Diagnosis of acute neurological emergencies in pregnant and post-partum women

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Acute neurological symptoms in pregnant and post-partum women could be caused by exacerbation of a pre-existing neurological condition, the initial presentation of a non-pregnancy-related problem, or a new acute-onset neurological problem that is either unique to or occurs with increased frequency during or just after pregnancy. Pregnant and postpartum patients with headache and neurological symptoms are often diagnosed with pre-eclampsia; however, a range of other causes must also be considered, such as cerebral venous sinus thrombosis and reversible cerebral vasodilatation syndrome. Precise diagnosis is essential to guide subsequent management. Our ability to differentiate between the specific causes of acute neurological symptoms in pregnant and post-partum patients is likely to improve as we learn more about the pathogenesis of these disorders.

Introduction

Acute neurological symptoms in pregnant and postpartum women could be caused by exacerbation of a pre-existing neurological condition (eg, multiple sclerosis or a seizure disorder) or by initial presentation of a non-pregnancy-related problem (eg, brain neoplasm). Alternatively, patients can present with new acute-onset neurological conditions that are either unique to or occur with increased frequency during and just after pregnancy; here we focus on diagnosis of this patient group. If specific treatments are not started promptly, many of these conditions can result in morbidity or mortality in these young, usually previously healthy individuals. The approach most commonly used to assess many of these symptoms—non-contrast brain CT—is often non-diagnostic. If a patient has a poor outcome, the medical, social, and medico-legal impact is often high. For all these reasons, prompt diagnosis is imperative.

In the past 5 years, the unique pathophysiological states of pregnancy and puerperium have been reviewed,1–3 raised oestrogen concentrations stimulate the production of clotting factors, which increases the risk of thromboembolism; increased plasma and total blood volumes increase the risk of hypertension; and raised progesterone concentrations towards the end of pregnancy enhance venous distensibility, and potential leakage from small blood vessels. The high oestrogen levels fall in the postpartum period. Combined, these hormonal changes can result in leaky capillaries and vasogenic oedema. Pre-eclampsia is defined as the new onset of hypertension and proteinuria after 20 weeks in a previously normotensive woman. Diagnostic criteria for mild pre-eclampsia are blood pressure greater than or equal to 140/90 mm Hg and proteinuria greater than or equal to 0·3 g in a 24-h urine specimen. Criteria for severe pre-eclampsia are two occasions of hypertension (ie, blood pressure greater than or equal to 160/110 mm Hg) at least 6 h apart, proteinuria greater than 5 g per 24 h, and other signs of end-organ injury. Pre-eclampsia occurs in 2–8% of all pregnancies.4 Eclampsia is defined as pre-eclampsia and a grand mal seizure in the absence of other conditions that could account for the seizure. Up to 0·6% of mildly pre-eclamptic women and 2–3% of severely pre-eclamptic women have eclamptic seizures.5 Maternal mortality rates for eclamptic women have been reported to be 0–14% during the past few decades, and are higher in poor countries than in high-income countries.6 The most common cause of death in eclamptic women is brain ischaemia or haemorrhage; however, the neurological events of eclampsia are usually acute and transient, and long-term deficit is rare in properly managed patients.7

Because pre-eclampsia and eclampsia are common, they are often the default diagnoses in pregnant and postpartum women who present with acute neurological symptoms. However, there are other conditions that overlap with eclampsia and with each other in terms of their presentations, including acute ischaemic stroke (AIS), intracerebral and subarachnoid haemorrhage (ICH and SAH), and cerebral venous sinus thrombosis (CVT). Severe vasoconstriction often develops in women with pre-eclampsia—especially when blood pressure is poorly controlled—and can cause brain infarction and haemorrhage. A reversible cerebral vasoconstriction syndrome (RCVS; also referred to as postpartum angiopathy and Call-Fleming syndrome) can develop during puerperium in the absence of hypertension or other features of pre-eclampsia. Pre-eclampsia, eclampsia, and RCVS can all be complicated by posterior reversible encephalopathy syndrome (PRES). In fact, 8–39% of patients with RCVS also have PRES.8,9 PRES is not a primary diagnosis, but a clinical and imaging syndrome caused by vascular abnormalities that are present in pre-eclampsia and eclampsia, RCVS, and other conditions. The continuum between potential causes of some neurological problems that can arise in pregnancy must be recognised, and we need to understand that various diagnoses can arise independently or simultaneously, and are not mutually exclusive. Additionally, whereas eclampsia is specific to pregnancy, PRES, RCVS, and CVT occur in non-pregnant individuals too.

Here we review clinical presentations and diagnostic evaluation of common and serious neurological emergencies that present in pregnant and post-partum

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women, with the aim to help clinicians to avoid misdiagnosis in these high-risk patients. We restrict our discussion to clinical manifestations and diagnoses, because after a diagnosis is established, specific treatments should naturally follow. We have organised data by both presenting symptoms and specific diagnosis, and we have created clinical algorithms on the basis of our interpretation of available literature and our own practice.

**Headache**

Primary headache disorders, tension-type and migraine, are the most common causes of headache in both pregnant and post-partum women. Paradoxically, this can make diagnosis more difficult unless physicians pay careful attention to the so-called red flags that are suggestive of a secondary cause (figure 1). An estimated 40% of post-partum women have headaches, often within the first week after delivery. Migraine usually improves during pregnancy, but often returns postpartum when oestrogen concentrations fall. When pregnant patients get new, worsening headaches or when headaches change in character, secondary causes might exist. Although new migraines can develop during pregnancy, clinicians should be cautious about making that diagnosis. The presence of multiple episodes—ie, five or more episodes in patients with migraine and ten or more in those with tension-type headache—is crucial in the diagnosis of migraine and tension-type headache; therefore, a first new headache that develops during pregnancy or puerperium cannot be definitively diagnosed as a primary headache disorder.

Pre-eclamptic patients often have bilateral throbbing headaches accompanied by blurred vision and scintillating scotomata. Pregnant women with new headaches must be screened for pre-eclampsia. They could have accompanying hypertension, epigastric or right upper-quadrant abdominal pain, oedema, increased deep tendon reflexes, proteinuria, and occasionally agitation or restlessness. Other laboratory findings that raise concern for patients with pre-eclampsia include thrombocytopenia, haemoconcentration, transaminitis, and raised creatinine concentrations.

Patients with abrupt onset of a severe, unusual headache—a so-called thunderclap headache—need prompt investigation. Hormonal changes affecting cerebral blood vessels and surges in blood pressure caused by pushing during labour are two mechanisms that are suggested to increase the incidence of aneurysmal SAH. Large studies have investigated the possible increased incidence of SAH in pregnant and post-partum patients, but have mixed results, possibly because of different methods of case acquisition and some non-aneurysmal cases of SAH. Patients who present with a thunderclap headache need a thorough evaluation to exclude SAH, usually a CT followed by lumbar puncture if the CT is non-diagnostic. However, if the work-up for SAH is negative, disorders such as PRES, CVT, RCVS, and cervico-cranial arterial dissections need to be considered (figure 1). Because CT and lumbar puncture might both be negative in these conditions, physicians should strongly consider following up a non-diagnostic CT and lumbar puncture with MRI sequences that include vascular studies of the arteries and veins, and MRI with diffusion-weighted imaging.

Post-partum primary headache disorders are common; in a study of 95 patients with severe postpartum headache, 37 (39%) had tension-type, 23 (24%) had pre-eclampsia or eclampsia, 15 (16%) postdural puncture headache, 10 (11%) had migraine, three each (3%) had pituitary haemorrhage or venous sinus thrombosis. This study was skewed towards hospitalised patients with headaches resistant to standard treatment. In patients given a spinal anaesthetic, postdural puncture headache is an important consideration. Headaches—often nuchal and occipital, caused by low intracranial pressure due to a CSF leak—typically begin 1–7 days post partum, worsen upon standing and resolve by lying flat for 10–15 mins. This incidence is roughly 0.5–1.5% in women given neuraxial anaesthetics, and symptoms usually resolve within 48 h of a blood patch procedure. Patients who have not had a spinal anaesthetic can also have low-pressure headaches, presumably due to dural tears from labour-related pushing. Although most patients with postdural puncture headache do well, rare complications include subdural haematoma, PRES, and CVT. Low intracranial pressure can cause subdural haematoma, presumably from the tearing of taut bridging veins in a slack brain. These patients might not have the postural component of headache because of the offsetting effects of low pressure from the dural tear and raised pressure from the subdural haematoma. Another diagnostic clue is no response to a blood patch. Most of the serious causes of headache are more common post partum than during pregnancy; therefore, if migraine or postdural puncture headache is unlikely on the basis of an individual patient scenario, physicians must consider these other causes.

**Acute neurological deficit**

Pregnant or post-partum patients who present with persistent acute motor, sensory, or visual findings—with or without headache—might have more serious causes and usually need urgent, thorough investigations (figure 1). Pregnant patients with transient motor, sensory, or visual symptoms commonly have migraine with aura, even if they have no headache. Using different methods, two studies found that in pregnant patients referred for transient neurological motor, sensory, or visual symptoms, most cases could be attributed to migraine with aura. Historical clues to the migrainous cause exist in these patients. Neurological symptoms begin gradually and are more likely to include positive (eg, brightness or shimmering) than negative phenomena.
(eg, blackness or loss of vision). Positive phenomena—brightness or sparkling in vision, tingling, or prickling feelings in the limbs or body—spread gradually and often lead to loss of function, such as scotoma or numbness. Symptoms often clear in one modality, for example vision, and then begin and spread in another modality.

The neurological symptoms develop and usually disappear in 20–30 min. Because visual symptoms are common with pre-eclampsia, diagnosis should not be made without a consideration of other disorders that affect the visual pathways, such as PRES, pituitary apoplexy, and strokes. Another consideration is orbital...
haemorrhage, which presents as acute diplopia, proptosis, and eye pain, and can arise during the first trimester (from hyperemesis) and during labour (from pushing).11

Stroke in pregnant and post-partum women is rare; however, risk is increased compared with non-pregnant age-matched controls, especially in late pregnancy and early puerperium.21,22 Recent evidence suggests that the rate of strokes occurring during pregnancy and postpartum is increasing, substantially for ICH and CVT.21 The ranges of event rates per 100 000 deliveries are 4–11 (AIS), 3.7–9.0 (ICH), 2.6–7.0 (SAH), and 0.7–24.0 (CVT).21,33–35 These studies varied in their methods (table 1). The extreme range for CVT probably results from different case-finding definitions and technological evaluations used in various studies. Additionally, the very low stroke rate in the most recent study (table I) is very likely attributable to the exclusion of post-partum patients (ie, the period of highest risk).19

Pre-eclampsia and eclampsia have causal roles in 25–50% of patients with stroke (table I).21,33,35,38 Other stroke risk factors in these women include older age, African-American race, concurrent hypertension and heart disease, caesarean delivery, migraine, thrombophilia, systemic lupus erythematosus, sickle cell disease, and thrombocytopenia.24,36–38 Thrombocytopenia also suggests the HELLP syndrome (ie, haemolysis, elevated liver enzymes, low platelets) and thrombotic thrombocytopenic purpura, the incidence of which is increased in pregnancy and which can present with stroke-like symptoms.40 Another unusual cause of stroke in pregnant and post-partum women is cervicocranial arterial dissection. Although some reports have shown an increased frequency in pregnant and post-partum women, no strong epidemiological evidence that the incidence of cervicocranial arterial dissection is heightened in this population exists.41 Patients with cervico-arterial dissections often present with isolated headache without neurological deficit,42 but they can also have brain infarctions.43 Possible causal factors are labour-related Valsalva or neck hyperextension during anaesthesia; however, no convincing epidemiological evidence for this exists. In the largest reported series of eight postpartum cases, the only differences between post-partum and non-post-partum cases were coincidental PRES, RCVS, and SAH, which further complicated the occurrence of overlapping clinical syndromes in these patients.43 Most of these dissections occur during the post-partum period, but they have also been reported during pregnancy.44

In patients with ICH and SAH, underlying structural lesions such as vascular malformations and aneurysms are common.33,35,38,40 SAH that occurs around the Circle of Willis is suggestive of an aneurism, whereas high convexal SAH suggests RCVS or CVT. Brain infarction and haemorrhage can result from many of the vasculopathies, including RCVS and pre-eclampsia. Finally, thrombotic thrombocytopenic purpura, pituitary apoplexy, amniotic fluid embolism, chorioangioma, air embolism, and cardioembolism from post-partum cardiomyopathy are rare causes of stroke in this population.45 Extensive diagnostic testing including vascular imaging must be done in these patients to identify specific treatable causes.

Seizures

Pregnant or post-partum women can be grouped into three categories: first, and most common, are patients with an established seizure disorder before pregnancy; second are patients with a new non-pregnancy-related seizure disorder, such as a new seizure from an undiagnosed brain tumour or hypoglycaemia; third are patients with new seizures that are pregnancy related (caused by eclampsia, ICH, CVT, RCVS, PRES, or thrombotic thrombocytopenic purpura). Whereas in patients with PRES, seizures are common and usually occur at presentation in the absence of prodromal symptoms, in CVT seizures usually occur later and nearly always after headache; brain CT can be normal in both conditions. Seizures are much less common in

<table>
<thead>
<tr>
<th>AIS</th>
<th>ICH</th>
<th>SAH</th>
<th>CVT</th>
<th>Eclampsia (%)</th>
<th>Method</th>
<th>Total deliveries</th>
<th>Years of study</th>
</tr>
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<tbody>
<tr>
<td>Jaigobin et al (2000)35</td>
<td>11.1</td>
<td>3.7</td>
<td>4.3</td>
<td>6.9</td>
<td>23% AIS, 38% CVT, 17% ICH, 0% SAH</td>
<td>Referral single-centre Canadian study</td>
<td>507 00</td>
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<tr>
<td>Lanska and Kryscio (2000)37</td>
<td>13</td>
<td>..</td>
<td>..</td>
<td>..</td>
<td>Not reported</td>
<td>USA national inpatient database</td>
<td>1 408 015</td>
</tr>
<tr>
<td>Salonen et al (2001)34</td>
<td>4.0</td>
<td>3.8</td>
<td>2.4</td>
<td>..</td>
<td>Not reported</td>
<td>Population-based national Swedish study</td>
<td>1 003 489</td>
</tr>
<tr>
<td>James et al (2005)38</td>
<td>9.2</td>
<td>8.6</td>
<td>..</td>
<td>0.7</td>
<td>15.7</td>
<td>USA national inpatient database</td>
<td>8 322 759</td>
</tr>
<tr>
<td>Kuklina et al (2011)34</td>
<td>11</td>
<td>7</td>
<td>7</td>
<td>24</td>
<td>Not reported</td>
<td>USA national inpatient database</td>
<td>8 785 475</td>
</tr>
<tr>
<td>Scott et al (2012)39</td>
<td>0.9</td>
<td>0.4</td>
<td>..</td>
<td>..</td>
<td>11% AIS, 33% ICH (pre-eclampsia and eclampsia)</td>
<td>UK national population-based cohort and nested case-control study</td>
<td>1 952 203</td>
</tr>
</tbody>
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AIS=acute ischaemic stroke. ICH=intracerebral haemorrhage. SAH=subarachnoid haemorrhage. CVT=cerebral venous sinus thrombosis. *Intrinsic to the studies that used the USA national database (the Nationwide Inpatient Sample) is a sampling of about 20% of patients; therefore, the reported number of deliveries is an extrapolated number. †The 13 include AIS, ICH, and SAH. §The authors do not directly state which strokes are eclampsia related, but do include an ICD-9 code for pregnancy-related cerebrovascular events separate from the ICD-9 codes for AIS, ICH, or CVT. ¶Includes pre-eclampsia only. **Includes CVT. Table 1: Incidence of stroke per 100 000 deliveries in pregnant and post-partum women.
RCVS. Other than to emphasise that pregnant and post-partum patients need the same systematic diagnostic approach to a new seizure as do all seizure patients, we will not focus on the first two groups.

No quality data inform the ideal initial work-up in patients in the third category. However, because of wide differential diagnosis and the poor sensitivity of CT, we believe that pregnant and post-partum patients with new-onset seizures—even those who have returned to normal and are neurologically intact—should undergo thorough investigation, usually including MRI sequences, to establish the cause of the seizure. The one exception to routine imaging is the patient whose seizures are consistent with typical prenatal eclampsia (figure 1).

**Individual conditions that cause acute neurological symptoms**

**Clinical features**

The clinical presentations of acute neurological symptoms in pregnant and post-partum women have substantial overlap between them, and several disorders can even coexist. However, the details—eg, headache characteristics, evolution of symptoms over time, and frequency of some symptoms such as seizures or visual problems—can often help to distinguish between them (table 2).

**Cerebral venous sinus thrombosis**

A rare cause of stroke overall, CVT is an important consideration in pregnant and post-partum women. A spike in incidence in the first trimester might be attributable to women who become pregnant with an underlying thrombophilia, but more than 75% of cases of CVT are post partum. Risk factors include caesarean section, dehydration, traumatic delivery, anaemia, raised homocysteine concentrations, and low CSF pressure due to dural puncture from a neuraxial anaesthetic. CVT is believed to be more common in poor countries than in high-income countries because of the higher frequency of poor nutrition, infections, and dehydration. Patients with CVT caused by pregnancy or the use of oral contraceptive generally have better long-term outcomes than do men or women with CVT that is unrelated to pregnancy.

Most patients present with a progressively severe, diffuse, constant headache, although 10% have thunderclap headache. Other findings include dizziness, nausea, seizures, papilloedema, lateralising signs, lethargy, and coma. The specific presentation depends on the extent and location of the dural sinuses and draining veins involved, collateral circulation, effects on intracranial pressure, and the presence of associated haemorrhage. Symptoms vary and can fluctuate over time. Non-contrast CT scans are often negative, but 30% of cases might show a clot or signs of infarction (figure 2). Ischaemic infarcts often undergo haemorrhagic transformation. CT venography often shows the clot, but magnetic resonance venography—especially with gradient spin-echo sequences—is diagnostic and generally the imaging study of choice.

**Reversible cerebral vasoconstriction syndrome**

RCVS is characterised by abrupt onset of thunderclap headaches and multifocal, reversible cerebral vasoconstriction. Two-thirds of patients with RCVS develop

<table>
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<tr>
<th>Mode of onset</th>
<th>PRES</th>
<th>RCVS</th>
<th>CVT</th>
<th>Eclampsia</th>
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<tr>
<td>Rapid (hours)</td>
<td>Rapid (hours), usually post partum</td>
<td>Abrupt, usually post partum</td>
<td>Third trimester or post-partum, symptoms often progress over days</td>
<td>Antepartum, intrapartum, or post partum (10–50%)</td>
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<tr>
<td>Key findings</td>
<td>Early prominent seizures, other symptoms (eg, stupor, visual loss, and visual hallucinations) usually accompany seizures; headache dull and throbbing, not thunderclap</td>
<td>Thunderclap headache, multiple episodes; seizures occur but are less common than in PRES; transient focal deficits (could become permanent in cases with intracerebral haemorrhage or infarction)</td>
<td>Headache nearly universal at onset, generally progressive and diffuse, thunderclap in small minority; seizures occur in roughly 40% of patients; focal signs might develop later</td>
<td>Seizures, frequent visual symptoms, abdominal pain, hyper-reflexia, hypertension, and proteinuria</td>
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<td>Evolution over time</td>
<td>If blood pressure is controlled, symptoms resolve within days to weeks</td>
<td>Dynamic process over time, generally, headaches common during first week, intracerebral haemorrhage during second week, and ischaemic complications during third week</td>
<td>Evolves over several days, non-arterial territorial infarcts and haemorrhages might develop</td>
<td>Can evolve (from pre-eclampsia) gradually or abruptly</td>
</tr>
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<td>CSF findings</td>
<td>Usually normal, might have slightly raised protein</td>
<td>Often normal (unless complicated by subarachnoid haemorrhage), but 50% of patients have slight pleocytosis and protein increases</td>
<td>Opening pressure raised in about 80% of patients, roughly 35–50% will have slightly raised protein or cell counts</td>
<td>Usually normal unless complicated by haemorrhage</td>
</tr>
<tr>
<td>Imaging aspects</td>
<td>CT positive in about 50% of patients; MRI shows prominent T2-weighted and FLAIR abnormalities nearly always in parieto-occipital lobes, but can involve other brain regions; intracerebral haemorrhage in about 15% of patients</td>
<td>CT usually normal (if no subarachnoid haemorrhage); 20% show localised convexal subarachnoid haemorrhage on MRI; CT angiogram and magnetic resonance angiogram usually show typical string-of-beads constriction of cerebral arteries; digital subtraction angiogram is more sensitive; might have associated cervical arterial dissection; initial arteriogram might be negative</td>
<td>CT often negative; MRI might show non-arterial territorial infarcts; haemorrhage common; MRV shows intraluminal clot flow voids; although MRV is preferred, CT venogram is also sensitive</td>
<td>Same as for PRES, some patients have coincident acute ischaemic stroke or intracerebral haemorrhage</td>
</tr>
</tbody>
</table>

PRES=posterior reversible encephalopathy syndrome. RCVS=reversible cerebral vasoconstriction syndrome. CVT=cerebral venous sinus thrombosis. FLAIR=fluid-attenuated inversion recovery. MRV=magnetic resonance venogram.
sustained within 1 week of delivery and after a normal pregnancy. RCVS is associated not only with the postpartum state but also with the use of immunosuppressive drugs, vasoactive substances (including serotonin reuptake inhibitors, cocaine, and phenylpropanolamine), various other medications, blood products, catecholamine-secreting tumours, cranio-cervical arterial dissections, and other conditions. Recurring daily thunderclap headaches over several weeks after a single thunderclap headache are nearly pathognomonic. Heads are often accompanied by vomiting, confusion, photophobia, and blurred vision. When seizures occur or focal neurological deficits develop, they nearly always follow the headache. Symptoms usually subside over 2–3 months. Although most patients have good outcomes, much variability exists, and fatal outcomes have been reported in post-partum patients with RCVS. Complications include brain haemorrhage and infarction and nonaneurysmal convexal SAH, which is more common than parenchymal ICH. Haemorrhagic complications usually precede ischaemic ones. In patients without infarction, the disease resolves over time. A small proportion of patients with RCVS also have cervicocranial arterial dissections. Unless there is a complicating haemorrhage, the CSF is usually normal but can show small numbers of lymphocytes and a mild rise in protein concentrations.

In the absence of haemorrhage, CT is usually normal. With respect to vascular testing, it is important to recognise that RCVS is a dynamic process. Transcranial doppler and various forms of angiography are useful aids, but could be normal early in the course of the disease. Angiography and transcranial doppler might be discordant. Angiography after the third day usually reveals multifocal segmental arterial constriction and can detect arterial dissections. Non-invasive CT or magnetic resonance angiography is positive in about 80% of patients, and shows the diagnostic pattern of alternating dilatation and constriction, which resembles a string of beads (figure 2). Transcranial doppler can be used to follow resolution of the vasoconstriction.

**Posterior reversible encephalopathy syndrome**

PRES is characterised by headache, seizures, encephalopathy, and visual disturbances in the setting of reversible vasogenic oedema on CT or MRI. PRES arises in patients with acute hypertension, pre-eclampsia or eclampsia, renal disease, sepsis, and other conditions and in those exposed to immunosuppressant and other drugs. Symptoms develop without prodrome and progress rapidly over 12–48 h. About 90% of patients have seizures, which might be focal to start with and then tonic-clonic, and generally precede visual changes or headache, which is generally dull, bilateral, and not thunderclap. Severe symptoms can occur even in the absence of severe hypertension.

Because the vasogenic oedema nearly always involves the occipital lobe, about 40% of patients have visual symptoms such as visual hallucinations, blurred vision, scotoma, and diplopia; 1–15% of patients have transient cortical blindness. The retina and pupils are normal. Many patients are confused and have poor memory. EEG monitoring can detect ongoing seizure activity. CT will show oedema in roughly 50–60% of patients; however, MRI should be done when PRES is suspected.

MRI reveals focal oedema, particularly in the parieto-occipital lobes (figure 2). Unlike posterior cerebral artery lesions, the occipital lesions spare the medial occipital lobe and calcarine cortex. About a third of patients have oedema in other areas of the brain, but nearly all have concurrent posterior involvement. Visual symptoms often resolve completely in hours to days; resolution of the oedema on imaging lags behind. In eclamptic patients, PRES is not the only potential explanation for seizures; rarely, pregnant or post-partum women develop PRES for other reasons (such as medication use or RCVS) and not as a result of eclampsia. Thus, although there is overlap in most patients, eclampsia and PRES can occur independently.

Studies comparing clinical and radiological features of PRES in non-pregnant versus pregnant patients have reported mixed results. Although a small study (21 patients) found no differences, a larger study (96 patients) showed that eclamptic or pre-eclamptic patients with PRES more commonly presented with headache, were less likely to be confused, and were more likely to have visual symptoms than were non-eclamptic or pre-eclamptic patients with PRES. On imaging, pregnant patients had less oedema, fewer haemorrhages, and more complete resolution. In view of the small numbers of patients in both of these studies, it is difficult to draw firm conclusions about these differences.

**Neurological complications of eclampsia**

Seizures are the hallmark of eclampsia. Eclamptic seizures are usually tonic-clonic and last for about 1 min. Symptoms that can precede seizures include persistent frontal or occipital headache, blurred vision, photophobia, right upper-quadrant or epigastric pain, and altered mental status. In up to a third of cases, blood pressure is less than 140/90 mm Hg before the seizure or no proteinuria exists. Although the exact mechanism of eclamptic seizures is unknown, several hypotheses exist. Cerebral over-regulation in response to hypertension might lead to cerebral arterial vasospasm and ischaemia, resulting in cytotoxic oedema. Alternatively, loss of autoregulation in response to hypertension might lead to endothelial dysfunction, capillary leak, and vasogenic oedema. This vasculopathy can also result in PRES or regions of infarction and haemorrhage. Although focal vasogenic oedema is characteristic of eclampsia, up to a quarter of patients have areas of persistent cytotoxic oedema.
consistent with infarction or focal haemorrhage. Thus, components of PRES, areas of ischaemia or haemorrhage, and even RCVS can contribute to eclamptic seizures.

Roughly 90% of eclampsia cases occur at or after 28 weeks of gestation. Just over a third of eclamptic seizures occur at term, and develop intrapartum or within 48 h of delivery. So-called late post-partum eclampsia—ie, eclampsia that arises more than 48 h after delivery—is being increasingly reported. In one large study of post-partum eclampsia, two-thirds of patients were discharged and re-admitted because of late post-partum pre-eclamptic symptoms, most commonly headache. The proportion of pre-eclampsia and eclampsia diagnosed post partum is 11–55% and the figures might increase with improved antepartum recognition. Post-partum patients sometimes ignore early symptoms—eg, headache or abdominal pain—and only seek medical care later, after a seizure.

Patients with post-partum eclampsia, especially those with late post-partum eclampsia, have a higher incidence of CVT, ICH, and AIS than do eclamptic patients diagnosed pre partum. Although most women with typical eclampsia do not need brain imaging, post-partum eclamptic patients, those with focal neurological deficits, persistent visual disturbances, and symptoms refractory to magnesium and antihypertensive treatment should undergo thorough diagnostic testing, preferably including MRI. Imaging might also reveal areas of vasoconstriction consistent with RCVS and, rarely, pregnant patients, especially those with RCVS, develop craniocervical arterial dissections. Thus, the range of neurological imaging findings in pre-eclamptic and eclamptic patients includes infarction, haemorrhage, vasoconstriction, dissection, and both vasogenic and cytotoxic oedema.

Rare conditions that cause acute neurological symptoms

Amniotic fluid embolism and metastatic choriocarcinoma are two pregnancy specific conditions that can present with neurological symptoms. Amniotic fluid embolism causes agitation, confusion, seizures, and encephalopathy in the context of cardiovascular and respiratory collapse during or immediately after labour. Choriocarcinoma, a rare cancer of trophoblastic tissue, metastasises to the brain in 20% of patients. Because the tumour can cause mass effect, bleed, and invade cerebral vessels, its clinical and imaging manifestations are variable.

Air embolism occurs when air that enters the myometrium during delivery enters the venous circulation and right ventricle, reducing cardiac output and resulting in seizures and abnormal cognition during or just after delivery. Nearly any focal or generalised neurological symptom can also occur because of right-to-left intracardiac shunting of air via a patent foramen ovale. Presence of air in the retinal veins and a so-called mill-wheel cardiac murmur suggest the diagnosis.

**Figure 2:** Selected images from pregnant and post-partum women with neurological emergencies

(A) Non-contrast CT scan of a 21-year-old post-partum woman who presented with 7 days of increasing left-sided headache. A subtle increased density (red arrows) that is consistent with a clot in the left transverse sinus can be seen. (B) The magnetic resonance venogram from the same patient shows a clot in the left transverse sinus (wide arrow) and in the sigmoid sinus (thin arrow). (C) Selected images from a digital subtraction angiography of a patient with reversible cerebral vasoconstriction syndrome who presented with a thunderclap headache. The image on the left shows the diffuse nature of the vasoconstriction. The image on the right shows the classic so-called string of beads appearance (green arrows show the focal areas of vasoconstriction). Similar findings are found in most patients with non-invasive—CT or magnetic resonance—angiography. Reproduced from Caplan, by permission of Elsevier. (D) Two cuts from FLAIR sequences on an MRI that show increased signal in both parieto-occipital regions (blue arrows), slightly more on the right hemisphere, in a 29-year-old pregnant patient with posterior reversible encephalopathy syndrome. Diffusion-weighted imaging on this same patient was normal. Note that the findings spare the medial occipital lobe and calcarine cortex, unlike the posterior cerebral artery lesions that involve this region.
Wernicke’s encephalopathy can complicate hyperemesis gravidarum. In one study of 625 non-alcoholic patients with Wernicke’s encephalopathy, 76 (12%) were women with hyperemesis.\(^{101}\) Abnormal eye movements are nearly always present; however, the classic triad of confusion, ocular findings (eg, diplopia and nystagmus), and gait abnormalities occurs in a minority of patients.\(^{102}\)

Some patients have an otherwise unexplained metabolic acidosis.\(^{103}\) Neither biochemical confirmation nor MRI is necessary—the simplest test is the response to intravenous thiamine.\(^{100–101}\)

Pregnant women are at particular risk of thrombotic thrombocytopenic purpura, which most commonly presents late in the second or early third trimester.\(^{104}\) The classic pentad includes thrombocytopenia, microangiopathic haemolytic anaemia, fever, and neurological and renal dysfunction.\(^{105}\) Neurological manifestations, which arise in more than half of patients, include fluctuating headache, seizures, and generalised and focal neurological deficits. Coexistent PRES is common.\(^{106}\) Because the treatments are so different, distinction between thrombotic thrombocytopenic purpura (ie, plasma exchange) and HELLP (ie, magnesium and delivery of the fetus) is important.\(^{41,104,105}\) Since no one distinguishing feature exists, haematological consultation is strongly recommended.

Pituitary apoplexy, acute infarction, or haemorrhage of the gland—usually in the setting of a (previously undiagnosed) adenoma—present with headache, visual loss, and ophthalmoplegia and decreased consciousness. Although the pituitary gland enlarges during pregnancy, pregnancy rarely leads to pituitary apoplexy, acute infarction, or haemorrhage of the gland.\(^{107,108}\) Pituitary apoplexy is distinguished from Sheehan’s syndrome (hypopituitarism presenting indolently, weeks to months after severe post-partum haemorrhage)\(^{109}\) and lymphocytic hypophysitis (headache and visual symptoms that present acutely in pregnant patients but typically with a slower onset than in non-pregnant patients).\(^{109–110}\)

Rarely life threatening, chorea gravidarum is a condition characterised by irregular, brief, unpredictable jerky movements of multiple body parts. The condition, which is associated with rheumatic fever, antiphospholipid syndrome, stroke, Wilson’s disease, and thyrotoxicosis, typically begins after the first trimester, but can present post partum.\(^{111–113}\) Symptoms usually resolve spontaneously within several weeks to months, or might subside post partum.

**Neuroimaging and multidisciplinary coordination of care**

When brain imaging is used to make a specific diagnosis, several basic principles should be kept in mind. First, the clinician and the radiologist should discuss the case and differential diagnosis before imaging to minimise ionising radiation and intravenous contrast exposure, and to ensure that, when MRI is done, the correct sequences are obtained the first time to maximise the accuracy of the interpretation of the images. Second, the fetal radiation exposure from a non-contrast brain CT is negligible.\(^{114}\) Although CT is safe to perform in this population, clinicians must realise its diagnostic limitations for many of the target conditions—aneurysmal SAH is one exception. Third, because many conditions that cause acute neurological symptoms and signs in pregnant and post-partum patients need MRI to establish the diagnosis, the clinician’s threshold for proceeding directly to MRI must be accordingly low. MRI in pregnant patients is generally thought to be safe, although conclusive data do not exist.\(^{114–116}\) Fourth, as with any medication, intravenous contrast is, when possible, best avoided during pregnancy. The US Food and Drug Administration classifies iodinated contrast as class B and gadolinium as class C. Although no high-quality clinical studies exist, iodinated contrast agents are thought to be safer than gadolinium, which is best avoided unless the physician believes that the information to be gained by its use exceeds any potential risk.\(^{114–117}\) Authorities recommend that informed patient consent is obtained before these procedures are done and intravenous contrast agents are used.\(^{116,117}\) Babies exposed to iodinated agents should have their thyroid function checked after birth. Finally, because only very small amounts of both iodinated contrast and gadolinium are secreted in breast milk and because similarly small quantities are absorbed across an infant’s gut, both types of contrast are regarded as safe in post-partum women who are breastfeeding.\(^{114–117}\) There are no data on the effect on outcomes of location of care of pregnant and post-partum patients with acute neurological emergencies. We believe that because these situations are uncommon and intrinsically multidisciplinary, these patients are ideally cared for in hospitals with expertise in neurology, neurosurgery, advanced radiology, obstetrics, and critical care. Even in such centres, close coordination of care across various disciplines is crucial.

**Conclusions**

Pregnant and post-partum patients who present with new acute neurological symptoms need a thorough diagnostic evaluation that targets a range of pathological conditions that are either unique to or arise more frequently in this population. After an accurate diagnosis is made, specific treatment will follow. Because most of these conditions are multidisciplinary and infrequent, clinicians should consider early transfer of these patients to a centre that can deliver full diagnostic testing and potential care. Since the precise pathogenesis of most of these disorders is unknown, specific and sensitive diagnostic tests are scarce; however, as the science advances, our ability to diagnose and differentiate between the specific causes of acute neurological symptoms is likely to improve. For example, the initiating event in pre-eclampsia has been suggested to be reduced...
uteroplacental perfusion caused by abnormal cyto-
 trophoblast invasion of spiral arteries. Researchers have hypothesised that the ischaemic placenta secretes soluble factors into the maternal vasculature, causing endothelial dysfunction and the clinical features of pre-
eclampsia. Excess secretion of a naturally occurring antiangiogenic molecule of placental origin referred to as soluble fms-like tyrosine kinase-1 (sFlt-1) might have a role in pre-eclampsia.118,119 In the future, this and other soluble factors into the maternal vasculature, causing endothelial dysfunction and the clinical features of pre-eclampsia.118,119 In the future, this and other conditions, we searched PubMed for English language articles containing the terms “pregnancy” or “postpartum” in the abstract in conjunction with other key terms, including “pre-eclampsia”, “eclampsia”, “headache”, “seizures”, “stroke”, “visual symptoms”, “PRES”, “reversible cerebral vasoconstriction”, and “cerebral vein thrombosis”, in the title. We manually searched the article bibliographies and our personal files for other sources. We gave priority to papers published in the past 10 years that included new data on diagnosis in large numbers of patients and those addressing serious neurological conditions. We also searched the National Guideline Clearinghouse and modified our reference list on the basis of reviewers’ comments. Most of the articles that we identified in our literature search were case series (often in referral populations) and review articles with consensus-based recommendations. There were few systematic analyses of the diagnosis of consecutive patients in routine practice. We eliminated articles about minor (non-life-threatening) neurological conditions (eg, carpal tunnel syndrome or peripheral seventh nerve palsy).

Search strategy and selection criteria

We searched for literature published from Jan 1, 1980 to Sep 20, 2012. Because we were focusing on more than one condition, we searched PubMed for English language articles containing the terms “pregnancy” or “postpartum” in the abstract in conjunction with other key terms, including “pre-eclampsia”, “eclampsia”, “headache”, “seizures”, “stroke”, “visual symptoms”, “PRES”, “reversible cerebral vasoconstriction”, and “cerebral vein thrombosis”, in the title. We manually searched the article bibliographies and our personal files for other sources. We gave priority to papers published in the past 10 years that included new data on diagnosis in large numbers of patients and those addressing serious neurological conditions. We also searched the National Guideline Clearinghouse and modified our reference list on the basis of reviewers’ comments. Most of the articles that we identified in our literature search were case series (often in referral populations) and review articles with consensus-based recommendations. There were few systematic analyses of the diagnosis of consecutive patients in routine practice. We eliminated articles about minor (non-life-threatening) neurological conditions (eg, carpal tunnel syndrome or peripheral seventh nerve palsy).

Contributors

JAE wrote the first draft and assumes overall responsibility for the Review. All authors helped to organise the information, performed the literature searches, wrote and edited subsequent drafts of the article.

Conflicts of interest

JAE, LRC, and CDT receive fees for expert testimony; however, none are felt to represent a conflict for this article. KO’B declares that she has no conflicts of interest.

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