Diagnosis of Acute Neurologic Emergencies in Pregnant and Postpartum Women

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INTRODUCTION

Acute neurologic symptoms in pregnant and postpartum women may be owing to an exacerbation of a preexisting neurologic condition (eg, multiple sclerosis or a known seizure disorder) or to the initial presentation of a non–pregnancy-related problem.

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Keywords
- Eclampsia
- Posterior reversible encephalopathy syndrome
- Reversible cerebrovascular constriction syndrome
- Cerebral venous sinus thrombosis
- Pregnancy

Key Points
- Pregnant and postpartum patients with headache and seizures are often diagnosed with preeclampsia or eclampsia because they are the most common conditions; however, other etiologies must be considered.
- Most cases of cerebral venous sinus thrombosis present in the early postpartum period.
- Although stroke and other cerebrovascular diseases are uncommon in pregnant women, the incidence is higher than in age and sex-matched nonpregnant individuals.
- Computed tomography scanning is insensitive to many of the acute neurologic conditions that affect pregnant and postpartum women.
(eg, a new brain tumor). Alternatively, patients can present with new, acute onset neurologic conditions that are either unique to or precipitated by pregnancy.

In this review, we focus on these latter conditions. The most common diagnostic tool used in emergency medicine to evaluate many of these symptoms—noncontrast head computed tomography (CT)—is often nondiagnostic or falsely negative. Misdiagnosis can result in morbidity or mortality in young, previously healthy individuals. Therefore, if a poor outcome occurs, the medical, social, and medicolegal impact is usually high. For all of these reasons, prompt diagnosis is imperative.

The unique pathophysiologic states of pregnancy and the puerperium have been reviewed.1–4 Increasing concentrations of estrogen stimulate the production of clotting factors, increasing the risk of thromboembolism. Increases in plasma and total blood volumes increase the risk of hypertension. Elevated progesterone levels in pregnancy increase venous distensibility and, potentially, leakage from small blood vessels. The high estrogen levels decrease in the postpartum period. Combined, these hormonal changes can result in increased permeability of the blood–brain barrier and vasogenic edema.

Preeclampsia, the new onset of hypertension and proteinuria or laboratory abnormalities after 20 weeks in a previously normotensive woman, occurs in 2% to 8% of pregnancies.5 The incidence of preeclampsia has increased by 25% in the United States over the last 20 years,6 which has been attributed in part to the increase in maternal obesity and maternal age.7 Diagnostic criteria for preeclampsia were recently revised.8 Whereas previously preeclampsia was defined by systolic blood pressures of 140/90 mm Hg or greater and proteinuria of 0.3 g or greater of protein in a 24-hour urine specimen, the new criteria allow for the diagnosis of preeclampsia without proteinuria, permit the use of a spot protein/creatinine ratio or urine dip to diagnose preeclampsia, and rename what was previously called “mild preeclampsia” as “preeclampsia without severe features,” among other changes. Preeclampsia is now defined as blood pressures of 140/90 mm Hg or greater on 2 occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure, plus either proteinuria, or in the absence of proteinuria, thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or new-onset neurologic symptoms such as visual changes or headache. In practical terms, this means any woman with persistently increased blood pressure and a persistent new headache meets diagnostic criteria for preeclampsia, and the headache would confer the diagnosis of preeclampsia with severe features. However, other neurologic conditions requiring significantly different management than preeclampsia should be considered in these cases. Of note, the revised criteria state that severe range blood pressures (those \( \geq 160/110 \) mm Hg) “can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy,”8 to stress that antihypertensive therapy should not be delayed in these women to confirm a diagnosis.

Eclampsia is defined as preeclampsia plus a generalized tonic–clonic seizure in the absence of other conditions that could account for the seizure. Eclamptic seizures occur in up to 0.6% of women with preeclampsia without severe features, and in 2% to 3% of women with preeclampsia with severe features.9 Of note, eclampsia rarely can present atypically, without elevated pressures or proteinuria so it should remain on the differential for women with new-onset seizures in pregnancy even if the classic criteria of hypertension and proteinuria or laboratory abnormalities are not satisfied.10–12 Maternal mortality rates for eclamptic women have been reported to be as high as 14% over the past few decades, with the highest rates in developing countries.13 Although the most common causes of death in eclamptic women are brain ischemia and hemorrhage, most eclampsia-related neurologic events are transient, and long-term deficits are rare in properly managed patients.14
However, other conditions, which overlap with eclampsia and with each other, can present similarly. These include acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), and cerebral venous sinus thrombosis (CVT). Severe vasoconstriction often develops in women with preeclampsia, especially when the blood pressure is poorly controlled. This vasoconstriction can cause brain infarction and/or hemorrhage. A reversible cerebral vasoconstriction syndrome (RCVS)—also referred to as postpartum angiopathy and Call–Fleming syndrome—can develop during the puerperium without hypertension or other features of preeclampsia. Preeclampsia, eclampsia and RCVS can all be complicated by the posterior reversible encephalopathy syndrome (PRES). In fact, 8% to 39% of patients with RCVS have PRES as well. PRES is a clinical (headache, seizures, encephalopathy, and visual disturbances) and imaging (reversible vasogenic edema) syndrome that may occur in preeclampsia/eclampsia, RCVS, and other conditions. It is essential to recognize the significant overlap between these various etiologies, which can occur independently or simultaneously. Whereas eclampsia is specific to pregnancy, PRES, RCVS, and CVT also occur in nonpregnant individuals.

This review is intended to help clinicians avoid misdiagnosis in these high-risk patients. We therefore limit the review to clinical manifestations and diagnosis, because once a given diagnosis is established, specific treatments should naturally follow. We have organized the data by presenting symptoms as well as by specific diagnosis. Finally, we have created clinical algorithms based on our interpretation of the existing literature and our practice.

HEADACHE

Roughly 40% of postpartum women have headaches, often during the first week. Primary headache disorders—tension type and migraine—are the most common causes in both pregnant and postpartum women. This can paradoxically make correct diagnosis more difficult unless physicians pay careful attention to “red flags” that suggest a secondary cause (Fig. 1B). In 1 series, among 95 patients with severe postpartum headache, one-half had tension type (39%) or migraine (11%), followed by preeclampsia/eclampsia (24%) and postdural puncture headache (PDPH; 16%). Pituitary hemorrhage, mass lesions, and CVT each accounted for another 3%. This study was skewed toward sicker, hospitalized patients whose headaches were “resistant to usual therapy.”

In general, migraine improves during pregnancy and returns postpartum as estrogen levels decrease. Pregnant patients with new, worsening headaches, positional headaches, or headaches that have changed in character suggest the possibility of secondary causes. Although new migraines can develop during pregnancy, migraine should be considered a diagnosis of exclusion. Implicit in the diagnosis of migraine and tension-type headache is the presence of multiple episodes (≥5 episodes for migraine and ≥10 for tension-type headache). Therefore, one cannot definitively diagnose a first new headache that develops during pregnancy or the puerperium—or in any other patient for that matter—as a manifestation of a primary headache disorder.

Preeclamptic patients often have bilateral throbbing headaches accompanied by blurred vision and scintillating scotomata. Pregnant women with new headaches must be screened carefully for preeclampsia. Hypertension, epigastric or right upper quadrant abdominal pain, edema, increased deep tendon reflexes, proteinuria, and occasionally agitation or restlessness may accompany the headache. Laboratory findings that increase the concern for preeclampsia include thrombocytopenia,
hemoconcentration, transaminitis, elevated creatinine, and elevated uric acid. Unfortunately, despite considerable research and progress, there is no current routinely available biomarker to definitively diagnose preeclampsia.\textsuperscript{30,31}

Patients with abrupt onset of a severe, unusual headache (“thunderclap headache”) require urgent investigation.\textsuperscript{32} Large studies evaluating the possible increased incidence of SAH in pregnant and postpartum patients report mixed results, possibly owing to varying methods of case acquisition, as well as the fact that some instances of SAH in these patients are nonaneurysmal.\textsuperscript{33–36} Hormonal changes affecting cerebral blood vessels and surges in blood pressure from pushing during labor are

![Fig. 1. Diagnostic algorithm for pregnant and postpartum patients presenting with acute neurologic symptoms. (A) Pregnant and post partum women with acute neurologic symptoms. (B) Pregnant and post partum women with isolated headache. (C) Patients with other neurologic symptoms or signs (with or without headache and not thought to be pure eclampsia) or eclamptic patterns not responding to treatment. CT, computed tomography; CVT, cerebral venous thrombosis; PRES, posterior reversible encephalopathy syndrome; RCVS, reversible cerebral vasoconstriction syndrome; SAH, subarachnoid hemorrhage.](image-url)
2 potential mechanisms for an increased incidence of aneurysmal SAH. All patients presenting with a thunderclap headache require a thorough evaluation to exclude SAH, usually a head CT scan followed by lumbar puncture if the CT scan is nondiagnostic.

However, if the workup for SAH is negative, disorders such as PRES, CVT, RCVS, and cervicocranial arterial dissections must be considered in pregnant and postpartum patients who present with thunderclap headache (Fig. 1). Because CT and lumbar puncture may both be negative in these latter conditions, physicians should strongly consider following up a nondiagnostic CT and lumbar puncture with MRI sequences including diffusion-weighted images as well as vascular studies of the arteries (MR angiogram) and veins (MR venogram). If arterial dissection is suspected, acquisition of T1 fat-saturated images should be considered to increase the sensitivity for detecting a thrombus within a dissection flap.

In patients who have had a spinal or epidural anesthetic, PDPH is an important consideration, and has been estimated to occur in 0.5% to 1.5% of these patients. Caused by low intracranial pressure owing to a cerebrospinal fluid leak, headaches, often nuchal and occipital, typically begin 1 to 7 days postpartum, rapidly worsen upon standing, and resolve upon lying flat over 10 to 15 minutes. Tinnitus, diplopia, and hypacusia may occur. Symptoms usually resolve within 48 hours of a blood patch. Patients who have not had a spinal or epidural anesthetic may also develop postpartum low-pressure headaches, presumably owing to dural tears from labor-related pushing.

Rare complications of PDPH include subdural hematoma, PRES, and CVT. Low intracranial pressure can cause subdural hematoma from the tearing of bridging veins that become taut as the brain sags. Clues to this complication include loss of the postural component of headache (owing to the offsetting effects of low intracranial pressure from the dural puncture and elevated pressure from the subdural hematoma) and lack of response to a blood patch.

Most serious causes of headache are more common postpartum than during pregnancy. Therefore, if migraine or PDPH is not likely based on the history and neurologic examination, physicians must consider these other etiologies.

ACUTE NEUROLOGIC SYMPTOMS AND DEFICITS

Pregnant or postpartum patients who present with acute motor, sensory, or visual findings (with or without headache) may have more serious causes and require urgent, thorough evaluation (see Fig. 1). Pregnant patients with acute neurologic deficits most often have migraine with aura, even in the absence of headache (ie, acephalgic migraine). Two studies using different methods both found that of pregnant patients referred for transient motor, sensory or visual symptoms, the vast majority could be ultimately attributed to migraine with aura.

Historical clues for a migrainous etiology include gradual onset of the neurologic symptoms and positive phenomenon (such as brightness or shimmering) as opposed to negative ones (blackness or loss of vision). The gradual onset and slow progression over 15 to 30 minutes differentiates migrainous symptoms from those attributable to cerebral ischemia, which are typically maximal at onset, and seizure, which spread more rapidly (ie, over seconds). Another clue that may help to differentiate migraine from vascular thromboembolic disease is the pathophysiologic process of cortical spreading depression that is believed to cause migrainous neurologic deficits often crosses vascular territories. Migrainous positive phenomena (brightness or sparkling in vision, tingling or prickling feelings in the limbs or body) often leave in their wake...
transient loss of function (scotoma or numbness). Symptoms affecting 1 modality (eg, vision) may clear and then involve another modality (eg, sensation).

Because visual symptoms are common with preeclampsia, one must be cautious not to make that diagnosis without considering other possibilities such as PRES, pituitary apoplexy or tumor growth, and strokes affecting the visual pathways. Because pituitary adenomas (micro or macro) may grow during pregnancy, any woman with a known pituitary tumor and new onset of headache with or without diplopia and a bitemporal field cut should undergo emergent pituitary imaging. Another consideration is orbital hemorrhage, which presents as acute diplopia, proptosis, and eye pain, and can occur during the first trimester (from hyperemesis) or during labor (from pushing).

Overall, stroke in pregnant and postpartum women is rare; however, the risk is increased compared with nonpregnant age-matched controls, especially in late pregnancy and the early puerperium. Recent evidence suggests that the rate of pregnancy- and postpartum-associated strokes is increasing. This epidemiologic trend is true for patients with and without pregnancy-related hypertensive disorders. The event rates per 100,000 deliveries range from 4 to 11 (AIS), 3.7 to 9 (ICH), 2.4 to 7 (SAH), and 0.7 to 24 (CVT). These epidemiologic studies varied in their methodology (Table 1). The wide range for CVT likely reflects variability in the case-finding definitions and radiologic modalities. Moreover, the extremely low stroke rate in the most recent study is likely owing to the fact that postpartum patients (the period of highest risk) were not included.

Preeclampsia/eclampsia plays an etiologic role in 25% to 50% of pregnant and postpartum patients with strokes: highest with ICH, lower in AIS, and lowest with CVT. Other stroke risk factors in these women include older age, African American race, congenital and valvular heart disease, hypertension, caesarian delivery, migraine, thrombophilia, systemic lupus erythematosus, sickle cell disease, and thrombocytopenia. In an analysis of 347 cases of fatal pregnancy-related strokes over a 30-year period in the United Kingdom, these patients accounted for 1 in 7 maternal deaths. Themes that emerged from analysis of these 347 fatal cases were failure to recognize and treat hypertension, delays in imaging owing to concerns about radiation exposure, delays in senior physician involvement, and diagnostic anchoring of “hysteria” or drug-seeking behavior.

Thrombocytopenia also suggests the HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) and thrombotic thrombocytopenic purpura (TTP), whose incidence is elevated in pregnancy and which can present with strokelike symptoms. These 2 conditions have very different clinical courses and management, so maternal–fetal medicine and hematology experts should be involved immediately in the evaluation, particularly if TTP is on the differential. One study of 1166 deliveries found 12 cases of HELLP syndrome of which 8 had neurologic complications—namely, seizures (4 patients), focal deficits (2 patients), and encephalopathy (2 patients). On imaging, 6 patients had PRES (3 with associated hemorrhages) and 2 had isolated ICH.

Another unusual cause of stroke in pregnant and postpartum women is cervicocranial arterial dissection. There may be an increasing frequency in pregnant and postpartum women, although comprehensive epidemiologic data are lacking. Patients with cervicocranial arterial dissections often present with isolated headache and/or neck pain without neurologic deficit, but they can also present with focal deficits owing to embolic strokes. There may be a predisposition for multiple vessel dissections. In the largest series of 8 postpartum cases, the only differences between postpartum cases and those occurring in nonpregnant/postpartum women were that...
Table 1
Incidence of stroke in pregnant and postpartum women, per 100,000 deliveries

<table>
<thead>
<tr>
<th>Study, Year Published</th>
<th>AIS</th>
<th>ICH</th>
<th>SAH</th>
<th>CVT</th>
<th>Eclampsia</th>
<th>Comments (Methods, Total Deliveries, Years of Analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaigobin &amp; Silver, 2000</td>
<td>11.1</td>
<td>3.7</td>
<td>4.3</td>
<td>6.9</td>
<td>23% of AIS 38% of CVT 17% of ICH 0% of SAH</td>
<td>Referral single-center Canadian study 50,700 deliveries 1980–1997</td>
</tr>
<tr>
<td>Lanska &amp; Kryscio, 2000b</td>
<td>13a</td>
<td>a</td>
<td>a</td>
<td>12.1</td>
<td>—</td>
<td>Not reported US national inpatient database 1,408,015 deliveries 1993–1994</td>
</tr>
<tr>
<td>Salonen Ros et al, 2001</td>
<td>4.0</td>
<td>3.8</td>
<td>2.4</td>
<td>—</td>
<td>—</td>
<td>Not reported Population-based national Swedish study 1,003,489 deliveries 1987–1995</td>
</tr>
<tr>
<td>James et al, 2005b</td>
<td>9.2</td>
<td>8.6</td>
<td>—</td>
<td>0.7</td>
<td>15.7c</td>
<td>US national inpatient database 8,322,799 deliveries 2000–2001</td>
</tr>
<tr>
<td>Kuklina et al, 2011b</td>
<td>11</td>
<td>7</td>
<td>7</td>
<td>24</td>
<td>—</td>
<td>Not reported US national inpatient database 8,786,475 deliveries 2006–2007</td>
</tr>
<tr>
<td>Scott et al, 2012</td>
<td>0.9d</td>
<td>0.4a</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>United Kingdom national population-based cohort and nested case-control study 1,958,203 deliveries 2007–2010</td>
</tr>
</tbody>
</table>

Note: included prenatal events only; see text

Abbreviations: AIS, acute ischemic stroke; CVT, cerebral venous thrombosis; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.

a The 13 includes AIS, ICH and SAH in this study.
b Intrinsic to the studies using the US national database is a sampling of approximately 20% of patients. Therefore, the reported number of deliveries is an extrapolated number.
c The authors do not directly state which strokes are eclampsia-related but do include an International Classification of Disease, 9th edition (ICD-9) code for “pregnancy-related cerebrovascular events” separate from the ICD-9 codes for AIS, ICH, or CVT.
d Includes CVT.
e Includes SAH.
simultaneous PRES, RCVS, and SAH were more often seen in the postpartum cases, again emphasizing the theme of overlapping clinical syndromes in these patients. The vast majority of these dissections occur postpartum.

Data from a small case series suggests that women with a prior cervical artery dissection without an underlying connective tissue disorder may not be at significantly increased risk for subsequent pregnancy-related dissections. Still, this series included only 11 women with completed pregnancies after the index event, only 1 of 11 had the initial event in the peripartum period, and 7 subsequent pregnancies were delivered by cesarean, suggesting possible confounding by indication, so the data must be interpreted with caution.

In patients with ICH and SAH, underlying structural lesions such as vascular malformations and aneurysms are relatively common. SAH that occurs around the circle of Willis suggests an aneurysm, whereas convexal SAH suggests RCVS or CVT (with or without an associated cortical vein thrombosis). Brain infarction and hemorrhage can result from many of the vasculopathies, including RCVS and preeclampsia. Finally, TTP, pituitary apoplexy, choriocarcinoma, amniotic fluid embolism, air embolism, and cardioembolism from postpartum cardiomyopathy are rare causes of stroke in this population. Sufficient diagnostic testing including vascular imaging must be performed in these patients to identify specific treatable causes.

SEIZURES

Pregnant or postpartum women with seizures can be grouped into 3 categories. The most common are patients with an established seizure disorder before pregnancy. Of note, again demonstrating the frequency of overlapping clinical syndromes, women with epilepsy before pregnancy have an increased likelihood of developing pre-eclampsia, and of progressing to eclampsia. The second group includes patients with a new non–pregnancy-related seizure disorder, such as a new seizure from an undiagnosed brain tumor or hypoglycemia. These pregnant and postpartum patients require the same systematic approach to a new seizure as in all seizure patients, but are not the focus of this review.

The third group has new seizures that are pregnancy related. Important causes include eclampsia, ICH, CVT, RCVS, PRES, and TTP. Seizures are very common in PRES and usually occur at presentation in the absence of prodromal symptoms, whereas in CVT seizures usually occur later and nearly always after headache. Head CT scans can be normal in each of these conditions. Seizures are much less common in RCVS.

Data are lacking to direct the initial workup in these patients. However, because of this wide differential diagnosis and lack of sensitivity of CT scanning, we believe that pregnant and postpartum patients with new-onset seizures, even those who have returned to baseline and are neurologically intact, should undergo sufficient workup, which usually includes MRI, to establish the cause of the seizure. Postpartum women, even those who are breastfeeding, should undergo the same neuroimaging study that would be done in any other patient for the same indication. For antepartum patients whose optimal neuroimaging would normally involve gadolinium, maternal–fetal medicine should be consulted to discuss the risks versus benefits of gadolinium administration in this setting.

INDIVIDUAL CONDITIONS

The clinical presentations of the specific conditions have considerable overlap and can coexist. However, the details (eg, characteristics of headache, evolution of
symptoms over time, and frequency of some symptoms such as seizures or visual problems) can often help to distinguish among them (Table 2).

CEREBRAL VENOUS SINUS THROMBOSIS

A rare cause of stroke overall, CVT is an important consideration in pregnant and postpartum women.71–74 There is a spike in the incidence during the first trimester, probably owing to women with an underlying thrombophilia who become pregnant,66, however, more than 75% of cases occur postpartum.75 Although the greatest risk for postpartum thromboembolism is in the first 6 weeks, the risk probably extends out to 12 weeks.75 Risk factors include caesarian section, dehydration, traumatic delivery, anemia, increased homocysteine levels, and low cerebrospinal fluid pressure owing to dural puncture.42,53 CVT is posited to be more common in developing countries owing to the increased frequency of poor nutrition, infections, and dehydration.77,78 CVT owing to pregnancy or oral contraceptive use tend to have better long-term outcomes than men or women with CVT unrelated to pregnancy.75

Most patients with CVT present with a progressive, diffuse, constant headache, although in 10% it is a thunderclap headache.79,80 However, 10% of patients with CVT may have no headache at all.81 Other findings include dizziness, nausea, seizures, papilledema, lateralizing signs, lethargy, and coma. The specific presentation depends on the extent and location of the involved dural sinuses and draining veins, collateral circulation, effects on intracranial pressure, and presence of associated hemorrhage.82 Symptoms vary and may fluctuate over time.42,71,78 Neurologic deficits do not follow arterial distributions.

Although D-dimer is usually increased in patients with CVT, most do not recommend its use in pregnant and postpartum women.83,84 These patients are often D-dimer positive, especially late in pregnancy and in the early puerperium.85 Pending further studies, we do not recommend using a negative D-dimer in pregnant or postpartum women to exclude CVT. Noncontrast CT scans are often negative, but may show a hyperdense venous clot or signs of infarction in 30% of cases84 (Fig. 2). Ischemic infarcts often undergo hemorrhagic transformation owing to venous hypertension. CT venography often shows the clot, but MRI with MR venogram, gradient recalled echo, and contrast-enhanced magnetization-prepared rapid gradient echo sequences is typically diagnostic and considered the imaging study of choice.84

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

RCVS is characterized by abrupt onset of usually multiple thunderclap headaches and multifocal, reversible cerebral vasoconstriction, typically occurring during the first week after delivery.86 Recurring daily thunderclap headaches over several weeks that follow a single thunderclap headache may be pathognomonic.86–88 When related to pregnancy, two-thirds of patients with RCVS develop symptoms within 1 week of delivery and after a normal pregnancy.18 RVCS is also associated with use of immunosuppressive drugs, vasoactive medications (eg, serotonin reuptake inhibitors and phenylpropanolamine), recreational drugs (eg, cocaine and marijuana), blood products, catecholamine-secreting tumors, cranio cervical arterial dissections, and various other miscellaneous conditions.18 In a review of a large series of RCVS and arterial dissections designed to identify patients with both conditions simultaneously, the postpartum state emerged as an association of this overlap.59 Vomiting, confusion, photophobia, and blurred vision often accompany the headaches. When seizures or focal neurologic deficits develop, they nearly always follow the headache.
<table>
<thead>
<tr>
<th></th>
<th>PRES</th>
<th>RCVS</th>
<th>CVT</th>
<th>Eclampsia</th>
</tr>
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<tbody>
<tr>
<td><strong>Mode of onset</strong></td>
<td>Rapid (over hours), usually postpartum</td>
<td>Abrupt, usually postpartum</td>
<td>Third trimester or postpartum,</td>
<td>Antepartum, intrapartum or postpartum (10%-50%)</td>
</tr>
<tr>
<td><strong>Prominent findings</strong></td>
<td>Early prominent seizures</td>
<td>Thunderclap HA, multiple episodes</td>
<td>HA nearly universal at onset,</td>
<td>Seizure, frequent visual symptoms and abdominal pain, hypertension, proteinuria</td>
</tr>
<tr>
<td></td>
<td>Usually seizures plus at least other symptoms (stupor, visual loss, visual hallucinations)</td>
<td>Seizures occur but much less so than in PRES</td>
<td>generally progressive and diffuse, thunderclap in small minority</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HA dull and throbbing, not thunderclap</td>
<td>Transient focal deficits (may become permanent in cases with ICH or infarction)</td>
<td>Seizures occur in ~40%</td>
<td></td>
</tr>
<tr>
<td><strong>Evolution over time</strong></td>
<td>Symptoms resolve over days to a week if blood pressure controlled</td>
<td>Dynamic process over time; as a general rule, HAs are common during first week, ICH during the second week and ischemic complications during the third week</td>
<td>Evolves over several days; nonarterial territorial infarcts and hemorrhages may develop</td>
<td>Can evolve (from preeclampsia) gradually or abruptly</td>
</tr>
<tr>
<td><strong>CSF findings</strong></td>
<td>Usually normal, may have slightly elevated protein</td>
<td>Often normal (unless complicated by SAH) but 50% will have slight pleocytosis and protein elevations</td>
<td>Opening pressure elevated ~80% of cases</td>
<td>Usually normal unless complicated by hemorrhage</td>
</tr>
<tr>
<td><strong>Imaging aspects</strong></td>
<td>CT positive in ~50% of cases MR prominent T2-weighted and FLAIR abnormalities nearly always in the parietooccipital lobes but can involve other parts of the brain ICH in ~15% of patients</td>
<td>CT usually normal (if no SAH) MR – 20% with localized convexal SAH CTA, MRA usually shows typical “string of beads” constriction of cerebral arteries DSA is more sensitive May have associated cervical arterial dissection Initial arteriogram may be negative</td>
<td>CT often negative MR may show nonarterial territorial infarcts Hemorrhage common MRV shows intraluminal clot flow voids Although MRV is preferred, CTV is also sensitive</td>
<td>Same as for PRES Some patients may have coincident AIS or ICH</td>
</tr>
</tbody>
</table>

**Abbreviations:** CSF, cerebrospinal fluid; CT, computed tomography; CTA, CT angiogram; CTV, CT venogram; CVT, cerebral venous thrombosis; DSA, digital subtraction angiogram; FLAIR, fluid-attenuated inversion recovery; HA, headache; ICH, intracerebral hemorrhage; MRA, MR angiogram; MRI, magnetic resonance imaging; MRV, MR venogram; PRES, posterior reversible encephalopathy syndrome; RCVS, reversible cerebral vasoconstriction syndrome.
Symptoms usually subside over several weeks. Although most patients have good outcomes, there is considerable variability in disease progression and fatal outcomes have been reported in postpartum patients with RCVS. The reversibility refers to the angiographic vasospasm, not to the clinical outcomes. Complications include nonaneurysmal convexal SAH, ICH, and AIS. Convexal SAH is more common than parenchymal ICH. Hemorrhagic complications usually precede ischemic ones. In patients without infarction, the disease resolves over time. Up to 10% of patients with RCVS may also have cervicocranial arterial dissections. Unless there is a complicating hemorrhage, the cerebrospinal fluid is usually normal, but may show small numbers of lymphocytes and mildly elevated protein.

Absent a hemorrhage, the CT scan is usually normal. With regard to vascular testing, it is important to recognize that RCVS is a dynamic process. Transcranial Doppler ultrasonography and various forms of angiography are useful tools; however, they may be normal early in the course of the disease. Angiography and transcranial Doppler ultrasonography may be discordant. By definition, focal areas of arterial constriction on catheter angiography are always present. However, it is important to recognize 2 limitations of noninvasive angiography (MR angiogram or CTA): (1) these modalities are only positive in approximately 80% of patients, showing the diagnostic pattern of alternating dilatation and constriction, simulating a “string of beads” (see Fig. 2) and (2) CTA and MR angiogram may be normal in the first 5 to 6 days of RCVS. Transcranial Doppler ultrasonography can be used to follow resolution of the vasoconstriction.

**POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME**

PRES is a syndrome characterized by headache, seizures, encephalopathy, and visual disturbances in the setting of reversible vasogenic edema on CT scan or MRI. PRES occurs in patients with acute hypertension, preeclampsia or eclampsia, renal disease, sepsis, exposure to immunosuppressant drugs, and numerous other conditions and drug exposures. In a single-center series, 46 of 47 patients with eclampsia (98%) had PRES, suggesting that in the setting of eclampsia, PRES is an integral part of the pathophysiology. Early diagnosis and management may improve outcomes.

Symptoms develop without prodrome and progress rapidly over 12 to 48 hours. Seizures, which occur in approximately 75% to 90% of patients, may be focal initially, then become generalized tonic-clonic. Severe symptoms can occur even in the absence of severe hypertension. Headache occurs in roughly 50% of patients. The headache is generally dull, bilateral, and not thunderclap in nature. Some degree of encephalopathy, ranging from mild confusion to stupor and coma, is present in 50% to 80% of patients.

Because the vasogenic edema typically involves the occipital lobes, approximately 40% of patients have visual symptoms, including visual hallucinations, blurred vision, scotomata, and diplopia. Transient cortical blindness occurs in 1% to 15% of patients. The retina and pupils are normal. Consider electroencephalographic monitoring to detect electrical seizure activity in encephalopathic patients without overt seizure activity (ie, nonconvulsive status epilepticus). CT scans will show edema in about 50% to 60% of patients. However, MRI should be performed when PRES is suspected because of its increased sensitivity for detecting vasogenic edema, microhemorrhages, and other PRES-related intracranial pathology.
Fig. 2. Selected patient images. (A) Noncontrast CT scan of a 21-year-old woman who presented with 7 days of increasing left-sided headache. A subtle increased density (black arrows) that is consistent with clot in the left transverse sinus can be seen. (B) The MR
MRI reveals focal edema, nearly always in the parietooccipital lobes (see Fig. 2). Although the mechanism of this posterior predominance has not been fully elucidated, it is hypothesized that the posterior cerebrovascular circulation has less autoregulatory capacity than does the anterior circulation in the setting of increased cerebral perfusion pressure. Nevertheless, regions of the brain supplied by the anterior cerebrovascular circulation are often involved concomitantly. The visual symptoms often resolve completely in hours to days; resolution of the edema on imaging lags behind. In eclamptic patients, PRES is not the only potential explanation for seizures. Although most pregnant or postpartum women with PRES have eclampsia, other contributing factors (such as medication use or RCVS) are also possible.

Studies comparing clinical and radiological features of PRES in nonpregnant versus pregnant patients have reported mixed results. One small study (21 patients) found no differences. In a larger study (96 patients), eclamptic or preeclamptic patients with PRES more commonly presented with headache, and were less likely to be confused and more likely to have visual symptoms. A third study (38 patients) also found less alteration in mental status in pregnant versus nonpregnant patients with PRES, as well as overall lower systolic blood pressures. On imaging, pregnant patients had less edema, fewer hemorrhages, and more complete resolution. In another study of 70 patients with “severe” PRES admitted to an intensive care unit, pregnancy or postpartum states (23% of the patients) were associated with better 90-day outcomes than other patients with PRES. Given the small numerators (pregnant and postpartum patients) and denominators (total PRES patients) of these studies, it is difficult to draw firm conclusions about the impact of pregnancy on presentation or prognosis.

NEUROLOGIC COMPLICATIONS OF ECLAMPSIA

Seizures are the hallmark of eclampsia. Eclamptic seizures are usually tonic–clonic and last approximately 1 minute. 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 one-third of cases, there is no proteinuria or blood pressure is less than 140/90 mm Hg before the seizure.

Although the exact mechanism of eclamptic seizures is unknown, several hypotheses have been proposed. Overactivity of cerebrovascular autoregulation in response to hypertension can lead to cerebral arterial vasospasm and ischemia, resulting in cytotoxic edema. Alternatively, loss of autoregulation in response to hypertension leads to endothelial dysfunction, capillary leak, and vasogenic edema. This vasculopathy can also result in PRES or regions of infarction and hemorrhage.

venogram from the same patient shows a clot in the left transverse sinus (short wide arrow) and in the sigmoid sinus (long thin arrow). (C) Selected images from a digital subtraction angiogram 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 “string of beads” appearance (black arrows show the focal areas of vasoconstriction). Similar findings are seen in most patients with noninvasive (computed tomography or MR) angiography. (D) Two images from the T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence on an MRI show increased signal in the bilateral parietooccipital regions (white arrows), slightly more on the right, in a 29-year-old patient with posterior reversible encephalopathy syndrome. Diffusion-weighted imaging on this same patient was normal. Note that the bilateral FLAIR hyperintensities, indicating vasogenic edema, spare the medial occipital lobe and calcarine cortex, which distinguishes this finding from posterior cerebral artery ischemic lesions.
Although focal vasogenic edema is characteristic of eclampsia, up to one-quarter of patients have areas of persistent cytotoxic edema consistent with infarction or focal hemorrhage.\textsuperscript{116} In 1 study, one-third of patients with “eclamptic encephalopathy” had cytotoxic edema.\textsuperscript{118} Thus, components of PRES, areas of ischemia or hemorrhage, and even RCVS may also contribute to eclamptic seizures.

Approximately 90% of eclampsia occurs at or after 28 weeks of gestation.\textsuperscript{13} Just more than one-third of eclamptic seizures occur at term, developing intrapartum or within 48 hours of delivery.\textsuperscript{13} Although a large population-based study in California suggests that the incidence of eclampsia in the United States is decreasing,\textsuperscript{119} recent data suggest an increase in “late” postpartum eclampsia (>48 hours after delivery).\textsuperscript{13} In 1 large study of postpartum diagnoses of preeclampsia/eclampsia, two-thirds of patients had been discharged and were readmitted because of late postpartum preeclamptic symptoms, most commonly headache.\textsuperscript{120} Of these 151 patients with delayed postpartum preeclampsia, approximately 16% of those readmissions were complicated by eclampsia. The proportion of preeclampsia/eclampsia diagnosed postpartum ranges from 11% to 55% and may be increasing owing to improved antepartum recognition.\textsuperscript{121–124} Postpartum patients sometimes ignore early symptoms, such as headache or abdominal pain, and only seek medical care later, after a seizure.\textsuperscript{121,125}

Patients with postpartum eclampsia, especially those with late postpartum eclampsia, have a higher incidence of CVT, ICH, and AIS.\textsuperscript{13,126} If an experienced clinician thinks that a woman has typical eclampsia, brain imaging is not necessarily indicated.\textsuperscript{13} However, in postpartum eclamptic patients, those with focal neurologic deficits, persistent visual disturbances, and symptoms refractory to magnesium and antihypertensive therapy or in patients for whom there is any diagnostic uncertainty, a thorough diagnostic workup, preferably including MRI, is recommended. Imaging may also reveal areas of vasoconstriction consistent with RCVS. Rarely, pregnant patients, especially those with RCVS, develop craniocervical arterial dissections.\textsuperscript{61–63,127} Thus, the spectrum of neurologic imaging findings in preeclamptic/eclamptic patients includes infarction, hemorrhage, vasoconstriction, dissection, and both vasogenic and cytotoxic edema.

### RARE CONDITIONS CAUSING ACUTE NEUROLOGIC SYMPTOMS IN PREGNANT AND POSTPARTUM WOMEN

Amniotic fluid embolism and metastatic choriocarcinoma are 2 rare pregnancy-specific conditions that can present with acute neurologic symptoms. In a single-center series, only 10 cases of amniotic fluid embolism were found over 30 years.\textsuperscript{128} One-half of these cases presented with postpartum hemorrhage and one-half presented with cardiovascular collapse.\textsuperscript{126} The latter presentation is associated with agitation, confusion, seizures, and encephalopathy with cardiopulmonary collapse occurring during or immediately after labor.\textsuperscript{129,130} Choriocarcinoma, a rare malignancy of trophoblastic tissue, metastasizes to the brain in 20% of patients.\textsuperscript{131,132} Because the tumor can cause hemorrhage, mass effect, and invasion of cerebral vessels, its clinical and imaging manifestations are variable.\textsuperscript{132,133}

Air embolism occurs when air that enters the myometrium during delivery is absorbed into the venous circulation and right ventricle, reducing cardiac output. Nearly any focal or generalized neurologic symptom can occur owing right-to-left intracardiac shunting of air via a patent foramen ovale.\textsuperscript{134} Alternatively, air may enter the left-sided arterial circulation via transpulmonary shunting of blood. Air emboli may then occlude the cerebral microvasculature, resulting in cerebral ischemia and/or
seizures during or just after delivery. The presence of air in the retinal veins and a “mill wheel” cardiac murmur suggest the diagnosis.

Another important consideration is Wernicke’s encephalopathy, which, although classically associated with alcohol use and malnutrition, can also complicate hyperemesis gravidarum. Among 625 nonalcoholic patients with Wernicke’s encephalopathy, 76 (12%) were in women with hyperemesis. Abnormal eye movements are nearly always present; however, the classic triad of confusion, ocular findings (diplopia and nystagmus), and gait abnormalities occurs in a minority of patients. Some patients have an otherwise unexplained metabolic acidosis. Neither biochemical confirmation nor MRI is necessary, the simplest test being the response to intravenous thiamine. It is essential to administer intravenous thiamine before administration of glucose-containing intravenous fluids in pregnant women with severe hyperemesis to avoid provoking neurologic injury in the setting of thiamine deficiency.

Pregnant women are at particular risk for TTP, which most commonly presents late in the second or early third trimesters. The classic pentad includes thrombocytopenia, microangiopathic hemolytic anemia, fever, and neurologic and renal dysfunction. Neurologic manifestations, occurring in more than one-half of patients, include fluctuating headache, seizures, and generalized and focal neurologic deficits. Coexistent PRES is common. Because the treatments are so different, distinction between TTP (plasma exchange) and HELLP (magnesium and delivery of the fetus) is important. Given that there is no single distinguishing feature, hematologic and maternal–fetal medicine consultation is strongly recommended.

Pituitary apoplexy, acute infarction, or hemorrhage of the gland, usually in the setting of a (previously undiagnosed) adenoma, presents with headache, visual loss, varying degrees of ophthalmoplegia, and decreased level of consciousness. Although the pituitary gland enlarges during pregnancy, pregnancy is a rare precipitant for pituitary apoplexy. Pituitary apoplexy must be distinguished from Sheehan syndrome (hypopituitarism presenting indolently, weeks to months after severe postpartum hemorrhage) and lymphocytic hypophysitis (presents in pregnant patients with headache and visual symptoms but typically with a slower onset).

NEUROIMAGING AND MULTIDISCIPLINARY COORDINATION OF CARE

Most of these patients require brain imaging to make a specific diagnosis. Several basic principles should be kept in mind. First, the emergency physician should discuss the differential diagnosis with the other consultants (including the radiologist) before imaging. The goals of imaging are to minimize ionizing radiation and intravenous contrast exposure, and ensure that, when MRI is being performed, the correct sequences are obtained the first time to optimize the diagnostic yield. Second, the fetal radiation exposure from a noncontrast brain CT scan is negligible. Although CT scanning is safe to perform in this population, clinicians must realize its diagnostic limitations for many of the target conditions. Third, because many of these conditions that cause acute neurologic symptoms and signs in pregnant and postpartum patients require 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 are lacking. Until recently, there were no reported teratogenic or other adverse fetal effects of iodinated contrast. In September 2015, a report was published describing thyroid dysfunction in 5 of 212 Japanese neonates born to women who underwent hysterosalpingogram with ethiodized oil (an iodinated contrast medium) before becoming pregnant. Given that this...
is a single report in the medical literature, as well as the lack of clarity as to how pre-
pregnancy hysterosalpingogram exposure to ethiodized oil relates to pregnant women
receiving intravenous iodinated contrast, this report must be interpreted very
cautiously. Because repeated supraclinical doses of gadolinium have been associated
with fetal demise and malformations in animal studies, gadolinium is best avoided un-
less the physician believes that the information to be gained by its use exceeds its po-
tential risk.145,152

Authorities recommend obtaining informed consent before these procedures and
use of intravenous contrast agents.145,146,152 However, in an emergent situation,
necessary imaging should not be delayed if the patient is unable to give consent
and a surrogate decision maker is not readily available. Last, because only minute
amounts of both iodinated contrast and gadolinium are secreted in breast milk and
because similarly minutes quantities are absorbed across an infant’s gut, both types
of contrast are considered to be safe in postpartum with respect to breast
feeding.145,152

No data address the effects on outcomes of location of care of pregnant and post-
partum patients with acute neurologic emergencies. Our opinion is that because these
situations are uncommon and inherently multidisciplinary, these patients are ideally
cared for in hospitals that have neurologic, neurosurgical, advanced radiological, ob-
stetric, and critical care expertise. Even in such centers, close coordination of care
across various disciplines is key.

SUMMARY

Pregnant and postpartum patients who present with acute neurologic symptoms
require a thorough diagnostic evaluation that targets a broad range of pathologic
conditions that are either unique to or occur more frequently in this population.
Once an accurate diagnosis is made, specific therapy can follow. Because of the
multidisciplinary nature and relative infrequency of most of these conditions, we
recommend that emergency physicians work closely with various consultants to co-
ordinate care in these patients. Early transfer of these patients to a center capable
of delivering the full range of diagnostic testing and potential care should be
considered.

REFERENCES

4. Hammer ES, Cipolla MJ. Cerebrovascular dysfunction in preeclamptic pregnan-


