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Case Report

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Complicated Preeclampsia; A rare case of concurrent PRES and CRVS

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Abstract

This case report explores the rare occurrence of simultaneous Posterior Reversible Encephalopathy Syndrome (PRES) and Cerebral Reversible Vasoconstriction Syndrome (CRVS) in a 32-year-old primigravida at 37 weeks' gestation with pre-eclampsia, requiring emergency caesarean section. This rare case highlights the overlapping clinical and radiographic features of PRES and CRVS, proposing shared pathophysiological mechanisms involving cerebral autoregulation failure and blood-brain barrier disruption. Discussion explores differential diagnoses, emphasizing the challenges of promptly diagnosing pre-eclampsia-associated neurological complications using an inter-disciplinary approach with specific attention to the interplay in treatment approach for PRES and CRVS.

Keywords: Posterior reversible encephalopathy syndrome (PRES); Cerebral Reversible Vasoconstriction Syndrome (CRVS); Pre-eclampsia

Introduction

Hormonal changes and hypercoagulability contribute to the increased incidence of headache in pregnancy when compared with the non-pregnant population. New headache complicates around 5% of pregnancies, approximately two-thirds of which are attributed to primary causes – namely tension, migraine and trigeminal cephalgia. In approximately one-third of cases, headache in pregnancy can result from secondary causes. The most common secondary causes are consequent to hypertensive disorders.

In patients with a known headache history prior to pregnancy, a change in quality/duration of headache during pregnancy is associated with a secondary cause. Furthermore, pre-partum migraine is an independent risk factor for secondary vascular causes of headache in pregnancy. Focal neurology, fever and hypertension constitute important clinical indicators that headache is of secondary origin in pregnancy [12].

Posterior reversible encephalopathy syndrome [PRES] describes a condition characterised by the region of radiographic change [posterior cerebrum], the typical prognosis [reversible], and the usual presentation [encephalopathy]. Cerebral reversible vasoconstriction syndrome [CRVS] is characterised by acute onset severe headache with or without focal neurology or seizures secondary to reversible cerebral vasospasm [2]. Whilst PRES and CRVS are independently recognised as complications of pre-eclampsia, both conditions may occur simultaneously as described here. The prescribed treatments for PRES in this scenario and CRVS are contrasting and a dilemma in determining management is found when finding the two in combination.

We report a case of a 32-year-old primigravida who simultaneously developed PRES and CRVS as a consequence of pre-eclampsia at 37 weeks' gestation.

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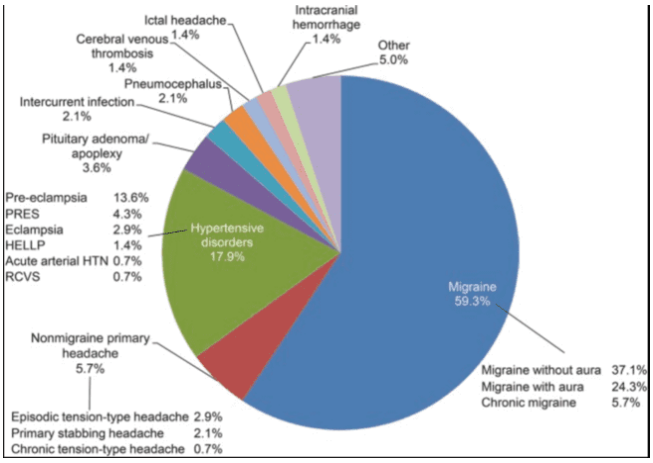

(Robbins et al., 2015) [13]

Case

A 32-year-old primigravida presented at 37 weeks and 5 days gestation to the maternity triage unit with subacute onset headache and vision loss over 48 hours. The headache was global and of moderate severity with a constant nature and no clear precipitating factors. The vision loss was bilateral and visual acuity limited to flashes of light bilaterally.

During the antenatal period, she had been diagnosed with gestational diabetes mellitus and declined pharmacotherapy. She underwent serial growth scans due to low PAPP-A which were deemed normal. She otherwise had no pre-natal comorbidities and was of normal BMI. She had a positive family history for paternal diabetes and hypertension.

At admission, she was noted to be hypertensive with a blood pressure of 180/125. Urinalysis revealed protein 4+ on dipstick with 5g/L on spot urinalysis. Renal function was intact. Heart rate, oxygen saturations, temperature and respiratory rate were within normal limits. On examination, she had pronounced peripheral pitting oedema in the upper and lower limbs. Reflexes were brisk in the absence of clonus. There was no discernible motor or sensory deficit on neurological examination of the peripheral nervous system. As such, she received 20mg modified release nifedipine orally and four boluses of labetalol 50mg intravenously, in addition to 4mg magnesium sulphate intravenously. Despite this, her blood pressure remained elevated and a further four boluses of hydralazine 5mg were given followed by a hydralazine infusion. Her blood pressure subsequently normalised and an uncomplicated emergency caesarean section was performed under spinal anaesthetic within four hours of presentation. CTG was normal to the point of caesarean section.

Post-operatively, an urgent CT head was performed due to refractory ongoing headache suggesting subarachnoid haemorrhage in the right anterior/high frontal regions, bilateral frontal parasagittal regions and left high parietal regions. In addition, subcortical low-density areas were noted in the right posterior parieto-occipital region. An urgent neurosurgical opinion was sought and nimodipine 60mg 4-hourly commenced orally with a target blood pressure of <160 systolic. Symptomatically, the patient's visual symptoms resolved progressively and ultimately completely within twelve hours post-operatively.

Further CT venogram, MRI head and MR-venogram were performed and specialist neuroradiologist advice sought. The appearances of the CT, MRI and MRV were consistent with a combination of reversible cerebral vasoconstriction syndrome (and associated convexity sulcal subarachnoid haemorrhage) with evidence of PRES in the occipital lobes.

The patient's headache continued to improve and resolved completely within one week of presentation and her resolution of symptoms is attributable to the appropriate treatment of her pre-eclampsia. On cessation of antihypertensive medications, a rebound hypertension of 170-180 systolic occurred, however the patient did not become symptomatic. Where the treatment of CRVS is to maintain a high systolic blood pressure (to overcome the vasoconstriction and permit adequate cerebral perfusion), the treatment of PRES is to treat the underlying cause. In this case, the patient's PRES was consequent to pre-eclampsia of which hypertension is a diagnostic feature. Therein lies the dilemma – do we prioritise treatment of pre-eclampsia associated PRES or CRVS? An MDT decision was made involving the acute medical, obstetric and neurology teams and the patient was discharged on oral nimodipine with regular outpatient blood pressure monitoring for a total duration of 21 days. Serial MRI head/MR-venogram at six weeks from presentation revealed complete resolution of PRES/CRVS changes [Figures 1 and 2]. She remains asymptomatic to date and has been discharged from follow-up from the Neurology team.

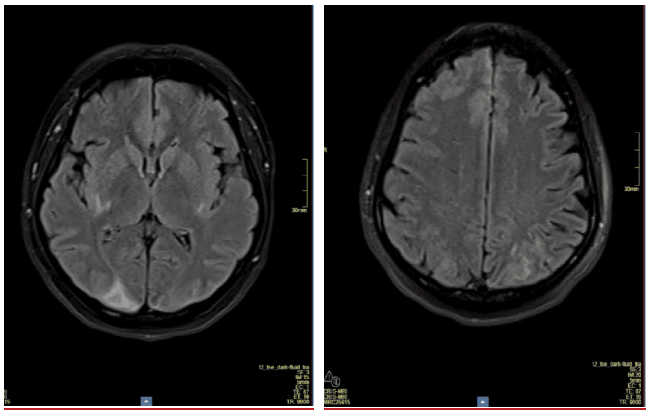

Figure 1: T2 MRI revealing an ill-defined gyral T2 hyperintensity is seen along the occipital cortex, with associated hyperintensities in the superior right frontal cortex and both anterior parafalcine frontal regions.

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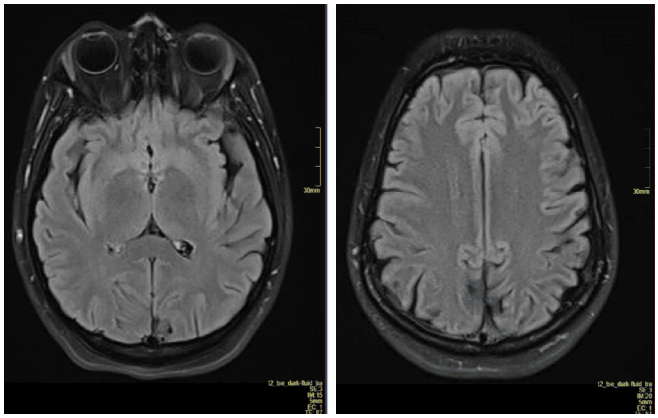

Figure 2: T2 MRI revealing resolution of PRES/CRVS changes shown in figure 1.

Discussion

In our case, the clinical presentation with the confirmation of pre-eclampsia suggested an intra-cranial cause of symptoms. In the absence of signs to suggest an infective process, the following differentials were considered: acute ischaemic or haemorrhagic stroke, cerebral venous sinus thrombosis, subarachnoid haemorrhage and PRES/CRVS.

Pre-eclampsia complicates around 4.6% of pregnancies worldwide and accounts for around 12% of maternal deaths [1]. Of the major risk factors for developing pre-eclampsia, this patient had three: low PAPP-A, gestational diabetes and nulliparity. Pre-eclampsia itself is associated with blurred vision, and as such the nature of the visual changes combined with ophthalmic examination can assist in the diagnostic process. Acute cortical blindness (as evidenced in this case) would be supported by a normal fundoscopic examination with preserved pupillary reflexes. It is important to recognise that cortical blindness in the context of pre-eclampsia is associated with occipital lobe oedema [4] which is also a radiographic hallmark of PRES. In the clinical environment however – especially in the out of hours context - the requisite to act promptly in treating pre-eclampsia often deem seeking formalised slit-lamp examination impossible.

PRES – in up to 90% of cases - is radiographically characterised by vasogenic oedema with a propensity to affect the parietal and occipital lobes observed as hypoattenuating zones on CT or hyperintensities in the white matter on T2/FLAIR MRI. However, it is recognised that a non-posterior distribution may be observed, and any region of the brain or spinal cord may be affected, most notably in those areas where major cerebral artery territories meet (aptly named 'watershed areas' (Bartynski & Boardman, 2007). In contrast to PRES, imaging for CRVS is often normal at the time of presentation with radiographic features appearing later. Once radiographic features have developed - and consequent to vasoconstriction of the cerebral vasculature - vasogenic oedema, infarcts in the watershed areas and haemorrhage are typically observed [18]. It is clear there is significant overlap in the radiographic findings in both conditions.

Initial CT findings in this case were suggestive of acute subarachnoid haemorrhage, whilst the history was not typical of acute subarachnoid haemorrhage – with headache being subacute and non-severe. Furthermore, the anatomical locations of small haemorrhages were multiple. Such 'convexity' subarachnoid haemorrhages are strongly indicative of CRVS in this clinical context. Furthermore, PRES in isolation can be complicated by intracranial haemorrhage, the most common of which is intracranial haematoma whilst subarachnoid haemorrhage is also recognised in the literature [8].

The pathophysiological mechanisms theorised to underly both PRES and CRVS are similar. Cerebral perfusion is tightly regulated by homeostatic control of the arteriolar diameter. This physiological process is complex and not fully understood [17]. In our case, the capacity of the cerebral autoregulatory system to accommodate an abrupt increase in blood pressure consequent to pre-eclampsia was exceeded, resulting in hyperperfusion, dysfunction of the blood-brain barrier and resultant vasogenic oedema. By this mechanism, conditions such as pheochromocytoma which cause abrupt fluctuations in blood pressure have also been complicated by PRES [7]. A second hypothesis for the of PRES is cerebral endothelial dysfunction. In our case, we theorise inflammatory cytokines released as a consequence of pre-eclampsia led to increased cerebral endothelial membrane permeability which in turn results in vasogenic oedema [11]. This mechanism also explains the association between PRES and sepsis and cerebral vasculitis. Substances directly toxic to the endothelium such as systemic chemotherapeutic agents used in cancers have been known to cause PRES in this fashion. CRVS shares endothelial dysfunction as a theorised pathophysiological precipitant with PRES for the reasons previously mentioned. Both pregnancy and pre-eclampsia are states of increased sympathetic drive, which perpetuate cerebral vasoconstriction in CRVS. In both CRVS and PRES, the failure of cerebral autoregulation and disruption of the blood-brain barrier result in cerebral oedema and haemorrhage, subsequent hypoperfusion can result in ischaemic infarcts [3].

There is no proven or established therapy for RCVS. While most patients fully recover with time, up to one-third can develop transient symptoms in the initial few days, and rare cases can develop a progressive clinical course. The goals of blood pressure control are controversial. High blood pressure (systolic >180 mmHg) can be treated with labetalol or nicardipine. Theoretically pharmacologically induced hypertension can induce further cerebral vasoconstriction or result in brain haemorrhage and, in the setting of cerebral vasoconstriction, even mild hypotension can trigger ischemic stroke [16]. The pain of RCVS-associated headache is extreme

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and frequently warrants the use of opioid analgesics in addition to nonsteroidal anti-inflammatory drugs (NSAIDs). Thunderclap headaches typically decrease in intensity and frequency over a span of days to weeks. Triptans and the ergot derivatives are contraindicated because of their vasoconstrictive actions [15]. Acute seizures warrant treatment with antiseizure medications, though seizures are usually present only upon presentation and do not recur. Therefore, long-term seizure prophylaxis is probably unnecessary. Clinical and angiographic resolution occur spontaneously without any medical intervention in approximately 90 percent of patients with RCVS, we generally do not use any agent to treat vasoconstriction. Data from two prospective case series suggest that nimodipine does not affect the time course of cerebral vasoconstriction. However, nimodipine might relieve the number and intensity of headaches and has documented effects on the smaller vasculature not easily imaged by angiography. Calcium channel blockers can be discontinued after resolution of symptoms or angiographic abnormalities if they are used.

In the acute setting, it is logical to avoid further exposure to any potential precipitating factors, such as marijuana, cocaine, exercise stimulants, amphetamines and triptans, serotonergic antidepressants, or other vasoconstrictive medications that can worsen the clinical course. Patients should avoid physical exertion, sexual activity, the Valsalva manoeuvre, and other known triggers of recurrent headaches for a few weeks. Laxatives and stool softeners should be used to avoid constipation (which can trigger the Valsalva manoeuvre), especially in patients receiving opioids for head pain. The risk of recurrent RCVS is low. The clinical outcome is benign in 90 to 95 percent of patients. Rare patients develop severe irreversible deficits or death from progressive strokes or cerebral oedema. Recurrence of an episode of RCVS are rare [9].

There is no specific treatment for PRES, other than removing or treating any underlying cause. 40% of all people with PRES are unwell enough to require intensive care unit admission for close observation and treatment of complications [14]. Those with PRES with seizures are treated using standard anticonvulsants used in other seizure disorders as there are no specific medications specific to PRES with seizures. However, in those with PRES due to pre-eclampsia or eclampsia, IV magnesium sulphate is the preferred medication for both seizures and hypertension. There are no universally accepted blood pressure lowering goals in those with PRES and hypertension, however, if there is a hypertensive emergency, the blood pressure may reduced quickly, but less than 25% within the first hour with the goal of blood pressure normalization within 24 to 48 hours [6]. There are no blood pressure lowering agents that are specifically used in PRES with hypertension, but commonly used agents include the intravenous medications nicardipine, clevidipine or labetalol which are fast acting, quickly adjustable, and can be given using continuous infusion with close monitoring. Of the blood pressure lowering agents available, nitrates may need to be avoided as there is a concern that this may aggravate the PRES even while lowering the blood pressure. The clinical outcome is benign in 90 to 95 percent of patients. Rare patients develop severe irreversible deficits or death from progressive strokes or cerebral oedema. Recurrence of an episode of RCVS is rare [10].

With adequate treatment, 70-90% of people with PRES make a full recovery within hours to days. 8–17% of people with PRES die, although this is not always a direct consequence of the PRES. Of those who have residual symptoms after PRES, this is attributable largely to haemorrhage. Non-resolution of MRI abnormalities has been linked with poorer outcomes. The presence of brain haemorrhage and cytotoxic oedema is also associated with a poor prognosis [19]. If PRES was caused by pre-eclampsia or eclampsia the prognosis is better than in PRES due to other causes. Factors that predict poorer prognosis are the person's age, the level of C-reactive protein, altered mental state at the time of diagnosis, and altered markers of coagulation. People with diabetes may have a worse outcome, and abnormalities in the corpus callosum on MRI have been linked with worse prognosis. Some patterns on electroencephalography (EEG) are also associated with a poorer outcome [5].

To conclude, we wish to offer three key lessons which this case highlights:

1. PRES and CRVS are rare but important differentials in the pre-eclamptic patient presenting with headache and vision loss.
2. There is increasing consensus amongst specialists that PRES and CRVS exist on a spectrum and in fact constitute the same condition.
3. The utmost importance of a multidisciplinary team (MDT) approach involving acute medical, obstetric, and neurology specialists to navigate treatment decisions and optimize patient outcomes in patients presenting with secondary headache.

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