Object: We report a case of endovascular surgery for subarachnoid hemorrhage (SAH) that developed in early pregnancy. Case Presentations: An 8-week pregnant 35-year-old female was admitted to our hospital with severe headache and loss of consciousness. Cephalic computed tomography (CT) revealed SAH (Hunt and Hess grade II). Digital subtraction angiography (DSA) demonstrated a 2.7 mm aneurysm at the right internal carotid artery-posterior communicating artery (IC-PC) bifurcation. We prioritized maternal treatment. Cerebral aneurysm coil embolization was performed on the 1st day under general anesthesia. During the operation, we tried to avoid irradiating the fetus by limiting the irradiation range and time. She was discharged on the 36th day of illness and gave birth to a 2532-g baby at 36 weeks of gestation. Conclusion: If SAH develops in early pregnancy, it is necessary to prioritize maternal treatment. Endovascular surgery should be considered as a treatment option.

Keywords ▶ subarachnoid hemorrhage, first trimester of pregnancy, coil embolization of intracranial aneurysms, radiation exposure

Introduction

The incidence of subarachnoid hemorrhage (SAH) during pregnancy is 0.01–0.05%, being rare. In addition, the prognosis of patients with ruptured aneurysms during pregnancy is markedly poor: additional hemorrhage, 31–50%; mortality rate, 50–68%.1,2 Therefore, if SAH develops, treatment must be performed as early as possible. Previous studies recommended that craniotomy be performed to treat SAH in pregnant women according to surgical indications.3,4 On the other hand, embolization of intracranial aneurysms has recently been performed for many patients, suggesting its efficacy for both mothers and fetuses.1,5–11 However, few studies have reported endovascular treatment in the first trimester of pregnancy, and the influence of fetal exposure to radiation and drugs remains to be clarified. We report a patient in whom coil embolization was performed to treat SAH related to a ruptured aneurysm at the right internal carotid artery-posterior communicating artery (IC-PC) bifurcation in week 8 of pregnancy.

Case Presentation

Medical history: Not contributory.

Present illness: After defecation in the toilet, headache involving the occipital region and transient fainting suddenly developed. She was brought to our hospital by ambulance.

Physical examination on admission: Regarding the consciousness level, the Japan Coma Scale (JCS) score was 1 and the Glasgow Coma Scale (GCS) score was E4V5M6. Headache and vomiting were noted, but there were no abnormal neurological findings.

Laboratory data on admission: Cephalic computed tomography (CT) revealed dominant SAH on the right side with the basal cistern and mild hydrocephalus (Fig. 1A). Digital subtraction angiography (DSA) of the right internal carotid artery through right brachial artery puncture demonstrated an aneurysm measuring 2.2 × 2.7 mm at the right IC-PC bifurcation (Fig. 1B). In general, aneurysms should be investigated using CT angiography, but in the present case, it was necessary to minimize the exposure dose and volume of contrast medium; therefore, DSA through right brachial artery puncture was selected. The neurological severity of SAH was evaluated as Hunt & Hess grade II and WFNS grade II.

![Fig. 1](image1.jpg)

Fig. 1 (A) CT on admission shows a diffuse subarachnoid hemorrhage and enlargement of the inferior horn of lateral ventricles. (B) Pre-embolization Rt.ICAG shows a small aneurysm at the internal carotid artery-posterior communicating artery bifurcation. (C) Post-embolization Rt.ICAG shows dome embolization of the ruptured aneurysm. Rt.ICAG: right internal carotid artery angiograms

![Fig. 2](image2.jpg)

Fig. 2 Postoperative MRA indicates no cerebral vaso-spasm. And the aneurysm was disappeared.

MRA: magnetic resonance imaging
Is Coil Embolization a Useful Treatment during Early Pregnancy?

Treatment: As SAH developed in the first trimester of pregnancy, maternal lifesaving-prioritized treatment was adopted. To reduce maternal invasiveness, coil embolization was selected. Under general anesthesia, a 6Fr long sheath was inserted into the right femoral artery. In addition to the systemic administration of heparin at 3500 units, continuous intravenous injection of 1300 units/h was started. To avoid pelvic exposure, a radiation protector was attached to the back, and fluoroscopy was performed only on the cephalic side to the diaphragm. A 6Fr Fubuki Guiding Catheter (Asahi Intecc Co., Ltd, Aichi, Japan) was inserted into the right internal carotid artery and an Excelsior SL-10 (Stryker, Kalamazoo, MI, USA) was guided into the aneurysm. Framing was initially conducted using a Target360 Ultra 2 mm × 3 cm (Stryker). Subsequently, Target 360 Nano coils measuring 1.5 mm × 2 cm and 1 mm × 2 cm, respectively, were inserted into the aneurysm. Cerebral angiography immediately after embolization revealed a neck remnant, but the complete disappearance of the dome was confirmed. Furthermore, to reduce exposure, the frequency of imaging was minimized (DSA: 5 times (including 3D-DSA and working-angle imaging), coil embolization: 8 times). However, in the present case, abdominal exposure monitoring was not performed, and the volume of contrast medium was not measured. At the site of puncture, hemostasis by manual compression was performed.

Postoperative course: After surgery, a lumbar drain was inserted and fasudil hydrochloride was intravenously administered for 14 days. In addition, cilostazol at 200 mg/day was orally administered for the same period. Magnetic resonance (MR) angiography 7 days after surgery did not demonstrate cerebral vasospasm or recurrent aneurysm (Fig. 2). Regarding the subsequent course, the patient was discharged on the 36th postoperative day with a modified Rankin Scale score of 0. On day 1 of week 36 of pregnancy, a baby weighing 2532 g was born transvaginally. Both maternal and neonatal courses have been favorable.

Discussion

SAH during pregnancy is markedly rare, but the maternal mortality rate is reportedly 13–35% and the fetal mortality rate is 7 to 25%.10) There is no unified view as to whether obstetric treatment or neurological treatment precedes when SAH developed during pregnancy, but it is recommended that treatment be performed in accordance with maternal lifesaving-prioritized treatment.12) A previous study reported that surgical intervention improved the fetal prognosis in addition to the maternal state2; therefore, it should be started as early as possible. In cases of SAH at a time when a fetus may survive in an extramaternal space, ruptured aneurysm treatment is routinely performed after extraction of the fetus.10) On the other hand, if extraction is difficult, treatment must be conducted while continuing pregnancy. In such cases, which of two procedures, craniotomy and embolization, should be selected remains controversial. We
examined whether coil embolization can be a pre-delivery treatment option for SAH in the first trimester of pregnancy.

Epidemiology

We investigated 167 previously reported patients including our patient. The distribution of patients with respect to the gestational age at the onset of SAH (Fig. 3A) and ruptured aneurysm sites (Fig. 3B) are presented. The incidence of SAH was low before week 15 of pregnancy, that is, the first trimester of pregnancy, whereas it was the highest in weeks 30–34. As for the timing of cerebral aneurysmal rupture in pregnant women, a peak was reported at 8 months of pregnancy. At this point, the risk of cerebral aneurysmal rupture is two times higher than that in non-pregnant women.4) This may be because the circulating blood volume after 7 months of pregnancy is approximately 1.5 times larger than that during non-pregnancy periods, and because an increase in the estrogen level leads to vasodilation.5) The most frequent site of aneurysmal rupture was the internal carotid artery (30%), differing from the rupture rate in non-pregnancy periods.

Radiation

The influence of radiation exposure on embryos/fetuses depends on the radiation dose and timing. In the organogenesis phase before week 8 of pregnancy, the radiation sensitivity of fetal anomalies is high, with a threshold of ≤500 mGy.13) Furthermore, the radiation sensitivity of the central nervous system is the highest between weeks 8 and 15 of pregnancy. Radiation exposure at approximately 1000 mGy may induce mental retardation at a high probability. According to the recommendations published by the International Commission on Radiological Protection (ICRP), a threshold, which is the limit dose for definitive effects on anomalies, is 100 mGy with respect to the influence of intra-uterine exposure on fetuses, and the threshold of psychomotor retardation is 100–200 mGy. However, fetal radiation exposure at ≤100 mGy cannot be accepted as a reason for abortion.14) A previous study examined the abdominal exposure dose under fluoroscopy/imaging conditions through a right brachial artery approach using a human body phantom, and found that the maximum radiation dose was approximately 800 mGy around the external occipital protuberance, whereas the mean and maximum radiation doses for the lower abdomen were 0.05 and 0.07 mGy, respectively, being markedly low.13) If the head is exposed to approximately 5000 mGy of radiation during neuroendovascular treatment, the reproductive gland radiation dose may be approximately 0.5 mGy, which corresponds to 0.01% of the maximum cephalic radiation dose; this is below the reference value published by the ICRP, ≤100 mGy. In addition, to reduce the exposure to fetuses (1) for postoperative hemostasis, hemostatic devices requiring fluoroscopy should not be used, and manual compression should be performed, (2) a transbrachial approach should be adopted, (3) the area below the diaphragm should not be irradiated, (4) a protector should be used on the patient’s back, and (5) the frequency of DSA and pulse rate should be reduced. Radiation protection for the abdomen involving the above points may reduce fetal radiation complications related to neuroendovascular treatment.

Contrast medium

The safety of iodine contrast medium in fetuses has not been established and its use should be avoided if possible. However, to prioritize maternal lifesaving, its use cannot be avoided.15) According to the European Society of Urogenital Radiology (ESUR) guidelines,16) no study has reported the teratogenicity of contrast medium. However, the Food and Drug Administration (FDA) classified contrast medium as Category B (no evidence regarding risks in humans) according to the fetal drug risk classification criteria. To our knowledge, no study has reported any disorder, including teratogenicity, related to endovascular treatment for ruptured aneurysms in pregnant women. In four patients, including ours, treatment was performed in weeks 4–15, that is, in the first trimester of pregnancy. However, there were no maternal or fetal complications in any patient after embolization. Michikawa et al. reported a patient who underwent embolization and extirpation for cerebral arteriovenous malformation in week 9 of pregnancy, leading to favorable maternal and fetal courses.17) Thus, in pregnant women, contrast medium should be used if necessary.

Anesthetics

Coil embolization can be performed under general or local anesthesia. From the viewpoint of maternal safety or intraoperative hemorrhage prevention, general anesthesia is recommended. After week 33, when the lungs become functional, it is possible to perform treatment after cesarean section, reducing the risk of general anesthesia. However, before week 33, there is only one option to continue pregnancy after treatment. In general, general anesthesia is selected after the second trimester of pregnancy (week 16 of pregnancy), when the organogenesis phase is almost completed. However, a previous study reported no teratogenicity.
even in patients in whom general anesthesia was adopted before week 16 of pregnancy. Therefore, considering the teratogenicity of anesthetics and their influence on the uterus/placenta, aneurysm treatment should be prioritized if necessary. In such cases, as labor pains may be induced during surgery through the actions of drugs, such as anesthetics, on the uterine muscle, caution is needed.

**Other drugs**

The FDA classified cilostazol as Category C (no controlled study involving humans has been conducted). Although no sufficiently managed study involving humans has been performed, cilostazol is available for pregnant women only when its benefits exceed its risks. A previous study involving the intravenous administration of fasudil hydrochloride to rabbit fetuses demonstrated the no-observed-effect level to be 6 mg/kg, and there were no unfavorable effects on fetuses in the third trimester of pregnancy. Regarding the use of ozagrel sodium in pregnant women, its safety has not been established, and it may be administered only when its therapeutic benefits are considered to exceed its risks. On the other hand, the oral administration of ozagrel sodium at 400 mg/day from week 20 of pregnancy until delivery did not induce any maternal or fetal adverse reactions. No study has examined the safety of fasudil hydrochloride in human fetuses; therefore, ozagrel sodium may be safer than fasudil hydrochloride.

Only seven patients with SAH in the first trimester of pregnancy, including our patient, have been reported, and endovascular treatment was performed for four patients (Table 1). Therapeutic strategies and fetal prognosis remain controversial, and management is difficult. The selection or timing of aneurysm treatment should be evaluated based on the pregnancy term, general condition, and maternal/fetal risk factors. In particular, treatment by coil embolization is minimally invasive for mothers. With respect to the influence of radiation or anesthetics on fetuses, there have been no serious adverse reactions. In the present case, we concluded that there was little influence of SAH treatment on the maternal or fetal states from coil embolization to delivery. However, few studies have examined endovascular treatment in the first trimester of pregnancy. In the future, this must be further investigated.

### Conclusion

We report a patient with SAH in week 8 of pregnancy for whom coil embolization was performed, leading to favorable

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**Table 1**

Summary of reported cases of endovascular treatment of aneurysmal subarachnoid hemorrhage in early pregnancy

| Author              | Year | Age (years) | H&H grade | GA (weeks) | Location | Size (mm) | Treatment | Material outcome | Fetus outcome | Delivery | Birth (weeks) | Current case | Year | Age (years) | H&H grade | GA (weeks) | Location | Size (mm) | Treatment | Material outcome | Fetus outcome | Delivery | Birth (weeks) |
|---------------------|------|-------------|-----------|------------|----------|----------|-----------|-----------------|--------------|----------|---------------|-------------|------|-------------|-----------|------------|----------|----------|-----------|-----------|-----------------|--------------|----------|---------------|
| M. Meyers          | 2000 | 34          | II        | 11         | PCA      | 20       | NE        | Favorable       | NE           | Vaginal delivery | 38          |      |             |           |            |           |          |           |          |                   |              |          |               |
| O. Ikarić           | 2003 | 25          | II        | 10         | P-com    | 10       | NE        | Favorable       | Favorable    | Abortion          | 38          |      |             |           |            |           |          |           |          |                   |              |          |               |
| K. Hasegawa        | 2003 | 35          | III       | 10         | A-com    | SC       | SC        | Favorable       | Favorable    | Abortion          | 38          |      |             |           |            |           |          |           |          |                   |              |          |               |
| H. Roman           | 2004 | 37          | III       | 12         | ICA      | SC       | SC        | Favorable       | Favorable    | Abortion          | 38          |      |             |           |            |           |          |           |          |                   |              |          |               |
| Andreas T          | 2009 | 32          | II        | 10         | ICA      | SC       | SC        | Short term      | Favorable    | Vaginal delivery | 32          |      |             |           |            |           |          |           |          |                   |              |          |               |
| M. Miyahara        | 2016 | 32          | V         | 9          | ICA      | 12       | NE        | Favorable       | Memory disorder | Caesarian section | 32          |      |             |           |            |           |          |           |          |                   |              |          |               |
| Current case       | 2019 | 35          | II        | 8          | P-com    | 2        | NE        | Favorable       | Vaginal delivery | 36          |          |               |           |            |           |          |           |          |                   |              |          |               |
maternal and fetal courses. As a rule, maternal lifesaving should be prioritized in the treatment of SAH in the first trimester of pregnancy. Endovascular treatment must be considered as an option.

Disclosure Statement
We declare no conflict of interest regarding this article.

References