

## CASE REPORT

## Cerebral-autoregulatory dysfunction syndrome

Ravindra Kumar Garg,<sup>1</sup> Hardeep Singh Malhotra,<sup>1</sup> Tushar B Patil,<sup>1</sup> Avinash Agrawal<sup>2</sup>

<sup>1</sup>Department of Neurology, Chhatrapati Shahuji Maharaj Medical University, Lucknow, Uttar Pradesh, India  
<sup>2</sup>Department of Internal Medicine, Chhatrapati Shahuji Maharaj Medical University, Lucknow, Uttar Pradesh, India

**Correspondence to**

Dr Hardeep Singh Malhotra, drhsmalhotra@gmail.com

**SUMMARY**

Reversible cerebral vasoconstriction syndrome and reversible posterior leukoencephalopathy syndrome are distinct clinicoradiological disorders which share certain features in terms of aetiology, pathogenesis and symptomatology. We present a case of a young primigravida with eclampsia who developed severe headache, vision loss and hemiparesis in the postpartum phase. MRI of the brain was suggestive of the involvement of anterior as well as posterior circulation and reversibility of widespread angiographic constrictions could be documented on follow-up. Despite the resolution of vascular changes, vision loss did not improve significantly in our case. Such an overlap of findings is unusual and probably represents the spectrum of cerebral-autoregulatory dysfunction occurring in these two syndromes.

**BACKGROUND**

Reversible cerebral vasoconstriction syndrome (RCVS) is a clinicoangiographic entity characterised by severe headaches occurring in varying combinations of neurological symptoms, and the constriction of large-sized and medium-sized cerebral arteries which resolves spontaneously within 12 weeks.<sup>1</sup> Reversible posterior leukoencephalopathy syndrome (RPLS) is a rapidly evolving neurological condition identified by headache, nausea and vomiting, seizures, visual disturbances and altered sensorium with reversible vasogenic oedema involving the parieto-occipital areas of the brain.<sup>2</sup> Considerable overlap, in terms of aetiology, pathogenesis and clinical features, exists between both these syndromes hence segregating the two is not always possible. RCVS and RPLS commonly occur in the postpartum phase which complicates the issue further.

**CASE PRESENTATION**

A 25-year-old primigravida, admitted in the department of obstetrics, developed three episodes of generalised tonic-clonic seizures with loss of consciousness 5 days prior to delivery of a child per vaginum. The patient was diagnosed as having eclampsia and was managed conservatively with parenteral magnesium sulfate. On the fourth postpartum day, the patient experienced a severe headache associated with multiple episodes of vomiting and blurring of vision. Over the ensuing 18 h she developed altered sensorium and was transferred to the department of neurology for further management. Her history was not suggestive of migraine, vasculitis or connective tissue disorder; medication history was non-corroborative. At the time of admission the patient was drowsy (Glasgow Coma

Scale 10/15) and movements were asymmetrical between the two sides of the body. Neurological examination revealed normal-sized reactive pupils, right-upper motor neuron facial palsy and right hemiparesis (Medical Research Council grade 2/5) with a right extensor plantar response. Other systemic examinations did not reveal any abnormality.

**INVESTIGATIONS**

Laboratory investigations revealed a normal haemogram, blood sugar, liver function tests, kidney function tests and coagulation profile; urine was positive for protein. Antinuclear antibody, extractable nuclear antibody profile and sepsis screen were negative. Chest x-ray and ultrasound of the abdomen did not reveal any abnormality. MRI of the brain showed involvement of the parieto-occipital regions, extending into the frontal lobes, and cerebellar hemispheres, left more than right, with evidence of restriction in the corresponding areas on diffusion-weighted images; apparent diffusion coefficient maps were suggestive of low values. There was no contrast extravasation on postcontrast T1-weighted images. MR angiography (MRA) revealed lack of visualisation of the left internal carotid artery and its divisions along with segmental constriction of the right vertebral artery; segmental narrowing and dilation of superior cerebellar and posterior cerebral arteries were additionally noted (figure 1). Ultrasound of the carotids in the neck did not reveal any abnormality. Cerebrospinal fluid examination was normal and was tested negative for varicella zoster virus, herpes simplex, Japanese encephalitis, dengue and enterovirus.

**TREATMENT**

In view of the clinical setting and angiographic findings the patient was initiated on nimodipine in anticipation of the development of ischaemia in the left internal carotid territory. The patient regained consciousness within 48 h and an improvement in weakness was observed; at 2 weeks no perceptible weakness existed on examination.

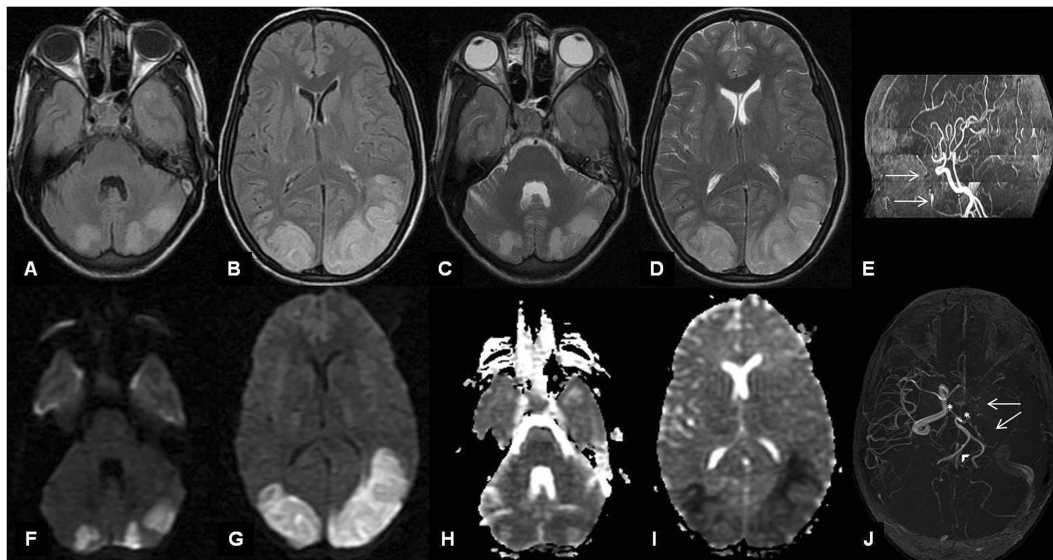
**OUTCOME AND FOLLOW-UP**

Follow-up MRI with MRA, carried out after 3 weeks, showed a decrease in the extent of involvement, and normalisation of flow in the left internal carotid artery (and its divisions), a resolution of the segmental constriction of the right vertebral artery, superior cerebellar arteries and posterior cerebral arteries (figure 2). A significant improvement in the patient's vision was not observed till the time of discharge at 4 weeks.



CrossMark

**To cite:** Garg RK, Malhotra HS, Patil TB, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201592



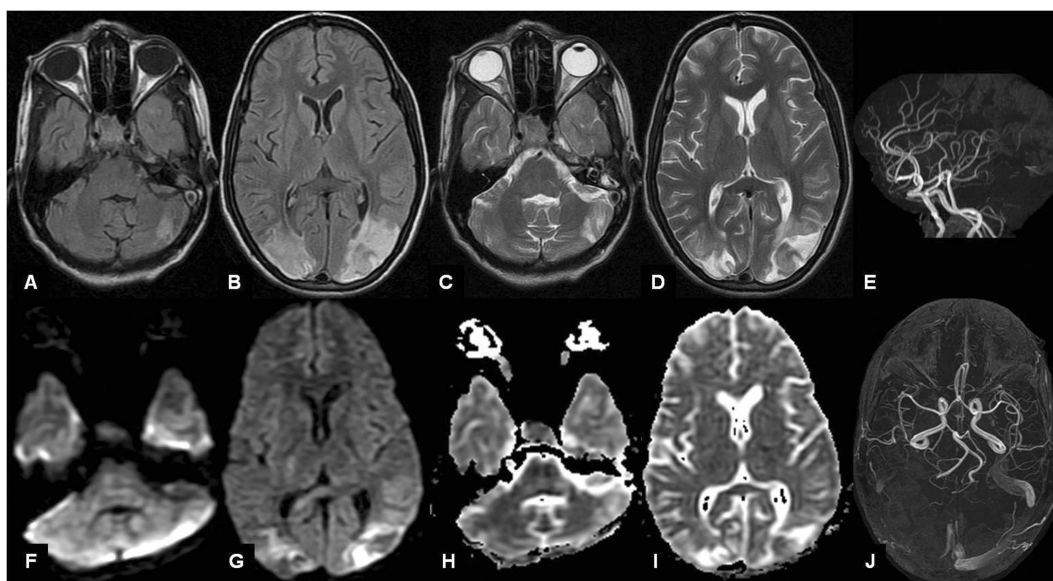
**Figure 1** Baseline MRI of the brain depicts hyperintensities involving the bilateral cerebellar hemispheres and the parieto-occipital regions on axial fluid-attenuated inversion recovery (A and B) and T2-weighted images (C and D), with corresponding diffusion-weighted images (F and G) showing restriction and apparent diffusion coefficient images (H and I) displaying low values. MR angiography (E and J) showing non-visualisation of the left internal carotid artery (arrows) and its divisions along with segmental constriction of the right vertebral artery (arrow head); segmental narrowing and dilation of superior cerebellar and posterior cerebral arteries is also evident (asterisk).

## DISCUSSION

In the background of eclampsia, our patient developed a severe headache and blurring of vision in the postpartum phase followed by hemiparesis. MRI with MRA of the brain demonstrated changes occurring beyond the conventional observation of parieto-occipital involvement with a striking non-visualisation of the left carotid artery along with changes observable in the right vertebral and both posterior cerebral and superior cerebellar arteries. Follow-up imaging revealed a persistence of, albeit decreased, cerebral-parenchymal changes but with remarkable

angiographic normalisation of the previously involved vessels. In view of the setting, symptomatology, the location of cerebral parenchymal changes with an admixture of vasogenic and cytotoxic oedema, and reversibility of angiographic changes the patient was classified as an overlap of RCVS and RPLS.

RCVS is a clinicoangiographic entity characterised by an acute-onset of severe headache (thunderclap headache), which may or may not be associated with neurological dysfunction, with reversible constriction of the large-sized and medium-sized cerebral arteries.<sup>1</sup> It is an underdiagnosed condition and the



**Figure 2** Follow-up MRI of the brain depicts hyperintensities, which have reduced in extent, involving the left cerebellar hemisphere and the parieto-occipital regions on axial fluid-attenuated inversion recovery (A and B) and T2-weighted images (C and D). Diffusion-weighted images (F and G) showing reduction in size while apparent diffusion coefficient (H and I) have increased from the baseline. MR angiography (E and J) showing normalisation of flow in left internal carotid artery (and its divisions), resolution of segmental constriction of the right vertebral artery, superior cerebellar arteries and posterior cerebral arteries.

exact incidence of the syndrome is not known; data available have been obtained from the various published case series.<sup>3-7</sup> It is an umbrella term comprising all aetiologically diverse disorders, viz. Call-Fleming syndrome, postpartum angiopathy, benign angiopathy of the central nervous system, migrainous vasospasm and drug-induced cerebral vasculopathy, where similar clinical and radiological findings are observed.<sup>8-9</sup> The key word 'reversible' in RCVS applies to the complete or near-complete normalisation of the angiographic findings within 12 weeks, and this may not necessarily be associated with the resolution of the clinical or cerebral-parenchymal findings.<sup>1</sup> MRI with MRA of the brain are the usual first-line imaging techniques to evaluate for RCVS; conventional catheter-based angiography, however, is the gold standard. The most specific evidence for RCVS is the demonstration of complete or near-complete reversibility of vasoconstriction, invariably within 3 months.<sup>1</sup> Besides angiography, transcranial Doppler study is an excellent tool for the initial assessment and follow-up of patients with RCVS. Since cut-off values similar to that in sickle-cell disease are not available for such patients, it is recommended that sequential studies be performed to look for the suggestion of vasospasm or improvement in the same.<sup>6</sup>

RPLS is identified by headaches, visual perception defect, altered sensorium and seizures, with the involvement of the parieto-occipital areas of the brain usually occurring in the setting of eclampsia, renal disease and hypertensive encephalopathy.<sup>2</sup> Most evident radiological findings on T2-weighted MRI are the hyperintense lesions located at the grey-white junction and involve the parieto-occipital regions bilaterally. Lesions can involve the frontal and temporal lobes, as well as the basal ganglia and cerebellar hemispheres; more extensive lesions have been associated with more severe clinical findings.<sup>10</sup> Resolution of the clinical symptomatology is evident as soon as the precipitant event is removed or managed, usually within a week, but the MRI findings resolve over a mean duration of 2-4 weeks.

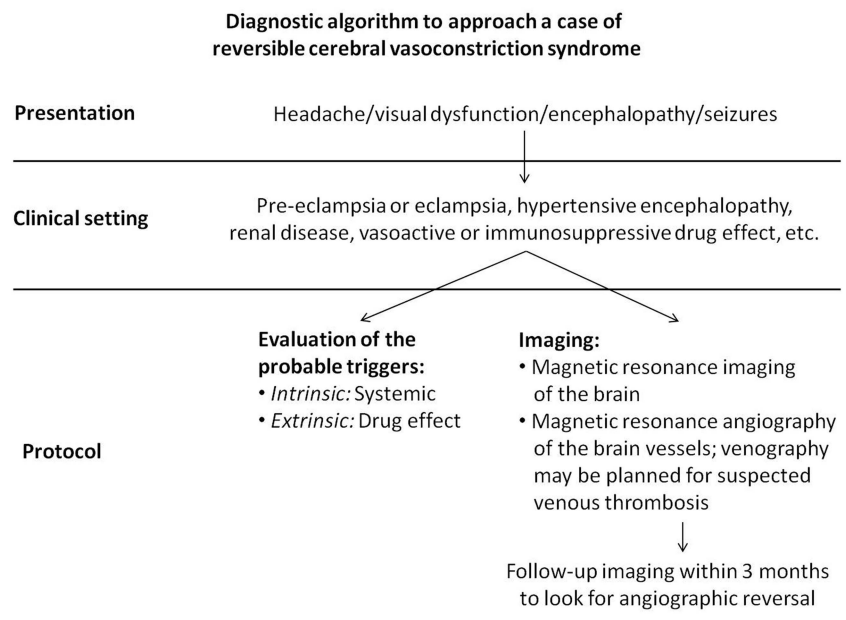
Although the aetiopathogenesis of RCVS and RPLS is not known precisely, a transient disturbance in the control of cerebral vascular tone has been hypothesised which leads to segmental and multifocal arterial constriction and dilatation.<sup>1-11</sup> The

development of these syndromes may be spontaneous, without any evidence of a trigger or underlying state, or secondary to eclampsia/pre-eclampsia and exposure to vasoactive substances (sympathomimetic/serotonergic) or systemic states mimicking the same. Several medical conditions including hypertensive encephalopathy and uraemia, and the use of cytotoxic and immunosuppressive drugs have also been associated with these syndromes.<sup>1-2-8</sup>

At the vascular front, RCVS seems to be associated with the constriction and/or dilation of large-sized and medium-sized cerebral arteries while RPLS has been related to endothelial dysfunction and cerebral-autoregulatory failure at the level of distal arterioles and capillaries.<sup>1-11-13</sup> As a corollary, we find actual strokes constituted by cytotoxic oedema in RCVS, but only changes attributed to vasogenic oedema are observed in RPLS; infarcts corresponding to arterial territories may therefore be more evident in cases with RCVS. The combination of changes, as observed in our case, can be explained if the pathophysiology is considered as a continuum of changes involving different parts of the cerebral vasculature (proximal vs distal) and the severity of cerebral-autoregulatory dysfunction. A mild-to-moderate grade dysfunction will thus lead to reversible ischaemia when proximal vessels are involved in RCVS, or vasogenic oedema upon involvement of the distal vasculature in RPLS. Similarly, severe dysfunction will lead to the development of stroke and manifest at locations depending on the location of arteries affected. The imaging findings in our case and the angiographic reversal attest that the pathophysiological mechanisms in these two syndromes represent a continuum manifesting as an overlap of RCVS and RPLS. A simple diagnostic algorithm to approach cases suspected of RCVS is depicted in figure 3.

RCVS can be associated with RPLS, regardless of the aetiology, in approximately 10% of the cases. A report of four cases of RCVS, described as postpartum angiopathy, and RPLS details the abnormalities in such patients similar to what was observed in our case.<sup>11</sup> In a recent larger series, 12 cases of RCVS in the postpartum phase have been described in one-third of those in which ischaemic changes were observed.<sup>7</sup> The present case reiterates the overlap between these two syndromes and also highlights the

**Figure 3** Diagnostic algorithm to approach a case of reversible cerebral vasoconstriction syndrome.



probability of extensive reversible vascular involvement. We have therefore preferred using the term 'cerebral-autoregulatory dysfunction' for appropriate categorisation.

The management of a patient with RCVS or RPLS depends upon the treatment of the underlying pathology or the removal of the triggering event. Adequate amount of fluids with maintenance of blood pressure help in limiting the cerebral hypoperfusion as well as vasospasm. Calcium channel blockers, nimodipine and verapamil, may be used in cases where vasoconstriction has been documented.<sup>1</sup> Stroke is seen in half of the patients with RCVS and seems to be the most important determinant of short-term and long-term morbidity; lethal fulminant course may also be seen in some patients.<sup>3 14 15</sup> The prognosis, otherwise, in RCVS and RPLS is good. Our patient had significant improvement in weakness but her vision did not improve significantly even after 1 month.

### Learning points

- ▶ Reversible cerebral vasoconstriction syndrome is an underdiagnosed condition and its documentation with reversible posterior leukoencephalopathy syndrome is sparse.
- ▶ Such an overlap probably represents the spectrum of the extent and severity of angiographic involvement occurring secondary to cerebral-autoregulatory dysfunction, central to both the syndromes.
- ▶ Residual defects may be seen even after complete reversal of cerebral angiographic findings.
- ▶ Appropriate fluid management and use of calcium channel blockers may help these patients.

**Competing interests** None.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

### REFERENCES

- 1 Calabrese LH, Dodick DW, Schwedt TJ, *et al*. Narrative review: reversible cerebral vasoconstriction syndromes. *Ann Intern Med* 2007;146:34–44.
- 2 Garg RK. Posterior leukoencephalopathy syndrome. *Postgrad Med J* 2001;77:24–8.
- 3 Hajji-Ali RA, Furlan A, Abou-Chebel A, *et al*. Benign angiopathy of the central nervous system: cohort of 16 patients with clinical course and long-term follow up. *Arthritis Rheum* 2002;47:662–9.
- 4 Chen SP, Fuh JL, Lirng JF, *et al*. Recurrent primary thunderclap headache and benign CNS angiopathy: spectra of the same disorder? *Neurology* 2006;67:2164–9.
- 5 Ducros A, Boukobza M, Porcher R, *et al*. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain* 2007;130:3091–101.
- 6 Chen SP, Fuh JL, Chang FC, *et al*. Transcranial color Doppler study for reversible cerebral vasoconstriction syndromes. *Ann Neurol* 2008;63:751–7.
- 7 Singhal AB, Hajji-Ali RA, Topcuoglu MA, *et al*. Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Arch Neurol* 2011;68:1005–12.
- 8 Ducros A, Boussier MG. Reversible cerebral vasoconstriction syndrome. *Pract Neurol* 2009;9:256–67.
- 9 Edlow JA, Caplan LR, O'Brien K, *et al*. Diagnosis of acute neurological emergencies in pregnant and post-partum women. *Lancet Neurol* 2013;12:175–85.
- 10 Schwartz RB, Feske SK, Polak J, *et al*. Preeclampsia-eclampsia, clinical and neuroradiographic correlates and insights to the pathogenesis of hypertensive encephalopathy. *Radiology* 2000;217:371–6.
- 11 Singhal AB. Postpartum angiopathy with reversible posterior leukoencephalopathy. *Arch Neurol* 2004;61:411–16.
- 12 Schaefer PW, Buonanno FS, Gonzalez RG, *et al*. Diffusion-weighted imaging discriminates between cytotoxic and vasogenic edema in a patient with eclampsia. *Stroke* 1997;28:1082–5.
- 13 Schwartz RB, Mulkern RV, Gudbjartsson H, *et al*. Diffusion imaging in hypertensive encephalopathy: clues to pathogenesis. *AJNR Am J Neuroradiol* 1998;19:859–62.
- 14 Singhal AB, Bernstein RA. Postpartum angiopathy and other cerebral vasoconstriction syndromes. *Neurocrit Care* 2005;3:91–7.
- 15 Fugate JE, Wijdicks EFM, Parisi JE, *et al*. Fulminant postpartum cerebral vasoconstriction syndrome. *Arch Neurol* 2012;69:111–17.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.  
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact [consortiasales@bmjgroup.com](mailto:consortiasales@bmjgroup.com)

Visit [casereports.bmj.com](http://casereports.bmj.com) for more articles like this and to become a Fellow