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Case Report

Thrombolysis and Mechanical Thrombectomy for Acute Ischemic Stroke in Pregnancy: A Case Report

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Objective: Intravenous (IV) recombinant tissue plasminogen activator (rt-PA) and mechanical thrombectomy (MT) are effective treatments for acute ischemic stroke (AIS). However, the treatment for AIS in pregnancy is not established because no clinical trials have included pregnant patients. We present a case of middle cerebral artery (MCA) M2 segment occlusion in pregnancy treated with IV thrombolysis and endovascular therapy.

Case Presentation: A 36-year-old woman being 6 weeks pregnant presented with right-sided hemiparesis and aphasia. MRI showed a high-intensity area on diffusion-weighted imaging of the left parietal lobe, and MRA showed left MCA M2 segment occlusion. She underwent IV rt-PA and MT and achieved thrombolysis in cerebral infarction 2b revascularization without complications. The protein S concentration was lower than that in the physiological changes during pregnancy. She was diagnosed with embolic stroke related to coagulopathy in pregnancy, and she underwent anticoagulation. At the 3-month follow-up, the modified Rankin Scale was 0. She miscarried at 4 months, and the fetal death was presumed to be obstetric cause.

Conclusion: IV rt-PA and MT may be effective and safe treatments for pregnant patients. Estimated fetal radiation exposure during MT is low and is presumed not to affect fetal development. We should mitigate the radiation dose and reduce the dose of iodinated contrast agents, particularly in pregnant patients.

Keywords ▶ pregnancy, mechanical thrombectomy, thrombolysis, ischemic stroke

Introduction

Acute ischemic stroke (AIS) in pregnancy is rare, with an incidence of 10.2 cases per 100000 deliveries in Japan[1)]; however, it is a cause of maternal and fetal morbidity and mortality. Although the efficacy of intravenous (IV) recombinant tissue plasminogen activator (rt-PA) and mechanical thrombectomy (MT) is established for AIS, pregnant women were not included in previous randomized controlled studies, and the efficacy and safety in pregnant patients with AIS are unclear.[2)] We report a case of middle cerebral artery (MCA) M2 segment occlusion in pregnancy treated with IV rt-PA and MT and present a literature review.

Case Presentation

A 36-year-old woman being 6 weeks pregnant (gravidity 4, parity 2, miscarriage 1) presented with right-sided facial paresis, hemiparesis, and motor aphasia. Her National Institutes of Health Stroke Scale (NIHSS) score was 2. MRI showed a high-intensity area on diffusion-weighted imaging of the left parietal lobe. MRA demonstrated left MCA M2 segment occlusion (**Fig. 1**). She had a history of Hashimoto's thyroiditis and received 75 μg of levothyroxine sodium hydrate per day. There was no problem of gestation, and no risk of hemorrhage. As there were no contraindications,

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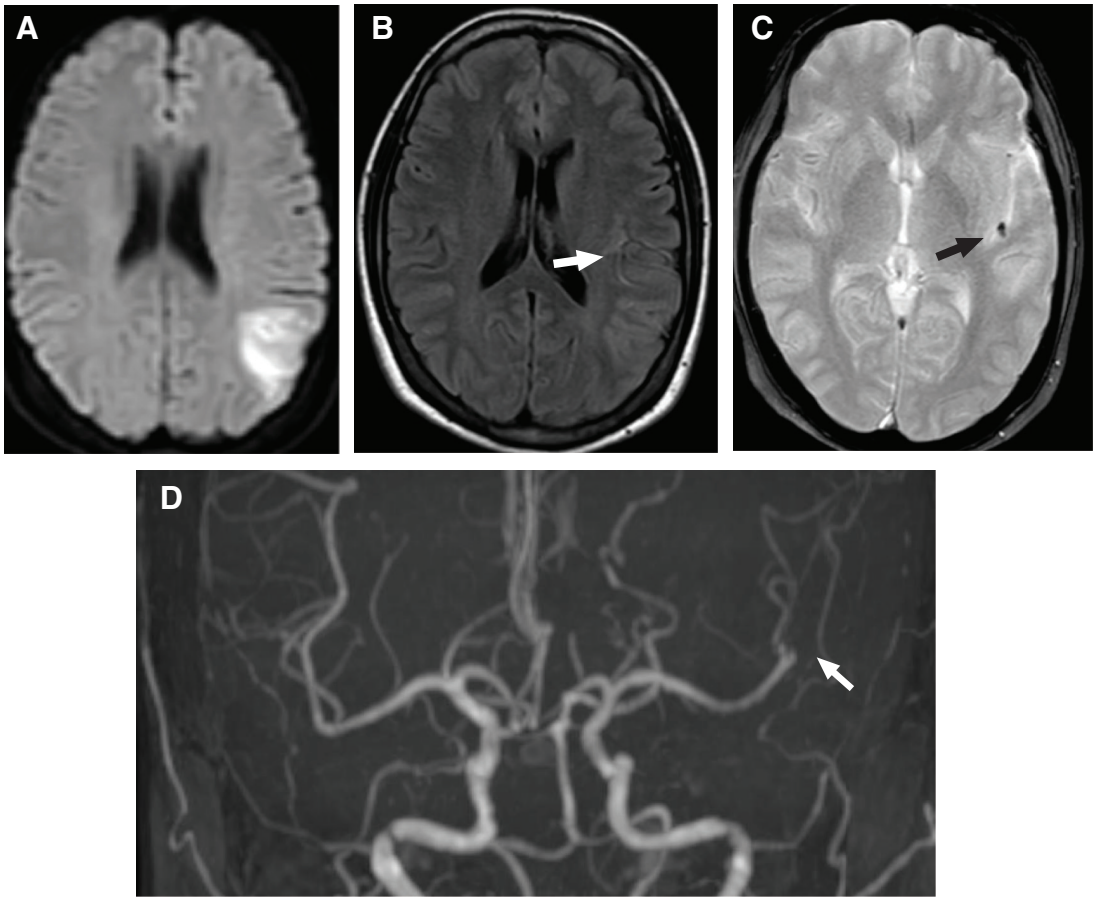

Fig. 1 (**A**) Diffusion-weighted imaging revealed a high intensity area of the left parietal lobe. (**B**) Hyperintensity vessel sign was positive on FLAIR (white arrow). (**C**) Susceptibility vessel sign was positive on T2*-weighted imaging (black arrow). (**D**) MRA revealed left MCA M2 segment occlusion (white arrow). MCA: middle cerebral artery

the patient underwent IV rt-PA 192 minutes after the onset of symptom. According to the guideline for IV thrombolysis (rt-PA), the third edition,[3] the dose of IV rt-PA was 0.6 mg/kg body weight, total of 10% was given as an initial bolus, and 90% was infused over 60 minutes. The aphasia was moderate and could be an obstacle to parenting and work. We explained to her husband who is a doctor about the efficacy and the risks of MT for the patient and her infant. After the discussion, we decided to let her receive MT. Groin puncture was performed with local anesthesia 202 minutes after the onset of symptom, and MT was performed. During the procedure, monoplane fluoroscopy was used. At first, a 9F Optimo catheter (Tokai Medical Products, Aichi, Japan) was placed in the left internal carotid artery. Occlusion of the left MCA M2 inferior trunk was confirmed (**Fig. 2A**). Using a Penumbra 3MAX catheter (Penumbra, Alameda, CA, USA) and Trevo 3 mm × 20 mm retriever (Stryker, Kalamazoo, MI, USA), first pass was performed in the left M2 (**Fig. 2B**). After first pass of the Trevo retriever with continuous manual aspiration of the 3MAX catheter, M2 inferior trunk was recanalized, but the superior trunk was occluded with the thrombus, which moved proximally (**Fig. 2C**). The second pass was performed in the occluded branch using the Trevo retriever and 3MAX catheter, and a red clot was retrieved. Post-thrombectomy angiography showed recanalization of the left MCA M2 segment (**Fig. 2D**). Endovascular treatment was performed within 52 minutes, resulting in successful revascularization and thrombolysis in cerebral infarction grade 2b (onset to recanalization time was 254 minutes). The total radiation dose for MT was 620.1 mGy, and the total exposure time was 20.5 minutes. The total use of iodinated contrast agents was 170 ml of iopamidol. After the procedure, the head CT showed no intracerebral hemorrhage. The patient's gravid uterus was protected using a lead protector during the endovascular procedure and head CT scanning.

She developed slight aphasia (NIHSS score 1) after MT and initiated rehabilitation. Initially, she was administered a

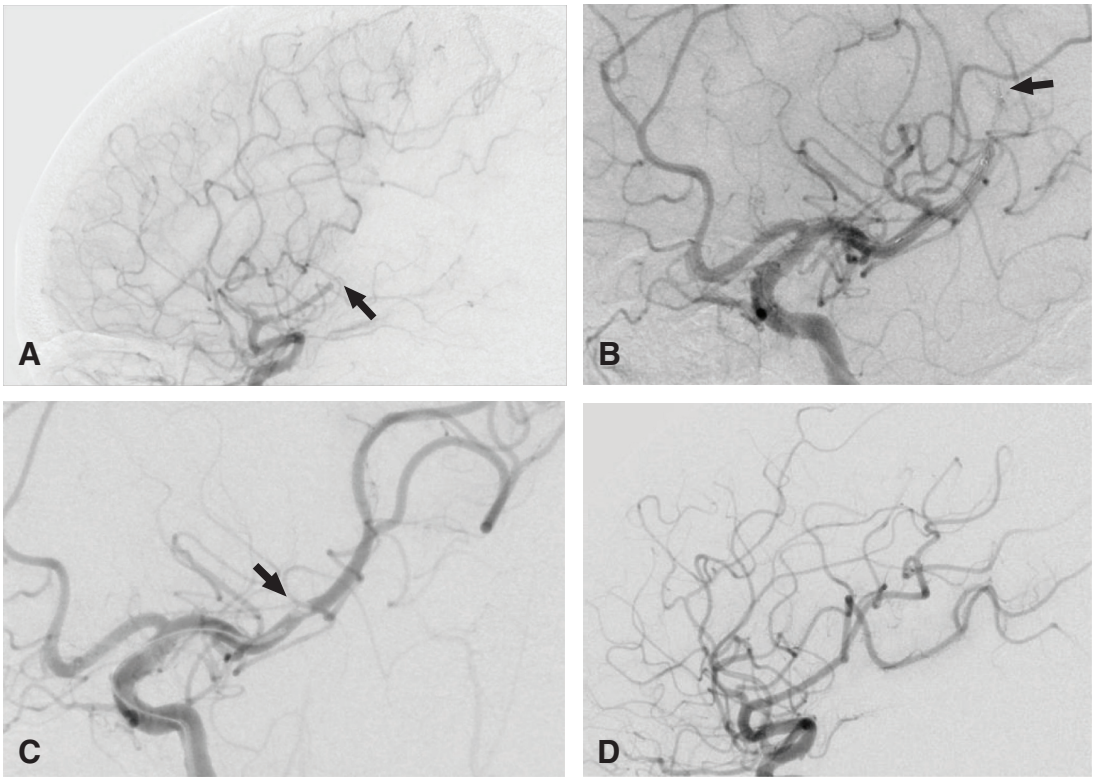

Fig. 2 (**A**) Left internal carotid artery angiography demonstrated occlusion of the left MCA M2 segment (black arrow). (**B**) Trevo 3 mm × 20 mm was deployed in the left MCA M2 segment. Black arrow shows the distal tip of the Trevo. (**C**) After first pass, angiography showed the inferior trunk recanalization and the superior trunk occlusion with the migrated thrombus (black arrow). (**D**) Post-thrombectomy angiography showed recanalization of the left M2 segment. MCA: middle cerebral artery

continuous heparin infusion. Electrocardiogram monitoring showed no atrial fibrillation. Laboratory results were as follows: red blood cell, 460 × 10^4/μl; hemoglobin, 13.3 g/dl; platelets, 21.8 × 10^4/μl; activated partial thromboplastin time (APTT), 32 seconds; prothrombin time-international normalized ratio (PT-INR), 1.03; d-dimer, 1.5 μg/ml; free protein S, 35 %; protein S activity, 28%; protein C activity, 72 %; and antithrombin III activity, 73%. Laboratory studies indicated reduced free protein S levels and its activity slightly lower than that in the physiological changes during pregnancy. Protein C activity was within the normal range, and the d-dimer was slightly high. Furthermore, thrombophilia screening yielded negative results for antinuclear antibody, anticardiolipin immunoglobulin, and lupus anticoagulant. Transthoracic echocardiography showed patent foramen ovale and a right-to-left shunt (high degree of shunting with the Valsalva maneuver). Deep vein thrombosis (DVT) was not confirmed on ultrasound. Therefore, continuous heparin infusion was replaced with subcutaneous injection based on the diagnosis of embolic stroke related to coagulopathy during pregnancy. Although the fetus growth was progressing well until 13 weeks of gestation, intrauterine fetal death (IUFD) was confirmed on ultrasound. The fetus was delivered at 15 weeks and 2 days (36 days after the onset of symptom). The cause of unexpected IUFD was unrevealed, but presumed to be an obstetric factor. After delivery, the protein S concentration returned to within the normal range; thus, she discontinued receiving subcutaneous heparin injections. She had no neurological deficit, and the modified Rankin Scale was 0 after the delivery.

Discussion

This case report described the treatments for MCA M2 segment occlusion in pregnancy: IV rt-PA and MT. Previous case reports and case series have shown the efficacy and safety of IV rt-PA.[4,5] Rt-PA has a large molecular size, so does not cross the placenta, and previous reports have demonstrated no effect of fetal development in animal models.[4)] Recently, case reports of MT for AIS in pregnancy have increased in number and suggested its efficacy and safety (**Table 1**).[4,6–10] In our case, although her NIHSS score was 2 and the site of occlusion was MCA M2 segment, the aphasia was moderate and could be an obstacle to parenting and work. The efficacy and

Table 1 Summary of reported cases of treated mechanical thrombectomy in pregnancy

Case	Author (year)	Age	Gestation (weeks)	IV rt-PA	TICI	Maternal outcome (mRS/time)	Fetal outcome
1	Aaron et al. (2016)	24	3rd trimester	(–)	Partial recanalization	0/after 6 months	Healthy
2	Aaron et al. (2016)	28	37	(–)	Partial recanalization	2/after 6 months	Healthy
3	Bhogal et al. (2017)	38	24	(–)	2b	1/after 8 years	Healthy
4	Bhogal et al. (2017)	36	25	(+)	NR	1/after 1 day	Pregnancy ongoing
5	Shah et al. (2018)	37	9	(+)	2b	1/after 3 months	Pregnancy ongoing
6	Watanabe et al. (2019)	36	21	(+)	2b	1/after 6 months	Healthy
7	Blythe et al. (2019)	29	39	(–)	3	0/after 6 weeks	Healthy
8	Tse et al. (2019)	28	39	(–)	3	1/after 5 days	Healthy
9	Tse et al. (2019)	27	36	(–)	3	0/after 2 days	Healthy
10	Tse et al. (2019)	36	8	(+)	2b	1/NR	Healthy
11	This case	36	6	(+)	2b	0/after 3 months	Death

IV rt-PA: intravenous recombinant tissue plasminogen activator; mRS: modified Rankin Scale; NR: not reported; TICI: thrombolysis in cerebral infarction

safety of MT for patients with M2 segment occlusion have not been established; however, Miura et al. suggested the efficacy and safety of MT for patients with M2 segment occlusion compared with medical treatment.[11] After a discussion about the efficacy and the complication of MT for MCA M2 segment occlusion with her husband, we decided to let her receive MT. The maternal outcome was good, but the fetal outcome was finally unfavorable.

Fetal radiation exposure during MT is estimated to be low.[12,13] The influence on the fetus is dependent on both the exposed dose and the developmental stage at the time of exposure. During the preimplantation phase (0–8 days), the radiation dose threshold of abortion (fetal death) is estimated to be 100 mGy. After the preimplantation phase, the influence of radiation on fetal death becomes lower. Normal maturation may be affected, when the gravid uterus was exposed to 100–200 mGy radiation dose in the organogenesis period (2–8 weeks). The radiation dose threshold of mental retardation is estimated to be 120 mGy in the organogenesis period (8–15 weeks).[12,13] Ishii and Miyamoto reported that the absorbed fetal radiation dose is measured to be 2.8 mGy in a general endovascular procedure (assuming that the radiation exposure durations of the groin is 30 seconds and head is 45 minutes).[12] Tanaka et al. reported that the estimated fetal mean radiation dose is approximately 0.05 mGy, when the maternal head maximum exposure is approximately 800 mGy.[13] In our case, the total radiation dose was 620.1 mGy and the total radiation duration was 20.5 minutes; thus, the estimated fetal radiation dose was low and not above the threshold of fetal death or malformation.

Clinical methods should be considered to minimize fetal radiation exposure during MT. Although the estimated fetal radiation dose is low during the procedure, lower exposure is desirable. Several clinical methods in order to reduce fetal radiation exposure have been suggested as follows: the use of monoplane fluoroscopy where feasible, shielding of the gravid uterus using a lead apron, insertion of a sheath with minimal scanning, performance of the procedure via transradial or transbrachial access, reduction of the air gap between the flat panel detector and patient, and minimal use of magnification.[8,10] In the present case, we performed these methods except for via transradial or transbrachial access, we underwent transfemoral MT. These clinical methods led to a reduction of fetal radiation exposure. Additionally, physicians should put a radio-photoluminescence dosimeter on her abdomen in order to get a more accurate dose of gravid uterus and consider the side-lying position during treatment after introducing the sheath in the third trimester of pregnancy.

IV iodinated contrast agents can be used in pregnancy, but its risk is uncertain, and caution is warranted. IV iodinated contrast agents have been shown to cross the placental blood barrier and enter the fetal circulation; however, in vivo tests in animals have shown no teratogenicity. A report has suggested that hypothyroidism develops in newborns after the administration of iodinated contrast agents during pregnancy; however, another report has suggested that there is no difference in neonatal thyroid function.[2,10] A report suggested that iodinated contrast agents could be used in pregnant patients in the same dose as in non-pregnant patients when needed.[14] In our case, we use 170 ml of

iodinated 300 mg/ml contrast agents. Iodinated contrast agents can be used in pregnant patients when it is significant to make diagnosis or treatment to the patients; however, we should keep in mind to keep it to the minimum dose.

The etiology of ischemic stroke in this case is uncertain, but reduced protein S activity may be related to the cause of stroke. During pregnancy, coagulation activity tends to increase. Several clotting factors increase, and anticoagulant factors such as protein S decrease with physiological changes.[2] Said et al. reported that the mean activity of protein S in pregnancy was about a half of that in non-pregnant woman.[15] In this case, protein S activity was slightly lower than that in the physiological changes during pregnancy. Because the patient's concentration of protein S returned to within the normal range after delivery, genetic protein S deficiency was ruled out. We considered the etiology of the infarction to be a paradoxical embolism, but DVT was not detected and there was no situation of her in the same posture for a long time until the symptom onset. Coagulopathy related with pregnancy may have caused ischemic stroke in the present case.

Conclusion

We reported a case of MCA M2 segment occlusion in pregnancy treated with IV rt-PA and MT. Although the maternal outcome was good, the fetal outcome was finally unfavorable. Estimated fetal radiation exposure during MT is low and is presumed not to affect fetal development. Physicians should always consider reducing the radiation dose and the dose of iodinated contrast agents.

Disclosure Statement

The authors have no conflicts of interest directly relevant to the content of this report.

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