De Novo Cerebral Aneurysms Manifesting as Repeated Subarachnoid Hemorrhage and Cerebral Ischemic Stroke
—Case Report—

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Abstract
A 29-year-old man suffered repeated subarachnoid hemorrhage and cerebral ischemic stroke over a period of 6 years. Cerebral angiography at each episode disclosed development of multiple de novo aneurysms at the bilateral middle cerebral arteries (MCAs), internal carotid arteries, right anterior cerebral artery, and right vertebral artery. Two of the ruptured aneurysms were treated by surgical and endovascular treatment, but he died of the effects of rupture of a de novo right MCA aneurysm. Histological examination at autopsy disclosed marked degenerative changes in all layers of the cerebral vessels, which were probably congenital in origin.

Key words: de novo aneurysm, subarachnoid hemorrhage, cerebral ischemic stroke, hypertrophy of intima, neuroradiological follow up

Introduction
De novo aneurysm is a newly formed aneurysm developing from a cerebral artery which previously appeared normal on angiography.5) The de novo aneurysm is comparatively rare and the annual incidence is 0.89–1.8%.3,18,19) The interval between the first angiography and occurrence is 3 to 20 years.17) We treated a patient who presented with multiple de novo aneurysms located on almost all of the cerebral arteries associated with repeated subarachnoid hemorrhage (SAH) and cerebral ischemic stroke.

Case Report
A 29-year-old man with no past and familial history suffered SAH due to rupture of a left middle cerebral artery (MCA) aneurysm on April 19, 1994 (Fig. 1 left). He developed vasospasm after clipping of the aneurysm (Fig. 1 right), but returned to normal social life after 1 month.

He presented with right hemiparesis, right cerebellar ataxia, and right sensory disturbance on July 5, 1997. Computed tomography (CT) detected no newly developed lesions. Cerebral angiography showed narrowing of the bilateral vertebral arteries (VAs) and basilar artery, and multiple aneurysms of the left MCA and internal carotid artery (ICA) (Fig. 2). He was treated medically.

He suffered sudden onset of headache and was transferred to our hospital on April 13, 1998. CT showed SAH, and cerebral angiography revealed a de novo left posterior communicating artery

Fig. 1 Oblique left carotid angiogram (left) showing the ruptured aneurysm in the M2 portion (arrow). Postoperative left carotid angiogram (right) demonstrating complete clipping of the aneurysm.
Fig. 2 Follow-up lateral left carotid angiogram (left) revealing multiple de novo aneurysms of the left middle cerebral artery and internal carotid artery. Lateral left vertebral angiogram (right) showing irregular narrowing of the vertebral and basilar arteries.

Fig. 3 Lateral left carotid angiogram (left) showing a de novo left posterior communicating artery aneurysm. Postoperative lateral left carotid angiogram (right) revealing Guglielmi detachable coils in the posterior communicating artery aneurysm.

Fig. 4 Follow-up anteroposterior (upper left) and lateral (upper right) right carotid angiograms demonstrating several aneurysms (arrows) of the middle cerebral artery and anterior cerebral artery. Anteroposterior (lower left) and lateral (lower right) left carotid angiograms revealing multiple aneurysms on both branching and non-branching locations of the middle cerebral artery and internal carotid artery.

aneurysm (Fig. 3 left). The aneurysm was considered to have ruptured based on the CT findings, and was treated with Guglielmi detachable coils (GDCs) (Fig. 3 right). He underwent ventriculoperitoneal shunt for hydrocephalus, and was discharged without neurological deficit.

He suffered repeated transient ischemic attacks about every 3 months from August 1999 to June 2000, manifesting as diplopia, right ptosis, right facial nerve paresis, and right hemiparesis. CT and cerebral angiography at each event revealed no remarkable changes.

Follow-up angiography showed development of de novo aneurysms of the right anterior cerebral artery (ACA) and right MCA on August 8, 2000 (Fig. 4). He suffered sudden onset of headache and CT showed third SAH on August 29, 2000. He was treated conservatively because cerebral angiography could not identify the ruptured aneurysm responsible for the SAH. He suddenly became comatose on September 12, and CT revealed massive right frontal intracerebral hemorrhage. He died on September 13 of progressive brain damage.

Autopsy examination found that the left MCA and ICA branches were irregularly dilated, with multiple saccular and fusiform aneurysms on both branching and non-branching locations of the bilateral MCAs, bilateral ICAs, right ACA, and right VA-posterior inferior cerebellar artery (Fig. 5A).

Histological examination found that the lumens of almost all vessels were partially narrowed by hypertrophy of the arterial intima. In particular, the thickened intima contained laminar structures. The arterial media contained fewer smooth muscle cells and increased fibrosis in almost all vessels. The walls between the aneurysms and the parent arteries...
Fig. 5  A: Autopsy photograph showing multiple saccular and fusiform aneurysms in the areas of the bilateral middle cerebral arteries (MCAs) and internal carotid arteries, right anterior cerebral artery (ACA), and right vertebral artery (VA)-posterior inferior cerebellar artery. Guglielmi detachable coils (arrow) are seen at the left internal carotid artery-posterior communicating artery and a clip (arrowhead) at the left MCA. BA: basilar artery.  B–D: Photomicrographs of cerebral artery sections taken at autopsy showing (B) intimal hypertrophy (I) and medial fibrogenesis (M) in the internal carotid artery (elastica van Gieson stain, × 40), (C) laceration of the elastic lamina (arrow), thinning of medial smooth muscle cells with fibroplasia (M), and invasion of monocytes in the right MCA aneurysm (elastica van Gieson stain, × 40), and (D) hematoma (H) and laceration of the vessel wall (arrow) at the rupture point of the right MCA (elastica van Gieson stain, × 200).

contained defects of the elastic lamina and arterial media with fibroplasia. Almost all aneurysm walls consisted of fibrous tissue, with a small number of monocyte invading the aneurysm wall, but no necrosis or organization of the wall was identified (Fig. 5B–D).

Discussion

Our patient presented with repeated development of de novo saccular and fusiform aneurysms on nearly all the cerebral vessels, manifesting as repeated SAH and cerebral ischemic stroke, in contrast to previous cases of de novo aneurysms which usually presented as a small number of saccular aneurysms.3,18,19) The normal structure of cerebral artery is different from other artery. Cerebral artery manifests thin arterial media, lack of external elastic lamina, and insufficient adventia.4,20) For these reasons, arterial media and internal elastic lamina play a key role in protecting cerebral artery from blood pressure.4,20)

Mural degeneration of the vessel is the predisposition for the development of a saccular aneurysm with subsequent growth due to distention of the vessel wall lacking an appropriate internal elastic lamina.17) De novo aneurysms are formed by similar mechanisms to other aneurysms. The risk factors for de novo aneurysms include congenital factors such as a medial defect and destruction of the elastic lamina, and acquired factors such as change in
hemodynamic stress, hypertension, smoking, and atherosclerosis. The present case had both saccular and fusiform aneurysms on the vessels of the circle of Willis and peripheral vessels. This unusual manifestation of multiple aneurysms suggests congenital degeneration of cerebral vessels. Variations in congenital connective tissue disorders including autosomal dominant polycystic kidney disease, Ehlers-Danlos type IV syndrome, and von Recklinghausen’s neurofibromatosis type I are associated with cerebral aneurysms. Alpha-1-antitrypsin deficiency and type 3 collagen deficiency may be associated with the pathogenesis of cerebral aneurysms. In our case, none of these diseases were present. However, fibromuscular dysplasia (FMD) could not be excluded because of the unusual aneurysms located in both the branching and non-branching sites. FMD is usually associated with disruption of the medial smooth muscle layer and fibrous proliferation, but the present case showed changes in the intimal rather than the medial wall. Recently, intimal wall damage was reported in FMD, suggesting that the present case was related to FMD.

The ischemic symptoms in our patient were probably due to the partial narrowing of the lumen of almost all vessels due to hypertrophy of arterial intima. Distal migration of thrombus from the aneurysms is another possible mechanism for the ischemic symptoms. Hypertrophy of the cerebral arterial wall may have prevented early rupture of the aneurysms.

Surgical treatment for de novo aneurysm is not curative because of recurrence and rupture in the same or another of the cerebral arteries. Treatment with GDCs can obliterate multiple aneurysms in both the anterior and posterior circulation less invasively in one session even in the acute phase of hemorrhage, which is potentially useful for de novo aneurysms. In our case, surgical or endovascular treatment for all of the aneurysms was impossible because of the high invasiveness of the required surgical approach and the unsuitability of GDCs for wide neck fusiform aneurysms.

Regular neuroradiological follow up is essential for younger patients with cerebral aneurysm considering the high risk of de novo aneurysm.

References
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