Long-term hemodynamic changes in cerebral proliferative angiopathy presenting with intracranial hemorrhage: illustrative case

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BACKGROUND Cerebral proliferative angiopathy (CPA) is a rare vascular proliferative disease; however, long-term follow-up reports are scarce. The authors report a rare case and document a patient’s medical history over 20 years.

OBSERVATIONS A 5-year-old girl developed left frontal lobe hemorrhage, presenting with headache. At 8 years of age, angiography showed diffuse capillary ectasia without an arteriovenous shunt. Single-photon emission computed tomography (SPECT) showed normal cerebral blood flow (CBF).

She had normal growth without systemic disease. At 25 years of age, an intraventricular hemorrhage occurred, presenting with sudden headache. Angiography revealed vascular lesion enlargement, increased feeding arteries, dural supply to the nidus and peri-nidal lesion, and flow-related aneurysm. SPECT showed remarkable decreases in CBF in the nidus and peri-nidal lesion. Cerebral proliferative angiopathy (CPA) was diagnosed, and the aneurysm arising at the lateral posterior choroidal artery caused the hemorrhage. Coil embolization of the aneurysm was performed with a flow-guide catheter and extremely soft platinum coils. New aneurysms were not noted 1.5 years after the procedure.

LESSONS This is the first report to demonstrate hemodynamic changes in CPA on angiography and SPECT over 17 years. The development of endovascular devices has enabled the embolization of ruptured aneurysms at the peripheral cerebral artery.

https://thejns.org/doi/abs/10.3171/CASE22437

KEYWORDS proliferative angiopathy; flow-related aneurysm; endovascular treatment; coil embolization

Cerebral proliferative angiopathy (CPA) is a rare cerebral vascular malformation that differs from the classic arteriovenous malformation (AVM) in that patients present with headache, epilepsy, intracranial hemorrhage (ICH), and cerebral ischemia. CPA has a proliferative character and gradually enlarges with intermingling brain tissues, hemodynamically impairs the lesion’s area, and induces adjacent brain lesions. However, reports of long-term follow-up of CPA are scarce. Cerebral blood supply in the ischemic lesions develops naturally from the perforator and dural arteries to the ischemic lesions, and flow-related aneurysms can arise due to vessel wall vulnerability, which carries the risk of rupture leading to ICH.

The treatment of flow-related aneurysms with CPA is complicated because it is located in the distal thin artery and supplies peripheral ischemic lesions. Endovascular glue embolization has been performed; however, this may cause peripheral cerebral ischemia leading to serious neurological deficits if eloquent cerebral areas are supplied. Bypass surgery from the external carotid artery systems or calvarial burr hole surgery can restore peripheral blood flow and reduce perfusion pressure on the collateral arteries; however, the dural and leptomeningeal collateral flows may complicate them.

The recent development of endovascular devices such as flow-guide microcatheters and extremely soft platinum coils has enabled aneurysmal embolization at the distal elongated lesion. We experienced a case of CPA with lobar hemorrhage at the frontal lobe in a 5-year-old girl, with a second hemorrhage occurring 20 years after the initial hemorrhage. Rupture of the newly arisen, flow-related aneurysm of the lateral posterior choroidal artery was the cause of ICH; therefore, the aneurysm was treated with coil embolization guided by a flow-guide microcatheter. We report this rare case and

ABBREVIATIONS ACA = anterior cerebral artery; AED = antiepileptic drug; AV = arteriovenous; AVM = arteriovenous malformation; CBF = cerebral blood flow; CPA = cerebral proliferative angiopathy; EDAS = encephalo-duro-arterio-synangiosis; ICH = intracranial hemorrhage; IVH = intraventricular hemorrhage; MCA = middle cerebral artery; MMA = meningeal artery; MR = magnetic resonance; PCA = posterior cerebral artery; SPECT = single-photon emission computed tomography.

INCLUDE WHEN CITING Published April 17, 2023; DOI: 10.3171/CASE22437.


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document her medical history over 20 years. The hemodynamic changes of CPA and treatment of flow-related aneurysms are discussed.

Illustrative Case

History and Presentation

In 2000, a 5-year-old girl with normal growth experienced the sudden onset of headache. Lobar hemorrhage in the left frontal lobe was diagnosed and treated with conservative therapy. Magnetic resonance (MR) imaging 3 months after the initial event revealed a diffuse nidal lesion in the left frontal lobe and scarring from the previous hemorrhage (Fig. 1A). Systemic convulsions continued, and oral antiepileptic drugs (AEDs) were administered, which controlled the seizures, and she grew with no neurological deficits.

A detailed examination, including single-photon emission computed tomography (SPECT), and angiography were performed when the patient was 8 years of age. Technetium-99m–labeled ethylcysteinate dimer–SPECT revealed normal cerebral blood flow (CBF) in the vascular and surrounding brain lesions (Fig. 1B). Angiography revealed diffuse vascular ectasia, which was mainly fed by the left anterior cerebral artery (ACA) and slightly by the left middle cerebral artery (MCA), but not provided by the posterior cerebral artery (PCA) (Fig. 1C–F). It persisted into the late arterial and early venous phase without arteriovenous (AV) shunt. Transdural supply into the capillary ectasias was not observed. Stenosis of the proximal arteries (bilateral internal carotid arteries, MCA, and ACA) was not observed. At that time, AVM was considered. The patient continued to have seizures, and AEDs were continued. She grew up with no neurological deficits and without systemic disease.

Serial MR imaging over time revealed gradual enlargement of the lesion (Fig. 2A–C). At the age of 24 years, MR angiography revealed a dilated left lateral posterior choroidal artery, which had no aneurysms (Fig. 2D).

At 25 years of age, she had a sudden headache and subsequent disturbance of consciousness, and she was transported to our hospital. She was in a somnolent state with no motor paresis. Plain computed tomography revealed an intraventricular hemorrhage (IVH) with a high-density spot at the posterior horn of the left lateral ventricle (Fig. 3A). MR angiography revealed an aneurysm of the left lateral posterior choroidal artery (Fig. 3B). Her level of consciousness improved with conservative therapy. Angiography 8 days after the second hemorrhage revealed enlarged diffuse capillary ectasias in the left frontal and parietal lobes fed by branching arteries of the left ACA and MCA, many perforator arteries, and dural arteries with no AV shunt. Perforator arteries had developed, and a saccular aneurysm had arisen from the left lateral posterior choroidal artery. The A1 and M1 feeding arteries were narrowed, and conversely, the peripheral branches of the ACA and MCA were enlarged. Transdural supply of the left middle meningeal artery (MMA) convexity branches, bilateral falcine arteries, and left ophthalmic artery appeared (Fig. 4). N-isopropyl-p-(123I) iodoamphetamine–SPECT at rest 18 days after the event showed remarkably decreased CBF in the left frontal and parietal lobes and a peri-lesion zone (Fig. 3C). The findings of angiography and SPECT diagnosed CPA. Flow-related aneurysm arose from the lateral posterior choroidal artery located at left lateral portion.

![Figure 1](image-url)
of the lateral ventricle. Therefore, the aneurysm was considered to be the cause of IVH. Recurrent hemorrhage was predicted from the aneurysm and endovascular treatment was planned. The patient's level of consciousness improved entirely with conservative therapy with no neurological deficits. Ventricle dilatation was not seen on follow-up imaging.

**Endovascular Treatment**

Forty-one days after the IVH event, endovascular coil embolization was performed. Preprocedural angiography showed a saccular aneurysm with a maximum diameter of 6 mm at the left lateral posterior choroidal artery (Fig. 5A and B). A 7-Fr guiding catheter was navigated to the left vertebral artery. A supercompliant 4- to 7-mm Shouryu balloon catheter (Kaneka Medics) and a Marathon flow-guide microcatheter (ev3, Inc.) were navigated from the guiding catheter. The Shouryu balloon was navigated to the main trunk of the left PCA, and the Marathon microcatheter was navigated to the aneurysm of the lateral posterior choroidal artery using a Tenrou 10 microcatheter (Kaneka Medics; Fig. 5C). An i-ED (0.010-inch) silky soft 3- to 6-cm coil (Kaneka Medics) was used as a framing coil, and a total of 6 i-ED coils (0.010-inch) with a total length of 15 cm were used to embolize the aneurysm, resulting in neck remnant obliteration (Fig. 5D and E). No intraprocedural complications occurred. The patient showed good recovery with no neurological deficits. An MR angiography 1.5 years after the procedure revealed no aneurysm recurrence (Fig. 5F). She has had no neurological deficits for 2 years and oral AEDs have been continued.

**Discussion**

CPA is a rare vascular malformation that differs from the classic brain AVMs. In 2008, Lasjaunias et al. proposed the concept of CPA, which differed from AVM in terms of unique characteristics, including response to peri-nidal oligomia and chromic cerebral ischemia, and reported that CPA accounts for 3.4% of brain AVMs. They presented its clinical course, imaging, and pathological descriptions in detail; and CPA presenting with ICH had a high recurrence rate of 67%. From then, a small number of cases have been reported. However, the natural history and therapeutic strategy for CPA have not yet been established.

CPA is discerned from classic AVM by its characteristic imaging features. The angiographic characteristics of CPA are proximal stenosis, absence of flow-related aneurysm, transdural arterial supply, puddling of contrast in the late arterial and early venous phase, poorly circumscribed nidus, peri-nidal angiogenesis, and a large area of arteriovenous shunting, but no early venous phase. In the CBF study, decreased CBF was seen both in the CPA and the area of the lateral ventricle.
adjacent to the CPA lesion; conversely, AVM shows increased CBF in the nidus.3

Observations
In the present case, at the first angiography at the age of 8 years, the findings of absence of dominant feeders, diffuse capillary angioectic aspect without AV shunt, and capillary, venous enlargement were characteristic of CPA. Conversely, stenosis of the proximal arteries and transdural supply, characteristic of CPA, was not observed. Angiography after the second hemorrhage, performed 17 years after the initial angiography, revealed enlargement of the diffuse vascular ectasias, stenosis of the proximal arteries, transdural supply, and perforator collateral flow with a flow-related aneurysm. Sequential MR imaging showed nidus localized in the frontal lobe only at first, which had gradually enlarged to the left parietal lobe, and the nidus with intermingled brain tissues. In the CBF study, normal CBF at the nidal lesion was observed at the age of 8 years, whereas decreased CBF in the left hemisphere with remarkably reduced CBF in the CPA lesion was observed at the second hemorrhage. During the 17 years between the first and second hemorrhages, the CPA proliferated, the proximal arteries of the CPA narrowed, the CBF in the CPA lesion and adjacent lesions decreased, and transdural and perforator Anastomosis had developed to supply peri-nidal blood perfusion. The year before the second hemorrhage, a flow-related aneurysm arose at the lateral posterior choroidal artery, which supplied the ischemic brain tissue of the left parietal lobe. The flow-related aneurysm was the source of the IVH.

There are no large-scale validation data on the natural course of CPA. Both favorable and unfavorable clinical outcomes have been previously reported with conservative management.1,2 Surgical removal, large nontarget embolization, and radiosurgery carry the risk of permanent neurological deficit because they interperse the normal neural tissue. The indications for surgery are confined very strictly to hemorrhage, identifiable fragile angioarchitecture, such as intranidal aneurysmal ectasias, uncontrolled seizures, and disabling headaches. Treatment with indirect revascularization such as calvarial burr hole, encephaloduarteriosynangiosis (EDAS), and encephalomyosynangiosis to the lesion where transdural supply was poor have been reported.1,2,4–6 Kono and Terada reported a patient with CPA who underwent EDAS, which relieved ischemic symptoms and improved CBF on SPECT. Other studies have reported improved clinical outcomes with indirect bypass surgery; however, there are no large-scale reports on surgery for CPA.5–8

Endovascular partial embolization was performed on the intra-nidal aneurysms that caused the source of the hemorrhage. Lasjaunias et al. reported that even partial treatment resulted in a sufficient control of the symptoms in the majority of selected patients. Glue embolization had been a main embolization method because flow-related aneurysm of the CPA had arisen at the distal portion. Sakata et al. reported an A1 perforator aneurysm treated by targeted embolization using n-butyl-2-cyanoacrylate. Giragani et al. reported a flow-related aneurysm in the anterior inferior cerebellar artery that was treated by Onyx (Medtronic) liquid embolic material. However, glue embolization can cause peripheral ischemia. The recent development of endovascular devices, including microcatheters and soft coils, has enabled targeted embolization of aneurysms at the distal elongated location. In this case, a flow-related aneurysm of the lateral posterior choroidal artery appeared 20 years after the initial hemorrhage, and the aneurysm was successfully embolized. The i-ED coil is a very soft coil for embolization using Marathon microcatheter due to the sound detach system of the i-ED coil.11

Calvarial burr hole and indirect bypass can carry the risk of cerebral ischemia at the lesion supplied by the dural anastomosis. In this case, dural supply was abundant, not only in the CPA lesion.
but also in the non-CPA parietal lobes. In the future, such additional treatment should be considered if the patient experiences ischemic events such as cerebral infarction, transient ischemic attack, or uncontrolled epilepsy.

Lessons
CPA can show proliferative and hemodynamic changes diagnosed by MR imaging, angiography, and CBF studies, even if asymptomatic. A flow-related aneurysm is one of the delayed changes that can arise due to hemodynamic changes, and coil embolization of the flow-related aneurysm is one of the treatment options to prevent the rupture of the aneurysm.

References

Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Author Contributions
Conception and design: Harada, Sanbongi. Acquisition of data: Harada, Saito, Kajihara. Analysis and interpretation of data: Harada, Kajihara. Drafting of the article: Harada, Kajihara. Critically revising the article: Harada. Reviewed submitted version of the manuscript: Harada, Kajihara. Approved the final version of the manuscript on behalf of all authors: Harada. Administrative/technical/material support: Sanbongi. Study supervision: Sanbongi, Fukuyama.

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