Giant fusiform aneurysm in an adolescent with PHACES syndrome treated with a high-flow external carotid artery–M$_3$ bypass

Case report and review of the literature

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✓The acronym PHACES describes a rare neurocutaneous syndrome that comprises posterior fossa malformations, facial hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, eye abnormalities, and sternal defects. Facial hemangiomas constitute the hallmark of this disorder. Giant intracranial aneurysms have not been previously reported in the literature as manifestations of PHACES syndrome and can present difficult therapeutic challenges. The authors describe a unique case of a 13-year-old adolescent boy with an incomplete phenotypic expression of PHACES syndrome who harbored diffuse cerebral angiodysplasia and a giant fusiform internal carotid artery (ICA) aneurysm extending from the distal cavernous segment to the supraclinoid segment. The aneurysm was successfully treated with a high-flow saphenous vein graft bypass from the external carotid artery to the distal middle cerebral artery followed by proximal ICA occlusion. This case represents a unique vascular manifestation of PHACES syndrome that required a complex management strategy. The authors review the literature on this rare disorder and emphasize the importance of considering the diagnosis of PHACES syndrome in child with a facial hemangioma.

KEY WORDS • cerebral revascularization • giant aneurysm • PHACES syndrome • high-flow bypass • pediatric neurosurgery

THE PHACES syndrome, which is characterized by posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, eye abnormalities, and sternal and supraabdominal raphe defects, is a rare pediatric congenital neurocutaneous syndrome, with facial hemangioma being the hallmark of the disorder.[1] The potential arterial anomalies include intracranial arterial dolichoectasia, arterial stenoses, and arterial agenesis, which can result in pediatric strokes or even a moyamoya-like syndrome.[4,21] To our knowledge, however, concomitant intracranial arterial dysplasia and giant aneurysms have not been reported in patients with PHACES syndrome.

In this article, we report a unique case of an adolescent boy with an incomplete phenotypic expression of PHACES syndrome who also harbored right hemispheric arterial dysplasia and a giant fusiform ICA aneurysm ipsilateral to the side of the facial hemangioma. The patient was successfully treated with a high-flow interpositional SVG bypass from

the ECA to the M$_3$ segment, followed by proximal ICA occlusion that resulted in flow reversal and subsequent thrombosis of the giant aneurysm.

Case Report

History and Presentation. This 13-year-old adolescent boy was referred to our neurosurgery clinic with a giant aneurysm, which had been detected on a CT scan obtained as part of the workup for headache and a facial hemangioma located on his forehead (Fig. 1). The patient and his parents reported that he had had a right forehead hemangioma since birth that did not regress. The rest of his medical history was noncontributory, and he denied any past neurological, cardiac, vascular, ophthalmological, or musculoskeletal disorder. Of note was a family history of lethal subarachnoid hemorrhage in a paternal aunt and a treated unruptured aneurysm in a paternal uncle.

Physical Examination. On examination, the patient had a large (5 × 4 cm), nontender hemangioma extending from his hairline down to his right forehead (Fig. 1). He was normocephalic, and no cranial or orbital bruit was noted. The results of his neurological and general examinations were otherwise unremarkable.

FIG. 1. Photograph of patient demonstrating facial hemangioma on the right forehead (*arrow*).

Neuroimaging. Contrast-enhanced CT scans demonstrated a giant ICA aneurysm with extensive osseous remodeling at the skull base and erosion into the sphenoid sinus (Fig. 2A). There were also significantly large vessels in the right sylvian fissure, an enhancing tuft of abnormal vessels in the right basal ganglia, and some midline shift (Fig. 2B and C).

Cerebral angiograms (Fig. 3) revealed a giant fusiform aneurysm of the right ICA, extending from the distal cavernous carotid segment to the supraclinoid segment of the ICA and measuring 15 × 25 mm. The right ophthalmic artery was originating from this aneurysmal dilation. There was significant dilation of the distal supraclinoid ICA, the A_1 segment (which was duplicated and tortuous), the M_1 segment, and both major divisions of the M_2 segments. There was also marked dilation of the right angular artery extending to the vertex, with dilated distal cortical branches. A myriad of small vessels with exaggerated parenchymal blush was present in the right posterior parietal lobe, the perisylvian region, and the right basal ganglia, consistent with diffuse angiodysplasia and proliferative angiopathy. No arteriovenous shunting was present. The right middle

meningeal artery and the right superficial temporal artery were supplying the scalp hemangioma. The left ICA and posterior circulations were within normal limits.

An accentuated vascular blush in the right orbit that was consistent with an orbital hemangioma was observed.

Surgical Decision Making. An incomplete phenotypic expression of PHACES syndrome was diagnosed on the basis of the coexistence of the facial hemangioma, orbital hemangioma, diffuse angiodysplasia of the intracranial vessels, and giant aneurysm. Given the risk of potential hemorrhage from a giant aneurysm in a young patient and the projection of the aneurysm into the sphenoid sinus and considering the strong family history of aneurysm, we recommended surgical treatment. We decided against merely packing the sphenoid sinus to prevent catastrophic rupture into the sphenoid, because the giant aneurysm involved the more distal carotid artery extending to the subarachnoid space as well. After review by our multidisciplinary neurovascular team, we believed that this giant fusiform aneurysm was not amenable to either microsurgical clipping or endovascular treatment. The patient underwent a balloon test occlusion of the right ICA and tolerated 30 minutes of occlusion. We therefore planned a Hunterian strategy to treat this aneurysm with proximal occlusion of the ICA. Although the results of the balloon test occlusion were negative, we planned for revascularization with an ECA-SVG-M_2 high-flow bypass to preserve the patient's cerebrovascular reserve because of his young age, the presence of angiodysplasia, and the risk of his developing more aneurysms in his lifetime if a large-caliber artery were to be sacrificed.

Operation. An ECA-SVG-MCA bypass was performed using the submandibular–infratemporal route (Fig. 4). The fine details of this procedure have been recently described by the senior author (W.T.C.).[6] Aspirin (two 325-mg tablets) was administered orally both in the evening and the morning before surgery. Intraoperative monitoring was performed using electroencephalography, somatosensory evoked potentials, and motor evoked potentials. The ECA was exposed in the neck and a recipient MCA vessel was isolated through a frontotemporal transsylvian exposure (Fig. 4). The branches of the MCA vessels appeared dilated, tortuous, and abnormal.
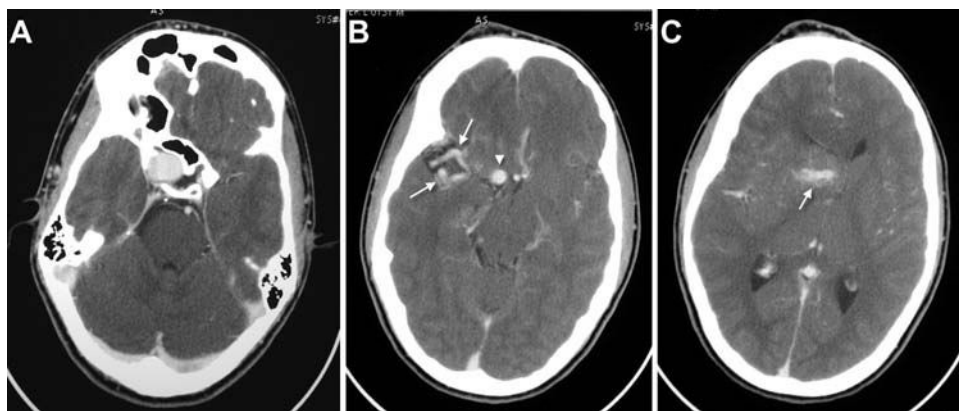

FIG. 2. Contrast-enhanced CT scans demonstrating a giant ICA aneurysm with extensive osseous remodeling at the skull base and erosion into the sphenoid sinus (A). The terminal segment of the supraclinoid ICA is markedly dilated (*arrowhead* in B). There are significantly large vessels in the right sylvian fissure (*arrows* in B) and an enhancing tuft of abnormal vessels in the right basal ganglia (*arrow* in C).
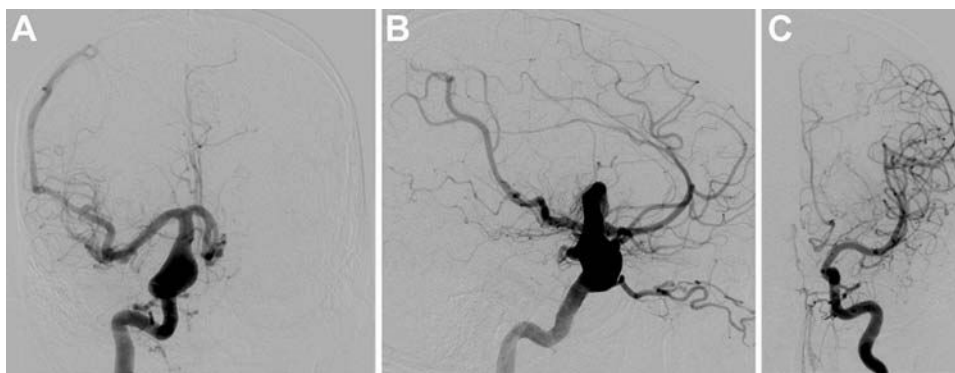
FIG. 3. Cerebral angiograms (right ICA injection, anteroposterior view [A]; right ICA injection, lateral view [B]; left ICA injection, anteroposterior view [C]) showing a giant fusiform aneurysm of the right ICA, extending from the distal cavernous carotid segment to the supraclinoid segment of the ICA. The right ophthalmic artery originates from this aneurysmal dilation. There is diffuse angiodysplasia in the right cerebral hemisphere, with significant dilation of the distal supraclinoid ICA, the A_1 segment, and the MCA and its distal cortical branches. The left ICA circulation (C) appears normal without any angiodysplasia.

After 5000 U of intravenous heparin was administered, the SVG was anastomosed to the ECA in an end-to-end fashion with interrupted 7-0 Prolene sutures (Fig. 4). The distal end of the SVG was then tunneled underneath the mandible and brought into the intracranial cavity through a bur hole created at the middle fossa skull base (the submandibular–infratemporal route) using a 14-F chest tube.

Electroencephalographic burst suppression was induced and maintained under hypothermic conditions for the distal anastomosis. We initially isolated an M_2 branch as the recipient vessel; however, the vessel was quite dysplastic. A more distal segment on the M_3 branch was identified and used as the recipient vessel. The distal end of the SVG was anastomosed to the M_3 branch in an end-to-side fashion with interrupted 9-0 nylon sutures (Fig. 4). An intraoperative micro-Doppler ultrasound examination of the bypass graft showed excellent flow and patency. Care was taken during dural closure and bone flap replacement to avoid compromising or kinking the bypass graft.

Postoperative Course and Proximal ICA Occlusion. The patient tolerated the procedure well and postoperative neurological examination revealed no deficits. Daily oral aspirin therapy was continued and strict blood pressure control (systolic range 100–120 mmHg) was maintained in the immediate perioperative period. Postoperative angiograms demonstrated patency of the bypass graft at both the proximal and distal ends (Fig. 5A). The right ICA just distal to the cervical carotid bifurcation was occluded with endovascular coil embolization. The patient tolerated proximal occlusion of the ICA without any neurological or visual deficits. The postocclusion angiogram demonstrated occlusion of the right ICA with thrombosis of the aneurysm (Fig. 5B). The MCA territory was supplied by the bypass graft with minimal retrograde flow to the terminal segment of the supraclinoid ICA. Although there was no filling of the right ophthalmic artery, there was collateral supply from the left ICA to the choroid of the right eye (Fig. 5C and D). The remainder of the patient's hospital course was uneventful, and he was discharged on postoperative Day 5 and instructed to continue the oral aspirin therapy regimen. A follow-up angiogram obtained 6 months after surgery revealed excellent patency of the SVG and complete thrombosis of the aneurysm. The patient remained neurologically intact with normal visual acuity (20/20) and full visual fields of his right eye at 1 year after surgery, with CT angiography showing no change in his arteriopathy.

Discussion

Hemangiomas are the most common benign tumors of infancy, occurring in up to 10% of infants.[2] They are rarely associated with other systemic abnormalities, and most of them regress spontaneously, with 98% resolving completely before the child reaches 9 years of age.[21] The association of facial hemangiomas with vascular and intracranial malformations was first described by Pascual-Castroviejo in 1978.[14] In 1996, Frieden et al.[8] proposed the acronym PHACE for a neurocutaneous syndrome characterized by posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and abnormalities of the eye. Posterior fossa malformations and arterial anomalies are the most common manifestations (occurring in 74 and 41% of cases, respectively).[1] The term has since been lengthened to PHACES to include midline sternal and ventral defects, which may be present in a minority of patients.[5,8]

The PHACES syndrome is a rare congenital anomaly, and its pattern of inheritance has not yet been established. The neural crest cells have been implicated as a common link to the pathogenesis of the different manifestations of the syndrome, including arterial anomalies, coarctation of the aorta, and cardiac and sternal defects.[22] The female predominance of 9:1 is especially striking.[2] Although in most cases (as in our patient) the phenotypic expression of the syndrome is incomplete, the facial hemangioma is the unifying feature that is present in all cases.[4,8,14,16,21] Unlike that of Sturge–Weber syndrome, the facial hemangioma associated with PHACES is typically a reddish, plaque-like lesion lying on one side of the midline, with no strict dermatomal distribution.[8] Because the expression of this syndrome is usually incomplete, careful ophthalmologic, neurological, cardiac, and sternal examinations along with neuroimaging (MR imaging and MR angiography) and echocardiography should be performed in children who have extensive, unilateral, plaque-like hemangiomas of the head and neck.
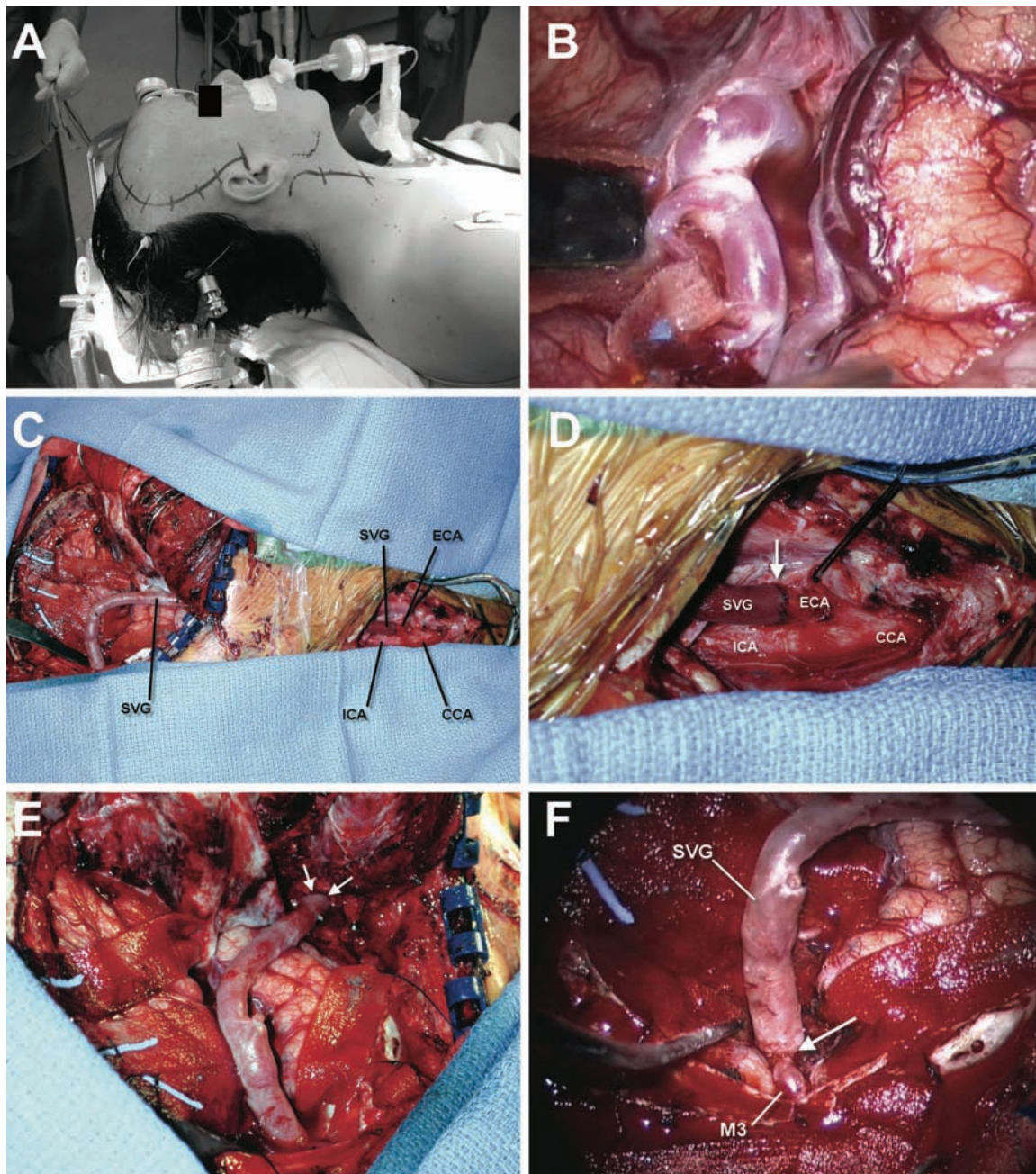
FIG. 4. Intraoperative photographs of ECA-SVG-M$_3$ bypass. A: Skin incisions for the frontotemporal craniotomy and cervical carotid exposure. B: The right M$_2$ segment has been exposed in the sylvian fissure and appears tortuous and dysplastic; it was unsuitable for bypass. A more distal M$_3$ branch was used as the recipient vessel. C: The SVG is shown anastomosed to the ECA proximally in the neck and to the M$_3$ distally in the head. D: The ECA is anastomosed to the SVG in an end-to-end fashion *(arrow)*. E: The SVG is tunneled underneath the mandible through the infratemporal fossa and brought into the intracranial space through a bur hole in the middle fossa *(arrows)*. F: The SVG is anastomosed to the M$_3$ segment in an end-to-side fashion *(arrow)*. CCA = common carotid artery.

Posterior fossa malformations associated with PHACES include Dandy–Walker malformation, cerebellar hemisphere hypoplasia (usually ipsilateral to the facial hemangioma), hypoplasia of the inferior vermis, and cerebellar cortical dysgenesis.[4,5,8,9,14,15] Abnormalities of the craniocervical vasculature are thought to be related to the excess of angiogenic factors such as basic fibroblast growth factor and vascular endothelial growth factor associated with proliferative cuta-

neous hemangiomas,[3] and they can be divided into two main subsets as follows: persistent embryonic arteries or arterial agenesis.[14] The most common persistent primitive artery is the trigeminal artery,[14] but cases involving persistent hypoglossal, proatlantal, or stapedial arteries have also been described.[1] The frequency of persistent primitive trigeminal artery has led some authors to believe that the putative insult occurs between 3.5 and 5.5 weeks' gestation, a period in
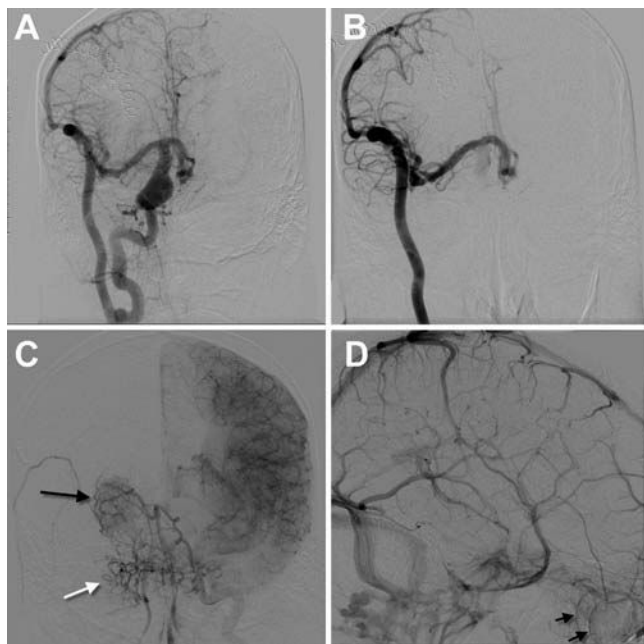
Fig. 5. A: Angiogram (right CCA injection, anteroposterior view) showing patent bypass graft and filling of the fusiform aneurysm. B: Right CCA postembolization angiogram (anteroposterior view) showing occlusion of the right ICA with thrombosis of the fusiform aneurysm. The middle carotid artery territory is supplied by the SVG bypass and there is minimal retrograde flow to the terminal segment of the supraclinoid ICA. The ophthalmic artery no longer fills, but the right eye is now supplied by collateral vessels from the left ICA circulation (see C and D). C: Left ICA angiogram (anteroposterior view) showing collateral blood supply to the right eye *(white arrow)* and also blood supply to the hemangioma on the right scalp *(black arrow)*. D: The venous phase of the left ICA injection (lateral view) shows the choroidal blush of both retinas *(black arrows)*.

which the trigeminal artery and other vasculature structures form and involute.[16] Arterial agenesis usually involves major arteries such as the ICAs and the vertebral arteries.[14] Segmental agenesis of the ICA and concomitant bilateral ICA agenesis and vertebrobasilar system agenesis have been reported.[12] Recently, intracranial arterial stenosis[4] and dolichoectasia (either focal or diffuse)[1] have been described as further arterial abnormalities of PHACES syndrome. We report the first case of a giant fusiform aneurysm associated with PHACES syndrome.

Revascularization techniques are important in the management of pediatric cases of ischemic brain disease, such as moyamoya or moyamoya-like syndromes. Revascularization procedures for vascular diseases other than moyamoya disease are performed very rarely in children but represent important strategies in the surgical treatment of skull base tumors and complex aneurysms that require parent vessel (for example, ICA) occlusion. In such cases, the ICA is often reconstructed or bypassed with the use of an interpositional SVG to ensure adequate cerebral blood supply. The goal of such high-flow revascularization is either to restore adequate flow in a patient with insufficient cerebrovascular reserve or to preserve cerebrovascular reserve and avoid excess hemodynamic stress on the remaining cerebrovasculature in a young patient with a long life expectan-

cy, as in our case. Moreover, preoperative balloon test occlusion is often unreliable or unfeasible in children, with authors reporting rates of false-negative results as high as 22%, resulting in ischemic complications after acute ICA sacrifice.[11,13,19] Consequently, some authors recommend a universal approach to revascularization to avoid an ischemic stroke whenever the ICA is sacrificed, although this recommendation remains controversial.[10,18]

Various high-flow bypass strategies using SVG reconstruction, among them cervical ECA–supraclinoid ICA and cervical ECA–M_2 bypass, have been described. In the present case, the more distal M_3 was the recipient because the more proximal M_2 was dysplastic and unsuitable for bypass. Fortunately, the M_3 in this case had a larger diameter and could serve as a suitable recipient vessel. The submandibular–infratemporal route of the graft permits a more direct routing of the bypass graft to the recipient vessel, thereby shortening the graft length and promoting patency.[6,7] Unlike the preauricular and postauricular subcutaneous tunneling techniques,[17,18,20] submandibular placement of the graft provides physical protection of the graft under the mandible and obviates a zygomatic osteotomy, thus preserving normal facial anatomy.[6]

Conclusions

The PHACES syndrome is a rare congenital neurocutaneous disorder that often manifests with incomplete phenotypic expression. Given its frequent association with posterior fossa malformations and intracranial vasculature anomalies, screening MR imaging and MR angiography should be performed in cases in which other characteristic symptoms are present or suspected. Rarely, the intracranial anomalies can manifest as aneurysms.

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