

Single Case – General Neurology

Multiple Endovascular Treatments for Hemorrhagic Cerebral Proliferative Angiopathy: A Case Report

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Keywords

Cerebral proliferative angiopathy · Endovascular procedures · Intracranial aneurysm · Cerebral hemorrhage · Embolization

Abstract

Cerebral proliferative angiopathy (CPA) is a rare vascular abnormality characterized by transdural supply, stenoses of feeding arteries, and intermingled normal brain parenchyma in abnormal vessels. CPA is often regarded as a separate entity from “classical” brain arteriovenous malformations in angioarchitecture, natural history, clinical presentation, and treatment. Bleeding from CPA is uncommon, but once bleeding occurs, the risk of rebleeding is high. Herein, we describe a case of cerebral hemorrhage caused by CPA. We performed two different endovascular treatments: partial embolization with glue for a ruptured aneurysm and coil embolization for an unruptured growing aneurysm. To our knowledge, this is the first report of serial endovascular treatments for hemorrhagic CPA that included a ruptured aneurysm and a growing unruptured aneurysm.

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Introduction

Cerebral proliferative angiopathy (CPA) is a rare vascular disease that constitutes only 3.4% of all arteriovenous malformations (AVMs) [1]. Lasjaunias et al. [1] retrospectively analyzed 1,434 AVM databases, where they identified CPA in 49 cases, and reported that CPA

has a lower risk for hemorrhage than do AVMs ($6/49 = 12\%$ vs. $583/1,385 = 42\%$). On the other hand, once hemorrhage occurs in CPA, its risk for rebleeding appears to be much higher than in AVM ($4/6 = 67\%$ vs. $24/583 = 4\%$) [1]. Therefore, if fragile lesions are identified in CPA with past hemorrhages, it is reasonable to treat those lesions. Here, we present a case of CPA with a hemorrhage that was treated not only as the bleeding source but also as an unruptured fragile lesion by using glue and coil embolization.

Case Report

Diagnosis

A 20-year-old man with repeated headaches and abnormal radiographic findings was referred to our hospital. Magnetic resonance imaging revealed large flow voids in the right hemisphere (Fig. 1a, b). Digital subtraction angiography showed a diffuse ill-defined nidus in the right temporal-occipital lobe, which was fed by a multitude of small arteries from the anterior cerebral artery, middle cerebral artery, and posterior cerebral artery (PCA) (Fig. 1c, d). Right external carotid angiography demonstrated a small supply from the middle meningeal artery through the dura mater. Compared with the large size of the nidus, the calibers of the feeding arteries were disproportionately small. Based on these radiological findings, CPA was diagnosed. Additionally, an aneurysm in the right distal PCA was detected. Because the patient had no symptoms other than intermittent headaches, we decided to treat him conservatively.

Hemorrhage

Two years after his initial visit to our hospital (at 22 years of age), the patient was brought to our hospital by ambulance with sudden onset seizures, vomiting, left hemiplegia, and disturbance of consciousness. Emergency computed tomography showed right thalamic hemorrhage with ventricular perforation and subarachnoid hemorrhage (Fig. 2a, b). Digital subtraction angiography showed a small aneurysm on a branch of the anterior choroidal artery (AChoA) (Fig. 2c), which was not confirmed in the previous study (Fig. 1d), and was suspected to be a cause of the hemorrhage. There was no remarkable change in the size of the PCA aneurysm.

First Embolization

Three weeks after the onset of the hemorrhage, follow-up angiography was performed, and enlargement of the distal AChoA aneurysm was noted (Fig. 2c, d). Because of its complicated angioarchitecture, it seems difficult to identify the aneurysm via direct approach. We decided to perform endovascular treatment. It was difficult to reach the aneurysm with a catheter; therefore, we performed targeted embolization to the branch of the AChoA using n-butyl-2-cyanoacrylate (NBCA), which resulted in complete disappearance of the aneurysm without any new neurological deficits (Fig. 2e, f). One month later, the left hemiparesis persisted, but the patient was able to ambulate and was discharged for rehabilitation.

Second Embolization

During follow-up, 2 years after the hemorrhage (at 24 years of age), an enlargement of the distal PCA aneurysm was noted (Fig. 3a, b). As the aneurysm had grown and was considered to have a high risk of rupture, coil embolization was performed. Angiography after endovascular treatment showed complete embolization of the PCA aneurysm (Fig. 3b, c). One week after the treatment, he was discharged from our hospital without any new neurological deficits, and there have been no further adverse cerebrovascular events to date, for over 7 months.

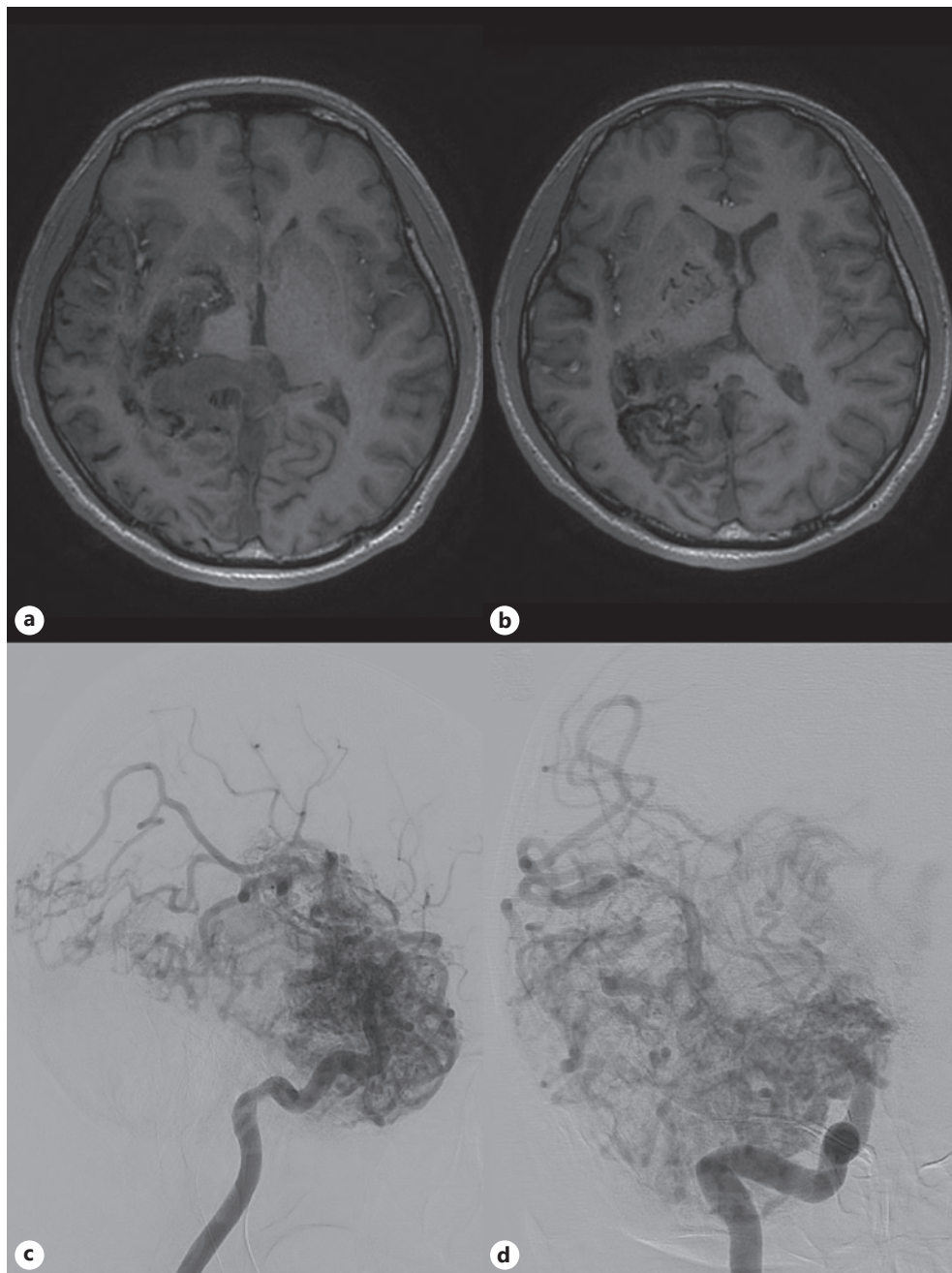


Fig. 1. Legend text. Magnetic resonance imaging at the time of diagnosis (**a, b**) showed large flow voids in the right hemisphere. Cerebral angiography of the right internal carotid artery (**c, d**) demonstrating an ill-defined diffuse nidus in the right hemisphere. During angiography, no dominant feeders were identified. No aneurysm was detected in the AChoA at the first angiography (**d**).

Discussion

CPA is a rare subset of AVM. It is composed of a large, very dense capillary network. Lasjaunias strictly distinguished CPA from “classical” AVM by the following diagnostic criteria: the presence of non-focal angiogenetic activity, that is, transdural supply and stenoses of

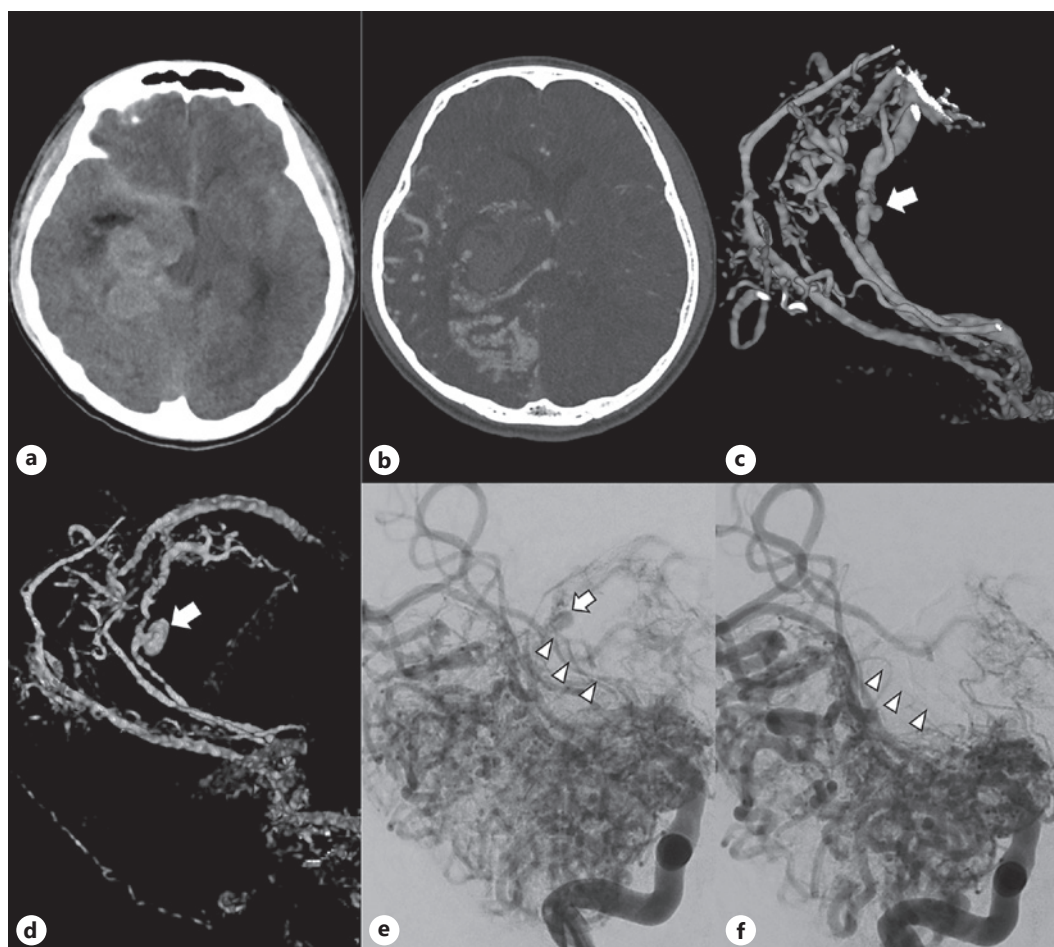


Fig. 2. Legend text. Non-contrast axial computed tomography image (a) showing thalamic hemorrhage with subarachnoid hemorrhage. Contrast-enhanced computed tomography (b) showing an oval-shaped lesion that appears to be an aneurysm (arrow). 3D rotational angiography (c) showing a small aneurysm fed by a branch of the AChOA (arrow). The aneurysm in the AChOA enlarged within 3 weeks after hemorrhage (d). Cerebral angiography performed before and after NBCA embolization (e, f) showing that endovascular treatment resulted in complete obliteration of the aneurysm (arrow) and its feeding artery (arrowheads).

feeding arteries [1]. The other angiomorphological points which help discern CPA from AVM are the absence of feeders or flow-related aneurysms, the large size of the nidus (which might be lobar or even hemispheric), the presence of capillary angioectasia, and smaller veins in comparison with the size of the nidus [1]. Intermingled healthy brain parenchyma within the abnormal vessel network is also the distinctive feature of CPA [1]. Because normal brain tissues exist in the abnormal vessels, surgical intervention can cause serious complications.

The most common symptoms of CPA are seizures and headaches; hemorrhagic events are uncommon [1]. Because of the high risk of intervention and mild symptoms, the main treatment for CPA is conservative therapy [1]. However, some CPAs are aggressive, and once hemorrhage occurs, the risk for recurrent hemorrhages is high. We surveyed the literature for all cases of hemorrhagic CPA, including the present case (Table 1), and found 18 cases of hemorrhagic CPAs [1–11]. Among the 18 cases, recurrent hemorrhages were observed in

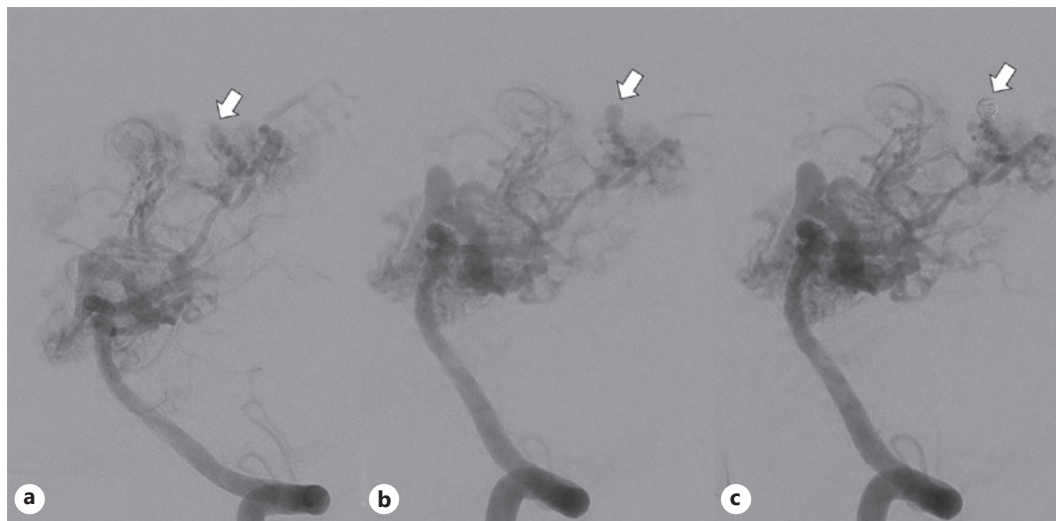


Fig. 3. Legend text. Cerebral angiography at the time of diagnosis (a) and 2 years after the occurrence of a hemorrhage (b) showing the enlargement of the distal PCA aneurysm (arrow) in 4 years (greatest dimension: 4.2 mm–5.5 mm). Angiography performed before and after coiling (b, c) showing complete obliteration of the PCA aneurysm (arrow).

eight [1–5], two of which involved the patient dying after rebleeding [1, 4]. Therefore, it is important to assess the treatment options for hemorrhagic CPA to prevent rebleeding.

Three previous reports of endovascular treatments for hemorrhagic CPA exist in the literature [1, 2, 6]. Unfortunately, no details were available from cases reported by Lasjaunias et al. [1], and the remaining two reports are focused on treatments for the bleeding source [2, 6]. Sakata et al. [2] embolized a ruptured pseudoaneurysm in the A1 perforator after a second hemorrhage using NBCA, and Giragani et al. [6] embolized a ruptured aneurysm in the anterior inferior cerebellar artery after initial hemorrhage using Onyx. Both cases yielded favorable results without any new neurological deficits. However, there is no previous report of the use of coil embolization for treating CPA, nor a description of treatment for “unruptured” lesions in CPA. If fragile lesions are identified in CPA with a past hemorrhage, targeted endovascular treatments, such as glue and coil embolization, might be required, considering the high rate of rebleeding. Maekawa et al. [4] reported a case of CPA with multiple recurrent hemorrhages in different lesions (initial hemorrhage in the left temporal lobe, followed by hemorrhages in the left thalamus, cingulate gyrus, and left temporoparietal lobe, and two intraventricular hemorrhages). This case suggests that in hemorrhagic CPAs, hemorrhages do not always occur in the same lesion; therefore, treating not only a bleeding source but also unruptured fragile lesions is important.

Regarding the location of the aneurysm, the present case indicates that fragile lesions in the CPA can be seen in uncommon areas. Aneurysms of the distal AChOA and distal PCA are both extremely rare [12, 13]. There are several possible hypotheses for the pathogenesis of these rare aneurysms. The enlargement of the AChOA aneurysm might be caused by thrombosis within the aneurysm by compression of hematoma or pseudoaneurysm formation at the tip of the aneurysm in the thick hematoma. Pseudoaneurysm in CPA has been reported as a source of bleeding in a previous study [2]. The distal PCA aneurysm might be a “flow-related aneurysm” commonly found in AVM. Flow-related aneurysm in AVM is thought to arise from increased hemodynamic stress [14]. According to Lasjaunias et al. [1], flow-related aneurysms are atypical findings in CPA; however, Giragani et al. [6] reported a flow-related aneurysm in CPA as a culprit lesion of hemorrhage. The case reported by Giragani et al. [6]

Table 1. Review of all hemorrhagic CPA studies

References	Sample size ^a	Treatment option	Source of bleeding/inspection method	Prognosis
Lasjaunias et al. [1]	6 (4)	NBCA	NA	NA (1 patient died of recurring hemorrhages)
Sakata et al. [2]	1 (1)	NBCA	Pseudoaneurysm (A1 perforator)/angiography	mRS 1
Bilaj et al. [3]	1 (1)	Craniotomy	Not identified/angiography	NA
Maekawa et al. [4]	1 (1)	Conservative	Not identified/angiography	Died
Ochoa et al. [5]	2 (1)	Surgical removal	NA/DSA	Asymptomatic
Giragani et al. [6]	1 (0)	Onyx	Flow-related aneurysm (AICA)/angiography	Asymptomatic
Kumar et al. [7]	1 (0)	Conservative	NA/DSA	Asymptomatic
Xia Y et al. [8]	1 (0)	Conservative	NA/DSA	Died
Kimiwada et al. [9]	1 (0)	IR	Not identified/angiography	Neurological aggravation
Beniwal et al. [10]	1 (0)	Conservative	NA/DSA	Asymptomatic
Maekawa et al. [11]	1 (0)	Conservative	Not identified/CT	Died
Current case	1 (0)	NBCA, coiling	Aneurysm (AchoA)/DSA	mRS 2, left hemiplegia

AchoA, anterior choroidal artery; AICA, anterior inferior cerebellar artery; CT, computed tomography; DSA, digital subtraction angiography; IR, indirect revascularization; mRS, modified Rankin Scale; NA, not available; NBCA, n-butyl-2-cyanoacrylate.

^aSample size, numbers in () refer to those with recurrent hemorrhage.

and the present case suggest that flow-related aneurysms, although rare, can occur in CPA. In past studies, hemorrhagic sources have not been identified in most cases of hemorrhagic CPA. Ten cases of hemorrhagic CPA have been reported in the literature in which the patient underwent cerebral angiography after hemorrhage [2–10], and in three of the cases, hemorrhagic sources could not be identified [3, 4, 9], whereas in five of them, a description of hemorrhagic sources was not available [5, 7, 8, 10]. We speculate that if small fragile angio-architectures (such as an aneurysm or aneurysmal ectasias) exist in uncommon deep areas, they may overlap with a multitude of adjacent abnormal vessels and be concealed.

Conclusion

We report a case of hemorrhagic CPA in which the patient underwent multiple endovascular treatments: NBCA injection for a ruptured aneurysm and coil embolization for an unruptured growing aneurysm. We emphasize that some CPAs are aggressive and paying special attention to detecting fragile lesions in CPA is crucial. If fragile lesions are noted in CPA, targeted endovascular treatments may be required, especially in cases of CPA with past hemorrhages. Further analysis is needed to clarify the clinical features and pathology and establish treatment options for hemorrhagic CPA.

Statement of Ethics

We have obtained written informed consent from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors declare that there is no conflict of interest associated with this manuscript.

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Author Contributions

Keijiro Shomura, Tomoya Kamide, Kouichi Misaki, Taishi Tsutsui, Iku Nambu, Naoyuki Uchiyama, and Mitsutoshi Nakada were involved in the diagnosis and care of the patient. Keijiro Shomura drafted the manuscript and reviewed literature. Tomoya Kamide revised and updated the manuscript. All of the authors read and approved the final version.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

- 1 Lasjaunias PL, Landrieu P, Rodesch G, Alvarez H, Ozanne A, Holmin S, et al. Cerebral proliferative angiopathy: clinical and angiographic description of an entity different from cerebral AVMs. *Stroke*. 2008 Mar;39(3):878–85.
- 2 Sakata H, Fujimura M, Sato K, Niizuma K, Endo H, Tominaga T. Development of abnormal hemispheric vascular networks mimicking cerebral proliferative angiopathy in a child originally diagnosed with deep-seated arteriovenous fistula. *J Stroke Cerebrovasc Dis*. 2016 Oct;25(10):e200–4.
- 3 Bilaj F, Rooji A, Enesi E, Ruka M, Petrela M. Cerebral proliferative angiopathy with tumor-like hemorrhage: a case report and literature review. *Neuroradiol J*. 2016 Oct;29(5):336–9.
- 4 Maekawa H, Terada A, Ishiguro T, Komiyama M, Lenck S, Renieri L, et al. Recurrent periventricular hemorrhage in cerebral proliferative angiopathy: case report. *Interv Neuroradiol*. 2018 Dec;24(6):713–7.
- 5 Ochoa A, Mantese B, Requejo F. Hemorrhagic cerebral proliferative angiopathy in two pediatric patients: case reports. *Childs Nerv Syst*. 2022 Apr;38(4):789–94. <https://doi/10.1007/s00381-021-05181-0>.
- 6 Giragani S, Pavunesan SK, Balasubramaniam A. Targeted endovascular treatment of haemorrhagic posterior fossa proliferative angiopathy. *Interv Neuroradiol*. 2018 Aug;24(4):440–3.
- 7 Kumar S, Sharma M, Srivastava T, Sinha V. Infratentorial hemorrhagic cerebral proliferative angiopathy: a rare presentation of a rare disease. *Asian J Neurosurg*. 2015;10(03):240–2.
- 8 Xia Y, Yu XF, Ma ZJ, Sun ZW. Hemorrhagic transformation of ischemic cerebral proliferative angiopathy: a case report. *World J Clin Cases*. 2021 Jul;9(20):5730–6.
- 9 Kimiwada T, Hayashi T, Takahashi M, Shirane R, Tominaga T. Progressive cerebral ischemia and intracerebral hemorrhage after indirect revascularization for a patient with cerebral proliferative angiopathy. *J Stroke Cerebrovasc Dis*. 2019 Apr;28(4):853–8.
- 10 Beniwal M, Kandregula S, Aravind, Rao KVLN, Vikas V, Srinivas D. Pediatric cerebral proliferative angiopathy presenting infratentorial hemorrhage. *Childs Nerv Syst*. 2020 Feb;36(2):429–33.
- 11 Maekawa H, Tanaka M, Hadeishi H. Fatal hemorrhage in cerebral proliferative angiopathy. *Interv Neuroradiol*. 2012;18(3):309–13.
- 12 Dolati P, Sutherland G, Wong J, Hudon M, Goyal M. Distal anterior choroidal artery aneurysm following iatrogenic posterior cerebral artery occlusion: a case report and review of literature. *Acta Neurochir*. 2012 Jan;154(1):53–7.
- 13 Yamahata H, Tokimura H, Hirabaru M, Hirano H, Arita K. Aneurysm on the cortical branch (P4 segment) of the posterior cerebral artery -case report-. *Neurol Med Chir*. 2010;50(12):1084–7.
- 14 Budohoski KP, Mohan M, Millar Z, Tajsic T, Barone DG, Cao JLL, et al. Longitudinal changes in size of conservatively managed flow-related aneurysms associated with brain arteriovenous malformations. *World Neurosurg X*. 2021 Oct;154:e754–61.