A Rare Case of Neurofibromatosis Type 1 Associated with Vertebral Arteriovenous Fistula and Moyamoya Syndrome

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Objective: We report a rare case of neurofibromatosis type 1 (NF-1) presenting with myelopathy due to the vertebral arteriovenous fistula (AVF), and major intracranial artery occlusions with moyamoya-like vessels.

Case Presentation: A 66-year-old woman of NF-1 suffered from neck pain, tetraparesis, and sensory disturbance of gradual onset. Cervical MRI showed a huge flow void, and the spinal cord was strongly compressed by the dilated vessels. Vertebral angiography revealed the AVF at the level of C4/5 fed by the left vertebral artery and drained into the dilated epidural spinal vein between C2 and C5 via the intervertebral veins. In addition, carotid angiography showed the occlusion of the right internal carotid artery and the left anterior cerebral artery associated with moyamoya-like vessels. She underwent endovascular treatment with careful attention to the intraoperative hypotension and the AVF was completely occluded. Her neurological symptoms were cured after the treatment.

Conclusion: We experienced a rare case of NF-1 coexisted with the vertebral AVF and moyamoya syndrome. In such a complicated condition, discreet attention for possible cerebral hypoperfusion during the perioperative period should be paid for the successful treatment.

Keywords ◄ arteriovenous fistula, endovascular treatment, moyamoya syndrome, neurofibromatosis type 1, vertebral artery

Introduction

Neurofibromatosis type 1 (NF-1) is an autosomal dominant inheritance disease with a dysplastic disorder of chromosome 17, and has ectodermal and mesodermal dysplasia such as café-au-lait spots or vascular abnormalities.1,2) A well-known craniocephalic vascular lesion associated with NF-1 is major intracranial artery occlusions with moyamoya-like vessels, so-called moyamoya syndrome.3–5) The prevalence of moyamoya syndrome in NF-1 patients is approximately estimated as 0.6%.6) On the other hand, arteriovenous fistulas (AVFs) in the vertebral artery are also occasionally involved.5–8) However, coexistence of both conditions in NF-1 patients is rare and only one case was previously reported.

Here, we present a case of NF-1 associated with moyamoya syndrome and vertebral AVF.

Case Presentation

A 66-year-old woman, previously diagnosed as NF-1 by café-au-lait spots and subcutaneous neurofibromas, was aware of the strong pain in the neck and left upper limb, and the pulsatile tinnitus for 9 months. The symptoms gradually worsened and she was referred to our clinical practice. Neurological examination revealed the left dominant paresthesia and motor weakness of both upper and lower limbs. She presented with spastic gait and vesicorectal disturbance. Plain cervical X-ray showed marked enlargement of the left intervertebral foramina from C2 to C5. CT scans of the cervical spine revealed a paravertebral enhanced lesion connecting with the spinal canal through the left intervertebral foramen mainly at the level of C4/5 (Fig. 1A). T2-weighted MRI showed a gigantic serpentine signal-void area at the
levels between the foramen magnum and C5 (Fig. 1B).

The spinal cord was strongly compressed dorsolaterally, but the intramedullary signal changes were unclear. The left vertebral angiography showed the direct arteriovenous (AV) shunt between the left vertebral artery and the vertebral venous plexus, which was draining into the intervertebral veins between C2 and C5 (Figs. 2A and 2B). The distal portion of the left vertebral artery was not revealed.

The right vertebral angiography showed the retrograde flow from the right vertebral artery to the AV shunts via left vertebral artery and no antegrade flow to the basilar artery (Fig. 2C). The right carotid angiography demonstrated occlusion of the right internal carotid artery with moyamoya-like vessels, but that the right posterior cerebral artery and basilar artery were supplied via the right posterior communicating artery. Blood flow of the right middle cerebral artery and anterior cerebral artery was supplied from the leptomeningeal anastomosis and moyamoya-like vessels (Fig. 2D). The left carotid angiography revealed occlusion of the left anterior cerebral artery with moyamoya-like vessels (Fig. 2E).

From these findings, she was diagnosed as NF-1 coexisted with the vertebral AVF and moyamoya syndrome (occlusion of the right internal carotid and the left anterior cerebral arteries with moyamoya-like vessels).

She underwent endovascular treatment for the left vertebral AVF and the shunt was occluded using detachable coils under general anesthesia. During the perioperative period, careful attention was paid for preventing cerebral hypoperfusion. A 6-French sheath was introduced into the right femoral artery, and a guiding catheter was placed into the left vertebral artery. Internal trapping of the parent artery was conducted at the AVF. A microcatheter was advanced distal to the fistula. Coiling of the fistulous segment was attempted with GDC-18 (Boston Scientific, Natick, MA, USA) and Detach-18 (Cook Medical, Bloomington, IN, USA). Endovascular coil embolization resulted in the successful obliteration of the vertebral AVF (Figs. 3A and 3B).

Post-embolization angiography demonstrated the complete occlusion of the AV shunt and the restoration of the normal antegrade flow to the basilar artery via the right vertebral artery (Fig. 3C), and the retrograde blood flow of the basilar artery from the right posterior communicating artery was also discontinued (Fig. 3D). Her neurological symptoms were significantly improved. Bypass surgery for the right middle and the left anterior cerebral arteries occlusion was not performed because of the absence of ischemic symptom. Follow-up MRI obtained at 4 months after the embolization showed the complete AV shunt occlusion.

## Discussion

### Vertebral AVF with NF-1

AVFs are abnormal communications of arteries and veins, and commonly caused by traumatic or iatrogenic etiologies. Spontaneous AVFs are less common and are related with vascular dysplastic conditions such as NF-1 or fibromuscular dysplasia. AVFs associated with NF-1 mostly occur in the vertebral arteries; in fact, 40 cases have been reported including the present case. The majority of the patients are females (67.5%). They commonly present with bruit over the neck (57.5%), myelopathy (22.5%), radiculopathy (25%), and radiculomyelopathy (25%), which might be induced by the spinal cord compression by the dilated draining veins, or the spinal cord ischemia by the steal phenomenon. Bruit and radiculomyelopathy due
to compression of the spinal cord and nerve roots by the enlarged draining veins were associated with the present case.

Two mechanisms of pathogenesis of the vertebral AVFs in NF-1 have been suggested.\(^1,9\) One is the primary occurrence as a congenital mesodermal dysplasia,\(^1\) and the other one is the rupture of an aneurysm, secondarily formed due to the vulnerability of the vertebral artery wall or the neurofibroma infiltrated into the vertebral artery wall, resulting in a fistula to the adjacent veins.\(^9\) The etiology of the present case is unknown; however, the congenital mesodermal dysplasia may be suspected because of the gradual onset of the symptoms although the age at onset was relatively high.

**Moyamoya syndrome in NF-1**

The prevalence rate of moyamoya syndrome in patients with NF-1, which is initially unilaterally and often involves
A Rare Case of Neurofibromatosis Type 1

Anterior vascular territories, is estimated as 0.6%, and more than 100 cases are reported in pediatric patients since 1976. Although there are increased risks for subsequent clinical and radiologic worsening, most cases are initially asymptomatic as shown in this present case. The initial symptoms are often ischemic events, such as transient ischemic attacks and completed ischemic strokes.

As regard the arterial occlusive lesions in NF-1, it has been suggested that the obliteration of the large-sized arteries is caused by the growth of the neurofibroma or ganglioneuroma in the tunica adventitia, and that of the small-sized arteries including cerebral arteries is caused by the proliferation of the smooth muscle cells. On the other hand, the gene abnormality in chromosome 17q25.2 has been reported in moyamoya disease, which is close to the NF-1 gene on chromosome 17q11.2. There are several reports concerning the association of moyamoya disease and NF-1, which could be explained by the close proximity of genes on chromosome 17.

The coexistence of vertebral AVF and moyamoya syndrome with NF-1

Only one case of NF-1 coexisted with vertebral AVFs and moyamoya syndrome has been reported until now. In this case, although the antegrade blood flow to the basilar artery via the left vertebral artery was not observed due to the vertebral AVF, all of the blood flow of the right vertebral artery was not stolen to the vertebral AVF and the antegrade blood flow to the basilar artery was preserved. Because the vertebral AVF was occluded with a detachable balloon with a preservation of the left vertebral artery, the antegrade blood flow to the basilar artery was restored. The myelopathy was completely relieved and no treatment was adapted to the asymptomatic occlusion of the right middle cerebral artery with moyamoya-like vessels.

In the present case, the antegrade blood flow to the basilar artery via the vertebral artery was not appeared because the blood flow of the bilateral vertebral arteries was stolen to the vertebral AVF. Subsequently, the retrograde flow via the right posterior communicating artery from the right internal carotid artery supplied the territory of the basilar artery. In addition, distal portion of the right internal carotid artery was occluded, and the leptomeningeal collateral flow via the right posterior communicating artery also compensated the territories of the right middle cerebral artery and the left anterior cerebral artery. Therefore, there might be a potential hypoperfusion in both territories although cerebral ischemic symptoms were not apparent. Furthermore, there might be a risk of cerebral aneurysms formation due to increase in hemodynamic stress to the
right posterior communicating artery. In the present case, the antegrade blood flow to the basilar artery via the right vertebral artery was restored after the treatment, and the retrograde blood flow to the basilar artery via the right posterior communicating artery was disappeared.

**Treatment of the vertebral AVFs or moyamoya syndrome with NF-1**

As for treatment of the vertebral AVFs, the direct surgery was formerly performed. Treatment has evolved considerably since 1990, and endovascular occlusion of fistulas is now the main option of the treatment. In the beginning of the endovascular era, detachable balloons were used as the material of the embolization. However, it cannot be used when a fistula site is not identified, or when there are multiple fistulas. In addition, although a shunt point embolization using the balloons or detachable coils via a transarterial or transvenous approach is useful in order to preserve the parent artery, the risk of the nerve root compression in the intervertebral foramen by the balloons or coils has also been pointed out. Recently, trapping of the parent artery using detachable coils has been adopted, and good results have been obtained with the relative simple technique. In addition, endovascular treatment with stent grafts for the vertebral AVFs with a large orifice has been reported. This method can maintain the patency of the parent artery although antiplatelet agents should be administered to prevent embolic events. In the present case, all blood flow of the left vertebral artery was drained through the AVF. In addition, the blood flow of the right vertebral artery was stolen partially by the AVF. Therefore, internal trapping of left vertebral artery was expected to terminate steal phenomenon of blood flow of the right vertebral artery, and to increase the blood flow to the basilar artery. We employed internal trapping for this case in consideration of a simplicity and a reliability. A balloon guiding catheter can control the blood flow of the parent artery and makes it easy to identify the shunt point and to prevent the coil migration to normal vessels. However, in this present case, because the AVF was clearly demonstrated by the angiography and coil migration would not happen because of steal phenomenon of the AVF, we used an usual guiding catheter.

On the other hand, for the treatment of moyamoya syndrome in NF-1, early diagnosis and appropriate surgical management are of utmost importance, which would improve the cerebral hemodynamics and reduce the incidence of subsequent ischemic events. However, close monitoring of these abnormalities is warranted because the long-term outcome is unknown. Further studies are needed, in large cohorts of NF-1 and moyamoya syndrome patients, for the understanding of the association between these conditions. In the present case, intraoperative anesthesia required scrupulous attention to cerebral circulation, since the AVF in the vertebral-basilar system should have a significant role in the collateral blood circulation of the internal carotid artery occlusion. The treatment of vertebral AVF was likely to contribute to the improvement of the cerebral hypoperfusion. Moyamoya syndrome was not treated surgically because any ischemic symptoms were not observed; however, the strict follow-up including the examination of the cerebral blood flow is required.

**Conclusion**

We experienced a rare case with NF-1 coexisted with the vertebral AVF and the occlusions of major intracranial arteries with moyamoya-like vessels. The vertebral AVF was treated with the endovascular coil embolization with careful attention of intraoperative hypoperfusion, and the compressive myelopathy was significantly improved postoperatively.

**Disclosure Statement**

The authors declare that they have no conflict of interest.

**References**


