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## CASE REPORT

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# Cerebral Proliferative Angiopathy: A Rare Type of Cerebral Vascular Malformation

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### ABSTRACT

*Cerebral proliferative angiopathy is a rare type of cerebral vascular malformation. It shows distinct angiomorphological features with a clinical presentation that differs to that of classic arteriovenous malformation of the brain. We describe a 15-year-old girl who presented with recurrent headache and limb weakness. A subsequent angiographic diagnosis of cerebral proliferative angiopathy was made. The clinical features, pathophysiology, and treatment of this condition are reviewed.*

*Key Words:* Adolescent; Cerebral angiography; Diseases/etiology; Intracranial arteriovenous malformations/classification; Magnetic resonance imaging

## 中文摘要

### 增生性腦血管病：一種罕見的腦血管畸形

謝志瀚、李騰飛、賴銘曦、陸嬈、梁錦榮、黃慧中

增生性腦血管病是一種罕見的腦血管畸形。它顯示出獨特的血管形態特徵，其臨床表現與大腦的典型腦血管畸形不同。本文描述一名15歲女性患者出現反覆頭痛發作和四肢無力。腦血管造影診斷為增生性腦血管病。本文同時綜述該病的臨床特徵、病理生理學和治療方法。

### INTRODUCTION

Cerebral proliferative angiopathy (CPA) is a rare and under-recognised cerebral vascular malformation. It is distinct to classic types of brain arteriovenous malformation (AVM) with pathognomonic angiographic findings. One of the major findings in CPA is the presence of brain parenchyma within the nidus of the lesion. Patients with CPA tend to present at a younger age, typically around age 22 years,<sup>1</sup> with fewer haemorrhages. Cerebral ischaemia is an important feature of this condition with implications for treatment strategy.<sup>2</sup> Similar to diffuse AVMs, there may be

disease progression and treatment can be challenging.<sup>3</sup> We present a case of CPA diagnosed by computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA).

### CASE PRESENTATION

A 15-year-old girl was admitted in March 2015 to a local hospital in Hong Kong for sudden-onset right-sided headache associated with left-sided limb weakness. She vomited twice. Further history revealed recurrent right-sided headaches and left-sided weakness for 6 months. The limb weakness usually lasted for 30 minutes

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Submitted: 13 Dec 2016; Accepted: 6 Feb 2017.

Disclosure of Conflicts of Interest: The authors have no conflicts of interest to disclose.

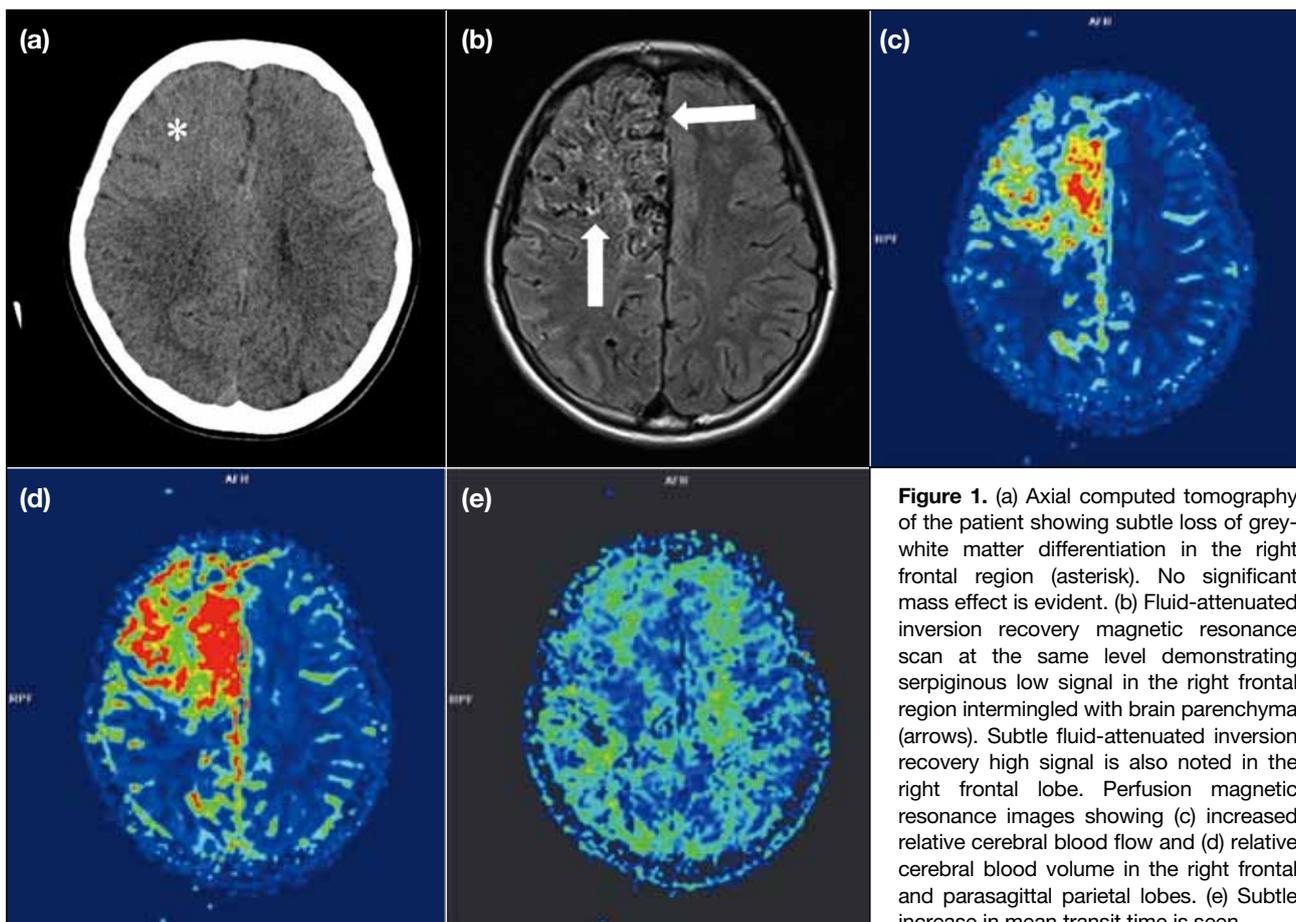
and then resolved spontaneously. No photophobia or visual blurring was noted and there was no history of convulsion. Physical examination revealed no focal neurological deficit.

Brain CT scan after admission showed subtle loss of grey-white matter differentiation in the right frontal lobe with sulcal effacement (Figure 1a). Nonetheless there was little mass effect and no associated oedema. In view of suspected underlying vascular or mass lesions, urgent brain MRI was performed. Fluid-attenuated inversion recovery (FLAIR) images showed a serpiginous low signal in the right frontal lobe and high right parasagittal parietal lobe compatible with abnormal vessels (Figure 1b), indicating the presence of vascular malformation. Intervening brain parenchyma was noted among the abnormal vasculature. Mildly dilated ipsilateral anterior, middle, and posterior cerebral arteries were noted. Small areas of T2-weighted and FLAIR hyperintensities were seen in the right frontal lobe. No definite haemorrhage was noted. Perfusion-weighted MRI demonstrated increased relative cerebral blood flow, relative cerebral blood volume, and mean transit time in the involved

region (Figure 1c-e).

DSAs of the bilateral carotid and vertebral arteries were subsequently performed (Figure 2a) and showed extensive abnormal vessels in the right frontal lobe. Scattered puddling of contrast material within the abnormal vessels with capillary ectasia was noted. Hypertrophied M2 branches of the right middle cerebral artery (MCA) were seen. Normal brain parenchyma was noted intermingled with the vascular spaces. Considering the size of the malformation, there was only mild arteriovenous shunting with draining veins towards the superior and inferior sagittal sinus. On external carotid artery DSA, supply of the vascular malformation by branches of bilateral middle meningeal arteries and the right superficial temporal artery was also present (Figure 2b). Supply of the right MCA territory at the right parietal lobe by the right posterior cerebral artery through pial-pial collateral was also evident in the right vertebral artery DSA (Figure 2c).

The overall imaging findings, particularly those of multiple arterial feeders, intermingling with normal



**Figure 1.** (a) Axial computed tomography of the patient showing subtle loss of grey-white matter differentiation in the right frontal region (asterisk). No significant mass effect is evident. (b) Fluid-attenuated inversion recovery magnetic resonance scan at the same level demonstrating serpiginous low signal in the right frontal region intermingled with brain parenchyma (arrows). Subtle fluid-attenuated inversion recovery high signal is also noted in the right frontal lobe. Perfusion magnetic resonance images showing (c) increased relative cerebral blood flow and (d) relative cerebral blood volume in the right frontal and parasagittal parietal lobes. (e) Subtle increase in mean transit time is seen.

brain parenchyma and a relatively small amount of shunting suggested the diagnosis of CPA. Because there was no history of bleeding, a high risk from intervention and relatively mild symptoms, she was managed conservatively.

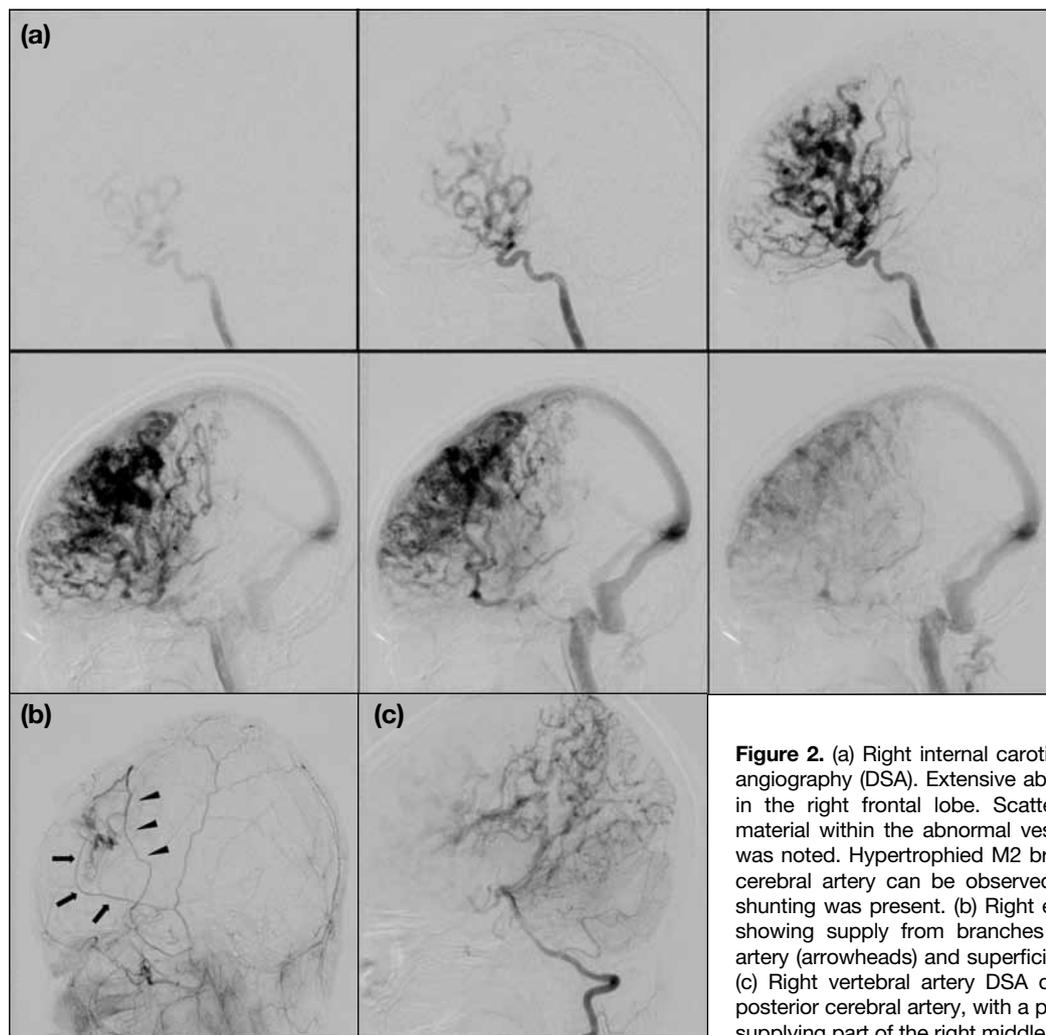
## DISCUSSION

Classic cerebral AVM refers to an abnormal transition between an artery and vein through a nidus. There is prominent shunting of blood from the arterial to the venous side.<sup>4</sup> This is a relatively uncommon entity. Nonetheless in the review by Lasjaunias et al,<sup>1</sup> about 3.4% of brain AVMs showed features distinct from classic brain AVM and these cases are termed CPA.

Angiomorphologically, CPA differs to classic AVM by the absence of dominant feeders or flow-related aneurysms, presence of proximal stenosis of the feeding arteries, extensive transdural supply to both

healthy and pathological tissue, large size, presence of capillary angioectasia and only moderately enlarged veins.<sup>1</sup> As seen in this case, the anterior, middle, and posterior cerebral arteries contributed to the vascular malformation. The draining veins were smaller than expected for an AVM of this size.

Histopathological study shows that the major difference between classic AVM and CPA, as seen in imaging studies, is the presence of identifiable neurons and normal brain tissue between the abnormal vessels in CPA. This is somehow analogous to capillary telangiectasia.<sup>5</sup> It is possible that CPA results from an early embryological event during angiogenesis.<sup>6</sup> One of the underlying causes may be hypoperfusion, as shown in perfusion-weighted MRI study.<sup>7</sup> This contrasts with classic AVM in which marked shunting is present. This hypoperfusion might lead to an uncontrolled angiogenic response, thus giving it its “proliferative” nature. Moreover, MRI perfusion



**Figure 2.** (a) Right internal carotid artery digital subtraction angiography (DSA). Extensive abnormal vessels are evident in the right frontal lobe. Scattered puddling of contrast material within the abnormal vessels with capillary ectasia was noted. Hypertrophied M2 branches of the right middle cerebral artery can be observed. Only mild arteriovenous shunting was present. (b) Right external carotid artery DSA showing supply from branches of the middle meningeal artery (arrowheads) and superficial temporal artery (arrows). (c) Right vertebral artery DSA demonstrating an enlarged posterior cerebral artery, with a prominent pial-pial collateral supplying part of the right middle cerebral artery territory.

study in our case demonstrated subtle increase in mean transit time in the involved region. The proposed mechanism for such finding is venous congestion with consequent ischaemia in the involved brain parenchyma. Ducreux et al<sup>8</sup> described one patient with identical MR perfusion findings that corresponded to increased regional vascularity with slow venous drainage on conventional angiography. Transdural supply is also thought to be a response to the ischaemic nature,<sup>9</sup> as seen in our patient with vascular supply from the external carotid artery territory. In addition, previous studies have also demonstrated reduced cerebrovascular reserve in these patients.<sup>10</sup> The role of vascular endothelial growth factor (VEGF) in this condition is also being investigated, with reports showing an increased level of cerebrospinal fluid VEGF level in CPA patients.<sup>11</sup>

Clinically, CPA tends to present in younger patients with a female-to-male ratio of 2:1 compared with the almost equal gender distribution in classic AVM.<sup>1</sup> Frequent presenting symptoms include seizure, headache, and progressive neurological deficits. Acute haemorrhage or neurological deficit are relatively less frequently encountered. Nonetheless when there is haemorrhage, the risk of re-bleeding becomes much higher, possibly due to vulnerability of newly formed vessels.<sup>1</sup>

There is currently no standard treatment for CPA. The usual treatment strategies of embolisation, surgery, or radiosurgery<sup>1,2</sup> all carry significant risks of injury to normal brain parenchyma since there is neuronal tissue interspersed with the abnormal vessels. Patients with haemorrhage, uncontrolled seizure or disabling headaches may still be managed by embolisation or surgery.<sup>1,12</sup> Since ischaemia is one of the pathogenic mechanisms of this condition, treatments aimed at improving blood supply to the ischaemic brain may be of value. This is analogous to cases of moyamoya disease.<sup>2</sup> Burr holes have been advocated by some as a means to improve the symptoms by increasing cortical blood supply through recruitment of additional dural blood supply.<sup>1</sup>

Encephaloduroarteriosynangiosis has also been reported to improve perfusion to the brain.<sup>13</sup> No established medical treatment is available for CPA at present. Although the use of anti-VEGF in AVM has been recommended, its role in CPA requires further investigation.<sup>2,13</sup>

The use of radiotherapy has also been recently reported in the literature. In one reported patient with CPA, the

patient presented with clinical and radiological response after radiation therapy.<sup>14</sup>

Like other brain vascular lesions, there may be progression of the vascular abnormality.<sup>1,2</sup> Whether to treat CPA patients with relatively mild symptoms and when to offer treatment remain uncertain. Further studies are required to delineate the pathogenic mechanism and natural history of this condition.

In conclusion, CPA is a rare and distinct type of cerebral vascular malformation. Clinicians and radiologists should be aware of this entity when encountering patients with vascular malformation of the brain and planning treatment.

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