

CASE REPORT

Recurrent Cerebral Hyperperfusion Syndrome After Intracranial Angioplasty and Stenting: Case Report with Review of Literature

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Received: 8 September 2013 / Accepted: 1 November 2013 / Published online: 5 December 2013

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Abstract Cerebral hyperperfusion syndrome (CHS) describes a syndrome of sudden onset focal neurological features, unilateral headache, and systemic hypertension. Recurrent CHS in the same patient has not been described to date. We describe a 55-year-old woman who first developed CHS post intracranial stenting with sudden-onset right focal seizures and associated acute focal edema on imaging. After one and half years, the patient developed symptomatic in-stent restenosis and underwent repeat angioplasty with stenting. Postprocedure, the patient had another episode of CHS in the form of acute bleed in the basal ganglia and died. A review of literature of patients for CHS postintracranial angioplasty and stenting also was performed. The present case describes a rare clinical scenario where the patient had recurrent CHS with different clinical and imaging features.

Keywords Recurrent cerebral hyperperfusion syndrome · Intracranial stenting · Intracranial angioplasty · Digital subtraction angiography

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Introduction

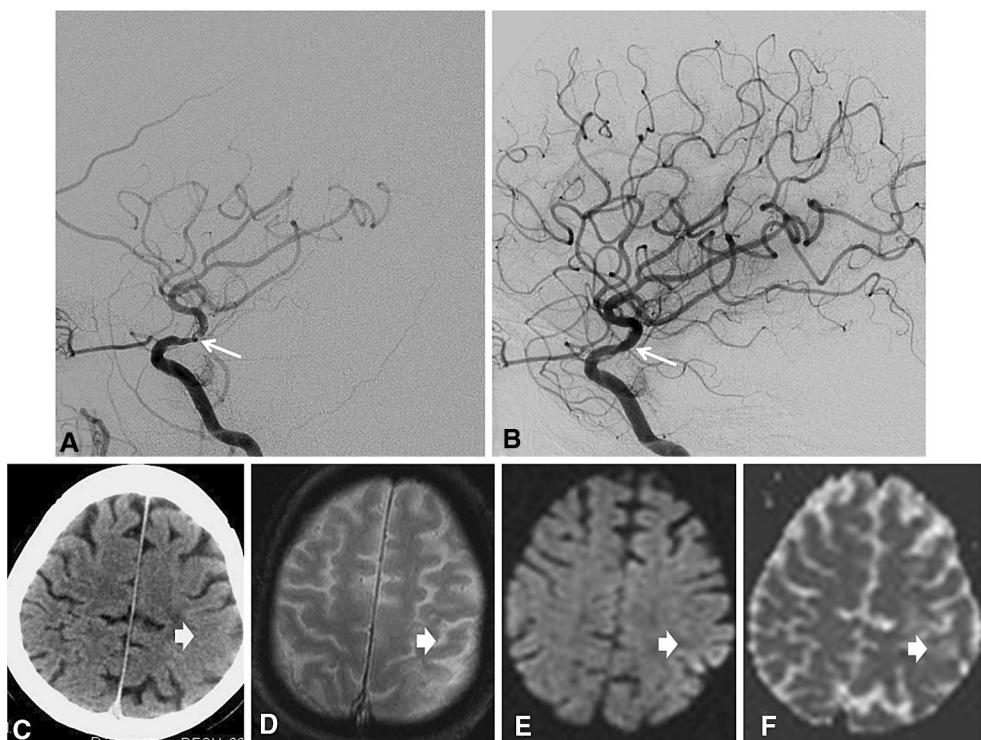
The term cerebral hyperperfusion syndrome (CHS) refers to a syndrome with sudden-onset focal neurological features, unilateral headache, and systemic hypertension. Sundt et al. [1] first described CHS in 1975 as sudden-onset atypical migrainous headaches, focal seizures, and intracranial hemorrhage after carotid endarterectomy (CEA). Bernstein et al. [2] first proposed the concept of impaired autoregulation as the underlying cause of CHS in 1984 [3]. CHS in patients undergoing CEA is well known. CHS in patients undergoing intracranial angioplasty and stenting is uncommon. There are only anecdotal case reports and series describing CHS in patients with intracranial stenosis.

Case Report

A 55-year-old woman presented with sudden-onset right upper limb weakness followed by partial recovery over 2 months. The patient had a history of minor stroke involving right faciobrachial region 4 months back. She was a known diabetic and hypertensive in good control. On clinical examination, the patient had right hand grip weakness.

The patient underwent magnetic resonance imaging (MRI) scan of the brain, which showed acute infarcts involving the left frontal periventricular deep white matter and head of caudate. Computed tomography angiography (CTA) was performed, and it revealed bilateral carotid artery disease at the internal carotid artery (ICA) origins causing mild (50 %) stenosis on the left and severe (more than 95 %) stenosis on the right. A high grade (more than 90 % stenosis) also was seen in the left supraclinoid ICA. Patient underwent a cerebral digital subtraction angiography (DSA) and

Fig. 1 Left supraclinoid ICA angioplasty and stenting. **A**, **B** Pre- and postangioplasty and stenting of the short segment, high-grade stenosis of left supraclinoid ICA (straight arrow). **C–F** Plain CT scan in the immediate postprocedure period shows effacement with thickening of the gyri in the left frontal and parietal lobes with vasogenic edema (block arrow). On the corresponding, gradient image there is no intracranial hemorrhage (block arrow). Also seen on the corresponding diffusion weighted and apparent diffusion coefficient images there is no acute infarct (block arrow)



stenting of the right ICA origin stenosis. The procedure was uneventful. Despite this, the patient continued to have episodic tingling numbness affecting her right upper limb and face with increasing frequency.

The patient underwent left supraclinoid ICA stenting with a 2.5×18 mm drug-eluting stent (Fig. 1A, B). Poststenting, patient had right focal seizures followed by secondary generalization. This was followed by epilepsia partialis continua involving right face and hand that was controlled with intravenous antiepileptics. There also was a rapid rise in blood pressure (200/120 mmHg) during the immediate postoperative period. Post-ictus, the patient developed right hemiparesis and facial palsy. Patient underwent CT and MRI scans of the brain. There was effacement with thickening of the gyri in the left frontal and parietal lobes with vasogenic edema. No intracranial hemorrhage (ICH)/acute infarct were seen (Fig. 1C–F). Patient was diagnosed to have developed cerebral hyperperfusion syndrome. She gradually recovered over a period of 1 month.

Patient underwent a control cerebral DSA at 6 months and was found to have severe in-stent restenosis (ISR) of 90 % in the left supraclinoid ICA. The entire left anterior circulation was dependant on the right ICA and was opacified through the anterior communicating artery. Because the patient was asymptomatic, she was managed conservatively with antiplatelet medications and strict control of hypertension and diabetes.

The patient presented one and half years later with sudden-onset right hemiparesis and facial deviation and history of similar episodes over a period of 2 days. There was rapid clinical deterioration over the next week with flurry of seizures and deteriorating sensorium. On MRI, diffusion weighted images (DWI) showed small infarcts in the left frontal subcortical white matter and centrum semiovale (Fig. 2A, B). However, MRI perfusion scan revealed a large region of mismatch in both the anterior cerebral arteries (ACAs) and the left middle cerebral artery (MCA) territories. MR angiogram of the circle of Willis showed a restenosis of the left supraclinoid ICA (Fig. 2C, D).

A cerebral DSA was performed that revealed a high-grade approximately 99 % ISR in the stented supraclinoid ICA. A balloon angioplasty followed by restenting of the left supraclinoid ICA stenosis was performed. Poststenting, there was significant improvement in the circulation with brisk filling of both the ACAs and MCA (Fig. 3A–C). There was no active contrast extravasation or persistent abnormal parenchymal staining anytime during or in the immediate postprocedure angiograms. However, the immediate postprocedure CT scan revealed a large 7×5 cm-sized left basal ganglia bleed with intraventricular hemorrhage (IVH) (Fig. 3D). Although the patient underwent decompressive craniectomy, the patient died on the third day after the procedure.

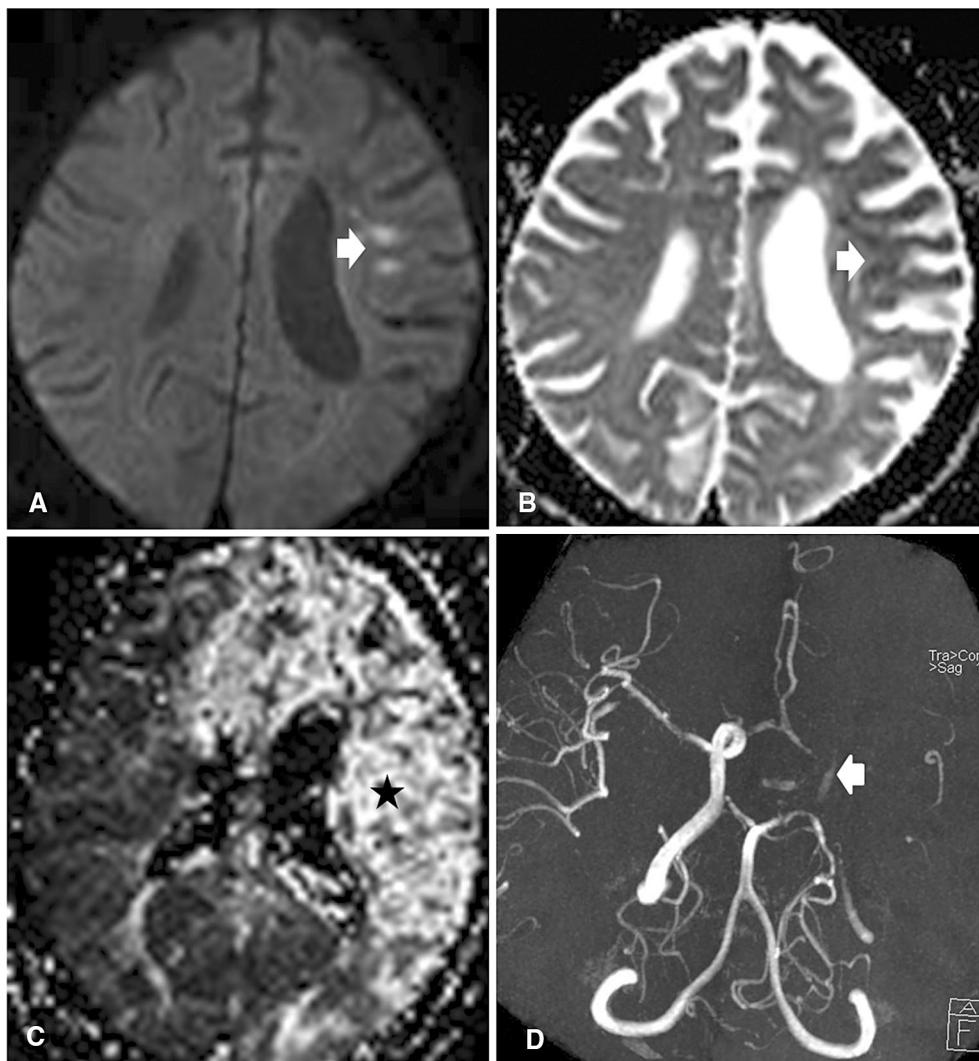


Fig. 2 MRI scan of the brain after one and half years in patient with recurrent symptoms of left anterior circulation insufficiency. **A, B** Diffusion weighted and apparent diffusion coefficient images reveal multiple small acute infarcts in the left frontal subcortical white matter and centrum semiovale (*block arrow*). **C, D** MRI perfusion

images revealed a large mismatch in both the anterior cerebral arteries and the left middle cerebral artery territories (*star*). MRA of the circle of Willis reveals a high-grade restenosis in the left supraclinoid ICA with poor visualization of the left MCA (*block arrow*)

Discussion

CHS has been a well-described entity in patients undergoing CEA. The incidence of CHS in patients undergoing CEA varies from 0.5 to 2.2 % with an incidence of 0.6 % ICH. In recent years, with CAS becoming an effective therapeutic option in patients with carotid stenosis, CHS has been reported in association with CAS as well. The incidence of CHS, post CAS is 1.1 % with an incidence of 0.7 % ICH [4, 5]. There are only isolated case reports describing CHS postendovascular management of intracranial stenosis and the exact incidence is unknown. On review of literature, there are no case reports describing recurrent CHS.

A variety of definitions of CHS have been proposed. The definition followed by most authors is a 100 % increase in the cerebral blood flow in the postprocedure period compared with baseline levels [6]. However, there are reports that this is not true in all cases [6]. Also, the data that describe CHS are very heterogeneous as the use of anticoagulants, antiplatelets, glycoprotein IIb/IIIa inhibitors, and blood pressure control in the perioperative period affect the incidence, manifestations, and mortality ascribed to CHS.

CHS has been described following procedures that entail a sudden increase or restoration of the cerebral blood flow. This increase is many-fold over the requirement of the previously hypoperfused brain. This sudden change in the status quo of the cerebral circulation combined with the

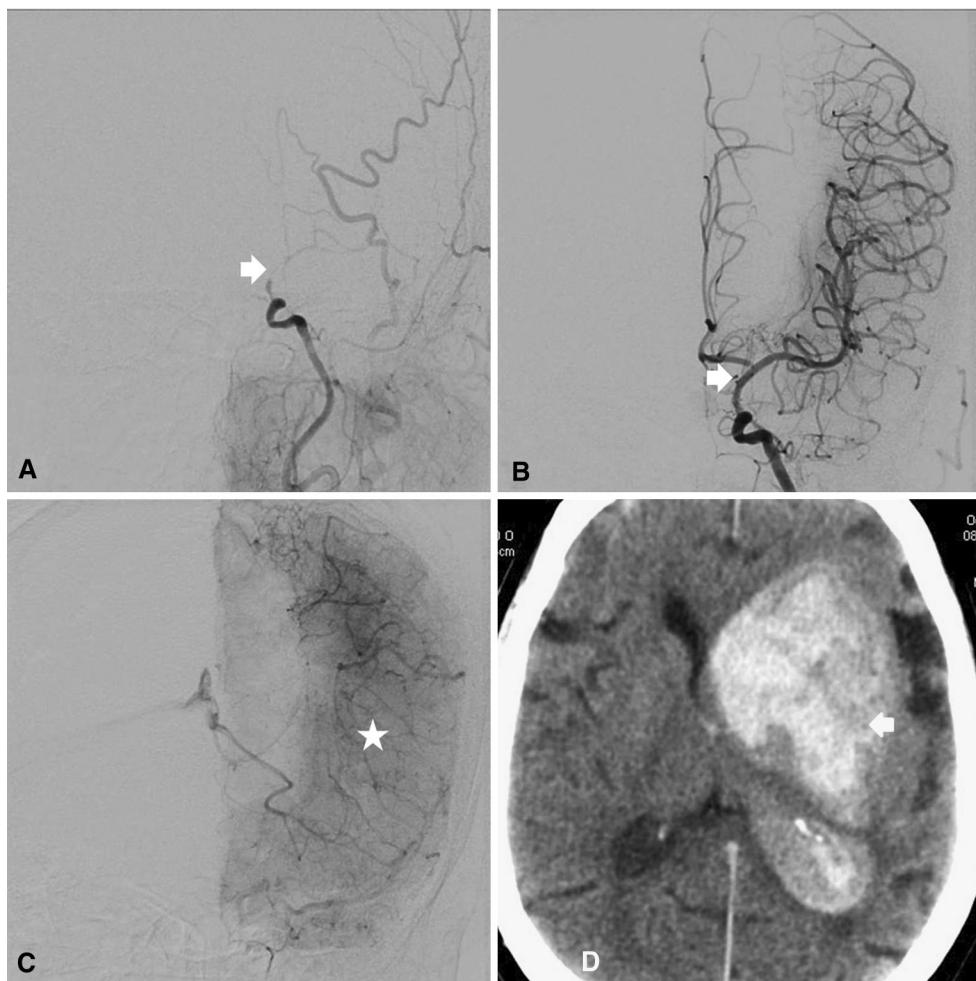


Fig. 3 Angioplasty with stenting for the supraclinoid ICA in-stent restenosis. **A, B** Left ICA angiogram demonstrates a high-grade in-stent restenosis in the supraclinoid ICA (block arrow). Postangioplasty with stenting shows good recanalization and brisk antegrade flow (block arrow). **C** Left ICA angiogram demonstrating dramatic

improvement in the left ICA territory perfusion (star) following angioplasty and stenting. **D** Immediate postprocedure CT scan demonstrating a large acute bleed in the left basal ganglia with intraventricular hemorrhage (block arrow)

decreased tone of the capillary resistance vessels as an adaptation to chronic hypoperfusion is proposed to cause a breakdown of the blood brain barrier (BBB) [7]. Oxygen-free radicals and nitric oxide play an important role both in neurogenic and myogenic autoregulation of cerebral perfusion [6]. In the more severe form, the resultant breakdown in the BBB results in intracranial hemorrhage [6, 7]. There is no experimental evidence for this, although studies have demonstrated defective capillaries, increase in permeability and loss of autoregulation in chronically ischemic brain [6]. The risk factors associated with development of CHS include a reduced cerebrovascular reserve, perioperative hypertension, severe or bilateral carotid stenosis, previous stroke, and poor collateral supply [6, 8].

CHS has been described to occur following CEA, CAS, intracranial percutaneous transluminal angioplasty and stenting (PTAS), vertebral and subclavian PTAS, aorto-

carotid bypass surgery, extracranial-intracranial bypass surgery, carotid-subclavian bypass surgery, innominate endarterectomy, dural arteriovenous fistula embolization, arteriovenous malformation resection, and clipping of giant ICA aneurysm [6].

Coutts et al. have classified CHS into three types:

1. Acute focal edema (AFE)
2. Acute intracranial hemorrhage (AIH)
3. Delayed classic presentation (DCP)

Patients with AFE develop vasogenic edema in the affected cerebral territory with no changes on DWI. These patients have lower mortality rates compared with those with ICH. Patients with AIH demonstrate parenchymal bleed, subarachnoid hemorrhage, intraventricular hemorrhage, or both. These patients have higher mortality compared with the patients with AFE. Patients with DCP

demonstrate the same imaging features as those with AFE or ICH but manifest more than 24 h after procedure. Patients in this group tend to have lower mortality rates but prolonged recovery times [8].

Meyers et al. [3] first described CHS in patients following angioplasty/stenting in intracranial cerebral blood vessels. A review of literature revealed a total of 14 patients who developed CHS following intracranial angioplasty or stenting. We have reviewed all the available literature indexed in MEDLINE, with search terms “cerebral hyperperfusion syndrome,” “carotid angioplasty”, “carotid stenting”, “CHS”, “internal carotid artery”, “middle cerebral artery”, “anterior cerebral artery”, “basilar artery”, “intracranial disease, arterial”, and “cerebral hemorrhage” with analysis of the reference lists and cases with intracranial hemorrhages following stenting or angioplasty of all the retrieved articles. A review of the patients with CHS following intracranial angioplasty and/or stenting for intracranial stenosis reveals that patients who develop ICH irrespective of acute or delayed presentation have a higher mortality (9/11) compared with patients who develop FE (0/2) (Table 1).

The available therapeutic options in the present case after failure of optimal medical management included an extracranial to intracranial bypass or angioplasty and/or stenting of the symptomatic intracranial ICA stenosis. However, two trials have shown the futility of extracranial to intracranial bypass surgeries in the treatment of symptomatic intracranial disease [9]. Therefore, the patient underwent stenting with angioplasty for the symptomatic intracranial ICA high-grade stenosis [10, 11]. It also is well known that patients with bilateral high-grade carotid stenosis are at a higher risk of CHS [8]. In an attempt to

decrease the risk of CHS, CAS of the asymptomatic right ICA origin stenosis was performed. However, the patient still developed CHS of the AFE type. A 6-month control cerebral DSA, revealed in-stent restenosis but the patient was asymptomatic and was managed conservatively. At 1½-year follow-up, patient developed symptoms of left ICA territory insufficiency and crescendo transient ischemic attacks (TIAs) and convulsions due to progressive increase in the degree of stenosis with severe hypoperfusion.

Although CHS presents with features of both cerebral edema and intracranial hemorrhage, a single theory of disturbed autoregulation with BBB breakdown has been proposed to account for them [7]. However, this is the only described clinical scenario to date wherein a patient had both the manifestations of CHS (FE and ICH). We believe this occurred in the present case due to ISR, which changed the patient’s hemispheric perfusion from a state of initial hyperperfusion in the immediate postprocedure back to a state of chronic hypoperfusion, thus resulting in the second fatal manifestation. Thus, this clinical scenario highlights the fact that, although AFE and AIH present with different clinical and imaging features they have the same underlying etiology.

The data from a large multicenter registry on intracranial stenting in patients with symptomatic high-grade stenosis has shown higher rates of stroke and death at 30 days in patients with symptomatic high-grade stenosis compared with patients with moderate-grade stenosis (9.6 vs. 4.4 %) [12]. Another similar large multicenter registry showed symptomatic ISR was most commonly detected in the first 6 months (80 %) and their rates decreased thereafter. However, patients with delayed symptomatic ISR (after

Table 1 Review of patients with CHS following intracranial angioplasty and/or stenting

Sl. no.	Author/s (year)	Location ICA/VA	Procedure	Number of patients	Imaging features AFE/AIH/DCP	Outcome
1.	Meyers et al. (2000)	VA (2)	PTAS	2	AFE (1) AIH (1)	Alive (1) Death (1)
2.	Bando et al. (2001)	VA	PTA	1	None*	Alive
3.	Liu et al. (2001)	MCA	PTA	1	AIH	Death
4.	Qureshi et al. (2002)	ICA (1) MCA (2)	PTA	3	AIH (3)	Death (3)
5.	García-Bargo et al. (2004)	ICA	PTAS	1	DCP-ICH	Death
6.	Rezende et al. (2006)	VA	PTAS	1	DCP-ICH	Alive
7.	Terada et al. (2006)	ICA (1) VA (1)	PTA PTAS	2	AIH (2)	Alive (1) Death (1)
8.	Jiang et al. (2007)	VB Jn.	PTAS	1	DCP-ICH	Death
9.	Zhang et al. (2009)	VA	PTAS	1	AIH	Death
10.	Wolfe et al. (2009)	MCA	PTAS	1	DCP-FE	Alive
11.	Present case	ICA	PTAS	1	AFE and DCP-ICH	Death

* CHS in this patient was diagnosed solely on SPECT findings. On MRI, there was no edema or ICH. Total number of patients given in parentheses
 AFE acute focal edema; AIH acute intracerebral hemorrhage; DCP-FE delayed classic presentation focal edema; DCP-ICH delayed classic presentation intracerebral hemorrhage; ICA internal carotid artery; MCA middle cerebral artery; PTA percutaneous transluminal angioplasty; PTAS percutaneous transluminal angioplasty and stenting; VA vertebral artery; VB Jn. vertebrobasilar junction

6 months) were found to have been symptomatic earlier with TIAs and despite repeated interventions ultimately presented with stroke. The registry also showed a high event rate (approx. 30 %/year) in patients undergoing intracranial stenting compared with medically managed patients in the WASID trial (22.5 %/year). Therefore, patients with recurrent TIAs carry a much higher risk with intracranial stenting [13, 14]. In the present case, although the patient was detected with high-grade ISR on the routine 6-month angiogram she became symptomatic for the ISR after one and half years and despite repeat angioplasty and stenting developed CHS with an ultimately fatal outcome.

The only therapeutic maneuver shown in studies to prevent CHS is comprehensive blood pressure control. The blood pressure in patients at high risk of CHS when strictly maintained below 120/80 mmHg has been shown to decrease the incidence of CHS (from 1.88 to 0.53 %) and produce a significant decrease in the incidence of ICH (from 1.1 to 0 %) [15]. However, some studies have failed to consistently demonstrate similar success in the prevention of CHS with strict blood pressure control [4]. In our institute, strict blood pressure control (normotension) is initiated at admission in all patients believed to be at high-risk of CHS following stenting. However, in the present case, following left supraclinoid ICA stenting the patient had focal seizures with secondary generalization followed by epilepsia partialis continua as an initial manifestation of CHS. The patient was rapidly loaded with antiepileptic agents before it was realized that the patient also had a sudden surge in the blood pressure to 200/120 mmHg. By the time antihypertensive medications had brought the blood pressure under control, the patient had already developed right hemiparesis with facial palsy. In the second instance, when balloon angioplasty and restenting of the ISR was performed, despite strict pre- and intraoperative blood pressure control, the patient was detected with a large ICH in the immediate postprocedure CT. The blood pressure was only marginally raised to 130/90 mmHg. Thus, although strict blood pressure control is known to decrease the incidence of CHS and ICH, patients may still develop CHS with a fatal outcome.

The present case is a rare case of recurrent CHS in the same patient with different imaging and clinical manifestations. Although rare, CHS in relation to intracranial stenting or angioplasty is associated with significant morbidity and mortality. Also, as illustrated by our case, patients who develop CHS poststenting are likely to develop recurrent CHS in the same territory if subjected to repeat stenting or angioplasty.

Conflict of interest The authors declared they have no conflict of interest.

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