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IMAGING (L MECHTLER, SECTION EDITOR)

Imaging of Headache in Pregnancy

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Abstract Pregnant women are most likely to have primary headaches, such as migraine and tension-type headaches, which can be diagnosed and treated without brain imaging. Primary headaches may even start de novo during pregnancy, especially in the first few months. However, when the headache occurs late in pregnancy or in the peripartum period, secondary causes of headaches need to be considered and evaluated by brain and/or vascular imaging, generally using magnetic resonance techniques. There is considerable overlap between the cerebrovascular complications of pregnancy, including preeclampsia/eclampsia, posterior reversible encephalopathy syndrome (PRES), reversible cerebral vasoconstriction syndrome (RCVS), and both hemorrhagic and ischemic strokes; although, their imaging may be distinctive. Imaging is necessary to distinguish between arterial and venous pathology causing headache in the peripartum patient, as there can be similar presenting symptoms. Mass lesions, both neoplastic and inflammatory, can enlarge and produce headaches and neurological symptoms late in pregnancy.

Keywords Headache · Pregnancy · Migraine · Eclampsia · Cerebral venous thrombosis · Reversible cerebral vasoconstriction syndrome (RCVS) · Ischemic stroke · Lymphocytic hypophysitis

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Introduction

Pregnancy is associated with physiologic changes that affect neurologic function and can cause different neurologic symptoms. Headache, of benign and concerning etiologies, is commonly associated with pregnancy and the peripartum period [1]. Differentiating between common, non-life-threatening types of headaches (primary headaches) and the secondary headaches due to conditions that require testing and specific treatment is extremely important for physicians caring for pregnant women. While most headaches experienced by pregnant and peripartum women are primary headaches, especially migraines, there are many causes of secondary headaches that are of concern in pregnant women (Table 1). Brain imaging is not needed for most headache patients who present with symptoms consistent with primary headaches, as described in the International Classification of Headache Disorders, third edition (beta version) [2•]. Neuroimaging is overutilized and is generally not indicated in the evaluation of patients with a history consistent with primary (especially migraine and tension-type) headaches [3]. However, brain imaging is generally advised in patients whose history and examination suggest secondary headaches, associated with underlying central nervous system (CNS) or systemic disorders. The choice of imaging modalities in a pregnant woman is crucial in achieving the correct diagnosis and starting appropriate treatment. It also requires the clinician to understand gestational physiology and to appreciate the needs of both the mother and the fetus.

Neuroimaging Safety

Risks, for both the mother and the fetus, associated with exposure to ionizing radiation and magnetic fields, must be weighed against the need for diagnostic imaging for the

Table 1 Major causes of headache in pregnancy

- Primary headaches
  - Migraine
  - Tension-type
- Secondary headaches
  - Cerebrovascular disease
    - PRES/reversible cerebral vasoconstriction syndrome spectrum
      - Preeclampsia, eclampsia, HELLP, postpartum cerebral angiopathy
    - Intracranial hemorrhage—ICH, SAH
    - Cerebral venous thrombosis (CVT) with infarct or hemorrhage
    - Arterial ischemic stroke
      - Thrombotic
      - Embolic (30 % cardioembolic)
        - Venous thrombosis (paradoxical embolization from peripheral source)
        - Fat
        - Amniotic fluid
        - Air (orogenital sex)
        - Choriocarcinoma
      - Arterial dissection
      - Arterial pathology (spasm, arteritis)
  - Mass lesions
    - Tumors
    - Vascular mass lesions—hemangioblastoma, cavernous malformation
  - Inflammation
    - Lymphocytic hypophysitis

pregnant woman with a headache [4•]. The effect of fetal exposure to ionizing radiation, as in plain X-rays and computed tomography (CT) scans, is dependent on the threshold of exposure and can include childhood malignancies, mutagenesis, infertility, and cataract formation. The effects of radiation depend on the absorbed radiation dose, the rate of absorption, and gestational age of the fetus. With contemporary clinical CT imaging, attributable risk of childhood cancer due to intrauterine fetus radiation exposure is believed to be low [5]. The rate of absorption depends on direct versus indirect radiation, with direct radiation being associated with a higher rate of absorption. The mother's body weight, area of radiation exposure, and her positioning during testing are major factors in decreasing the rate of fetal radiation dose absorption. Early gestational age is associated with growth retardation, congenital malformations, and neonatal death. Fetal exposure to ionizing radiation at 8–15 weeks is associated with higher risk of cognitive delay than is exposure at 15–25 weeks of gestation.

No known adverse effects are described with maternal or fetal MRI imaging using 3Tesla or lower magnets. Theoretical concerns include fetal exposure to the magnetic field, noise exposure with concern about fetal hearing loss, and exposure of the fetus to increased temperature. The use of intravenous (IV) iodinated contrast (FDA class B) should be avoided during pregnancy. Likewise, IV gadolinium should also be avoided during pregnancy. Gadolinium is classified as a class C drug by the FDA; in animal studies, it was shown to penetrate into fetal circulation, and was associated with developmental abnormalities and spontaneous abortion. Informed consent for any type of intravenous contrast should be obtained if such exposure is unavoidable in order to diagnose maternal, or fetal, disease [6]. The injection of gadolinium contrast should not interfere with breast feeding [4•].

Primary Headaches

Primary headaches in pregnancy are common and approximately 5 % of pregnancies are affected by a new onset or new type of headache, most often migraine [7]. Headaches occurring early during pregnancy are more likely to be primary headaches, or, if secondary headaches occur, they are likely to be unrelated to the woman's pregnant condition. While both migraine and tension-type headache are quite common in pregnancy and the postpartum period, the frequency and severity of migraine headaches tend to decrease during the later months of pregnancy due to the shifting ratio between maternal estrogen and progesterone [8]. About 40 % of postpartum women are thought to have headaches, often in the first weeks after delivery. Migraine headaches often return soon after delivery, especially if the woman is not breast-feeding, and in the setting of her stress, sleep deprivation, and abrupt hormonal changes. However, cerebrovascular disorders associated with pregnancy that can cause headaches, especially ischemic stroke, hemorrhagic stroke, and postpartum cerebral angiopathy are more likely to occur in the 6 months after delivery than they are during pregnancy itself. Taking an accurate history and looking for so-called red flags are very important in order to differentiate primary headaches from concerning neurological and medical conditions which can also present with headache, either related to the pregnancy or incidental. Some of the "red flags" that should guide the clinician toward the diagnosis of conditions other than primary headache include a significant change in the descriptive symptoms of the headache; poor or no response to the usual effective treatments; the presence of persistent or unusual visual, motor, or sensory symptoms; and altered consciousness or confusion associated with the headache. The presence of these symptoms indicates the need for prompt imaging studies [1, 9].

Secondary Headaches

Many of the secondary headaches most commonly associated with pregnancy are caused by cerebrovascular disease, especially in the later stages of pregnancy or in the weeks after delivery [10]. Even some nonvascular secondary headaches associated

with pregnancy may have cerebrovascular complications, such as inadvertent dural puncture headache that occurs with subdural hematomas or thrombosis of cerebral veins [11]. Low pressure headaches in pregnancy are similar clinically and radiographically to low pressure headaches in non-pregnant patients. They have a typical positional component with an acute onset of headache in upright position and fast resolution of headache after lying down (Fig. 1). However, occasionally, the positional complaints can be reversed with exacerbation of the headache pain when recumbent. Nausea, nuchal rigidity, tinnitus, and hyperacusis are common associated symptoms. In peripartum women, a dural puncture headache typically occurs after spinal or epidural anesthesia, occurring in about 1 % of pregnant women. Brain MRI reveals downward displacement of cerebellar tonsils, so-called brain sagging, and gadolinium injection reveals diffuse pachymeningeal enhancement. [5, 12]. Thrombosis of cortical veins with associated subarachnoid hemorrhage, as well as unilateral or bilateral subdural collections, can occur with a postdural puncture headache [13]. While both spontaneous CSF leak and post-dural puncture headaches are associated with intracranial hypotension and positional headaches, hemorrhage into an enlarged or neoplastic pituitary could mimic this with distinct positional components as well (Fig. 1).

Cerebral Venous Thrombosis

The increased risk of cerebral venous thrombosis (CVT) during pregnancy and up to 8 weeks postpartum is related to multiple factors, including iatrogenic intracranial hypotension from anesthetic dural puncture, postpartum hypercoagulability, and dehydration [14, 15]. Headache is the most common initial symptom and usually is of gradual onset and escalating severity. Other symptoms include change in mental status or alteration in level of consciousness, intracranial hypertension leading to papilledema with eventual visual loss, focal or generalized seizures, and focal neurological deficits due to venous infarcts [16]. The incidence of both hemorrhagic and ischemic stroke associated with pregnancy, especially CVT, is increasing, with hypertension as a major reason for this alarming increase in cerebrovascular complications of pregnancy [17•]. Epidemiologic data from the last decade shows increased rates of CVT in pregnancy: 0.7–24 %, with a less clear relationship to increasing maternal age than with arterial thrombosis or hemorrhage. MR venography, without need for contrast injection, is the preferred imaging used to evaluate pregnant patients with suspected CVT [18]. Time-of-flight (TOF) MR venography assesses flow in large draining cerebral veins and the dural sinuses. Interruption of flow-related signal is usually indicative of CVT; however, low flow pressure in cerebral veins and dural sinuses can also cause a dropout of TOF-related signal. The presence of thrombus in cerebral veins and sinuses is also associated with the absence of normal hypointense flow voids on brain MRI T1 and T2 sequences. MRI imaging with 3D T1-weighted gradient-recalled echo (GRE) contrast enhanced sequences may have the greatest diagnostic utility in the diagnosis of CVT after delivery [19, 20]. Cerebral venous infarction due to CVT is associated with more severe periinfarct edema than arterial infarction and is associated with a hyperintense signal on T2 and FLAIR sequences. A non-contrast head CT can reveal a hyperdense thrombus in the dural sinus or cortical vein. With contrast injection, the CT scan can show an empty delta sign due to the lack of flow outlining a triangular filling defect caused by a clot in the superior sagittal sinus and the dural sinus torcula. CT venography, with the need for iodinated contrast injection, can be used in the postpartum period. In cases of CVT complicated by intracranial hypertension, diffuse cerebral edema can be seen on both CT and MRI imaging. Other brain imaging findings associated with secondary intracranial hypertension, such as flattening of the posterior globe, protrusion of the globe, enlarged subarachnoid space around the optic nerves, and an empty sella, may be seen with CVT. Cases of CVT associated with posterior reversible encephalopathy syndrome (PRES) have been reported, illustrating the complex interplay between the various forms of cerebrovascular disease found in pregnant women [21].

Eclampsia and Preeclampsia

Preeclampsia is the most common hypertensive disorder of pregnancy which occurs in approximately 5 % of pregnancies. Preeclampsia is often heralded by a new onset of headache later in pregnancy [22]. Hypertensive disorders of pregnancy are more common in women with migraine headaches prior to pregnancy, further complicating the differentiation of headache types in pregnant women. Preeclampsia is a syndrome that includes the new onset of hypertension during the second half of pregnancy and up to 8 weeks postpartum. Blood pressure elevation is accompanied by new-onset proteinuria and/or other signs and symptoms of end-organ hypertensive damage such as headaches, vision changes, abdominal pain, and peripheral edema. The neurological manifestations of preeclampsia are caused by disordered cerebral vascular autoregulation, leading to endothelial damage, and capillary leakage with resultant cerebral edema. Certain circulating angiogenic factors released by the placenta are associated with preeclampsia and may reflect the severity of outcome of hypertensive disorders of pregnancy [23]. Based on the newer definition of preeclampsia, proteinuria is not required for the diagnosis [24]. This change in definition reflects the high variability in disease presentation and progression based on the various organs (e.g., brain, liver, spleen, kidneys) affected by the new onset of an often precipitous elevation in blood pressure. Eclampsia is defined as preeclampsia along with new onset of generalized seizures. Preeclampsia can progress to eclampsia in 1–2 % of cases and presents with seizures due to cerebral involvement [9]. Both conditions present with a holocephalic, throbbing headache associated with blurred vision and photophobia, often accompanied by confusion and alteration in the level of consciousness. Focal neurological findings can include brisk deep tendon reflexes. There are no pathognomonic

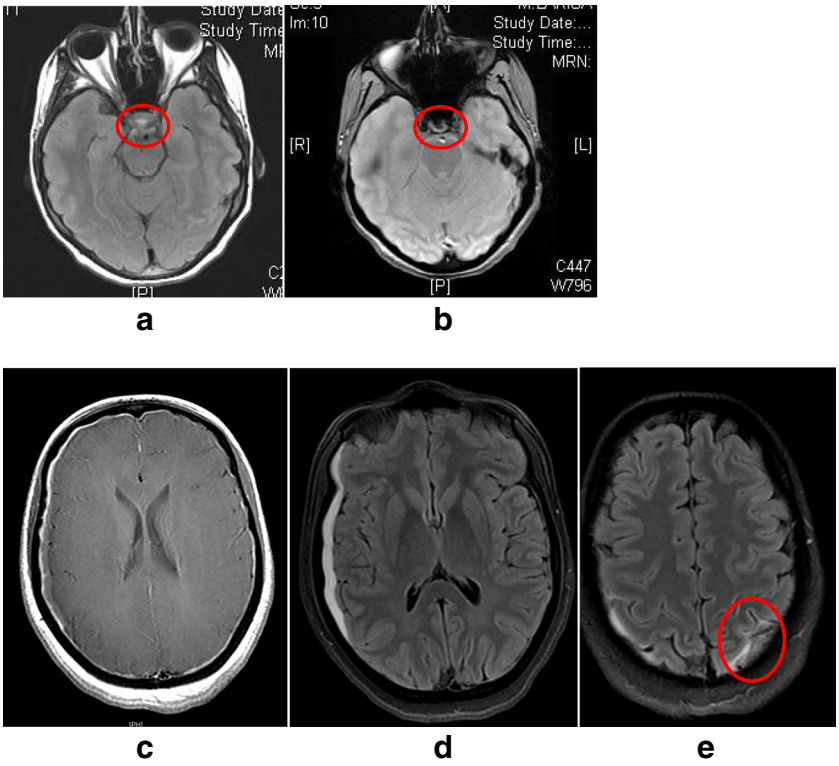

Fig. 1 **a**, **b** A 33-year-old woman, 31 weeks pregnant, developed spasm-like headaches whenever she bent over, lowered her head, sneezed, or coughed starting a couple weeks prior to imaging. Axial FLAIR imaging (**a**) shows increased signal intensity in the pituitary with decreased signal on GRE (**b**) consistent with a pituitary hemorrhage. **c**–**e** A 25-year-old woman developed a post-partum positional headache after sectioning under epidural anesthesia. Diffuse pachymeningeal enhancement, (T1 with contrast: **c**), a subdural hemorrhage (FLAIR: **d**), and a small subarachnoid hemorrhage near a cortical vein thrombosis (FLAIR: **e**) were consistent with a dural puncture

findings associated with these conditions on either brain MRI or head CT in the early stages of the blood pressure elevation. Nevertheless, non-contrast brain MRI should be performed to rule out other causes of headache, particularly preeclampsia complicated by stroke due to the hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, PRES, and reversible cerebral vasoconstriction syndrome (RCVS) [25, 26]. These cerebrovascular complications of pregnancy likely represent a continuum of disorders with overlapping presentations. Acute elevation in blood pressure is a hallmark of preeclampsia/eclampsia and is a major cause of PRES. Untreated preeclampsia/eclampsia can result in ischemic and hemorrhagic strokes, with progression to PRES and RCVS (Fig. 2). Interestingly, hypertension as a complication of pregnancy increases a woman's risk of stroke in the future, unrelated to future pregnancies.

Posterior Reversible Encephalopathy Syndrome

PRES is a clinical and radiographic syndrome presenting with a pressure-like dull holocephalic headache, encephalopathy, visual changes, and seizures, as can preeclampsia/eclampsia. Similarly, the underlying pathophysiology of this spectrum of disorders is thought to be due to the loss of cerebral autoregulation and increased capillary leakage resulting in vasogenic edema predominantly in the parietal and occipital lobes. However, imaging changes can be diffuse in the brain, and even rarely in the brainstem and spinal cord [27]. Pregnancy-related PRES is usually a complication of preeclampsia/eclampsia, but it can happen in normotensive women. Brain imaging is particularly important with a non-contrast brain MRI being the imaging modality of choice in pregnant patients. Patchy parietooccipital or diffuse hemispheric hyperintensities on T2 and FLAIR sequences and T1 sequence hypointensities are characteristic. Imaging with head CT reveals patchy posterior or diffuse hypodensities in the bilateral cerebral hemispheres. These changes do not follow a particular arterial distribution, differentiating them from cerebral arterial infarction but potentially confusing them with venous infarction associated with CVT. Recognition of the clinical symptoms and the significance of the elevated blood pressure should lead to the timely initiation of treatment with the resolution of clinical symptoms and radiographic findings. However, untreated PRES, as with preeclampsia/eclampsia, can lead to strokes, both ischemic and hemorrhagic. Pregnancy-related thrombotic thrombocytopenic purpura (TTP) complicating preeclampsia can trigger intracerebral hemorrhage that can be detected by the GRE sequence on brain MRI or non-contrast head CT [28]. As with eclampsia, there is an overlap in the physiologic mechanism of PRES and RCVS and cases of concurrent conditions are reported [25, 26, 29]. The presence of vasospasm in patients with PRES has been documented by catheter angiography and magnetic resonance angiography (MRA), emphasizing the overlap between cerebrovascular syndromes in pregnancy [30].

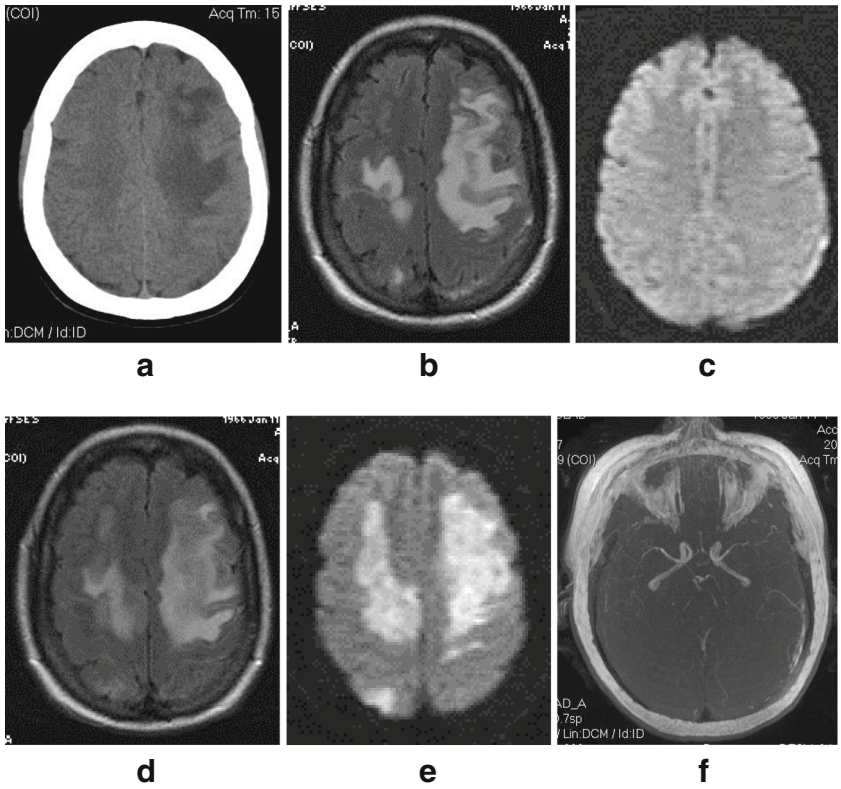

Fig. 2 A 40-year-old woman had a headache and elevated blood pressures that started 3 days after a normal sectioned delivery. Imaging was obtained on day 8. Regions of hypoattenuation were seen on CT scan (**a**). An MRI scan obtained on day 8 after delivery showed FLAIR signal abnormalities (**b**) without corresponding changes on DWI (**c**). On day 20 after delivery, her blood pressures were still elevated with a headache. An MRI scan showed increased FLAIR abnormalities of vasogenic edema (**d**), as well as corresponding new areas of cytotoxic edema on DWI (**e**). On postpartum day 22, MRA showed markedly constricted intracranial vessels (**f**)

Reversible Cerebral Vasoconstriction Syndrome/Postpartum Cerebral Angiopathy

RCVS is a clinical and radiographic syndrome of multiple etiologies, which is associated with a headache of generally abrupt onset and reversible multifocal vasoconstriction in large- and medium-size arteries (Fig. 3) [31–33]. Currently, the term RCVS spectrum is used to describe entities that represent the same or overlapping vasospastic disorders: postpartum angiopathy, Call–Fleming syndrome, drug-induced cerebral vasospasm, and benign cerebral angiopathy [34]. In many cases, the exact etiology is unknown. The majority (60 %) of women develop RCVS in the postpartum period. The cause is idiopathic or due to exposure to vasoactive substances such as medications or illicit drugs, such as cocaine and marijuana. The association of RCVS with the postpartum state is due to the presence of circulating angiogenic factors [35]. In uncomplicated cases not associated with progression to a stroke, brain imaging, both CT and MRI, may be unrevealing. Vasospasm, commonly described as beading, is confirmed by MRA, computed tomography angiography (CTA), or cerebral catheter angiography; although MRA, the preferred imaging modality in pregnant patients, may only reveal subtle or non-specific changes. CTA and cerebral angiography can be utilized in postpartum patients since iodinated contrast in breast milk is not associated with adverse effects on the infant [36–38]. Catheter angiography may be needed to confirm the diagnosis in a postpartum woman (Fig. 4). Generally, but not always, the characteristic pattern of vasospasm can be differentiated from the beaded and tapered vessels with cutoff and ballooning seen with central nervous system vasculitis. Repeat vascular imaging in 3 months is warranted to confirm the resolution of reversible cerebral vasospasm. Postpartum angiopathy can be complicated by ischemic stroke, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH). SAH is more common than ischemic stroke or ICH [39, 40]. As with CVT, the small volume of subarachnoid blood that can be associated with RCVS is usually cortical, as opposed to cisternal, in location. Radiographic features of SAH are the same as in non-pregnant patients. SAH may also be associated with CVT, and the area surrounding the hemorrhage should be evaluated for a thrombosed cortical vein (Fig. 1). The association of RCVS with PRES and preeclampsia/eclampsia syndrome was noted above; however, RCVS is usually benign and headache is the only presenting symptom. The RCVS-related headache may be treated with calcium channel blockers; although, it generally resolves without specific treatment, other than the removal of any known precipitating agent. Treatment usually results in resolution of headache as well as imaging findings.

Approximately 2 % mortality due to ICH and ischemic stroke has been associated with complicated cases of RCVS [41, 42]. Intracranial hemorrhage, both intracerebral and subarachnoid, while rare in pregnancy, constitutes the third leading cause of non-obstetric-related mortality in pregnant and postpartum women. The causes of hemorrhages in pregnancy are different from the general population and are largely related to physiologic changes in pregnancy such as increased blood volume and cardiac output, pregnancy-related hypertension, eclampsia/preeclampsia with or

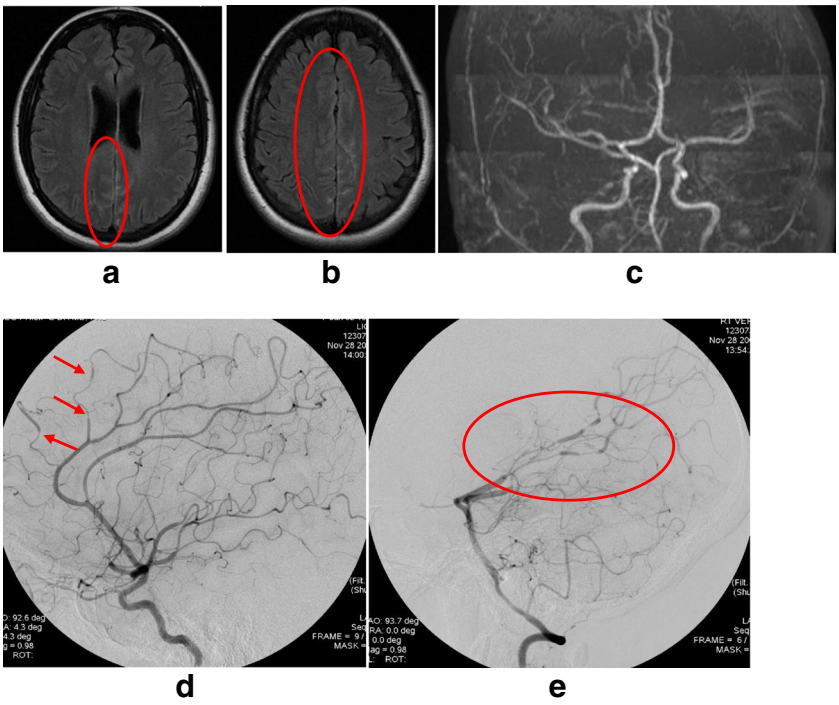

Fig. 3 A 40-year-old woman had a sudden onset of headache prior to delivery which persisted for 7 days after delivery. Her BP was 136/61 and her neurological examination was normal. Her CT scan of the head was interpreted as negative. Sulcal FLAIR hyperintensity in the fronto-parieto-occipital parasagittal regions bilaterally, more prominent on the left, is consistent with subarachnoid blood (**a**, **b**). Small-caliber supraclinoid internal carotid arteries bilaterally and areas of narrowing/dilatation of the M2 segment of the right internal carotid artery were noted on MRA (**c**). However, arterial pathology consistent with RCVS was better seen on catheter angiography (**d**, **e**)

without hypertension, loss of cerebral vascular autoregulation, and vascular wall remodeling. Arteriovenous malformations (AVMs), cavernomas, and intracerebral aneurysms are the most common lesions related to ICH [43]. The risk of hemorrhage from previously unruptured aneurysms does not increase during pregnancy. AVM rupture most commonly presents with parenchymal, followed by intraventricular, hemorrhage [44]. The risk of cavernoma-related symptomatic hemorrhages during pregnancy is not increased [45]. The risk of aneurysmal SAH during pregnancy and delivery is lower than in non-pregnant women [46]. However, the risk of hemorrhagic cerebrovascular disease, presenting with the apoplectic onset of a severe headache, is increased immediately after delivery. More than 50 % of SAH occur in the postpartum period [47]. Headache related to ICH is typically a severe holocephalic headache of sudden onset, when the hemorrhage causes increased intracranial pressure or dural irritation. SAH commonly presents with holocephalic headache, with characteristic abruptness of peak intensity at onset. Headache due to hemorrhage may be associated with nausea, vomiting, and photophobia, complicating the differentiation from the acute onset of a migraine headache. Focal and global neurological findings depend on the location and size of the ICH and the presence of increased intracranial pressure and hydrocephalus. Additionally, cerebral vasospasm and infarction occurring hours to days after SAH can cause worsening headaches, altered mental status, and focal neurological findings. A non-contrasted head CT has high sensitivity and specificity in detecting acute intracranial blood, including in the intraventricular and subarachnoid spaces. Vascular imaging is often required immediately, particularly in cases where a leaking cerebral aneurysm is suspected. While cerebral catheter angiography is considered a gold standard in the detection of SAH, CTA (a study with IV contrast) has a very high sensitivity and specificity as well, especially for aneurysms that are at high risk for rupture [48]. If fetal safety is a concern due to exposure to ionizing radiation and IV iodinated contrast, TOF MRA can be performed, but the technique has high sensitivity to motion artifact [43].

Ischemic Stroke

The risk of ischemic stroke is increased around the time of delivery and for 6 weeks postpartum. A study by Kuklina et al. [17•] showed a disturbing increase in the rate of antepartum and postpartum stroke in the last decade, likely related to an increase in traditional risk factors, including hypertension, in an older pregnant demographic. Pregnancy-specific ischemic stroke risk factors include estrogen-induced hypercoagulability, trophoblastic embolism, amniotic fluid embolism, cardioembolism, pregnancy-related hypertension, eclampsia/preeclampsia, reversible cerebral vasospasm, cerebral venous sinus thrombosis, cervical arterial dissection, and paradoxical embolism due to deep venous thrombosis (Table 1). Although headaches are not typical for patients with ischemic stroke, they are not

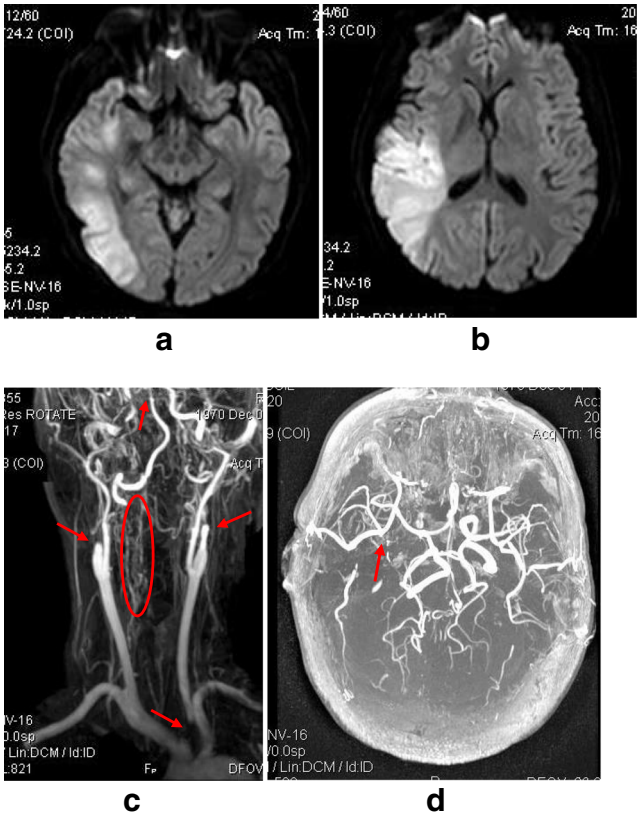

Fig. 4 A 36-year-old woman had an uneventful first pregnancy with vaginal delivery of a healthy infant. A week later she developed a headache, dizziness, and progressive left-sided weakness, without visual field deficit. Diffusion weighted imaging on MRI (**a**, **b**) showed an acute infarct in the territory of the posterior division of the right MCA. MRA of the neck (**c**) and head (**d**) showed bilateral internal carotid arteries, right common carotid artery, right vertebral artery, and basilar artery lesions due to multiple dissections. She had occlusion of the posterior division of the right MCA

uncommon in pregnant patients with ischemic stroke [10]. Otherwise, clinical presentations of ischemic stroke in pregnancy are not different from general population and include change in mental status, focal neurological deficit and, less commonly, seizures. Radiographic findings are similar to ischemic stroke imaging in the general population as well. Head CT reveals loss of gray-white differentiation, sulcal effacement, and hypoattenuation of the infarcted area. Chronic infarcts appear hypodense with associated volume loss. MRI reveals hyperintense lesions on DWI with correlating hypointense lesions on ADC sequences (restricted diffusion) from the first minutes of stroke onset. Later ischemic changes are associated with hyperintensities on T2 and FLAIR sequences and are hypointense on T1 sequence.

Tearing of the endothelial lining of the extracranial and intracranial arterial vessels can cause postpartum headache or neck pain, associated with focal (e.g., Horner's syndrome, lower cranial nerve paresis) or TIA/ischemic stroke symptoms and signs. Ischemic stroke is usually caused by clot embolization from a dissection flap to a distal vessel, with a hemodynamic cause from the dissection causing arterial occlusion being less common. Postpartum arterial dissection appears to be unrelated to the mechanics of childbirth and can present with headache prior to the development of focal neurological deficits. Arterial dissection can involve single or multiple posterior and anterior circulation vessels, occurring days to a month after vaginal or sectioned delivery (Fig. 4). Peripartum arterial dissection is not generally associated with underlying connective tissue disorders and can occur in cardiac and renal arteries, as well as intracranial or extracranial arteries. The reason for this postpartum vulnerability is unknown [49]. Dissection is best visualized by MRA of head and neck during pregnancy, with MRA of the neck with contrast obtained after delivery. Cross-sectional T1 imaging with fat suppression may show a characteristic crescent-shaped deformity in the wall of the dissected internal carotid artery.

Central Nervous System Mass Lesions

Rarely, an acute headache during pregnancy can be due to an expanding or hemorrhagic intracranial mass lesion, generally due to cardiovascular and hormonal changes in lesion morphology. A large proportion of tumors, both primary brain tumors and metastases, either becomes symptomatic, recur, or progress during pregnancy. Low-grade primary brain tumors become more aggressive in pregnancy. Intermediate and high-grade primary brain tumors, diagnosed prior to pregnancy, have been shown to develop altered more aggressive pathology and may recur or progress significantly during pregnancy [50–52].

During pregnancy, especially during the last trimester, increases in cardiac output, as well as whole blood and plasma volume, causes increased vascularity and increased hemorrhage risk in CNS mass lesions. Changes in progesterone, estrogen, and prostacyclins are also related to the noted expansion in primary and metastatic brain tumors. Headache may be caused by increased intracranial pressure due to intracranial hemorrhage or obstructive hydrocephalus from accelerated tumor expansion [53]. Elevated blood volume can increase risk of hemorrhage into either a normal pituitary or an associated neoplasm, causing an acute headache in pregnancy, with characteristic imaging changes (Fig. 1). Pituitary adenomas can become symptomatic during pregnancy due to vascular or endocrine mechanisms (Fig. 1) [54–57].

Primary brain or metastatic tumors that have a significant vascular component, causing increased bleeding

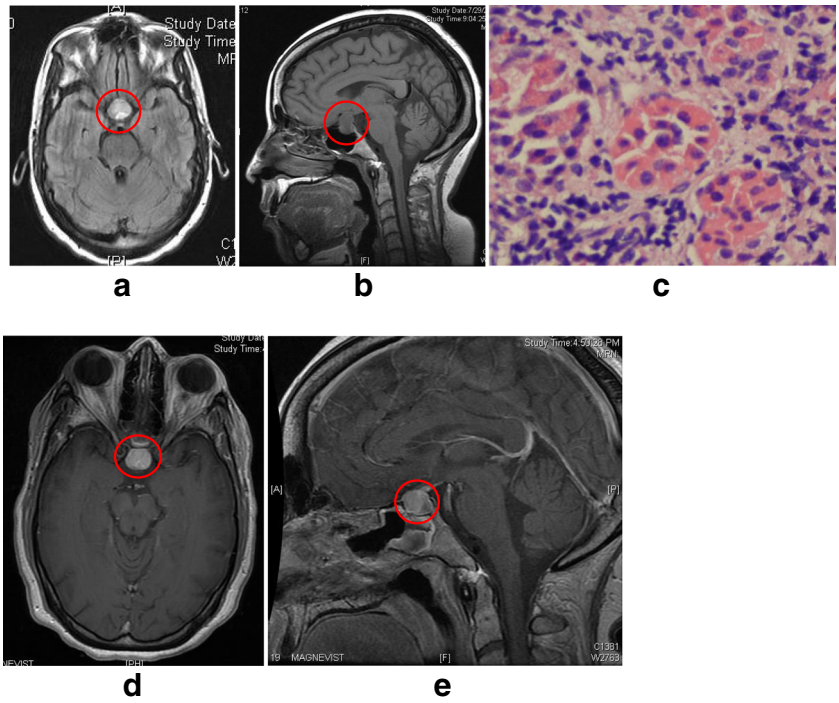

Fig. 5 A 34-year-old woman, 32 weeks pregnant, noted 3 weeks of holocephalic headaches with nausea and vomiting. For 2 weeks she noted left, then right, peripheral visual loss. She had a left afferent pupillary defect and an asymmetric bitemporal field cut. A pituitary lesion was seen on FLAIR (**a**) and sagittal T1 (**b**). A pituitary biopsy showed marked infiltration of lymphocytes (**c**). A contrast-enhanced T1 sequence (**d**) obtained after delivery showed a homogenously enhancing pituitary mass (**e**). Vision improved with steroids

risk in a non-pregnant state, are particularly susceptible to hemorrhage-related headaches during pregnancy. Choriocarcinomas are derived from the placenta during pregnancy and can metastasize to the central nervous system. When these rare tumors involve the brain or spinal cord in the peripartum period, they are often diagnosed after an acute headache and focal neurological deficits caused by hemorrhage [58]. Even benign vascular mass lesions such as intracranial or spinal hemangioblastomas can become acutely symptomatic during pregnancy because of vascular mechanisms causing expansion [59, 60].

Meningiomas are more frequent in women and express progesterone receptors on tumor cells; but, the mechanism of pregnancy-related expansion is probably more vascular than endocrinological [61]. Meningiomas, especially the more vascular (angiomatous) ones, tend to grow rapidly during pregnancy and may become symptomatic either due to their mass effect causing headaches and/or focal neurological deficits or by serving as a seizure focus. Parasellar meningiomas may present in the later months of pregnancy with headaches due to the expanding mass effects of the hydrocephalus. Headaches can be caused by elevated intracranial pressure, by the distortion of the diaphragm sella, or by parasellar dura irritation. Meningiomas may present on MRI during pregnancy as isointense T_1- and T_2-weighted lesions with a broad dural attachment, hyperostosis, and normal sellar dimensions. A dural tail may not be seen on an unenhanced scan obtained during pregnancy.

Central Nervous System Inflammation

Lymphocytic hypophysitis is an inflammatory autoimmune disease of the pituitary gland that characteristically presents as a perisellar expansion of the adenohypophysis, neurohypophysis, or infundibulum, with isodense or hypodense signals on T_1-weighted images [62]. Patients, who are often but not always peripartum women, present with headache, nausea, and vomiting, as well as a bitemporal visual field deficit (Fig. 5). If surgery, rather than empiric treatment with steroids, is deemed to be appropriate, then the diagnosis may be made on pathological examination of a frozen biopsy specimen, so as not to remove a functioning pituitary gland. The diagnosis should be suspected in a peripartum woman with a non-hemorrhagic enlargement of the pituitary, and prompt steroid treatment after confirmation by biopsy generally leads to return of the pituitary to its usual size and function [63].

Conclusion

While the complaint of a new-onset headache is always concerning in a pregnant woman, magnetic resonance brain and/or vascular imaging is generally only obtained when a new-onset headache occurs in the peripartum period, especially when accompanied by focal neurological symptoms or elevated blood pressure. Headache associated with elevated blood pressure is variably associated with MRI and MRA changes; but,

lowering the elevated blood pressure can treat the headache and prevent preeclampsia/eclampsia and its multiple cerebrovascular complications. Mass lesions, both neoplastic and vascular, may enlarge most aggressively in the later months of pregnancy. Contrast is rarely given, but non-contrasted MRI, MRA, and MRV studies can be obtained safely in the pregnant patient with a concerning headache.

Compliance with Ethical Standards

Conflict of Interest Maryna Skliut and Dara G. Jamieson declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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