

# Headache, blindness and a seizure after childbirth

H Mehta,<sup>1</sup> T Khan,<sup>1</sup> T F Ismail,<sup>1</sup> A Rogers,<sup>1</sup> A Wallis,<sup>1</sup>  
D Collas,<sup>1</sup> W R J Wallis,<sup>1</sup> M J van der Watt,<sup>1</sup>  
D J Werring<sup>1,2</sup>

A previously fit and well 17-year-old primiparous woman presented 5 days following the uncomplicated delivery of her first child with a gradual onset, severe, throbbing, predominantly left sided headache. There was no nausea, vomiting, neck stiffness or photophobia. Her past medical history was unremarkable, apart from heterozygosity for factor V Leiden, for which she was screened because of a history of thrombophilia in her mother. On initial assessment, no abnormality was detected other than an elevated blood pressure of 180/100 mm Hg. There was no evidence of oedema or proteinuria. Two days later, her visual acuity deteriorated over 12 h from 6/6 to perception of hand movements bilaterally, precipitating referral to the medical team. She then had a generalised tonic-clonic seizure, which was terminated within 5 min using intravenous magnesium and diazepam. She was subsequently loaded with phenytoin with no further seizures. On examination by the medical team, blood pressure remained elevated at 180/110 mm Hg. Visual acuity was reduced to perception of hand movements, pupillary responses were normal and there was no papilloedema. Tone, power, coordination and sensation were normal throughout. Reflexes were brisk, particularly in the left arm, and the plantars were extensor bilaterally. Other than mildly elevated inflammatory markers compatible with recent parturition, her blood tests and urine dipstick were unremarkable.

## QUESTION 1: WHAT IS THE DIFFERENTIAL DIAGNOSIS?

At this stage, the differentials that need to be considered in a peripartum woman with headache, neurological deficits,

<sup>1</sup> Department of Medicine, Watford General Hospital, Watford, UK; <sup>2</sup> Institute of Neurology, University College London, National Hospital for Neurology and Neurosurgery, London, UK

**Correspondence to:** Dr D J Werring, Stroke Research Group, Department of Brain Repair and Rehabilitation, Institute of Neurology, Queen Square, London WC1N 3BG, UK; [d.werring@ion.ucl.ac.uk](mailto:d.werring@ion.ucl.ac.uk)

seizures and a family history of thrombophilia include:

- ▶ pre-eclampsia/eclampsia
- ▶ dural venous sinus thrombosis
- ▶ cerebral infarction
- ▶ cerebral haemorrhage
- ▶ posterior reversible encephalopathy syndrome (PRES).

## QUESTION 2: HOW SHOULD THE PATIENT BE FURTHER INVESTIGATED TO RESOLVE THE DIFFERENTIAL DIAGNOSIS?

The patient's primiparity, young age, and family history of thrombophilia are significant risk factors for pre-eclampsia.<sup>1</sup> Eclampsia—characterised by hypertension, proteinuria and neurological symptoms including visual disturbance and seizures—usually occurs in the last trimester or within a few days of delivery, but may occur up to 23 days post-partum.<sup>2</sup> Eclampsia is usually associated with significant proteinuria (>300 mg/24 h), but urine dipsticks are not reliable in excluding this; furthermore, even without proteinuria, the index of suspicion should remain high in a peripartum patient with hypertension, visual disturbance and seizures.<sup>1,2</sup> Cerebrovascular disorders—including cerebral infarction and cerebral venous sinus thrombosis—are rare complications of pregnancy and the puerperium,<sup>3</sup> but must be carefully considered in the context of both the inherited and acquired thrombophilic tendency of the patient, and the presence of focal neurological deficits complicated by seizures. Cerebral haemorrhage can also give rise to these features, and cannot be reliably excluded without brain imaging. The radically different management strategies needed (anticoagulation for cerebral venous sinus thrombosis, possible intra-arterial thrombolysis for basilar artery thrombosis or antiplatelet agents for other types of cerebral infarction, and aggressive medical and supportive therapy to reduce haematoma expansion for

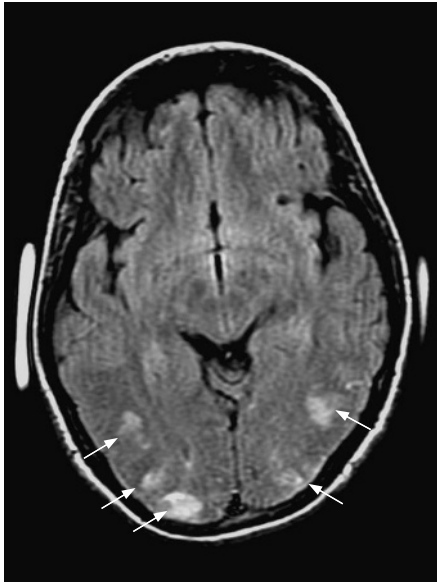
haemorrhage) make the need for urgent neuroimaging all the more pressing.

A computed tomography (CT) scan of the head was undertaken and revealed subtle reduced attenuation in bilateral occipitoparietal regions, worse on the right than the left, but no evidence of venous sinus thrombosis (fig 1). CT may show acute thrombus in the sagittal or lateral sinuses, but even with contrast techniques is not sufficiently sensitive to completely exclude cerebral venous sinus thrombosis.<sup>4,5</sup> In view of the hypercoagulable state engendered by recent pregnancy, and the patient's factor V Leiden status, urgent magnetic resonance imaging (MRI) with MR venography and diffusion weighted sequences was arranged to exclude more definitively venous sinus thrombosis or infarction. The venous sinuses were patent but the FLAIR (fluid attenuated inversion recovery) sequences revealed patchy increased signal in a similar distribution to the abnormalities noted on CT (fig 2). The diffusion weighted images showed no significant restriction of diffusion, suggesting vasogenic oedema rather than the cytotoxic oedema typical of cerebral infarction, which causes restricted diffusion. These characteristic neuroradiological findings in conjunction with the patient's clinical presentation and the absence of evidence of venous sinus thrombosis suggested a diagnosis of posterior reversible encephalopathy syndrome (PRES).



**Figure 1** Axial CT scan of the head showing subtle, patchy low attenuation in bilateral parieto-occipital regions.

## Self-assessment questions



**Figure 2** MRI of the brain (axial FLAIR sequence) at initial presentation showing patchy parieto-occipital increased signal (arrows).

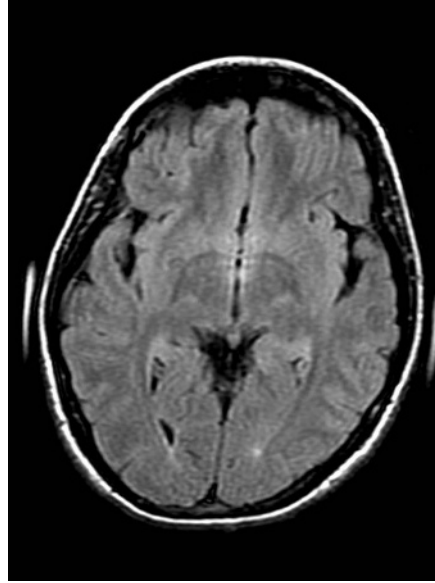
### QUESTION 3: HOW SHOULD THE PATIENT BE MANAGED?

The management priorities are to remove any precipitants, aggressively lower blood pressure and treat any seizures. Accordingly, intravenous labetalol was started to reduce the patient's blood pressure to <140/80 mm Hg, a manoeuvre which could have been deleterious had primary cerebral infarction and venous sinus thrombosis not been confidently excluded. Anticonvulsants are used as in any setting of acute prolonged generalised seizures.<sup>6</sup> In our patient, phenytoin was continued at the usual oral maintenance doses for seizure prophylaxis and her electrolytes were carefully monitored and tightly controlled.

Over the next 48 h, the patient reported that her vision had returned to normal apart from a small area of blurriness in her left hemi-field, which resolved fully over the next few days. The headache also subsided and at follow-up 8 weeks later, she was asymptomatic with no further seizures or visual disturbance. Her blood pressure was well controlled on oral labetalol and a repeat MRI brain showed complete resolution of the original changes (fig 3).

### DISCUSSION

PRES is an unusual but readily treatable cause of acute headache, altered consciousness, visual disturbance and seizures.<sup>7</sup> Since the original description of the syndrome in 1996, a number of triggers have been characterised for the



**Figure 3** MRI of the brain (FLAIR sequence) at 8 weeks follow-up.

syndrome including pregnancy (sometimes with eclampsia), severe hypertension, immunosuppressive treatment and uraemia.<sup>7-9</sup> The exact pathogenesis remains obscure,<sup>7</sup> though it is thought that disturbed cerebral autoregulation with endothelial injury or dysfunction results in increased vascular permeability in the posterior circulation.<sup>7 10 11</sup> The resultant leakage of fluid across the blood-brain barrier impairs neuronal function causing an encephalopathy (headache, impaired consciousness, seizures) with pronounced visual disturbance.<sup>10</sup> Untreated, this vasogenic oedema may compromise the integrity and function of the local cerebral microcirculation, thereby producing cell death and permanent neurological sequelae.<sup>12 13</sup> Structures supplied by the anterior circulation may be involved, though the disorder shows a predilection for posterior vascular territories.<sup>7 10</sup> This may reflect the relative paucity of sympathetic fibres innervating the posterior circulation in comparison to the anterior circulation,<sup>10 14</sup> making the posterior vasculature more vulnerable to failure of autoregulation and endothelial leakage.<sup>11 14</sup>

MRI with FLAIR and diffusion weighted sequences is the modality of choice for clarifying the diagnosis and distinguishing the syndrome from cerebral infarction or venous sinus thrombosis.<sup>12 13</sup> Rapid early diagnosis is essential as blood pressure lowering may worsen outcome from cerebral infarction due to thrombotic occlusion of the vertebrobasilar artery or cerebral venous sinuses, yet this measure is the cornerstone of managing PRES.

T2 weighted sequences (especially FLAIR) reveal patchy hyperintense lesions, predominantly affecting but not necessarily confined to the posterior white matter (fig 1).<sup>12</sup> Diffusion weighted imaging techniques can be used to seek the restricted diffusion characteristic of cytotoxic oedema in cerebral infarction, by contrast with the generally increased diffusion due to vasogenic oedema seen in PRES.<sup>15</sup> However, PRES can also result in permanent cerebral infarction,<sup>11</sup> causing a more complex pattern of diffusion changes.

The management of PRES is directed towards, wherever possible, removal of the original insult that precipitated endothelial dysregulation, and aggressive control of blood pressure and seizures.<sup>10</sup> Worsening hypertension escalates further endothelial damage, thereby creating a vicious circle of further cerebral injury and worsening hypertension.<sup>9</sup> Generalised seizures may result, increasing cerebral oxygen consumption and exacerbating cerebral oedema at a time when cerebral autoregulation and microvascular integrity are already compromised. Thus, if untreated, PRES may not be reversible but can result in severe neurological sequelae or even death. Blood pressure should therefore be expeditiously lowered in a controlled manner using parenteral antihypertensives such as labetalol with invasive blood pressure monitoring.<sup>9 10</sup> Sodium nitroprusside and glyceryl trinitrate may also be used, but, by increasing cerebral vasodilatation, may worsen vasogenic oedema.<sup>9</sup> While doubt remains regarding the safety of the latter drugs in this context, and in the absence of compelling contraindications, labetalol may therefore be the agent of choice in PRES.<sup>10</sup> Seizures should be promptly arrested with intravenous lorazepam followed by phenytoin

### Learning points

- ▶ Posterior reversible encephalopathy syndrome (PRES) is a rare but potentially reversible cause of headache, visual disturbance and seizures.
- ▶ Early recognition and prompt treatment is required to prevent permanent neurological sequelae or death.
- ▶ Early diagnosis is facilitated by prompt neuroimaging with magnetic resonance imaging.
- ▶ Treatment is directed towards removing precipitants, lowering blood pressure, and controlling seizures.

(or magnesium sulfate in the obstetric setting if pre-eclampsia is suspected).<sup>6-10</sup> The rarity of the condition and its diverse aetiologies are likely to preclude randomised controlled trials. Thus, management is likely to continue to be guided by our limited understanding of the underlying pathophysiology of PRES, highlighting the urgent need for more basic and clinical research.

## CONCLUSIONS

PRES is a rare but treatable cause of headache, visual disturbance and seizures. Clinicians from a variety of backgrounds and disciplines should consider PRES in the differential diagnosis of headache, altered consciousness and seizures. The index of suspicion should be high in patients who are peripartum or who have received immunosuppressive drugs with potentially neurotoxic adverse effects. The importance of early recognition is underscored by the potential reversibility of the condition and the development of

neurological sequelae and even death in the absence of prompt treatment.

## FINAL DIAGNOSIS

Posterior reversible encephalopathy syndrome (PRES).

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