British Journal of Medicine & Medical Research
12(2): 1-5, 2016, Article no.BJMMR.22113
ISSN: 2231-0614, NLM ID: 101570965

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Reversible Cerebral Vasoconstriction Syndrome – A Systematic Approach

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Authors' contributions

This work was carried out in collaboration between all authors. Author RP found the case. Authors SG and RR designed the study. Author SG wrote the protocol, and wrote the draft of the manuscript. Author SI managed the literature searches and helped in preparing the draft. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/22113
Editor(s):
(1) Vijay K. Sharma, Division of Neurology, Yong Loo Lin School of Medicine, National University of Singapore, National University Hospital, Singapore.
Reviewers:
(1) Takao Yasuhara, Okayama Univ, Japan.
(2) Rajendra Nath, King George's Medical University, Lucknow, India.
Complete Peer review History: http://sciencedomain.org/review-history/12065

Case Study

Received 18th September 2015
Accepted 13th October 2015
Published 2nd November 2015

ABSTRACT

Aims: Reversible cerebral vasoconstriction syndrome (RCVS) is a rare idiopathic clinical syndrome presenting as reversible multifocal segmental vasoconstriction of cerebral arteries, typically affecting middle aged women. A 52 year old lady with radiological features of RCVS is presented.
Presentation of Case: A 52 year old lady presented with recurrent thunderclap headache. Initial laboratory and radiological investigations were normal. Over the course of two weeks she developed stroke like symptoms with haemorrhagic transformation. Serial imaging revealed development and resolution of cerebral arterial stricture.
Discussion: RCVS is often an under-diagnosed entity in patients with thunderclap headache. The initial MRI may be normal but the repeat MRI after two to three weeks may show features of stroke with associated vascular abnormalities. The follow up of these cases with radiological investigations may help in precise diagnosis.
Conclusion: Differentiating RCVS from other causes of thunderclap headache can significantly alter the management options and further prognosis.

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Keywords: Thunderclap headache; resolving cerebral vasoconstriction; benign CNS arteriopathy; migrainous vasospasm.

1. INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) is a rare idiopathic clinical syndrome presenting as reversible multifocal segmental vasoconstriction of cerebral arteries, typically affecting middle aged women. The dreaded complications are ischemic and haemorrhagic stroke. The definitive diagnosis of the syndrome depends on the radiological demonstration of spontaneous resolution of the angiographic findings within two to six weeks [1,2]. The widespread usage of imaging modalities have increased the rate of detection of more cases, raising the incidence. The pathophysiological mechanism causing RCVS is still not well understood. Awareness of this clinical entity will increase the detection and facilitate improvement in the treatment options.

2. PRESENTATION OF CASE

A 52 year old multiparous post-menopausal woman presented with sudden onset of excruciating headache while she was swimming, that peaked in around two minutes. The headache was occipital, which rapidly progressed to involve the entire head. An associated visual disturbance was present in the form of multi-coloured circles in the left visual field. She had episodic attacks of migraine which were relieved by taking non-steroidal anti-inflammatory drugs (NSAID). There was no history of any other comorbidity. A computerised tomography (CT) scan was done on the same day and CT scan showed no significant abnormalities. The symptoms resolved after eight hours.

Similar episodes of headache recurred daily, which were associated with, but not relieved with vomiting. A magnetic resonance imaging (MRI) of the brain with magnetic resonance angiogram (MRA) and magnetic resonance venogram (MRV) was done three days later. T2 weighted images showed hyper intense regions the left parietal lobe, suggestive of small vessel ischemic disease. MRA and MRV were normal. Symptomatic NSAIDs were prescribed. However, episodes of headache continued.

Four days later she developed similar episodes of headache, which was associated with left lower limb monoparesis and lower back ache. The power of the left lower limb was four out of five, according to Medical Research Council (MRC) scale. No sensory deficit was elicited and deep tendon reflexes were normal. No associated fever, seizures, palpitations or altered sensorium was present. She got admitted in a nearby hospital for the same. Routine blood investigations and electrocardiogram were normal. MRI scan of the brain and spine was performed which revealed acute infarct with minimal haemorrhagic transformation in left parietal lobe (Figs. 1a, 1b, 1c), with normal MRA. The symptoms resolved in six hours.

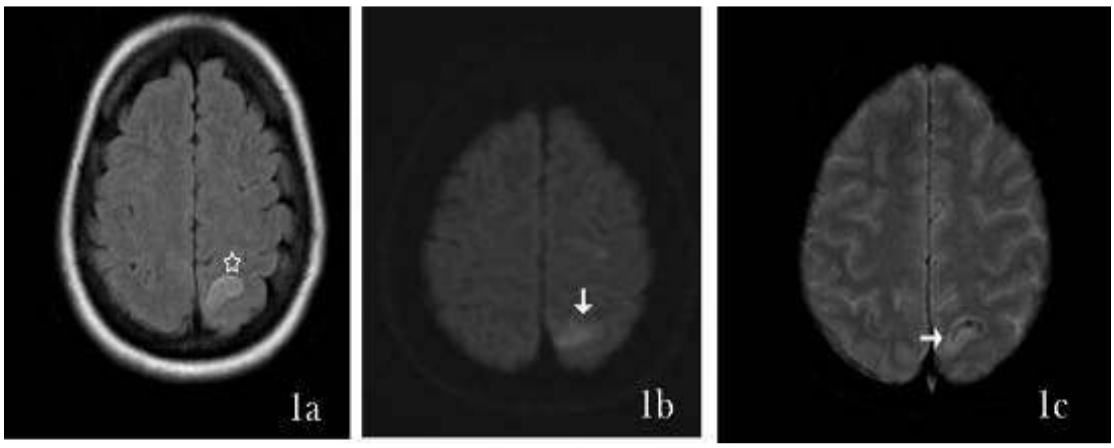

Fig. 1a, 1b and 1c. Axial sections of the brain shows an area of FLAIR hyper intensity involving the left parietal lobe (asterix) and restricted diffusion on DWI (down arrow) with foci of blooming on GRE (right arrow) suggestive of acute haemorrhagic infarct

After three days, the lady was shifted to our institution for further management in view of worsening headache, progressive right side weakness and loss of vision. We did a vasculitis workup and cerebro-spinal fluid (CSF) analysis, both of which turned out to be normal. MRI study was repeated which showed fresh acute infarcts in bilateral occipital lobe with increase in parietal infarct size with haemorrhagic transformation (Figs. 2a, 2b). MRA showed irregularity and narrowing of bilateral middle cerebral arteries and narrowing of the bilateral posterior cerebral arteries (Fig. 2c). Patient was started on oral Nifedipine. The symptoms resolved within 3 hours with partial restoration of vision. However, the symptoms progressed the next day and another MRI was done. There was increase in the size of the infarcts in bilateral occipital regions (Fig. 3a), whereas MRA showed resolution of vascular changes (Fig. 3b). Due to systemic compromise, patient went in for asystole and succumbed to complications.

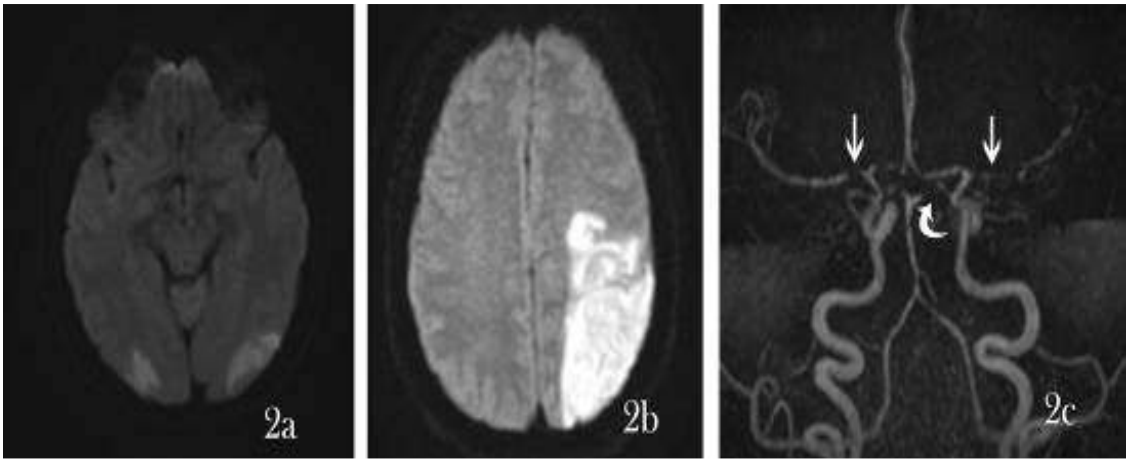

Fig. 2a, 2b and 2c. Diffusion weighted imaging shows areas of restricted diffusion in bilateral occipital lobe and left parietal lobe and MRA showing irregularity with beaded appearance involving bilateral middle cerebral arteries (down arrow) and bilateral posterior cerebral arteries (curved arrow)

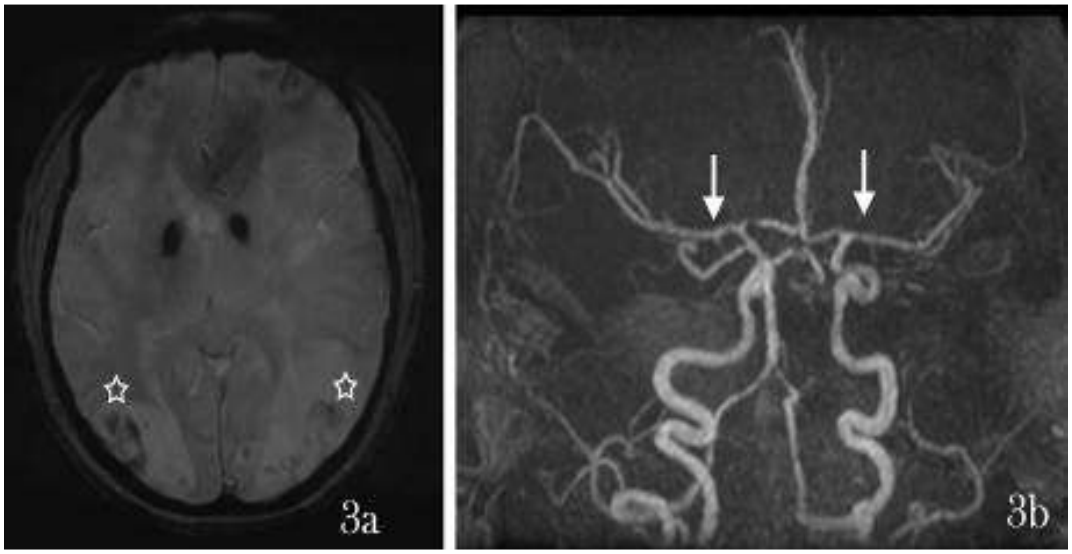

Fig. 3a and 3b. Axial gradient sections of the brain shows bilateral haemorrhagic infarcts involving bilateral occipital lobes (asterix) and reversal of the beaded appearance in bilateral middle cerebral arteries

3. DISCUSSION

RCVS is mostly an imagiological diagnosis. In the present scenario, the syndrome is almost exclusively diagnosed based on imaging findings of multifocal segmental vasoconstriction of cerebral arteries resolving within few weeks, with no other obvious diagnosis [3]. RCVS is synonymous with migrainous vasospasm or migraine angitis, Call-Fleming syndrome, benign angiopathy of the central nervous system, postpartum angiopathy and drug-induced arteritis [4].

The syndrome is most common in women with a female to male ratio of 3:1 [5]. The mean age of occurrence is around 42 years and ranges from 10 to 76 years [4]. No geographical or racial predilection has been reported. The recent increases in incidence may be due to increased physician awareness or improvement in imaging techniques or due to true increase in the disease [5].

RCVS can be spontaneous (37%) or secondary due to other triggering factors (63%) including use of vasoactive drugs (37%) and the postpartum state (5%). The pathogenesis is primarily idiopathic but may be due to transient disturbance in the control of cerebral vascular tone, which may be induced by sympathetic over activity, endothelial dysfunction, or oxidative stress. No active inflammation or vasculitis has been demonstrated in histologic or electron microscopic analysis [5].

The clinical manifestations range from pure cephalalgic forms with recurrent thunderclap headaches over one to two weeks to rare catastrophic forms with multiple haemorrhagic and ischemic strokes, brain oedema and death.

Thunderclap headache is the term used for sudden onset excruciating headache that peaks within seconds to few minutes. The most important differential diagnosis is sub-arachnoid haemorrhage due to a ruptured aneurysm. Thunderclap headaches occur in 94%–100% of patients with RCVS with a characteristic waxing and waning [5]. Thunderclap headache can also be associated with various other medical conditions, including aneurysmal subarachnoid haemorrhage, primary headache disorder, pituitary apoplexy, cerebral venous sinus thrombosis, unruptured cerebral aneurysm, cervical arterial dissection, and third ventricle colloid cyst, among others [6]. All the conditions associated with thunderclap headache can be diagnosed by MRI and MRA with confidence, whereas plain CT scan can be normal. So we recommend MRI with MRA in all patients with thunderclap headache.

Photophobia, phonophobia, nausea, vomiting, seizures, focal neurological deficits or symptoms relating to complications can also manifest.

Initially, conventional cerebral angiography was the primary diagnostic modality showing diffuse, multifocal, segmental narrowing involving large and medium-sized arteries in the anterior and posterior circulations, with occasional dilated segments, like ‘strings and beads’ or ‘sausage strings’ [7], which reverses when repeated within a few weeks.

More recently, non-invasive investigations such as magnetic resonance angiography (MRA) and transcranial Doppler (TCD) have promised to demonstrate similar efficacy in the assessment and follow-up of vasoconstriction [8,9].

Cerebro-spinal fluid analysis will be normal or near normal and the vasculitis workup will be normal. RCVS should be suspected in a patient presenting with thunderclap headache in which the initial imaging findings are normal.

Various complications were observed, in different time courses. The early complications usually occur within one week and are cortical subarachnoid haemorrhage (22%), posterior leuko-encephalopathy (9%), intra-cerebral haemorrhage (6%) and seizures (3%). The late complications occurring mainly during the second week are ischaemic events, including transient ischemic attacks (TIAs) (16%) and cerebral infarction (4%). Stroke can be haemorrhagic or non-haemorrhagic leading to neurological deficits or even death (5-10%).

Risk factors for the development of intracranial haemorrhage in patients with RCVS include a history of migraines, older age, and female sex [10]. No definite clinical or radiological prognostic indicators have been identified. Severe course may be associated with a high level of urine 8-Iso-prostaglandin F2α [11] or with BDNF Val66Met gene polymorphism [12].

No high level evidence exists for the optimal management of RCVS. Intensive unit level care with withdrawal of any suspected exogenous triggers and symptom relief with analgesics, blood pressure control, and seizure prophylaxis are advocated. Reversal of vasoconstriction by

calcium channels blockers such as Nimodipine or Nifidipine is found to be useful in controlling attacks. These measures have not been proven to change the course of the disease [3].

The actual magnitude of RCVS is still not understood. The incidence might be higher than predicted earlier. And including the disease in the differential diagnosis may be helpful in detecting the cases and formulating the optimal treatment.

4. CONCLUSION

To conclude, in patients presenting with thunderclap headache, the initial MRI might be normal. A repeat MRI with MRA within one or two weeks may help in precise diagnosis which aids in optimizing further management and prognosis of the disease.

CONSENT

Informed consent was obtained from the patient's relatives for publishing the case and the radiological images. No information that will reveal the identity of the patient has been included in the article.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/12065