Reversible Cerebral Vasoconstriction Syndrome: Treatment with Multiple Sessions of Intra-Arterial Nimodipine and Angioplasty

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Summary

Reversible cerebral vasoconstriction syndrome (RCVS) is characterized by acute severe headache with or without additional neurological symptoms and reversible cerebral vasoconstriction. Unruptured aneurysms have been reported in some cases with RCVS. We describe a severe case of a 50-year-old woman with RCVS presenting as cortical subarachnoid hemorrhage. Cerebral angiogram demonstrated the typical angiographic findings of RCVS and two very small unruptured aneurysms of the left internal carotid artery. The patient was treated with calcium channel blockers and the two aneurysms were successfully treated endovascularly. On day 16 the patient developed new focal neurological symptoms (severe paraparesis) and was successfully treated with intraarterial nimodipine and angioplasty in multiple sessions.

Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a term used to describe a reversible segmental and multifocal vasoconstriction of cerebral arteries, and severe headaches with or without focal neurological deficit or seizures¹. The most common clinical feature of RCVS is a severe acute headache, often qualifying as thunderclap headache a sudden excruciating headache that peaks in less than 1 min, like a 'clap of thunder', mimicking that of a rup-

tured aneurysm². Brain imaging is typically normal, although some cases have presented intraparenchymal (6%) or subarachnoid hemorrhages (SAH) (22%) attributed to reperfusion³.

The course is usually benign, even without treatment. The major complication of RCVS is stroke, -ischemic or haemorrhagic- eventually leading to permanent sequelae and even death⁴. The exact incidence of stroke is unknown, but has been estimated to range from 7%⁵ up to 54%¹.

Here, we describe a case of RCVS, where a complicated course of severe, symptomatic vasoconstriction led to serious neurological deficits and resolved after serial intra-arterial applications of nimodipine and balloon angioplasty.

Case Report

A 50-year-old woman presented to us after she experienced an unusual, short-lasting (30-75 minutes) thunderclap headache six hours before admission. Neurological examination was normal on admission. She had no other medical history and no history of drug use. Vital signs were normal. Computed tomography (CT) of her brain showed small left-sided SAH at the high convexity. Cerebral magnetic resonance imaging (MRI) confirmed CT findings without additional information (Figure 1). Cerebral angiogram showed two small (3 mm and 2 mm) parophthalmic saccular aneurysms and

↑ *Figure 2* Digital subtraction angiogram, right internal artery injection, oblique view, shows segmental areas of vasoconstriction of both middle and anterior cerebral arteries (arrows).

← *Figure 1* Brain MRI, FLAIR sequence, shows hyperintensity over the left frontal lobe, corresponding to blood in the subarachnoid space.

Figure 3 Cerebral angiogram, left internal carotid artery injection, oblique view shows two small (less than 3 mm) parophthalmic aneurysms. Segmental areas of vasoconstriction are also evident (arrow).

Figure 4 Post-embolization cerebral angiogram, shows complete occlusion of the aneurysms.

multiple segmental arterial narrowing in distal branches of the both middle and left posterior cerebral arteries (Figures 2 and 3). However, the localized cortical subarachnoid blood in this patient was clearly remote from the left IC aneurysm. Moreover, it appears extremely unlikely that minimal localized bleeding at the surface of the brain could explain the subsequent diffuse and multifocal vasoconstriction affecting medium- and large-sized arteries remote from the site of bleeding in this patient. Full vasculitic screen was negative. Cerebrospi-

nal fluid examination was normal. The patient was treated with intravenous administration of nimodipine (intravenous infusion 1 mg/h) and analgesics (paracetamol) due to mild headaches. Taking into account the fact that aneurysms were treatable we proposed endovascular treatment. The following day the patient underwent successful endovascular embolization of both aneurysms (Figure 4). The patient had an uneventful postoperative course and remained asymptomatic and fully mobilized. Follow-up CT on day 14 was normal.

On day 16 the patient developed severe paraparesis (Medical Research Council [MRC] grade 1/5). On neurologic examination the patient was alert and oriented. MRI showed bilateral anterior cerebral arteries ischemic lesions. MRA showed diffuse vasospasm in bilateral anterior and middle cerebral arteries more prominent in the anterior. The vasospasm was evident in the entire course of the vessels and it was equally prominent in distal segments of multiple branches of both anterior and middle cerebral arteries. The patient underwent cerebral angiogram under mild sedation and under continuous monitoring of her vital signs. The DSA confirmed the MRA findings (Figure 5A,B). The patient underwent selective intra-arterial infusion of nimodipine 6 mg in each ICA over 30 minutes (1 lt normal saline 0.9% with 12,500 IU heparin and 10 mg of nimodipine with a flow rate of 20 ml/min) in both ICAs. Balloon angioplasty was started 30 minutes after the onset of intrarterial infusion of nimodipine on both anterior and middle cerebral arteries (A1 and M1 segments). At the end of the procedure the diameter of the vessels normalized. Only distal branches of the anterior and the middle cerebral arteries showed minor irregularities.

After the procedure, the patient was transferred in the ICU and was treated with intravenous (IV) administration of nimodipine at a dose of 1 mg/hour. We also maintained generous hydration and iatrogenic hypertension for systolic blood pressure between 160 mm Hg and 180 mm Hg.

The patient showed remarkable neurological improvement (Medical Research Council [MRC] grade 3/5) within four hours after the procedure.

The clinical improvement after each intervention lasted for less than 24 hours despite the medical treatment and therefore the patient underwent, in total, four sessions of intra-arterial infusion of nimodipine and angioplasty with the same protocol. After the last session, the angiographic result remained stable (Figure 5C,D), as follow-up MRA showed, and the paraparesis gradually improved within 48 hours. A follow-up MRI done one and six months (Figure 6) after neurological deterioration showed bilateral anterior cerebral arteries ischemic lesions.

The patient was discharged on day 28. During the following 12 months the patient showed remarkable neurological improvement, and she is able to walk without assistance. Follow-up MRAs at three and six months were normal.

Discussion

Reversible cerebral vasoconstriction syndrome (RCVS) is a cerebrovascular disorder associated with multifocal arterial constriction. The typical patient with RCVS is a woman between the ages of 20 and 50 years presenting with a hyperacute severe headache, often called a "thunderclap headache"¹. Historically, this refers to a severe headache that reaches its peak intensity within seconds, like a "clap of thunder". It has been described under various names, including Call-Fleming syndrome, benign angiopathy of the nervous system and postpartum angiopathy. RCVS may be spontaneous, more than half of the cases occur in special circumstances such as postpartum or after an exposure to sympathomimetic or serotonergic substances. For the diagnosis of RCVS the patient should have all of the following features: multifocal, segmental cerebral arteries vasoconstriction, no evidence of aneurysmal subarachnoid hemorrhage, normal or near-normal cerebrospinal fluid analysis and reversibility of vasoconstriction within 12 weeks after onset. Recent reports⁴ and case series^{6,7} have suggested that intracranial hemorrhages may be frequent and have different patterns in RCVS, including cortical subarachnoid hemorrhages (cSAHs), intracerebral hemorrhages (ICHs), and subdural hemorrhages (SDHs).

ICH and cSAH are usually early complications (in the first three and ten days respectively). Ischemic events occur significantly later (12-15 days)⁴.

Cortical subarachnoid hemorrhage (cSAH) is an unusual presentation of subarachnoid bleeding, in which the bleeding is localized to the convexities of the brain without involvement of the adjacent parenchyma or extension into the interhemispheric fissures, basal cisterns, or ventricles. Since most saccular aneurysms arise from the circle of Willis, aneurysmal rupture is an unlikely source of cSAH. Diverse etiologies have been posited for its occurrence, including cortical vein occlusions, reversible cerebral vasoconstriction syndrome (RCVS), lupus vasculitis, cavernoma, and cerebral amyloid angiopathy (CAA) etc.^{7,8}. Localized convexity subarachnoid hemorrhage occurs in 22% of patients with RCVS, mainly within the first week of the course of the disease².

Neurovascular imaging in patients with RCVS shows alternating areas of arteries constriction and dilatation in the large and medium

Figure 5 A,B) Right and Left internal carotid artery angiogram shows marked narrowing of middle and anterior cerebral arteries. C,D) Post-treatment angiogram shows improvement in the diameter of both anterior and middle cerebral arteries. E,F) After four serial sessions of intra-arterial nimodipine infusion and angioplasty marked improvement is noted. Segmental vasoconstrictions of distal branches were also improved.

Figure 6 Follow-up MRI (6 months), FLAIR sequences shows bilateral anterior cerebral arteries chronic ischemic lesions.

and peaks between days four and 11. Acute vasospasm on the day of onset is extremely rare. Other arterial abnormalities have been reported in patients with RCVS like small unruptured aneurysms and dissections⁴. There are also several reports of RCVS with cSAH and small unruptured aneurysms which were treated either surgically or endovascularly, or left untreated.

The optimal management of acute neurologic deficits caused by RCVS is uncertain. Patients with RCVS might be responsive to the calcium channel blockers such as nimodipine or verapamil. Calcium-channel blockers should be administered with caution because of the risk for brain infarction in cerebral regions with reduced perfusion by a severely constricted cerebral artery. Alternatively, short-term high-dose glucocorticoids have been reported to be effective.

By definition RCVS is a spontaneous reversible condition. Permanent neurological deficits were noted in only 3-6% of patients in two large prospective series. Higher percentages of stroke, up to 54%, have been suggested in literature reviews and retrospective series, with ICH in 14-25% and infarctions in 14-31%².

In post-SAH vasospasm the most commonly used endovascular therapies are intra-arterial vasodilators and balloon angioplasty. Nimodipine, verapamil and milrinone have recently been demonstrated to be safe and effective when administered intra-arterially for the treatment of severe segmental vasoconstriction in patients with RCVS^{9,10}. Direct intra-arterial application of vasodilators has an immediate effect and permits preferential intracranial arterial dilation while minimizing systemic hypotension¹⁰.

In our case the angiographic result was excellent and the patient showed remarkable recovery after every session of intrarterial infusion and angioplasty. Due to the neurological deterioration of the patient within 18 to 24 hours we decided to repeat the treatment in three additional sessions.

We recommend intrarterial administration of nimodipine and/or balloon angioplasty as a possible treatment for patients with RCVS with severe neurological deficits due to reduced perfusion, but there is only limited sustained improvement in vasodilation that may require repetitive treatments.

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