course After the Second Embolization. After this treatment, the patient’s truncal ataxia and left arm paresis markedly improved, in part because a regimen of steroid medication was initiated immediately after the procedure. The dose of the steroid agent was later tapered and finally discontinued. The woman was discharged 11 days postprocedure with persistent swallowing disturbance and mild dysarthria. She was readmitted 1 month later because of a deterioration in gait disturbance. Neuroimaging examinations demonstrated no recanalization of the aneurysm (Fig. 2c), although increased brainstem edema was evident on MR images (Fig. 2d). Dynamic MR imaging to the origin of the PICA (Fig. 1d). The lumen of the left VA had a similar caliber. Three-dimensional digital angiography revealed the ipsilateral PICA and AICA sweeping around the neck of the aneurysm.
enhanced by intravenous infusion of Gd–diethylenetriamine pentaacetic acid revealed an early and marked enhancement of the small area packed with GDCs and a late and less marked enhancement of the peripheral portion of the thrombosed aneurysm (Fig. 2e and f). These findings indicated that the neovascularization process and repeated minor hemorrhages into the aneurysm might have led to the deterioration in the woman’s condition.

**Operation.** The patient underwent right suboccipital craniectomy and thrombectomy followed by partial aneurysmectomy. Interestingly, markedly developed vasa vasorum were seen on the proximal VA and the aneurysm neck, which had been packed with coils (Fig. 3a). The aneurysm wall near the neck also received an arterial supply from small branches of the right AICA as well as from the vasa vasorum of the parent artery (Fig. 3b). The vasa vasorum on the right VA seemed to derive from the dura mater close to its entrance to the intracranial cavity (Fig. 3c). The patent portion of the proximal VA was clipped immediately distal to the origin of the posterior meningeal artery. The origin of the PICA was then also occluded with clip placement. When the middle of the adjacent VA segment, which appeared to be completely occluded on the angiogram, was cut using microscissors, blood oozed through the coils packed within the parent artery on the side on which the aneurysm lay (Fig. 3d). After the PICA was clipped off near its origin, the VA immediately distal to the neck of the aneurysm was dissected and also occluded by clip placement. When the aneurysm was opened, the packed coils were found to be embedded in the partially organized thrombus. Even after the distal side of the right VA was clipped, oozing at the thrombus persisted. The packed coils and friable clot were removed, leaving the outer shell of the aneurysm attached to the brainstem. Oozing of blood was found to stop gradually during removal of the clot and coils in response to coagulation of the aneurysm wall, which was achieved by using bipolar cautery.

**Pathological Examination and Findings.** Surgical specimens selected for pathological examination were immediately fixed in a 10% buffered formalin solution and left overnight. Specimens without GDCs were embedded in paraffin and cut into 4-μm-thick sections. Some parts of the specimens, which were attached to GDCs and embedded in glycol methacrylate (Historesin Plus; Leica Co., Heidelberg, Germany), were cut using a tungsten carbide knife (Superhard Knife; Meiwa Corp., Tokyo, Japan), as previously described. The sections were stained with hematoxylin and eosin, Masson trichrome, and elastica van Gieson stains. To recognize neovascularization of the aneurysm, factor VIII–related antigen (von Willebrand factor) and rabbit polyclonal anti–human antibody (Dako, Kyoto, Japan) were also applied to the paraffin-embedded sections. Immunohistochemical stains were applied using the streptavidin–biotin method (LSAB; Dako).

The aneurysm lumen, mostly occupied by tissue organizing around the GDCs, consisted of many fibroblasts, newly formed capillaries, inflammatory cells such as lym-
phocytes, hemosiderin-laden macrophages, and foreign body–type giant cells (Fig. 4a). The aneurysm wall was thin and displayed complicated atherosclerosis with focal calcification. Fresh fibrin mural thrombus and coagula were situated along the aneurysm wall. Interestingly, there were hemosiderin-laden macrophages scattered close to capillary vessels near the coils. In the adventitia of the aneurysm wall, a plexus of small arterioles compatible with vasa vasorum was seen (Fig. 4b). In the resected V A, small capillary vessels and accumulation of inflammatory cells were noted around the packed coils. Incomplete organization of the thrombus around the coils may explain the lack of symptom relief afforded by the previous endovascular procedures (Fig. 4c).

Postoperative Course. The patient showed a marked improvement in her gait disturbance as well as in her lower cranial nerve palsy, despite a transient increase in her swallowing disturbance and the new development of a right partial sixth cranial nerve palsy. She was discharged home and remained well at the 5-month follow-up examination, at which the edema in her brainstem was found to be decreasing.

Discussion
The present case is unique in that the thrombosed giant aneurysm continued to enlarge despite the persistent lack of angiographically demonstrated filling and after successful endosaccular embolization and trapping of the VA with coils. The optimal treatment of intracranial aneurysms is to eliminate them from the intracranial circulation while preserving the parent vessel. Some thrombosed giant aneurysms, however, cannot be successfully obliterated at the neck by surgical clip attachment or endosac-
cular coil embolization due to the presence of atherosclerosis or calcification within the neck, intraaneurysmal thrombosis, or anatomical factors such as the width of the aneurysm neck. For those formidable giant aneurysms, proximal arterial (hunterian) ligation or trapping by surgical or endovascular methods should be considered as valid alternatives.\textsuperscript{2,6,16} Complete thrombosis is usually observed within 1 month after this therapeutic maneuver. Steinberg, et al.,\textsuperscript{16} reported that in patients with giant aneurysms of the VA there was an 87\% complete and a 13\% incomplete rate of thrombosis after ipsilateral VA occlusion. These researchers found that for relief of neurological symptoms, complete or near-complete thrombosis was essential; 67\% of their patients with incomplete thrombosis suffered neurological complications, 86\% of which were fatal. Even those patients in whom angiograms reveal complete absence of aneurysm filling immediately after hunterian ligation should be followed up closely, because authors of several studies have documented recanalization with or without subsequent rupture or enlargement, even after complete thrombosis of giant aneurysms.\textsuperscript{4,11,12,19} Based on these findings, some neurosurgeons have tended to favor complete aneurysm trapping, either surgically or endovascularly. Although trapping and aneurysmectomy by surgery is the established method for the treatment of giant thrombosed aneurysms,\textsuperscript{14,17} endovascular trapping and endosaccular coil embolization can be important alternatives because of their less invasive nature. Nevertheless, the efficacy and safety of these alternatives for giant thrombosed aneurysm remains uncertain. Halbach, et al.,\textsuperscript{7} reported on the efficacy of endosaccular embolization of intracranial aneurysms in patients presenting with a mass effect, showing improvement of symptoms in the majority, especially those in whom there was less calcification and a shorter duration of symptoms. In cases of partially thrombosed giant aneurysms, however, the efficacy of endosaccular embolization has been doubted because of the documented growth potential of these lesions, even after complete thrombosis.\textsuperscript{7}

The enlargement of intracranial aneurysms has been explained by repeated hemodynamic injury to the aneurysm wall.\textsuperscript{4,18} On the other hand, there is no consensus on the mechanisms underlying the increase in partially thrombosed giant aneurysms in patients presenting with mass lesions. Schubiger, et al.,\textsuperscript{15} postulated, based on computerized tomography scans and MR images, that recurrent intramural hemorrhages at the highly vascularized wall are factors contributing to aneurysm growth. Nagahiro, et al.,\textsuperscript{14} reviewed the outcome in patients treated for thrombosed giant aneurysms of the VA and suggested that formation of intrathrombotic vascular channels and subsequent establishment of blood flow between the parent artery and channels may be important factors in the growth of thrombosed aneurysms. Kwan, et al.,\textsuperscript{10} suggested that transmitted pulsations may result in enlargement of a treated aneurysm, with subsequent distal migration of the balloons (“water-hammer effect”). In the present case, we eliminated the aneurysm from the circulation by endo-

\textbf{FIG. 4.} Photomicrographs of specimens of the resected aneurysm. a: Mixed inflammatory reactions with foreign-body giant cells, macrophages, and lymphocytes are seen around the coils in the organizing thrombus of the lumen. Neovascularization (asterisk) and hemosiderin-laden macrophages (arrows) are apparent in the organizing tissue surrounding the GDCs. b: Factor VIII–related antigen is positive for newly formed vessels (arrows) in the organizing thrombus. c: The aneurysm wall displays atherosclerosis. Arrowheads indicate the atheromatous core. Arrows show organizing thrombus of the lumen. Masson trichrome staining, original magnifications \( \times 400 \) (a); \( \times 100 \) (b); \( \times 40 \) (c).
vascular trapping together with endosaccular embolization— theoretically the best endovascular treatment— to prevent the establishment of blood flow between the parent artery and intrathrombotic vascular channels. The details in the present case highlight the unique problems in treating partially thrombosed giant aneurysms by using the endovascular method.

The most important finding in this study is the persistence of a greatly retarded blood flow in the VA, which apparently was completely occluded by the endovascular method. When oozing blood was noted from the cut lumen of the completely occluded VA, both the proximal VA and the PICA had already been clipped. Therefore, this intraoperative finding suggested that the transmural vascular connections through the well-developed vasa vasorum may play a critical role in the greatly retarded blood flow in a VA that apparently has been completely occluded by the endovascular method. In support of the view posited by Nagahiro et al., the histological findings in the present case showed the relatively low density of the vasa vasorum on the fundic side of the aneurysm, thus suggesting a major role of the transmural connection at the neck side in the recanalization of completely occluded thrombosed aneurysms. On Gd-enhanced T₁-weighted images, the location of persistent, marked enhancement after embolization at the aneurysm neck and the finding of an originally patent lumen coincided with intraoperative and histological findings. This suggests that Gd enhancement may be a useful tool to detect the density of the induced vascular network on the aneurysm wall after endovascular treatment.

The exact mechanisms underlying such a transmural vascular connection remain unknown. The accumulation of inflammatory cells was noted in the unorganized thrombus around the coils, indicating that the inflammatory process may induce neovascularization around the neck of the aneurysm. Therefore, the development of transmural vascular connections between the well-developed vasa vasorum and the unorganized thrombus around the coils at the neck of the aneurysm appears to be a key event in continuous aneurysm growth, probably due to recurrent minor hemorrhaging after endovascular treatment.

A rich adventitial neovascularization of the parent artery occluded by coils could provide potential routes of blood supply to the aneurysm neck from surrounding dural and leptomeningeal arteries. This is important because, theoretically, endovascular trapping, unlike surgical trapping, cannot block such blood flow to the aneurysm neck beyond the occluded arterial segment through vasa vasorum on the adventitia. Furthermore, histological findings indicated that microscopic intravascular neovascularization within the packed coils might be the potential source of recanalization to the thrombosed aneurysm. Therefore, it is important to understand the pathophysiological role of intracranial vasa vasorum in the treatment of partially thrombosed giant aneurysms.

Vasa vasorum are adventitial vessels and are considered to be essential for supplying nutrients and oxygen to adventitia and media and for removing metabolic waste from the outer vessel wall. Data from recent studies have shown that intracranial arteries do not have vasa vasorum except for the proximal segments of the intracranial internal CA and the VA piercing the dura. The vasa vasorum might derive from the leptomeningeal or dural vessels or simply represent an intracranial extension of the vasa vasorum complex in the extracranial segments of the internal CA and the VA. Authors of previous studies reported the absence of vasa vasorum in intracranial arteries in neonates and children as well as the increased density of vasa vasorum in proximal segments of atherosclerotic intracranial arteries. These findings may indicate that vasa vasorum in proximal segments of intracranial arteries in adults are acquired and reactive in nature. The presence of complex adventitial neovascularization in occluded CAs in children with sickle cell disease and in intracranial VA thrombosis indicates that vascular occlusion is a more potent stimulus—probably through arterial wall hypoxia—than atherosclerosis alone for inducing intra- or extravascular neovascularization. In the present case, the well-developed vasa vasorum were seen on the VA that had been occluded with coils, mainly on the neck of the aneurysm. Although the PICA was occluded without any clinical sequela after the patient passed the balloon test occlusion, hypoxia in the cerebellum of the PICA territory together with the thrombosed aneurysm may have induced neovascularization involving vasa vasorum of the occluded VA and the neck of the aneurysm.

Conclusions

The present difficult case clearly illustrates the pitfall of endovascular treatment for partially thrombosed giant VA aneurysms. The intraoperative findings at the aneurysmectomy suggested that adventitial neovascularization by the vasa vasorum on the VA occluded with coils may play a key role in the persistent enlargement of such aneurysms even after apparently complete endovascular occlusion. Surgical clip placement and aneurysmectomy should be considered for the relief of symptoms in such cases that are refractory to endovascular treatment.

References

Continued growth of a giant aneurysm after endovascular treatment


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