Pregnancy-associated Intracranial Hemorrhage: Results of a Survey of Neurosurgical Institutes across Japan

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Background: Pregnancy-associated hemorrhagic stroke is considered a serious complication. Although coagulopathy, pregnancy-induced hypertension, eclampsia, and other systemic complications have been emphasized, pre-existing cerebrovascular diseases (CVDs) have not been fully analyzed. To clarify the role of these vascular lesions more in detail, the Japan Neurosurgical Society conducted a nationwide survey on all the neurosurgical institutes across Japan. *Methods:* This 2-year survey focused on hemorrhagic stroke occurring in pregnancy, delivery, and puerperium. Clinical data based on retrospective chart review were obtained through a questionnaire and analyzed according to the time of onset, underlying CVDs, obstetric systemic complications, therapeutic approaches, and maternal and neonatal prognoses. *Results:* The survey identified 97 hemorrhagic strokes that were associated with pregnancy. Baseline CVDs responsible for hemorrhage were detected in 54 cases (55.7%), among which 47 lesions (87.0%) had been undiagnosed before stroke onset. The detection rate of baseline CVDs before the 32nd week of gestation was significantly higher than that after the 32nd week (90.0% versus 53.3%, $P = .0017$). Arteriovenous malformations (AVMs) were the most frequent CVDs causing intracranial hemorrhage, occurring at 1.8 times the frequency of ruptured aneurysms during pregnancy. Poor outcomes, including 10 deaths, were seen in 36.1% of the cases despite aggressive treatment. *Conclusion:* Pregnancy-associated hemorrhagic strokes frequently concealed baseline CVDs, especially when they occurred before the 32nd week of gestation. AVMs were the predominant bleeding source. For appropriate treatment, therefore, close examination for cerebral vascular lesions is essential when a pregnancy-associated hemorrhagic stroke is encountered. **Key Words:** Pregnancy—stroke—intracranial hemorrhage—arteriovenous malformation—cerebral aneurysm—moyamoya disease.

Introduction

Pregnancy-associated hemorrhagic stroke is well recognized as a serious complication.[1,2] In previous studies conducted mainly by neurologists and obstetricians, systemic obstetric complications including coagulopathies, pregnancy-induced hypertension, and eclampsia were identified as the causes of hemorrhage.[2-7] Pre-existing cerebrovascular diseases (CVDs) such as cerebral aneurysms and arteriovenous malformations (AVMs) were also reported,[4,8] but their incidence and treatments were not fully analyzed. The Japan Neurosurgical Society, therefore, set out to conduct a survey of neurosurgical institutes across Japan regarding pregnancy-associated hemorrhagic stroke with a special focus on identifying underlying CVDs.

Methods

This study is a retrospective analysis based on the clinical chart review in each neurosurgical institute and was

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conducted in 2 phases (primary and secondary surveys) in 2012 as an official project of the Japan Neurosurgical Society. The society has 109 main training institutes across Japan under which 755 affiliated local training institutes participate in providing neurosurgical services. The target of the primary survey was all strokes occurring during pregnancy, delivery, and puerperium (no later than 6 weeks after delivery) that were treated in these institutes between January 2010 and December 2011. In the primary survey, all 109 main training institutes were assigned to compile the number of pregnancy-associated strokes treated in their own hospitals or affiliated local training institutes during the earlier mentioned period. The results were e-mailed to the survey office without any clinical information, and only the e-mail address of the corresponding physician in each case was provided. In the secondary survey, a questionnaire requesting detailed clinical information on each case was e-mailed to each corresponding physician and returned to the survey office without any personally identifying information attached. The clinical information included stroke type and time of stroke onset (gestational age or time after delivery), causes of hemorrhage, types of underlying CVDs, types of obstetric systemic complications, therapeutic procedures for strokes, methods of delivery, and maternal and neonatal prognoses.

Feedback on the primary survey was obtained from 102 (93.6%) main training institutes covering 729 affiliated local training institutes. The survey office sent secondary survey questionnaires to the 126 attendant physicians who had declared their experience with pregnancy-associated stroke and received feedback from 100 physicians (79.4%). After determining the eligibility of each case and eliminating duplications resulting from patient transfer between institutes, the authors extracted 134 cases. These strokes were divided into 97 hemorrhagic strokes (intracerebral or subarachnoid hemorrhage) and 37 other strokes (eg, cerebral arterial infarction or venous infarction), and the former 97 cases were submitted for the further analysis. Intracranial hemorrhage was confirmed by computed tomography (CT) or magnetic resonance (MR) imaging in all cases, and bleeding sources were further examined by MR angiography, digital subtraction angiography, or CT angiography except for a few cases of early death that could not allow further examinations.

Statistical Methods

The data were presented as frequency or means within a standard deviation. Fisher exact probability test and Mann–Whitney *U* test were applied to categorical data. All analyses were performed with Statcel 3 software (OMS Publishing, Inc., Tokorozawa, Japan). Prognosis of the patients was expressed with the modified Rankin Scale (mRS)[9] at discharge.

Table 1. *Demographics of patients with pregnancy-associated hemorrhagic stroke*

	n = 97 (100%)
Mean age (y)	32.2 ± 5.4
Timing of onset	
During pregnancy	
Number of cases	60 (61.9%)
Mean gestational age at onset (wk)	27.7 ± 10.1
At delivery	
Number of cases	13 (13.4%)
Mean delivery weeks	38.4 ± 3.7
Puerperium	
Number of cases	24 (24.7%)
Time after delivery	
<24 h	8
1-3 d	4
3-7 d	3
8-42 d	8
Unknown	1

Results

Patient Demographics

Table 1 summarizes the patient demographics. Among the all 97 hemorrhagic strokes, 60 (61.9%) occurred during pregnancy, 13 (13.4%) at delivery, and 24 (24.7%) during puerperium. Mean gestational age at the onset of hemorrhage during pregnancy was 27.7 ± 10.1 weeks.

Causes of Hemorrhage in Each Period

Figure 1, A shows the causes of hemorrhagic stroke throughout all periods (pregnancy, delivery, and puerperium). Baseline CVDs responsible for hemorrhage were detected in 54 cases (55.7%). Among all vascular lesions, AVMs are the most frequent cause of hemorrhage, followed by cerebral aneurysms and moyamoya disease. Another 3 lesions were also detected, including 2 cavernous malformations and 1 hemorrhage from the vasculature of an intraparenchymal tumor. Of all the detected CVDs, only 7 lesions (13.0%) had been diagnosed before pregnancy, and 47 lesions (87.0%) including all the aneurysms, 92.0% of AVMs, and 60.0% of moyamoya diseases had remained undiagnosed before stroke onset. Fourteen obstetric complications were identified, including pregnancy-induced hypertension, HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome, eclampsia, and disseminated intravascular coagulation. Because 2 of these complications were accompanied by bleeding from the AVM and moyamoya disease, they were categorized as “baseline CVDs,” and the other 12 cases were categorized as “obstetric complication” in Figure 1. The cause could not be determined in 31 cases (32.0%). Figure 1, B illustrates the causes of hemorrhage in each period. The CVD detection rate was