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Severe reversible cerebral vasoconstriction syndrome in a postpartum patient treated successfully with direct instillation of intra-arterial verapamil during cerebral angiography

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CASE

A 36-year-old woman developed a sudden onset thunderclap headache and visual disturbance, while undergoing a caesarean section for her second pregnancy. Ten minutes after delivery, she suffered a sustained, generalized tonic-clonic seizure and required intubation and, following intubation, was transferred to the intensive care unit.

Following cessation of seizure activity, the patient was extubated and on examination was found to be neurologically intact. A noncontrast CT brain was unremarkable; however, intracranial MRI and MR angiography (MRA) demonstrated multifocal, low-grade arterial stenoses in several vascular territories without evidence of infarction or hemorrhage. The two major differentials of these MR findings were cerebral vasculitis and reversible cerebral vasoconstriction syndrome (RCVS), and given the patient's postpartum presentation, RCVS was considered the most likely diagnosis. Four days after delivery, the patient was neurologically intact and experiencing only minor headaches and, therefore, was discharged on oral calcium cannel blockers for treatment of cerebral vasoconstriction and oral pregabalin for seizure prophylaxis.

One week later, the patient represented to hospital with severe headaches and was found to be markedly hypertensive with a systolic blood pressure over 190 mm Hg. Neurological examination identified bilateral agraphesthesia without other focal neurological deficits. Repeated MRI/MRA performed at this time demonstrated significant progression of disease; multiple bilateral cortical watershed infarcts [Figure 1(A)] had developed since initial MRI and multiple high-grade stenosis were now seen within the anterior, middle, and posterior cerebral arteries bilaterally and within the basilar artery [Figure 1(B)].

In order to better define the extent of arterial pathology and to exclude other potential causes of the patient's clinical and radiological findings, a digital subtraction cerebral angiogram (DSA) was then performed. The DSA demonstrated extensive and severe beading of large and medium caliber intracranial arteries; multiple segments of smooth and high-grade stenosis were interspersed with normal caliber arterial segments [Figure 2(A) and (B)]. No intracranial aneurysm was identified and the arteries of the external carotid artery circulation were found to be normal.

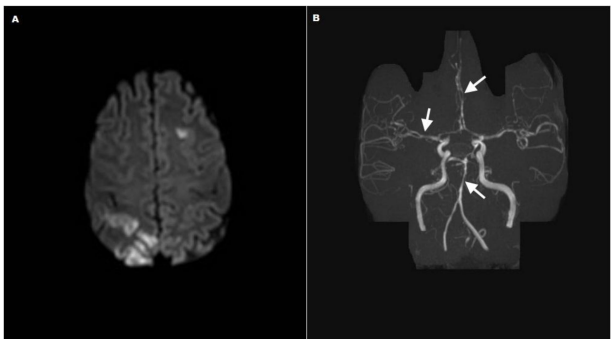

Figure 1. (A) Diffusion weighted imaging demonstrating multiple foci of high signal consistent with multiterritory, acute watershed infarcts. (B) Time-of-flight MRA demonstrates diffusely abnormal intracranial arteries with extensive multiterritory stenoses (white arrows) involving ACAs, MCAs, and vertebro-basilar system.

Given that the DSA findings suggested RCVS and given the severity of the arterial stenoses, 10mg of verapamil was instilled into each internal carotid artery and into the left vertebral artery. This administration of intra-arterial calcium channel blockers produced a dramatic angiographic result with near complete resolution of the multifocal arterial stenoses [Figure 2(C)].

Although the patient's headaches persisted for three more days, her blood pressure normalized, she was found to be neurologically intact and she was discharged from hospital four days after the DSA.

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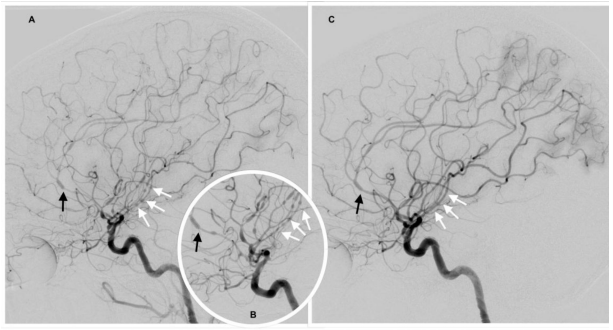

Figure 2. (A) Initial DSA images of left ICA territory and (B) magnified image demonstrate the classic "string of beads" sign of RCVS (white arrows) with multifocal arterial stenoses interspersed with normal caliber segments. Multiple further focal stenoses are also demonstrated (e.g., the stenosis identified by the black arrow). These findings almost completely resolve following administration of (C) IA verapamil

DISCUSSION

RCVS is an uncommon phenomenon, classically presenting as a severe headache with or without seizures or focal neurological deficits. Although the condition is usually self-limiting, cerebral infarction, edema, or hemorrhage can result in significant morbidity in approximately 5% of cases [1].

The underlying pathophysiological process appears to be a transient loss of cerebral vascular tone resulting in the development of multifocal stenoses of the large and medium caliber intracranial arteries. The reason for the loss of arterial tone is poorly understood; however, it has been noted that the majority of cases occurs in the postpartum period or following exposure to adrenergic or serotonergic drugs [2], indicating that endogenous and exogenous triggers for the condition exist.

Angiography is a requirement for the diagnosis of RCVS. The noninvasive modalities of CT angiography and MR angiography (MRA) will demonstrate the multifocal arterial stenosis seen in RCVS in many cases [3]; in addition, these techniques have the advantage of imaging the cerebral parenchyma and identifying potential sequale of RCVS such as intracranial hemorrhage or infarction.

However, DSA with its higher spatial resolution remains the gold standard imaging technique for RCVS allowing accurate assessment of extent and severity of disease. The "string of beads" sign, multiple smooth arterial stenoses interspersed with segments of normal arterial caliber, is the classic angiographic finding in RCVS and is well demonstrated in this case [Figure 2(A) and (B)]. DSA is also better able to differentiate between RCVS and its mimics; namely, cerebral vasculitis or vasospasm secondary to aneurysmal SAH. Reversibility of arterial stenoses following administration of vasodilators [Figure 2(C)] is suggestive of RCVS with vasculitis rarely responding in a similar fashion due to established arterial wall fibrosis [4]. Involvement of the external carotid circulation suggests the presence of a systemic vasculitis but does not exclude a primary cerebral vasculitis. Vasospasm due to aneurysmal SAH rarely elicits the arterial "beading" seen in RCVS and is highly unlikely if an aneurysm is not identified on DSA.

Treatment of RCVS involves analgesia, antiseizure prophylaxis, and administration of agents to reduce the degree of cerebral arterial vasoconstriction, most commonly the calcium channel blockers verapamil and nimodipine. These agents are most commonly administered orally; however, as demonstrated in this case and in other small case series [5], the direct intra-arterial administration of these agents during DSA maybe a useful adjunct in the treatment of severe cases of RCVS.

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