Imaging of Neurologic Disorders Associated with Pregnancy and the Postpartum Period

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Diverse pathologic conditions affect the central nervous system (CNS) and pituitary gland during pregnancy and the puerperium. Some are specific to the physiologic process of reproduction (e.g., eclampsia, postpartum cerebral angiopathy, Sheehan syndrome, lymphocytic adenohypophysitis). Others are nonspecific but occur more often in pregnant women (e.g., cerebral infarction, dural venous thrombosis, pituitary apoplexy). Recognition of the characteristic imaging findings in eclampsia, for example, may allow exclusion of other disorders. Even when imaging changes are nonspecific, knowledge of those entities associated with pregnancy and awareness of the increased likelihood of certain diseases in pregnancy will allow a more informed differential diagnosis. Differentiation of primary nonaneurysmal subarachnoid hemorrhage (SAH) from aneurysmal SAH is an example. Moreover, earlier use of imaging will result in fewer delayed diagnoses. For example, magnetic resonance venography allows early diagnosis of cerebral venous thrombosis. Even when the imaging changes are less specific, knowledge of likely possibilities will lead to more appropriate earlier use of imaging. For example, the stimulatory effects of pregnancy on prolactinoma, meningioma, hemangioblastoma, vestibular schwannoma, and metastatic tumors such as breast cancer and choriocarcinoma suggest the early use of CNS imaging to avoid the consequences of a delayed diagnosis.

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Abbreviations: CNS = central nervous system, CVT = cerebral venous thrombosis, FLAIR = fluid-attenuated inversion recovery, PCA = postpartum cerebral angiopathy, SAH = subarachnoid hemorrhage

RadioGraphics 2007; 27:95–108 • Published online 10.1148/rg.271065046 • Content Codes: NR OR

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Introduction

Pregnant women experience significant improvement of migraine headache during pregnancy. However, headache remains the commonest symptom encountered due to intracranial disease during the course of pregnancy and the puerperium. Thus, the development of acute headache should be taken seriously (1). There is considerable overlap of the clinical features of different disease entities affecting the central nervous system (CNS). There is a general tendency for delayed diagnosis of uncommon but serious conditions during pregnancy because of a reluctance to perform imaging studies.

This article surveys the neurologic disorders that occur during the course of pregnancy and the postpartum period. Cerebrovascular complications are classified into ischemic infarctions, subarachnoid hemorrhage, eclamptic encephalopathy, postpartum cerebral angiopathy, and cerebral venous thrombosis. The neuroendocrine disorders of the pituitary gland are classified into pituitary apoplexy, Sheehan syndrome, and lymphocytic adenohypophysitis. Neoplastic disorders include pituitary adenomas, primary CNS tumors, and intracranial metastatic disease.

Cerebrovascular Complications

Cerebrovascular disorders can be classified into ischemic stroke, subarachnoid hemorrhage, eclamptic encephalopathy, postpartum cerebral angiopathy, and cerebral venous thrombosis.

Ischemic Stroke

Pregnancy and the puerperium are considered hypercoagulable states. Factors leading to hypercoagulability of blood include low levels of inhibitors of the coagulant protein S; elevated levels of inhibitors of protein C; increased levels of fibrinogen, factor VII, factor VIII, and factor X; and an enhanced ability to neutralize heparin (2).

The risk of ischemic stroke increases with age, particularly after age 35 years. Black women are at a higher risk. Other risk factors include lupus, blood transfusion, and migraine headaches (3).

The risk of both ischemic infarction, which accounts for 60% of all strokes, and intracranial hemorrhage is high in the peripartum period and puerperium, but not during the 9-month course of pregnancy itself (4).

Thrombotic infarcts result from hypercoagulable states and thrombosis on top of existing atherosclerotic plaques (Fig 1). Embolic infarcts can result from dissections due to prolonged difficult labor, cardiac valvular disease, and the rare dilated peripartum cardiomyopathy (5). In those conditions, infarctions typically occur in the major arterial distributions. Watershed infarcts can result from dissections and significant obstetric hemorrhage (Fig 2).

Subarachnoid Hemorrhage

Subarachnoid hemorrhage (SAH) is a rare occurrence during pregnancy. Even during pregnancy and the puerperium, rupture of an intracranial aneurysm still remains the commonest cause of SAH. Pregnancy may increase the risk of aneurysm rupture due to the hemodynamic and hormonal alterations (6). The reported prevalence of SAH during pregnancy is 1 in every 10,000 patients. This translates to a prevalence five times higher than in nonpregnant women (7). SAH due to aneurysmal rupture commonly occurs in young primigravidas during the third trimester (8). Ruptured aneurysms should be treated just as they would be in patients who are not pregnant. Unruptured aneurysms should be treated only if they are symptomatic or enlarging (6). Successful endovascular coil treatment of aneurysms during pregnancy has been reported (9).

Primary nonaneurysmal SAH due to pregnancy-induced hypertension is an extremely rare event. Autopsy studies have shown leptomeningeal petechial hemorrhages in women who died of eclampsia. On rare occasions, pregnancy-induced hypertension has been linked to significant SAH that was detectable at CT (10). Shah (10) reported three patients with primary nonaneurysmal SAH associated with pregnancy-induced hypertension. All three women presented with acute sharp headache and focal seizures within 2 days after delivery. All three women were black and had no history of sickle cell disease. CT typically
Figure 1. Reversible ischemia in an 18-year-old woman with sickle cell trait who developed weakness 4 days after cesarean section. (a) Axial fluid-attenuated inversion-recovery (FLAIR) magnetic resonance (MR) image shows bilateral gyral thickening (arrows) in the frontal and parietal lobes, which is presumably due to cytotoxic edema. (b) Axial gadolinium-enhanced T1-weighted MR image shows cortical enhancement (arrows), a finding characteristic of reversible or incomplete ischemia. Computed tomography (CT) performed 6 weeks later showed mild encephalomalacia.

Figure 2. Complete (irreversible) cerebral infarctions in a 24-year-old woman who developed cortical blindness after difficult labor. (a) Axial diffusion-weighted MR image shows restricted diffusion in both occipital lobes, primarily in the arterial watershed zones. (b) Axial FLAIR MR image shows corresponding edema and mass effect. MR imaging performed 7 weeks later showed corresponding laminar necrosis and cortical atrophy.
shows a limited amount of unilateral SAH over the frontal or parietal convexities (Fig 3). Unlike patients with aneurysmal rupture, none of these patients showed hemorrhage within the basal cisterns or ventricles (10). All three women underwent cerebral angiography within 2 days of CT, and no aneurysms were found. Shah (10) hypothesized that SAH is possibly related to sudden hypertension and failure of cerebral autoregulation with propagation of the high arterial pressure waves to the relatively thin-walled pial veins, resulting in their rupture (10).

**Eclamptic Encephalopathy**

Eclampsia is a serious complication that occurs in 5% of pregnancies and accounts for 10% of the deaths related to pregnancy. Eclampsia is defined clinically as seizure or coma associated with pregnancy-induced hypertension. Patients typically present with headache, altered mental status, cortical blindness, and seizures (11).

Eclampsia as well as several other pathologic entities may result in the posterior reversible encephalopathy syndrome. The exact mechanism remains unknown. However, it is likely to be multifactorial and involves cytotoxic effects on the vascular endothelium leading to increased permeability and vasogenic edema (12). In addition, acute fluctuations of blood pressure can result in variable degrees of vasospasm and vasodilatation. This impairment of the cerebral autoregulation eventually leads to disruption of the blood-brain barrier in the posterior circulation. The predilection for the posterior circulation and watershed zones is believed to be related to its sparse vasomotor sympathetic innervation (13,14).

The imaging findings in patients with eclampsia are identical to those of hypertensive encephalopathy (15,16). CT demonstrates transitory posterior areas of patchy low attenuation. MR imaging is superior to CT in imaging patients with eclamptic encephalopathy. Lesions are characterized by low signal intensity on T1-weighted images and high signal intensity on T2-weighted images in the posterior cortex and subcortical white matter (Fig 4). Lesions typically show no diffusion restriction.
is particularly useful in distinguishing the reversible vasogenic edema from the cytotoxic edema of complete infarction (17). There is also occasional involvement of the basal ganglia and brainstem (18) (Fig 5). Catheter angiography typically shows vasospasm in the medium and large cerebral arteries, particularly of the basilar artery (19).

Treatment of eclampsia is supportive, with priorities set out for controlling seizures and hypertension, as well as maintaining a stable hemodynamic state. Magnesium sulfate is the drug of choice to prevent recurrent convulsions in eclampsia (20).

**Postpartum Cerebral Angiopathy**

Postpartum cerebral angiopathy (PCA) is a unique and poorly understood cerebrovascular disease that occurs in normotensive postpartum women within 1–4 weeks of delivery. Unfortunately, the term has been used loosely in the literature to describe any form of cerebral angiopathy in the puerperium including the hypertension-induced angiopathy of eclampsia. There are two recognizable forms of PCA described in the literature. Idiopathic PCA is a reversible nonrelapsing angiopathy that occurs in normotensive postpartum women who present with severe headache, seizures, and focal neurologic deficits due to intracerebral hemorrhage (21–24). In some patients, PCA may be discovered early, before the development of intracerebral hemorrhage. Idiopathic PCA is also known as Call-Fleming postpartum angiopathy (24). Iatrogenic PCA occurs anytime during the puerperium after administration of bromocriptine to suppress lactation (25), administration of ergot alkaloids to control postpartum hemorrhage (26), or use of sympathomimetics in cold medicines and nasal decongestants (27).

The diagnosis of PCA should be considered in normotensive postpartum women presenting with intracerebral hemorrhage. At imaging, there is intracerebral hemorrhage with local mass effect.
Patients with PCA may also develop reversible high T2 signal abnormalities anywhere in the brain cortex or white matter (24,28). The angiographic features are characterized by reversible multifocal stenoses and a beaded appearance of the medium- and small-caliber cerebral arteries in the anterior circulation (21–23) (Fig 6c, 6d). This is in contradistinction to eclampsia, which affects large and medium-sized arteries in the posterior circulation. Transcranial Doppler ultrasonography (US) depicts vasoconstriction by recording high velocities. Transcranial Doppler US is particularly useful in monitoring the effect of treatment and confirming reversibility of the vasoconstriction (29,30).

**Figure 6.** PCA in a 38-year-old woman who experienced a severe headache and a seizure 2 weeks after childbirth. (a) Axial unenhanced CT scan obtained at admission shows a cerebral hematoma in the left frontal lobe. (b) Axial T2-weighted MR image obtained after 2 days of evacuation shows a new hematoma in the right frontal lobe and residual hemorrhage in the left frontal lobe. (c, d) Right carotid angiogram (c) and magnified view with region-of-interest circles (d) show multifocal stenoses and a beaded appearance of the peripheral branches of the anterior and middle cerebral arteries. The findings are characteristic of the angiitis of PCA, which affects the small- and medium-caliber arteries beyond the proximal segments of the major cerebral arteries.
Treatment of PCA is controversial. Patients may improve after symptomatic treatment (24). Steroids are commonly used (21,28), and hyperosmolar hypervolemic infusions have been suggested (31). Intracranial balloon angioplasty is rarely needed (23).

Cerebral Venous Thrombosis
Cerebral venous thrombosis (CVT) accounts for 6% of maternal deaths (32). CVT may occur anytime during the course of pregnancy and the puerperium, but the risk seems to be highest during the first 2 weeks of the puerperium (33,34). There is increased risk of CVT in young mothers and after cesarean section (35,36). CVT is not as severe or rare as previously assumed. The clinical presentation varies from headache to coma, depending largely on the severity and extent of thrombosis as well as the mode of onset (37). A patient with CVT may present with focal neurologic deficits depending on the sinus or major cerebral vein involved. The superior sagittal sinus is most commonly involved in nonseptic CVT, whereas cavernous and lateral sinus thromboses are more often the result of sepsis (38).

At CT, there is hyperattenuation of the thrombosed sinuses with or without venous infarction (Fig 7a). Contrast-enhanced CT may show the typical filling defect commonly referred to as the

Figure 7. Thrombosis of the superior sagittal sinus and venous infarction in a 25-year-old woman who was 34 weeks pregnant and developed headaches and blurring of vision. (a) Axial CT scan shows high attenuation in the superior sagittal sinus (curved arrows) and focal hemorrhage in the left parietal lobe at the gray-white matter interface (straight arrow). (b–d) Sagittal T1-weighted (b), axial T2-weighted (c), and axial FLAIR (d) MR images show high signal intensity in the superior sagittal sinus (arrow). (e) Axial gadolinium-enhanced T1-weighted MR image shows a filling defect (empty delta sign) (arrow) in the superior sagittal sinus. (f) On a three-dimensional time-of-flight MR venogram, the superior sagittal sinus is not visualized because of extensive thrombosis.
empty delta sign. However, it may take 7–10 days for the empty delta sign to show on CT scans after the onset of symptoms (39). MR imaging is more sensitive than CT in early detection of thrombosis and more accurate in depicting the extent and complications of CVT. Simultaneous high signal intensity of the venous sinuses with all routine sequences (T1-weighted, T2-weighted, and FLAIR) is a reliable sign of CVT (Fig 7b–7d) (39). High signal intensity on T1-weighted images with a corresponding filling defect after gadolinium enhancement may develop within the first week after clinical onset (Fig 7c). Lack of physiologic enhancement of the venous sinus is an early sign and is typically seen within the first week of CVT on both CT and MR images (39). MR venography can add to the diagnostic value of routine MR imaging and better demonstrates the layout of the major cerebral veins and dural venous sinuses (Fig 7f). Other parenchymal signs of CVT include diffuse mass effect, localized sulcal effacement, and venous infarcts. Venous infarcts typically do not conform to the arterial territories and are often associated with hemorrhage at the gray-white matter interface (39–42). Catheter angiography is not needed to confirm the diagnosis of CVT. However, it may be useful in delivering local thrombolytic agents and in thrombus retrieval. Although anticoagulation is the first line of treatment (43,44), some references advocate early thrombolysis and have reported good outcomes even in the presence of hemorrhagic infarctions (45,46).

Pituitary Disorders

The rising levels of estrogen during pregnancy cause hypertrophy of prolactin-producing lactotrophs, which result in progressive enlargement of the adenohypophysis. This is paralleled by the rising levels of prolactin in the circulation. Prolactin levels may reach 35 ng/mL during the first trimester, 175 ng/mL during the second trimester, and up to 210 ng/mL during the third trimester (47). The pituitary gland achieves its maximum size during the first 3 days of the puerperium in preparation for lactation. There is an increased chance of pituitary hemorrhage, infarction, and accelerated prolactinoma growth during the course of pregnancy and the puerperium (48,49).

Pituitary Apoplexy

Pituitary apoplexy is defined as acute hemorrhagic infarction in an existing pituitary adenoma or otherwise physiologically enlarging pituitary gland. Clinically, the patient may present with severe headache, vomiting, and visual disturbances including visual field defects and restricted eye movements (50). Occasionally, there is a small amount of SAH that may irritate the adjacent meninges. Patients may also develop dizziness or altered mental status, thought to be the result of hemodynamic instability presumably due to acute hypopituitarism (51). Pituitary apoplexy is a rare occurrence during pregnancy and may be thought of as a presentation of pituitary microadenoma (52,53). CT and MR imaging show hemorrhage in a prominent pituitary gland (Fig 8). However, not all patients with apoplexy show intrasellar hemorrhage (Fig 9).

Treatment of pituitary apoplexy is supportive with hormonal replacement if needed. Transsphenoidal surgery although safe is rarely needed (52).

Sheehan Syndrome

Sheehan syndrome is a clinical state of panhypopituitarism due to pituitary infarction that occurs after an obstetrically related hypotensive episode around the time of delivery. Pituitary infarction in the setting of an obstetric hemorrhage should be suspected if hypotension and tachycardia persist after adequate initial treatment of the inciting event. Additional early signs of hypopituitarism may include hypoglycemia and failure of lactation (54,55). Owing to a deficiency of pituitary hormones, patients may subsequently present with a
myriad of clinical signs and symptoms, including chronic fatigue, dizziness, postural hypotension, cold intolerance, hypopigmentation, myxedema, loss of pubic and axillary hair, decreased libido, breast atrophy, and amenorrhea (56). At imaging, there is usually the appearance of a partial or complete empty sella (Fig 10) (54–56).

**Lymphocytic Adenohypophysitis**

Lymphocytic adenohypophysitis is a rare inflammatory disorder of the anterior lobe of the pituitary gland that may affect young women in the peripartum. The disorder has been reported only rarely in males, with a female-to-male ratio of approximately 10:1 (57). This disorder is considered an inflammatory autoimmune disease and has been associated with other autoimmune diseases such as autoimmune thyroiditis and pernicious anemia.

Lymphocytic adenohypophysitis results most often in early failure of adrenocorticotropic hormone and thyroid-stimulating hormone, whereas nonfunctioning adenoma causes early failure of growth hormone and gonadotropins (57). Postpartum hypoprolactinemia (level < 150 ng/mL) is seen in the majority of patients with lymphocytic adenohypophysitis. This is attributed to pituitary parenchymal damage caused by the severe inflammatory reaction (47,49). Hyperprolactinemia is seen in less than one-third of patients. This may be attributed to compression of the pituitary infundibulum, thus preventing the transport of prolactin-inhibiting factor to the adenohypophysis, or may be related to the presence of prolactin-stimulating antibodies (57).

At imaging, there is enlargement of the pituitary gland with suprasellar extension in 60%–80% of patients. In lymphocytic adenohypophysitis, the pituitary gland may have variable appearances on MR images. In the majority of patients, there is early and homogeneous enhancement of

![Figure 9. Pituitary apoplexy in a 44-year-old woman who developed headaches 3 weeks after childbirth. Her prolactin level was 19.9 ng/mL. (a) Coronal T1-weighted MR image shows an enlarged, poorly enhancing pituitary gland (arrow). (b) MR image obtained 4 weeks later shows atrophy of the pituitary with a partial empty sella appearance.](image)

![Figure 10. Sheehan syndrome in a 37-year-old woman who presented with a clinical picture of panhypopituitarism 3 months after complicated delivery. Sagittal gadolinium-enhanced T1-weighted MR image shows an empty sella with herniation of the optic chiasm (arrow) into the sella turcica.](image)
the pituitary gland (58) (Fig 11). However, heterogeneity of the enlarged pituitary gland may also be seen. Hemorrhage has not been reported in lymphocytic adenohypophysitis, to our knowledge. Thickening of the infundibulum and involvement of the neurohypophysis resulting in diabetes insipidus are reported in 15% of patients (57). There are no imaging features that distinguish lymphocytic adenohypophysitis from pituitary adenoma (47,49). After recovery, there is regression of the pituitary gland to normal or small size, resulting in the appearance of a partial or total empty sella (57).

Although recovery may occur spontaneously, steroids have been advocated as the main line of treatment. Not only do glucocorticoids replace the shortage of a vital hormone, but they also have a potent anti-inflammatory effect (57,59).

**Neoplastic Disorders**

Hormonal changes during pregnancy can enhance the rate of growth of prolactinomas, while hemodynamic alterations may increase the capillary bed of some vascular benign tumors. Intracranial metastasis can be the first manifestation of an extracranial malignancy. Symptoms may be masked by other existing pathologic processes such as migraine or preeclampsia.

**Pituitary Adenoma**

Prolactinomas are the most common pituitary tumors occurring during pregnancy. The stimulatory effect of elevated estrogen on prolactinoma growth is well recognized. Molitch (49) analyzed results of several series totaling 376 women with microadenomas and 151 women with macroadenomas. Only six women (1.6%) with microadenomas developed signs and symptoms of tumor enlargement. Of 86 women with macroadenomas who had no prior treatment, 20 (23.3%) developed symptomatic tumor enlargement.

Clinical evaluation of a pituitary mass poses a significant challenge during pregnancy. This is in part due to the continuously rising level of prolactin. Pituitary evaluation is further hindered by our reluctance to administer gadolinium contrast material during pregnancy. Prolactin levels may vary in the presence of a prolactinoma, and periodic measurements are of little help. Surveillance for tumor growth is usually performed by periodic clinical assessment and visual field testing (48). If imaging becomes necessary, high-resolution MR imaging sequences without contrast material can be performed. In the proper clinical context, a pituitary adenoma may be present if the pituitary height exceeds 12 mm (49) (Fig 12).

Treatment options are meticulously considered and individualized. Medications such as bromocriptine or cabergoline are considered the treatment of choice for prolactin-secreting microadenoma and adenomas confined to the sella.

**Figure 11.** Lymphocytic adenohypophysitis in a 28-year-old woman who developed a severe headache 4 days after normal vaginal delivery. (a) Sagittal T1-weighted MR image shows mild enlargement and homogeneous enhancement of the pituitary gland (arrow). (b) Sagittal T1-weighted MR image obtained 3 weeks later shows spontaneous regression of the pituitary to a normal size.
Transsphenoidal surgery may become necessary in uncontrollable suprasellar macroadenomas. Adenomas secreting adrenocorticotropic hormone should always be surgically removed. Surgery and medication are not indicated in growth hormone–secreting adenomas and nonfunctioning adenomas. Patients with thyroid-stimulating hormone secreting tumors should receive only antithyroid medications to control hyperthyroidism (48).

**Primary Intracranial Tumors**

Pregnancy has no significant effect on the incidence or behavior of glioma. However, pregnancy appears to enhance the growth of meningioma (60). About 70% of meningiomas express progesterone receptors and 30% express estrogen receptors. Serial imaging has shown regression of meningiomas after delivery. These observations suggest that progesterone influences tumor growth (60,61). In addition, there are a few reports in the literature that document accelerated tumor growth in hemangioblastoma (62) and vestibular schwannoma (63) during the course of pregnancy.

**Intracranial Metastasis**

Cerebral metastasis can be the initial presentation of breast cancer and choriocarcinoma. The relatively dense and firm breasts during pregnancy and lactation may hinder early diagnosis of breast cancer. It is well recognized that pregnant women with breast cancer present with more advanced disease than nonpregnant women (64). Choriocarcinoma is the severest form of trophoblastic disease and can rarely coexist with a normal pregnancy. Intracerebral hemorrhage can be the first presentation of gestational choriocarcinoma. In the indexed literature, there are four reported cases of metastatic gestational carcinoma to the brain (65–67). Hemorrhage was seen in two (50%) of the cases.

**Conclusions**

Imaging abnormalities in the CNS are produced by a spectrum of diseases that may occur during pregnancy and the puerperium. Some are specific to the physiologic process of reproduction, eclampsia being one of the more common, while others are the result of diseases that are seen regularly in the adult population albeit sometimes with increased frequency in pregnant women, such as dural sinus thrombosis. Recognition of the characteristic imaging findings in eclampsia may, for example, allow confident exclusion of more serious disorders like stroke. Even when CNS imaging changes are nonspecific, an awareness of the increased likelihood of certain diseases in pregnancy as well as knowledge of those entities more or less specific to pregnancy and the
puerperium will allow a more informed differential diagnosis. Differentiating primary nonaneurysmal SAH from aneurysmal SAH is an example. PCA with its underlying changes of vasculitis is another entity that should be considered in addition to the other common causes of intracerebral hemorrhage.

Moreover, earlier use of imaging will result in fewer delayed diagnoses. Modalities such as CT and MR venography enable early noninvasive diagnosis of CVT. Simple unenhanced CT or preferably MR imaging allows safe confirmation of pituitary apoplexy. Furthermore, even when the imaging changes are less specific, knowledge of likely possibilities will lead to more appropriate earlier use of imaging. For example, awareness of...
the stimulatory effects of pregnancy on prolactinoma, meningioma, hemangioblastoma, and vestibular schwannoma, as well as metastatic tumors such as gestational choriocarcinoma and breast cancer, suggests the early use of CNS imaging to avoid the consequences of a delayed diagnosis. The last example illustrates the importance of early imaging in making a definitive diagnosis that may have saved the patient’s life (Fig 13).

References


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