

# Posterior reversible encephalopathy syndrome: a case following reversible cerebral vasoconstriction syndrome masquerading as subarachnoid haemorrhage

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Received: 22 September 2011 / Accepted: 23 December 2011 / Published online: 12 January 2012  
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**Abstract** Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic clinico-radiological diagnosis typically presenting with headache, encephalopathy and visual disturbance accompanied by a unique neuroradiological pattern of symmetrical parieto-occipital vasogenic oedema. Here we present the case of a 51-year-old woman who presented to hospital following a thunderclap headache, initially thought to be secondary to a subarachnoid haemorrhage (SAH). A tiny anterior choroidal artery aneurysm was demonstrated on cerebral angiogram. At surgical clipping, no evidence of haemorrhage was observed. Post-operatively, the patient developed delayed right-sided hemiparesis, managed with aggressive hypertensive treatment, and later, with onset of septicaemia, central visual loss. Computed tomography (CT) brain scans demonstrated oedematous changes within the parieto-occipital regions bilaterally and later areas of infarction. The initial diagnosis of SAH was revised to reversible cerebral vasoconstriction syndrome (RCVS), which gave rise to PRES. To our knowledge, this is the first reported case of RCVS with concomitant PRES and cerebral infarction.

## Introduction

Posterior reversible encephalopathy (PRES) is a clinico-radiological diagnosis that has gained substantial recognition since its initial description by Hinchey et al. in 1996 [12]. It is characterised by an acute headache, visual disturbance, seizures, variable focal neurological deficits and reversible vasogenic oedema on neuro-radiological imaging. The vasogenic oedema is often widespread but has a predilection for the parietal and occipital regions [12]. Despite the syndrome's name, vasogenic oedema is also observed in the cortex, frontal lobes, basal ganglia and brainstem [3]. Controversy exists as to the mechanism underlying the cerebral oedema; the favoured pathogenic theory suggests an autoregulatory disturbance with hyperperfusion, resulting in blood brain barrier breakdown with reversible oedema, without infarction [4]. The second theory is related to endothelial cell dysfunction/injury leading to blood-brain barrier damage, with resultant cortical and subcortical vasogenic oedema [4]. The imaging appearances have been noted in patients with pre-eclampsia, following transplant surgery and in the setting of severe hypertension [11], whilst haemorrhage has been considered both an atypical aetiology and feature [2, 10, 12]. Here we present the first documented case of PRES leading to cerebral infarction in the context of reversible cerebral vasoconstriction syndrome (RCVS).

## Case report

A 51-year-old woman presented to hospital 7 days after a sudden onset explosive headache associated with nausea and vomiting. There was no photophobia or neck stiffness. On neurological examination she had a Glasgow Coma Score (GCS) of 15/15 and was blind in the left eye (since

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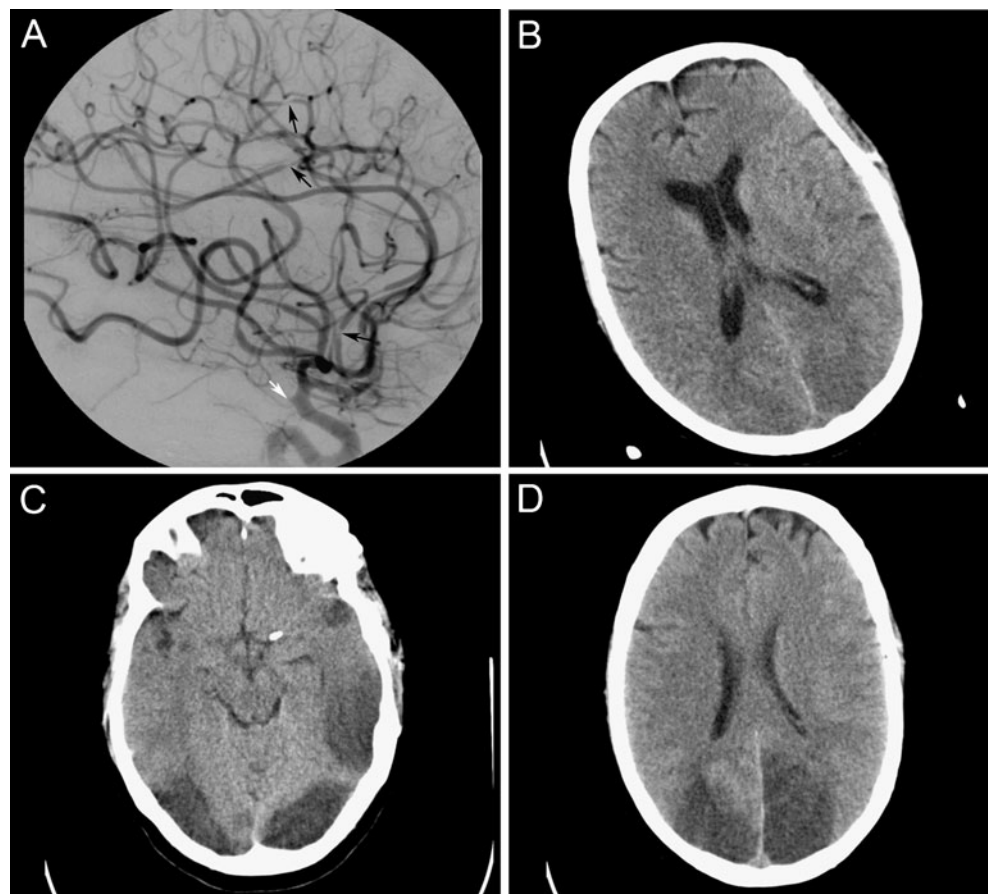
birth). There were no other deficits. A computed tomography (CT) brain scan was performed, which appeared normal. Lumbar puncture revealed a red cell count (RCC)  $>5,000$  and bilirubin 0.007 absorbance units (AU). CT angiogram demonstrated a possible abnormality of the left supraclinoid internal carotid artery. A repeat lumbar puncture was performed: RCC 2,410 and bilirubin 0.006 AU, with normal protein and glucose. A subsequent catheter cerebral angiogram demonstrated a wide-necked 2-mm bleb at the origin of the left anterior choroidal artery. Numerous areas of narrowing were noted, affecting branches of both the anterior and posterior circulation, suggestive of vasospasm (Fig. 1a). A diagnosis of subarachnoid haemorrhage (SAH) due to rupture of the aneurysm was felt most likely, despite bilirubin being just below the laboratory cut-off value for the diagnosis (0.008 AU). The focal vasospasm and cerebrospinal fluid (CSF) findings were felt to be due to the delay in presentation.

The following day the patient underwent left pterional craniotomy and clipping of the aneurysm. Intra-operatively no evidence of haemorrhage was noted. Following clipping, thorough lavage was performed and good haemostasis was achieved; tiny fragments of haemostatic gauze were applied to three tiny raw areas on the opercula of the Sylvian fissure. Papaverine, 40 mg diluted to 5 ml in 0.9% saline, was

instilled (as a matter of routine) and the dura was closed. Intra-operatively, motor evoked potentials and video-microangiography were not used. Post-operatively, the patient awoke neurologically unchanged.

Overnight she developed dysphasia responsive to triple-H therapy [15] despite no defects on the CT perfusion scan. Fluctuating motor deficit, responsive to vasopressors developed on the fifth post-operative night in concert with rising transcranial Doppler velocities (from 80–90 cm/s on day 4 to 175 cm/s on day 6). Focal neurological deficit continued to fluctuate, whilst Gram-negative sepsis from intravenous line infection was successfully treated with antibiotics from the tenth post-operative day. Doppler velocities remained fast throughout. Nineteen days following surgery, a further episode of line sepsis precipitated fever of 40°C, disorientation and permanent right-sided hemiplegia despite re-introduction of vasopressors. A CT brain scan was performed after the patient developed sudden central visual loss, which demonstrated bilateral occipital and left parietal regions of low attenuation interpreted as PRES (Fig. 1b) and pressors were withdrawn. Within 4 days established infarction was evident (Fig. 1c, d). On the basis of the clinical, operative and radiological findings, the initial diagnosis of SAH was revised to reversible cerebral vasoconstriction syndrome (RCVS). We presume PRES with cerebral

**Fig. 1** Radiological imaging. **a** Initial angiogram showing anterior choroidal artery aneurysm (*white arrow*) and with evidence of vasospasm (*dark arrows*). **b** CT scan initially interpreted as demonstrating PRES. **c, d** CT scan 4 days after **b**, demonstrating established bilateral occipital and left temporal infarcts



infarction followed due to increased vascular permeability from sepsis superimposed on therapeutic hypertension for the neurological deficits. During the period of convalescence magnetic resonance imaging (MRI) was performed, which confirmed multiple ischaemic lesions. The patient was later transferred to a neuro-rehabilitation unit with a GCS of 15, right sided hemiparesis and near blindness (light perception only). She remains disabled by these deficits.

## Discussion

Reversible vasoconstriction syndrome is characterised by a severe acute “thunder-clap” headache, peaking within 1 min mimicking that of a ruptured cerebral aneurysm [6, 7]. It is an increasingly recognised condition with an incidence estimated at 40/100,000 [13], with a 2:1 female preponderance, presenting typically in the fourth decade of life [8]. The syndrome was first described in a clinical-angiographic case series of four patients who were found to have transient, fully reversible vasoconstriction and dilatation involving the arteries of the circle of Willis [5]. Subsequent studies described diffuse, multifocal, segmental narrowing involving large and medium-sized arteries in the anterior and posterior circulations, with occasional dilated segments like “string and beads” observed on catheter cerebral angiography [8].

In addition to the stereotypical headache, there may or may not be focal neurological deficits, seizures, cortical SAHs and ischaemic or haemorrhagic strokes [9, 10]. In the absence of a cerebrovascular event the syndrome is completely reversible with an ensuing resolution of the transient disturbance of arterial tone regulation [9]. Reversible vasoconstriction syndrome has been described as giving rise to PRES in the context of immune manipulation and in septic shock [9]. Here we present the first detailed report (to our knowledge) of RCVS that gave rise to PRES and cerebral infarction. The largest case series to date of RCVS has demonstrated that in the absence of a cerebrovascular event up to 2% of cases can develop PRES and this figure more than doubles in the presence of cortical SAH [10]. Of the 89 patients in this recent study, only a single case developed both PRES and cerebral infarction [10].

The clinical presentation of RCVS is very similar to that of an aneurysmal SAH [6, 7]. In addition to its clinical masquerade as SAH, catheter cerebral angiography demonstrates diffuse vasospasm [8]. This is different from vasospasm secondary to an aneurysmal SAH, which usually correlates with the location and amount of bleeding and is rarely multifocal [8]. The use of calcium channel blockers is the primary treatment of RCVS. The use of triple-H therapy in RCVS raises the pressure in already constricted vessels. Combined with the failure of the cerebrovascular auto-

regulatory mechanism, we and others postulate that this can give rise to a “hyperperfusion state” and extravasation of fluid into the brain parenchyma [1, 14]. This same physiological state is also the leading hypothetical mechanism underlying the development of PRES [4]. We believe the use of triple-H therapy in our case of RCVS may have played a central role in the development of PRES. The continued use of triple-H in the context of septicaemia is likely to have given rise to cerebral infarcts.

In conclusion our case highlights a common pathological mechanism linking RCVS and PRES. It seems most likely that a disturbance in vascular autoregulation resulting in hyperperfusion gives rise to reversible cerebral oedema. Additionally, the case described herein highlights the complexity of managing patients who present with symptoms consistent with SAH but have both negative findings on biochemical and radiological investigation. Such patients should be approached with caution and a diagnosis of RCVS should be explored early, prior to the judicious use of triple-H therapy and vasoactive agents.

**Acknowledgements** We thank the Neurology, Neuroradiology and Neuro-intensive Care Departments of the Wessex Neurological Centre, Southampton General Hospital. A.R.S. is in receipt of the Jason Brice Fellowship in Neurosurgical Research.

**Conflicts of Interest** None.

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