Natural Course and Pathogenesis of Transient Focal Neurologic Symptoms During Pregnancy

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Objectives: To determine the pathogenesis and course of transient focal neurologic symptoms in pregnant women and to identify prognostic variables that will enable targeted workup.

Design: Case-control series.

Setting: Tertiary care university hospital.

Patients: Pregnant patients with acute transient focal neurologic symptoms. Women with histories of migraine, recurrent thromboembolism, or cerebrovascular disease were excluded.

Interventions: Diffusion-weighted imaging (DWI), perfusion-weighted imaging, fluid-attenuated inversion recovery (FLAIR) imaging, gradient-recalled echo imaging, and magnetic resonance venography (MRV) and angiography to determine the presence of brain ischemia and venous thrombosis. Patients underwent echocardiography, carotid duplex ultrasonography, and a battery of hypercoagulability tests and were followed up a mean of 12 months after the event.

Results: Twenty-eight controls and 14 patients were enrolled from 23,773 pregnancies. Mean age was 31.2 (range, 24-41) years and mean gestational age at symptom onset was 28 (range, 17-44) weeks. No controls reported transient focal neurologic symptoms, migraine aura, or headache. Presenting symptoms included dysphasia (6 patients) and hemisensory (5) and hemimotor (7) syndrome. In 4 patients, these symptoms were preceded by scintillating scotoma; in 9 patients, focal symptoms were followed by a first-ever, throbbing, migraine-like headache. Only 1 patient had evidence of frank infarction on magnetic resonance imaging (MRI); 2 patients had single, small, hyperintense bright foci on FLAIR imaging without accompanying lesions on DWI, and 11 patients had normal MRI and MRV results. Echocardiography, carotid duplex ultrasonography, and hypercoagulability results were negative in all patients. None of the patients had ischemic events and 4 (29%) developed migraines with aura headaches during follow-up.

Conclusions: Focal neurologic symptoms in healthy pregnant women are frequently preceded by aural visual phenomena and can usually be attributed to a first-ever migraine attack. Cerebral ischemia is less common than migraine and can be reliably diagnosed with MRI. Extensive evaluations to assess a putative hypercoagulable state and cardiocerebrovascular pathology may not be warranted in all such patients.

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ISCHEMIC CEREBROVASCULAR COMPLICATIONS during pregnancy are rare, with an estimated incidence of 8 to 68 events per 100,000 pregnancies. Approximately half of cases are arterial ischemia and half are venous strokes. Many pathologic states are linked to stroke during pregnancy, including eclampsia, arteriovenous malformation, cardiomyopathy, and systemic lupus erythematosus. Focal transient neurologic symptoms during pregnancy may be transient ischemic events. The most frequently entertained differential diagnosis in such cases is migraine with aura, even in patients without a history of migraine headaches. Indeed, epidemiological studies found that migraine can first present during pregnancy in 1.9% of patients. The diagnostic dilemma is accentuated when symptoms are not accompanied by a typical migraine-like headache, in which a diagnosis of “migraine sin migraine” is frequently made.

The many possible etiologies of transient focal neurologic symptoms during pregnancy frequently lead to costly and time-consuming investigations. Therefore, the main purpose of our study was to evaluate the natural course of such symptoms in previously healthy pregnant women and to predict the necessity of the extensive diagnostic workup these patients usually undergo.
Detailed history revealed that in 4 of 14 patients (29%), and in another 2 patients they continued for 3 to 4 hours. Symptoms lasted a few minutes to 1 hour in most patients, but in 1 patient they persisted for up to 24 hours. Women with a familial history of hemiplegic migraine were also excluded. Patients with no record of ever reporting focal neurologic symptoms were matched for age and pregnancy stage and were randomly selected as controls from a large cohort of pregnant women observed at our center to evaluate the frequency of unreported focal symptoms in otherwise normal pregnancies.

All patients underwent magnetic resonance imaging (MRI) using a modified stroke protocol that included diffusion-weighted imaging (DWI), perfusion-weighted, fluid-attenuated inversion recovery, and gradient-recalled echo imaging; and magnetic resonance angiography and venography at presentation. All women who were included were admitted and evaluated with transesophageal echocardiography, carotid duplex ultrasonography, and a battery of hypercoagulability tests, which included protein C and S levels, activated protein C resistance, and anticardiolipin and lupus anticoagulant tests. Following discharge, patients were followed up at 3-month intervals at our outpatient clinic.

Fourteen patients were enrolled in the study of the total 23 773 pregnancies registered at our center during the study, yielding a frequency of 58 of 100 000 pregnancies. The baseline characteristics of our patients are summarized in the Table. The mean age was 31.2 (range, 24-41) years and the mean gestational age at the onset of symptoms was 28 (range, 17-44) weeks. Twenty-eight controls were also included. Presenting symptoms in our patients included dysphasia (6 patients) and hemisensory (5 patients) or hemimotor (7 patients) symptoms. Symptoms lasted a few minutes to 1 hour in most patients, but in 1 patient they persisted for up to 24 hours and in another 2 patients they continued for 3 to 4 hours. Detailed history revealed that in 14 of 14 patients (29%), these symptoms were preceded by scintillating scotoma, and in 9 patients (64%), the focal symptoms were followed by a first-ever, throbbing, migraine-like headache. Importantly, the presence of visual phenomena and headache were not immediately evident and were not stated as the chief complaint. Rather, the presence of such symptoms only became evident after specific targeted questioning. In 7 of 9 patients, the headaches were described as mild to moderate; the other 2 patients had severe headache. None of the controls had focal neurologic symptoms reported at any time during pregnancy.

Only 1 patient had evidence of frank infarction on DWI; another 2 patients had single, small, hyperintense, bright foci on fluid-attenuated inversion recovery imaging without accompanying lesions on DWI; and 11 patients had normal MRI and magnetic resonance venography results. Echocardiography, carotid duplex ultrasonography, and hypercoagulability results were negative in all patients.

None of the patients had recurrent focal motor or language symptoms or had a clinical stroke. Four patients (29%) developed recurrent migraine with aura headaches during follow-up.

Our main finding is that focal transient neurologic symptoms in otherwise healthy pregnant women are not uncommon and have a generally benign course. They can usually be attributed to first-ever migraine with aura attacks, especially when preceded by visual phenomena, such as scintillating scotomata, even in the absence of a migraine headache. The presence of scotoma or headache was not immediately evident and a high index of suspicion and specific questioning were needed to get this information from the patients.

Headaches occurred during or shortly after cessation of the focal symptoms in 64% of patients. Most headaches were mild but fulfilled the International Headache Society criteria for migraine. Only 29% of our patients developed recurrent migraine headaches during follow-up. This suggests that pregnancy could lower the threshold for migraine attacks in a subset of women, resulting in a
single episode. We could not identify predictors for the development of recurrent headaches in our patients. In contrast, none of the controls reported ever having a transient focal deficit during their pregnancies and none developed migraine headaches at any time during or after pregnancy. Nevertheless, we cannot rule out the possibility that some cases are routinely missed due to underreporting, because not all patients were screened for neurologic symptoms during pregnancy. However, the occurrence of focal symptoms is usually very alarming to patients and physicians alike and typically triggers prompt evaluation at the emergency department; therefore, we believe that most patients were not missed. Most of the focal symptoms occurred during the third trimester or shortly after delivery, which coincides with the hypercoagulable period during pregnancy. The major differential diagnoses in women presenting with focal symptoms late during pregnancy are arterial ischemia, venous thrombosis, and migraine-induced phenomena. The occurrence of migraine aura without headache is well documented, but its occurrence in the special circumstances of pregnancy triggers extensive workup, because the first 2 diagnoses could be potentially life threatening and therefore it is imperative to rule them out. This can be safely achieved with the advent of a modified stroke MRI protocol, such as the one we presented here, which included DWI, perfusion-weighted imaging, fluid-attenuated inversion recovery imaging, magnetic resonance angiography, magnetic resonance venography, and gradient-recalled echo imaging. Diffusion-weighted imaging is highly sensitive for detecting ischemic changes and its results are also positive in a high percentage of patients with clinical transient ischemic attacks. In contrast, DWI results are negative in cases of migraine with aura except for rare reports in patients with familial hemiplegic migraine. Such patients were not included in the current series. A normal result on DWI obtained at presentation practically ruled out the possibility of arterial or venous ischemia in our series and none of the patients with normal MRI results developed stroke during or after the pregnancy. Therefore, we suggest MRI as the primary diagnostic modality in pregnant healthy women with focal symptoms.

The outcomes of our patients were benign, with only 1 patient developing mild stroke as determined by DWI. These findings agree with those of a previous study that showed that patients with typical migraine aura without headache were not found to have an increased frequency of cerebral ischemic events. Importantly, none of our patients had abnormal carotid duplex ultrasonography or echocardiography results. In contrast with another case series, none of our patients had coagulation abnormalities. This difference could be explained in part by the fact that we excluded patients with a history of prior stroke or transient ischemic attack and prior deep vein thrombosis in contrast with previous reports. Therefore, these tests should not be performed unselectively in all patients with such transient events but rather saved for those with a positive family history and those with previous thrombotic events.

In conclusion, our data suggest that the occurrence of focal reversible neurologic symptoms during pregnancy carries a benign outcome and is frequently caused by the first attack of migraine with aura. Screening with MRI rules out more ominous causes of focal symptoms in pregnancy, including arterial or venous ischemia, and obviates the need for extensive and costly evaluations, including hypercoagulability testing, transesophageal echocardiography, and carotid duplex ultrasonography. 

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REFERENCES