CLINICAL UPDATE

Acute obstructive hydrocephalus in posterior reversible encephalopathy syndrome

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Posterior reversible encephalopathy syndrome (PRES) is an uncommon, subacute neurological disorder that presents radiologically with a pattern of bilateral parieto-occipital areas of vasogenic oedema. Conditions commonly associated with PRES include autoimmune disorders, cytotoxic drugs, metabolic abnormalities and, most frequently, hypertensive emergencies. Clinically, headache, visual disturbances, seizures and an altered level of consciousness are often reported. The outcome is favourable if the underlying cause is addressed. Posterior fossa involvement resulting in obstructive hydrocephalus is a rare presentation and may be misdiagnosed as a mass lesion or infection, leading to delayed or unnecessary treatment. We describe the clinical presentation, findings on neuroimaging and conservative management of a man with PRES resulting in severe cerebellar oedema and acute obstructive hydrocephalus. This case illustrates that awareness of atypical neuroimaging in PRES is important for the management of these patients and to avoid morbidity and mortality.

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In 1996, Hinchey *et al.*[1] described the first 15 patients with posterior reversible leukoencephalopathy syndrome (PRES). The authors identified an abrupt increase in blood pressure, with or without renal impairment, as well as immunosuppressive therapy as risk factors. PRES affecting predominantly the posterior fossa and leading to acute hydrocephalus is extremely uncommon. The earliest cases in the literature, reported by Verrees *et al.*[2] and Adamson *et al.*[3] in 2003 and 2005, respectively, illustrated the unique presentation of three patients with altered mental status, hypertensive crisis and cerebellar oedema with obstructive hydrocephalus. These patients underwent emergency ventriculostomy and had full resolution of their neurological deficits.

We report the clinical and neuroradiological findings in a patient with severe hypertensive encephalopathy and renal impairment who was found to have an unusual variant of PRES. The patient did not receive cerebrospinal fluid (CSF) diversion and recovered fully with blood pressure management alone.

Case study

A 50-year-old man with no previous history of arterial hypertension was brought to the emergency department by his sister after having collapsed, with generalised seizures and confusion. The blood pressure at presentation was 280/185 mmHg. He had a reduced level of consciousness, but no clear cranial nerve fall-out or focal neurological deficit. After recovery, he retrospectively reported having had a severe headache for a few days prior to admission.

A non-contrast computed tomography (CT) scan of the brain showed marked global cerebral and cerebellar oedema, as well as basal cistern and fourth-ventricle effacement with subsequent supratentorial obstructive hydrocephalus. Additionally, there was periventricular transependymal oedema, and bilateral symmetrical centrum semiovale and corona radiata white-matter hypodensities were prominent. Other findings included a right basal ganglia hypodensity, suggestive of a lacunar infarct, and multiple widespread parenchymal punctate calcifications thought to be chronic calcified granulomas from previous neurocysticercosis (Fig. 1A - D). A small subgaleal haematoma indicated some additional trauma, probably related to the initial seizures.

A CSF diversion was planned, and the patient was transferred to a high-care facility to achieve blood pressure control. Owing to the initial diagnostic uncertainty, meningitis as well as space-occupying lesions were considered, and he was treated with broad-spectrum antibiotics, intravenous corticosteroids and antiepileptic medication. To plan the neurosurgical approach, a CT scan with contrast or a magnetic resonance imaging (MRI) scan was requested but could not be performed because the patient had renal impairment. Despite intravenous administration of labetalol and consecutive introduction of several antihypertensive agents, it was difficult to control the blood pressure. On day 2, the blood pressure remained high, fluctuating around 190 - 200/130 - 140 mmHg, and several more days of therapy were needed to reduce the blood pressure to only moderately increased levels. The patient slowly improved, and a brain MRI scan was performed on day 6.

MRI supported the CT findings, with significant bilateral symmetrical white-matter high signal on T2-weighted imaging (T2WI) and fluid-attenuated inversion recovery. This involved the frontal and parietal centrum semiovale, corona radiata and periventricular subependymal areas. Parenchymal calcifications shown on CT were demonstrated as foci of blooming artefact on susceptibility-weighted images, but some of these did not correlate with the calcifications on CT and may have represented parenchymal microhaemorrhages. Additionally, an acute infarct was demonstrated in the left basal ganglia caudate nucleus. The cerebellar oedema had resolved, and the fourth ventricle was no longer effaced (Fig. 2A - G).

A follow-up brain MRI scan after 2 weeks showed improvement of the acute hydrocephalus and transependymal oedema. There was improvement but persistence of the bilateral white-matter changes, in keeping with small-vessel disease (Fig. 3A - C).

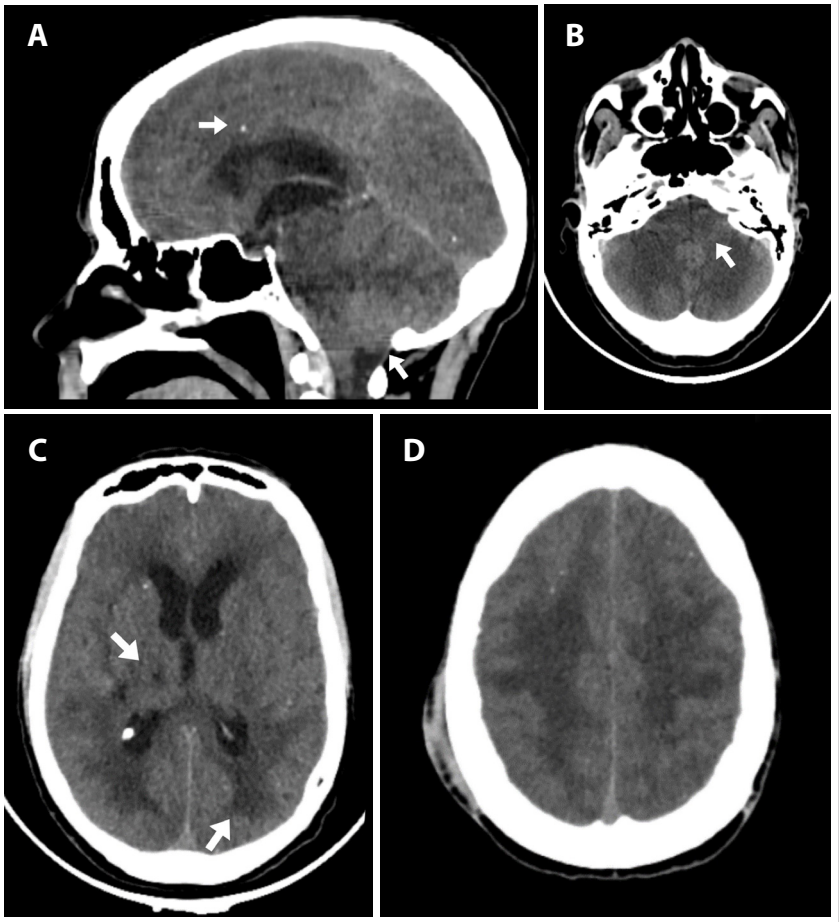

Fig. 1. A midline sagittal CT brain scan (non-contrast) (A) demonstrates effacement of the fourth ventricle and cisterna magna (lower arrow) with multiple parenchymal calcifications (upper arrow), an axial CT scan at the level of the pons (B) shows effacement of the basal cisterns (arrow), an axial CT scan at the level of the thalami (C) shows enlarged lateral and third ventricles as well as periventricular transependymal oedema (lower arrow) and a right basal ganglia chronic lacunar infarct (upper arrow), and an axial CT scan at the level of the centrum semiovale (D) shows bilateral symmetrical white-matter hypodensities and effacement of the sulci. In addition, a right parietal subgaleal haematoma and soft-tissue swelling are present. (CT = computed tomography.)

The patient continued to improve with conservative management and was discharged without neurological sequelae on seven oral antihypertensive drugs after 3 weeks in hospital. Electrocardiographic and echocardiographic changes in keeping with hypertensive cardiomyopathy, and small kidneys on ultrasonography with proteinuria, implying hypertensive nephropathy, were indicative of pre-existing but undiagnosed hypertension.

Ethical clearance to publish this case study was granted by the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria (ref. no. 24/2022).

Discussion

This case report contributes to the limited data on PRES manifesting with predominant posterior fossa oedema and secondary obstructive hydrocephalus. Although more cases have been reported in recent years, the literature mostly consists of small case series of 1 - 3 patients.[4-6]

With better availability of and improvements in brain imaging, the list of conditions associated with PRES has become more extensive. Among others, autoimmune diseases, especially systemic lupus erythematosus, bone marrow and solid organ transplants, and liver disease are frequently associated with PRES.[7-10] Nevertheless, hypertensive emergencies, as in our case, remain the most common underlying cause.

Although the pathophysiology of PRES is not fully understood, two main theories are considered. The first one, applicable to our case, results from the observation that most patients with PRES experience a rapid increase in blood pressure, exceeding the limits of cerebral autoregulation and resulting in hyperperfusion and consecutive breakdown of the blood-brain barrier with subsequent vasogenic oedema.[11,12] The resolution of radiological findings as well as symptoms in patients with consistent blood pressure reduction seem to support this theory.

However, up to 25% of patients do not have arterial hypertension or only demonstrate blood pressures below the levels of cerebral blood flow autoregulation failure.[13] In some of these patients, but also in reported cases with hypotension at presentation, e.g. PRES associated with sepsis, a different mechanism must be presumed.

The second theory addressing the aetiology of PRES in patients without hypertension therefore favours endothelial dysfunction and an inflammatory response with circulating cytokines as triggering mechanism, leading to increased vascular permeability and interstitial brain oedema.[13,14]

Clinically, our patient presented with two typical features of PRES, namely confusion and seizures. The initial clinical picture mainly depends on severity and anatomical distribution of the lesions, but in a larger study of 113 patients from the Mayo Clinic, the authors found seizures in 74%, encephalopathy in 28%, headaches in 26% and visual disturbances in 20%.[15] Because accurate visual testing is often hindered or impossible in the acute setting due to confusion, the presence of visual symptoms may be underestimated. In addition, bilateral parieto-occipital brain lesions can result in visual anosognosia, with patients denying visual impairment or even blindness. This is called Anton syndrome.

In the same cohort,[15] the most commonly identified anatomical area was parieto-occipital in 94%, coinciding with the imaging findings in the initial study from 1996. Other commonly involved brain regions were the frontal lobes in 77%, followed by the temporal lobes in 64% and less often the cerebellum.[15] Interestingly, the lesions were asymmetrical in nearly half of these cases (48%), with one patient having unilateral lesions.

The term posterior reversible encephalopathy syndrome is regarded as inaccurate by many clinicians, for two reasons. Firstly, PRES can extend beyond the parieto-occipital areas or spare them altogether. Secondly, some patients can progress and develop permanent neurological deficits.

Treatment of PRES is nonspecific and mainly consists of addressing the assumed trigger, i.e. blood pressure reduction, discontinuation of offending drugs, or

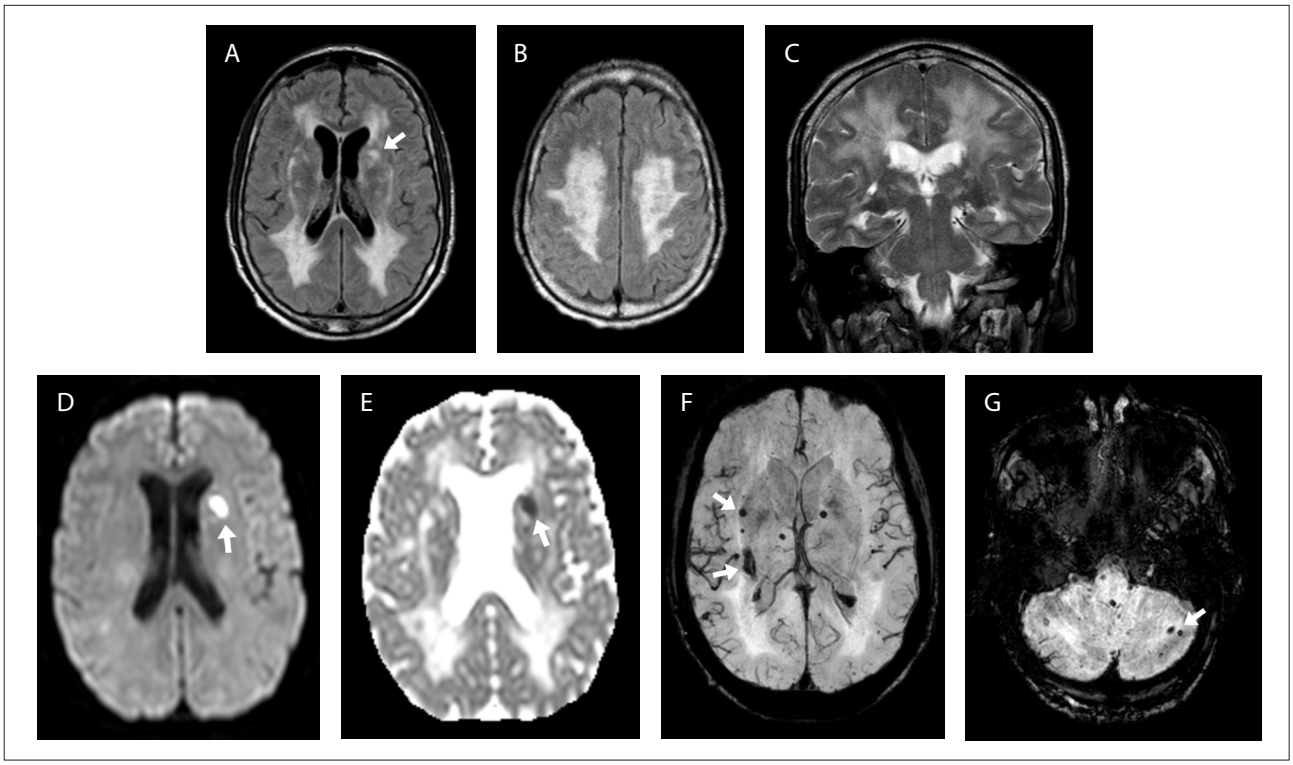

Fig. 2. Selected axial (FLAIR) and coronal (T2WI) images of the brain (A, B and C), showing extensive bilateral symmetrical white-matter T2WI/FLAIR hyperintensity. Additionally, there is an acute infarct in the left caudate nucleus that appears hyperintense on T2/FLAIR (A, arrow). The infarct demonstrates diffusion restriction on diffusion-weighted imaging and apparent diffusion coefficient (D and E, arrows). Axial susceptibility-weighted images (F and G) demonstrate multiple parenchymal punctate calcifications (arrows) shown as foci of blooming artefact. (FLAIR = fluid-attenuated inversion recovery; T2WI = T2-weighted imaging.)

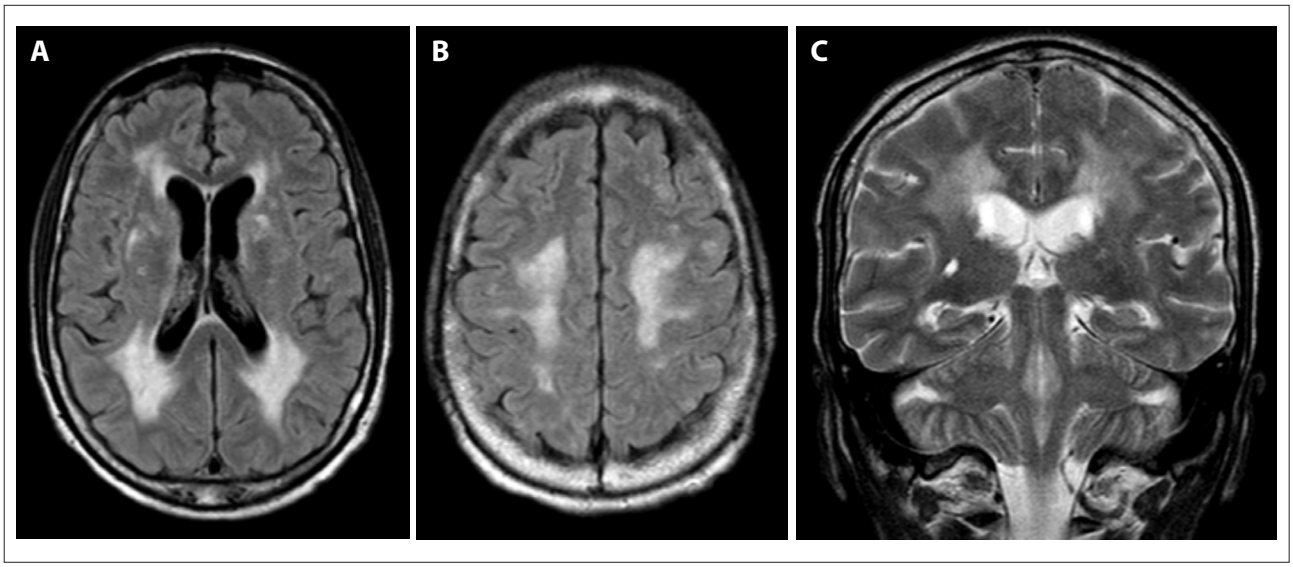

Fig. 3. Follow-up MRI scans of the brain (2 weeks later) showing residual but improved bilateral symmetrical white-matter high signal on axial FLAIR (A and B) and coronal T2WI (C). These selected images were taken at the same level as those in the initial MRI scans shown in Fig. 2. (MRI = magnetic resonance imaging; FLAIR = fluid-attenuated inversion recovery; T2WI = T2-weighted imaging.)

other specific steps such as treating septicaemia or prompt delivery of the baby in a woman with eclampsia. In addition, symptomatic treatment such as initiation of anticonvulsive drugs may be required. The outcome of PRES depends on rapid recognition of the disorder and reversal of causative conditions. While it was previously regarded as a benign, 'reversible' condition, studies over the past few years have shown that morbidity and mortality can be substantial, depending on the underlying cause and management.[16] In a recent retrospective cohort study including 44 patients with PRES, 86% needed intensive care and the in-hospital mortality rate was 11.4%.[17]

Time to causative factor control was a predictor of outcome. Other risk factors for poor outcome included severe encephalopathy, hyperglycaemia or a neoplastic cause.[16] In a recent meta-analysis from 2018, patients with PRES associated with pre-eclampsia and

eclampsia had a reduced risk of poor outcome, but haemorrhages and cytotoxic oedema on imaging increased the odds ratio for poor outcome.[18]

In cases with cerebellar involvement and obstructive hydrocephalus, neurosurgical intervention remains an essential part of management, often resulting in rapid improvement and prevention of long-term neurological disability. In two larger case series, from Li *et al.*[19] (2015) with 11 cases and Kumar *et al.*[20] (2012) with 18 cases, CSF-diverting surgery was reported in approximately half of all patients and the overall outcome was good with only one death due to sepsis. In our patient, CSF diversion was intended, but it was delayed because of the persistently high blood pressure and lack of contrast imaging. Our patient, although confused and unco-operative, did not require intubation and did not show upper motor signs, which were features that prompted urgent intervention in other instances.[21,22]

Interestingly, our patient remained conscious, despite the extent of cerebral oedema on initial imaging. In a recent study from 2017, Schweitzer *et al.*[23] looked for an association between poor outcome and radiological findings and, apart from extensive vasogenic oedema, identified the presence of haemorrhage and restricted diffusion as risk factors for poor outcome. While microhaemorrhages, as found in our patient, were relatively common, being detected in >50% of patients if susceptibility-weighted imaging was performed,[24] larger haemorrhages with mass effect are probably expected to affect patient outcome.[23] The absence of larger areas with restricted diffusion on MRI, which indicate additional cytotoxic oedema with possible infarction and therefore a worse outcome, is another possible factor contributing to our patient's positive outcome despite extensive vasogenic oedema. Similarly, in a study from 2016, the authors could demonstrate a correlation between MRI imaging severity and clinical outcome, while the presence and pattern of gadolinium enhancement did not affect the prognosis.[25]

In summary, we present a rare radiological variant of PRES with extensive brain oedema, predominantly affecting the posterior fossa and resulting in obstructive hydrocephalus. The positive outcome with conservative treatment only may be attributed to firstly the underlying cause being hypertensive encephalopathy, which could be reversed, and secondly the absence of larger haemorrhages and areas of restricted diffusion on MRI, which often result in permanent neurological deficit.

Conclusion

PRES is well characterised by clinical presentation and, typically, supratentorial distribution of radiological findings on brain imaging. Unusual radiological findings such as severe cerebellar oedema resulting in obstructive hydrocephalus can make a timely diagnosis challenging and jeopardise optimal management or result in unnecessary treatment. Recognising PRES as an unusual cause of acute obstructive hydrocephalus is crucial to initiate best medical therapy swiftly and, depending on the clinical picture, to decide whether ventriculostomy is needed or can be withheld without compromising the patient's outcome.

Teaching points

- PRES presents radiologically with a pattern of bilateral parieto-occipital areas of vasogenic oedema.
- Clinically, a combination of confusion, headaches and visual disturbances is common.
- Atypical imaging can include predominantly posterior fossa involvement resulting in obstructive hydrocephalus.
- Recognition of the underlying cause, often a hypertensive crisis, and its timeous treatment are of paramount importance for a favourable outcome.

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Author contributions. JH: conceptualised the update and wrote the clinical case study and discussion; TNA: provided the images and the description of the radiological findings.

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Conflicts of interest. None.

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