Special Theme Topic:
Stroke During Pregnancy or Delivery

Subarachnoid Hemorrhage From Intracranial Aneurysms
During Pregnancy and the Puerperium

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Abstract
Subarachnoid hemorrhage (SAH) due to the rupture of an intracranial aneurysm (IA) is a rare but serious complication of pregnancy and is responsible for important morbidity and mortality during pregnancy. This study reviewed reports of ruptured IA during pregnancy and the puerperium, and our own cases of ruptured IA in pregnant women. Hemorrhage occurred predominantly during the third trimester of pregnancy, when maternal cardiac output and blood volume increase and reach maximum. Physiological and hormonal changes in pregnancy are likely to affect the risk of IA rupture. Ruptured IAs during pregnancy should be managed based on neurosurgical considerations, and the obstetrical management of women with ruptured IAs should be decided according to the severity of SAH and the gestational age. Emergent cesarean section followed by clipping or coiling of aneurysms is indicated if the maternal condition and the gestational age allow such interventions. Although SAH during pregnancy can result in disastrous outcomes, the necessity of intracranial screening for high-risk pregnant women is still controversial.

Key words: intracranial aneurysm, pregnancy, subarachnoid hemorrhage, clipping, coiling

Introduction
Intracranial hemorrhage is the second leading cause of death during pregnancy in Japan and accounts for 5% to 12% of all maternal deaths during pregnancy in the United States.¹,² In particular, subarachnoid hemorrhage (SAH) is the third most important cause of maternal mortality during pregnancy in the United States.³ Maternal mortality due to rupture of an intracranial aneurysm (IA) ranges from 13% to 35%.³,⁴ As IA rupture is rare during pregnancy, and SAH is sometimes difficult to differentiate from eclampsia, inappropriate management may compromise maternal and fetal outcome. We report our own experience with IA rupture during pregnancy.

Epidemiology
The frequency of SAH in pregnancy is 5.8 per 100,000 deliveries according to nationwide data in the United States.⁴ The etiologies of SAH in pregnancy are diverse, so the rate of clipping or coiling in patients with pregnancy-related SAH in this study was only 12.7%, suggesting that peripartum SAH is less frequently aneurysmal than SAH occurring without pregnancy. The incidence of ruptured IA in pregnancy has been difficult to assess because of the varying figures reported so far, but is estimated to range from 3 to 10 per 100,000 pregnancies.³,¹³,²³-²⁵

Pregnancy was previously reported to not increase the likelihood of hemorrhage.¹,¹² On the other hand, the frequency of aneurysmal SAH during pregnancy increased with advancing gestational age, with more than 50% of IA ruptures occurring in the third trimester (Fig. 1).⁷ The observed increase is likely to be related to the hemodynamic and hor-
Fig. 1 Timing of subarachnoid hemorrhage from ruptured intracranial aneurysms during pregnancy and the puerperium.

Fig. 2 Location of ruptured intracranial aneurysms during pregnancy and the puerperium. ACA: anterior cerebral artery, AcomA: anterior communicating artery, ICA: internal carotid artery, MCA: middle cerebral artery, NS: not stated, PcomA: posterior communicating artery, VBA: vertebrobasilar arteries.

Monal changes in the gravid state. Cardiac output increases by 60% at the end of the second trimester. Progressive increases in blood volume and blood pressure reach the maximum values at term. Increased exposure of hormones such as estrogen, progesterone, human chorionic gonadotrophin, and relaxin may result in potential predisposition to IA formation, enlargement, and rupture. Indeed, IA growth during pregnancy was previously reported.

The aneurysmal topography is different from that of the general population. About 50% of ruptured IAs are found in the internal carotid artery (Fig. 2), whereas the most common site of IAs in the general population is the anterior communication artery (39.2%). The parity of patients was not associated with the incidence of IA rupture.

Management Strategy for IA Rupture During Pregnancy

Ruptured IA in a pregnant patient should be treated as in the non-pregnant patient. Surgical treatment should be carried out immediately in order to avoid rebleeding and ischemic complication due to vasospasm. A meta-analysis demonstrated that both mother and fetus benefit from surgical treatment after aneurysmal SAH during pregnancy. Although there are no formal studies to guide the optimal obstetric management of pregnant women with aneurysmal SAH, emergent cesarean section should be performed followed by the aneurysm exclusion procedure, if a fetus grows mature enough for survival outside the uterus. Predicted survival of preterm infants improves after 28 weeks’ gestation. During the period when intact survival of the fetus can be little expected (less than 24 weeks), surgical intervention for IAs should proceed with maintaining pregnancy. If SAH occurs between 24 and 28 weeks, therapeutic strategy should be decided individually according to the maternal and fetal status. For patients presenting with high intracranial pressure caused by massive intracerebral hematoma or acute hydrocephalus, hematoma evacuation or ventricular drainage is required in an emergency. In such a case, intraoperative fetal monitoring is important. If continuous fetal distress is discovered by monitoring, the intracranial procedure should be suspended and emergent cesarean delivery should be performed. In this situation, multidisciplinary management involving neurosurgeons, anesthesiologists, obstetricians, and neonatologists is essential. In our institution, the method and timing of neurosurgical intervention and obstetric management are determined through mutual consultation among neurosurgeons, anesthesiologists, obstetricians, and neonatologists.

Fetal cardiotocography is performed by obstetricians during the waiting time for operation and during operation, and information about fetal status is conveyed by the obstetricians as needed.

Clipping for IA Rupture During Pregnancy

Microsurgical clipping has been the method of
choice of managing patients with ruptured IAs during pregnancy. In a series of 106 patients who underwent aneurysm clipping during pregnancy, the overall maternal mortality was 11% with 5% of fetal mortality. The maternal mortality correlated with the initial clinical grade. Table 1 shows our own cases with ruptured IAs during pregnancy in the National Cerebral and Cardiovascular Center. In 4 cases, ruptured IAs were treated by clipping and resulted in satisfactory maternal and fetal outcomes, in spite of a variety of complications including rebleeding, symptomatic vasospasm, and postpartum cardiomyopathy in the peripartum period. In order to prevent delayed cerebral ischemia due to vasospasm, patients were treated with triple H therapy (hypertensive-hypervolemic-hemodilution therapy). Case 2 presented with left hemiparesis due to vasospasm on the 10th day of the onset, but developed severe congestive heart failure on the 11th day which was diagnosed as postpartum cardiomyopathy. Postpartum cardiomyopathy is a form of dilated cardiomyopathy of unclear etiology affecting women after delivery without preexisting heart disease. Even though not diagnosed as postpartum cardiomyopathy, left ventricular function of women in late pregnancy or in the puerperium is jeopardized by increased circulatory blood volume. Therefore, the fluid balance for such a patient should be managed deliberately. Fortunately, our patient recovered from both neurological symptom and heart failure after multidisciplinary treatment.

Obstetric management has changed with the times. In the earliest case, a ruptured aneurysm was clipped while maintaining pregnancy. With advances in neonatal care, cesarean section and aneurysm clipping were simultaneously performed in the following 3 cases. Normally, microsurgical clipping for ruptured IAs requires low blood pressure and induced hyperventilation to control the intracranial pressure. As these neurosurgical considerations could do harm to the fetus, we recommend cesarean delivery before aneurysm clipping if possible. Our Case 5 had a miserable outcome with maternal and fetal death. This 42-year-old woman received outpatient treatment for pregnancy complicated with hypertension. In her 28th week of pregnancy, she was found in a comatose state and transferred to our institution by ambulance. On her arrival, cardiopulmonary arrest was confirmed. Although her spontaneous circulation returned once after resuscitation, she died on the second day. Autopsy revealed a ruptured basilar tip aneurysm of 11 mm in maximal diameter (Fig. 3). This case prompted us to debate the necessity of intracranial screening for high-risk pregnant women.

Coiling for IA Rupture During Pregnancy

Coiling has become the treatment of choice for ruptured and unruptured IAs. Successful endovascular
treatment for ruptured IAs during pregnancy has been reported. In endovascular treatment during pregnancy, fetal exposure to radiation is a concern. The irradiation risk to the fetus in coil embolization during pregnancy was assessed by a phantom study. Assuming screening duration ranges for the groin of 0–30 seconds and for the head of 15–45 minutes, the absorbed fetal dose ranged from 0.17 to 2.8 mGy, which were far below the risk of hereditary disease at birth or the natural cumulative risk of fatal childhood cancer by age 15 years.

Iodinated contrast agents used for angiography also pose little risk to the mother and fetus, as far as maternal hydration is maintained in order to avoid fetal dehydration. Rather, the problem lies in the use of heparin and the difficulties in performing obstetric management in the unfamiliar environment of the angiographic suite. Endovascular surgery requires heparin-induced systemic anticoagulation to reduce the thromboembolic complications for at least the duration of embolization. Intravenous heparinization, sometimes together with antiplatelet agents, carries the risk of hemorrhagic implications when labor spontaneously commences during embolization or if emergency cesarean section should be performed before or during embolization. Another problem can arise when either spontaneous precipitous labor or sudden fetal distress occurs during embolization. Emergent cesarean section is difficult to perform in the angiographic suite. Indeed, simultaneous coiling and cesarean section has not been reported so far. In principle, the treatment of choice for aneurysms should be decided depending on the type, shape, size, and location of aneurysms even in pregnant patients. However, given the above-mentioned problems, clipping would be recommended over coiling if an aneurysm can be safely treated by both procedures. As incomplete obliteration of IAs can result in coil compaction or re-growth of the residual neck especially during pregnancy, tight packing of coils must be achieved in pregnant patients.

### Intracranial Screening for High-Risk Pregnant Women

There is no evidence-based consensus or guidelines about the management strategy for unruptured IAs in pregnant women. In our institution, we have performed intracranial screening for high-risk cases selected by the criteria listed in Table 2 after the stage of organogenesis (after the 12th week of preg-

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**Table 2 Criteria for intracranial screening for high-risk pregnant women in the National Cerebral and Cardiovascular Center (since January 2009)**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Chronic hypertension</td>
<td>( \geq 160/110 \text{ mmHg} )</td>
</tr>
<tr>
<td>2: Past history of CVD</td>
<td></td>
</tr>
<tr>
<td>3: Age ( \geq 40 \text{ yrs} )</td>
<td></td>
</tr>
<tr>
<td>4: Family history of CVD in parents</td>
<td></td>
</tr>
<tr>
<td>5: Chronic headache</td>
<td></td>
</tr>
<tr>
<td>6: Pregnancy-induced hypertension</td>
<td></td>
</tr>
<tr>
<td>7: Obesity (BMI ( \geq 25 \text{ kg/m}^2 ))</td>
<td></td>
</tr>
</tbody>
</table>

Head magnetic resonance angiography is indicated if a patient meets either criteria 1 or 2, AND any combination of 2 or more of the criteria 3, 4, 5, 6, 7. BMI: body mass index, CVD: cerebrovascular disease.

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**Table 3 Results of intracranial screening for high-risk patients (2009–2011)**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>1: Chronic hypertension</th>
<th>2: Past history of CVD</th>
<th>3: Age (yrs)</th>
<th>4: Family history of CVD</th>
<th>5: Chronic headache</th>
<th>6: Pregnancy-induced hypertension</th>
<th>7: BMI (kg/m²)</th>
<th>Results of MR angiography</th>
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<td>no</td>
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<td>no</td>
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<td>37</td>
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<td>no</td>
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<td>41</td>
<td>no</td>
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<td>no</td>
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<td></td>
</tr>
</tbody>
</table>

**Shaded columns indicate cases which meet the criteria.** BMI: body mass index, CVD: cerebrovascular disease, MR: magnetic resonance.
nancy) since 2009. From 2009 to 2011, 11 patients were screened by magnetic resonance (MR) angiography and an unruptured IA was detected in 2 cases (Table 3). MR angiography screening was primarily proposed by obstetricians and, if any intracranial vascular lesions were detected, neurosurgeons were consulted about the risk of hemorrhage or infarction in each case. The delivery method and surgical indication for intracranial lesions were decided through discussion between neurosurgeons and obstetricians.

Case 9 was a 38-year-old woman referred to our institution because of pregnancy-induced hypertension. She had a family history of SAH and suffered from chronic headache. She was complicated with hypertension and obesity (body mass index [BMI] 26 kg/cm²). MR angiography for intracranial screening showed a saccular aneurysm in the left vertebral artery of 4 mm in diameter. At her 37th week of pregnancy, she underwent elective cesarean section because of further elevation of blood pressure and proteinuria. The aneurysm has been closely followed up without surgical intervention.

Case 12 was a 37-year-old woman, complicated with hypertension, diabetes mellitus, and obesity (BMI = 41.3 kg/cm²). She had a family history of SAH. MR angiography for intracranial screening revealed an unruptured anterior communicating artery aneurysm of 8 mm in diameter. Her blood pressure was strictly controlled until the 37th week of pregnancy when she underwent elective cesarean section. The aneurysm was treated by endovascular coil embolization one year after delivery.

The necessity of intracranial screening for high-risk patients is controversial and its cost effectiveness should be discussed. The best way of delivery for pregnant women harboring unruptured IAs has not been determined. Recently, no increased association was reported between pregnancy or delivery and the risk of rupture of IAs. Cesarean delivery was considered not necessary in pregnant women complicated with IAs. However, I wonder if this rule should also be applied to high-risk cases, for example, patients complicated with marked hypertension. Given the devastating consequence of SAH, we should try to find some kinds of solution to reduce its incidence. At least, appropriate counseling is needed if an unruptured IA is found in a woman who desires to bear children.

Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

References


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