CASE REPORT

An Early Pregnant Chinese Woman with Cerebral Venous Sinus Thrombosis Succeeding in Induction of Labor in the Second Trimester

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Abstract Cerebral venous sinus thrombosis (CVST) is a rare condition in early pregnancy. A 22-year-old Chinese woman at 10 weeks of pregnancy requested induced abortion and was diagnosed as CVST for a severe headache accompanying with nausea and vomiting. The patient was treated successfully with anticoagulation, followed by amniocentesis, and finally succeeded in induction of labor safely. The diagnosis, treatment and prognosis for this rare condition are discussed in this paper.

CEREBRAL venous sinus thrombosis (CVST) is a rare and life-threatening condition, accounting for about 0.5-1% of all strokes.¹ It usually occurs in infant, young adults, and female, especially during late pregnancy and puerperium, and relatively rare in early pregnancy. The experience in management of such patient is limited according to the literatures available by far. Here, we present a pregnant woman requesting induced abortion who was diagnosed as CVST in the first trimester, recovered after anticoagulation therapy, and succeeded in induction of labor in the second trimester without

any complication.

CASE DESCRIPTION

A 22-year-old Chinese woman, gravida 1 para 0 at 10 weeks of pregnancy, was admitted to the Family Planning ward for a request of induced abortion as she was unmarried. Three days after admission, she suffered from continuous severe headache, accompanying with nausea and vomiting. She had no other symptoms, such as abdominal pain, vaginal bleeding, fever, rash, seizure or diplopia. The headache progressed in severity the next day. The patient recalled her migraine headache occurred every summer since she was 14-year-old, but the headache was mild and automatically resolved in several days, only occasionally gastrodia was applied to relieve the pain. The patient declined any personal history of cerebral trauma, other medical diseases, and family history of similar condition.

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The vital signs were stable at admission. Physical examination showed a stiff neck without focal neurological findings. Blood examinations excluded connective tissue diseases and infectious diseases. Anticardiolipin antibodies in serum by enzyme-linked immunosorbent assay were negative. The d-dimer was abnormally elevated to 5.01 mg/L, but her coagulation profile was normal. The general screening of thrombophilia including protein C and protein S revealed a decreased level of protein S. Homocysteine in serum was normal. Cerebral CT showed a high intensity in the right parietal lobe (**Fig. 1A**). Magnetic resonance image (MRI) revealed an iso-signal intensity lesion on T1-weighted image (T1WI) (**Fig. 1B**) and a hypo-signal intensity lesion on T2-weighted image (T2WI) in superior sagittal sinus. Magnetic Resonance venography (MRV) showed that the superior sagittal sinus, right transverse sinus were completely occluded (**Fig. 1C, 1D**). Magnetic Resonance Angiography (MRA) did not show any abnormality.

The patient was diagnosed as cerebral venous

sinus thrombosis after consulting with the neurology team and was transferred to the neurological ward. To control intracranial hypertension, mannitol was administered intravenously and low molecular weight heparin (LMWH) subcutaneously with dose adjusted by her weight soon after admitted. One week after the initiation of the treatment, warfarin was added orally. The dose of warfarin was strictly adjusted according to her International Normalized Ratio (INR), targeted between 2.0 to 3.0. In the third week of anticoagulation treatment, the INR reached the targeted level. The headache started to resolve gradually. Then we stopped LMWH and only warfarin was given orally.

Post-treatment CT scan one month after the diagnosis showed the cerebral venous sinus thrombosis had disappeared. As the patients requested induced abortion, she was then transferred to the Family Planning ward again. Considering the possibility of hemorrhage during induction of labor, warfarin was replaced by LMWH. The ultrasound examination of uterus demonstrated a pregnancy at about 14-week gestation.

Figure 1. Medical imaging of cerebral venous sinus thrombosis of a young lady in early pregnancy.

A. Non-contrast CT image showed high density (arrow) in the area of right parietal lobe, which was suspicious for thrombosis; B. Sagittal T1WI MRI image revealed an iso-signal intensity (arrow) in superior sagittal sinus; C. Sagittal image of reconstructed MRV, a thrombus filling defect in superior sagittal sinus (arrow) was observed; D. Coronal image of reconstructed MRV, a thrombus filling defect in right transverse sinus (arrow) was observed.

Amniocentesis was performed and rivanol, also known as ethacridine which was a type of disinfectant, was injected into her amniotic cavity. Two days later, the patient spontaneously delivered a lifeless fetus and the placenta was delivered by vaginal with no complication. She was informed to take warfarin for 3 months after induction of labor.

DISCUSSION

CVST is an abnormal condition with a variety of symptoms and signs, affecting about 5 people per million.¹ It may lead to many emergent or life-threatening situations, such as cerebral edema, cerebral hemorrhage, hernia of brain, so early diagnosis and early therapy is crucial.

The underlying risk factors of CVST include prothrombotic conditions, hyperhomocysteinemia, pregnancy and puerperium, positive antiphospholipid antibodies, protein C and protein S deficiency, oral contraceptives, cancer, preeclampsia, etc.² In contrast to other subtypes of stroke, the incidence of CVST decreases with age.^{3,4} CVST is more common seen in young adult, and pregnancy related CVST occurs in the third trimester or puerperium because of the hypercoagulation state. Besides, hypercoagulability may worsen by anemia, dehydration, preeclampsia and trauma.⁵ The case we present was in early pregnancy, which was a rare type. The mechanisms of CVST during pregnancy and postpartum are still unclear. A cross-section study showed that women with pregnant associated stroke had fewer vascular risk factors but were more likely to have cerebral venous thrombosis than non-pregnant women with stroke, which indicated CVST may have a unique pathophysiology related to pregnancy.⁶

Clinical manifestations of CVST are of diversity and depend on the location and severity of thrombosis. Because of its non-specific symptoms, it is difficult to distinguish from other diseases such as hypertension, intracranial infection, and cranial space occupying lesions. Many data have shown that headache is the most common symptom clinically, no matter with or without any other complaint.^{7,8} Other common signs are nausea, vomiting, blurred vision, focal neurological deficits, seizures and disturbance of consciousness. During early pregnancy, the prodromal symptom of CVST, such as nausea and vomiting, may be misdiagnosed as hyperemesis gravidarum. Imaging can reveal the occluded vessels and thrombus in cerebral veins

or sinus, so it plays an important role in diagnosis of CVST. MRI/MRV, CT/CTV, and angiography are commonly used. The typical manifestation on CT for CVST, "the empty delta sign", usually presents 7 to 10 days after symptoms onset, while it is usually normal or non-specific in up to 30% CVST cases, and CT venography is suggestive.^{2,4} MRI is noninvasive, more sensitive and specific compared with CT scan. The MRI signal varies with not only the localization of involved vessel or sinus, but also with aging of the thrombus. In the first 3 to 5 days, the thrombus shows isointense on T1WI and hypointense on T2WI. Then its signals increase on both T1WI and T2WI with time going on. The golden standard for CVST is the combined visualization of thrombosed vessel or sinus on MRI and absence of the vessel or sinus on MRV.^{2,4} Studies have demonstrated that MRI during pregnancy has no harm to the fetus.⁹ Therefore, MRI and MRV are recommended as the first choice of imaging examination for screening of CVST in pregnant patients. Intra-artery angiography is currently rarely performed because it's invasive. In our case, CT, MRI, MRV and MRA were performed timely, all of which helped to make a quick and standing diagnosis of CVST.

According to the guideline of the American Heart Association/American Stroke Association, once CVST is diagnosed, anticoagulant therapy should be initiated if no major contraindications.² The first line treatment for CVST in acute phase usually start with intravenous heparin or subcutaneous LMWH. It has been supposed that anticoagulation treatment is beneficial to prevent enlargement of thrombosis, decrease the incidence of pulmonary embolism, and promote the recanalization.² There has been no evidence showing the treatment of anticoagulation for CVST with intracerebral hemorrhage increase the risk of bleeding.^{8,10} However, follow-up imaging is needed to exclude intracerebral hemorrhage during anticoagulant therapy.

The experience in the treatment for pregnant women with CVST is limited, and all data are from case reports or small sample size studies. Heparin or LMWH could be used in full dose throughout the pregnancy till delivering, because of their feature not being transferred into placenta. The dose of heparin needs to be adjusted between 3000 U to 5000 U, while the dose of LMWH be adjusted by patients' body-weight.^{11,12} There is no data on the difference of outcomes between heparin and LMWH in CVST patients.

The time of using oral anticoagulation postpartum depends on the underlying etiology of CVST. For CVST

patients who have transient risk factor, such as pregnancy while using oral contraceptive, warfarin should be continued for 3 to 6 months. For CVST patients related to inherited prothrombotic condition, warfarin should be continued for 6 to 12 months or indefinitely.^{2,13} It was recommended to continue the anticoagulation for at least 6 weeks postpartum, accompanied with oral warfarin or other vitamin K antagonist to keep a target INR between 2.0 to 3.0.^{10,12,13} Nonetheless, warfarin is forbidden in first trimester of pregnancy for its teratogenic effects. In this case, we gave anticoagulation therapy with combination of LMWH and warfarin. When her condition became steady, she was continually put on oral warfarin for 3 months due to the transient risk of pregnancy.

Some small cases series suggested that endovascular thrombolysis, no matter mechanical or chemical, may be safe and efficient for CVST patients who was on anticoagulation but got worse. Local injection of recombinant tissue plasminogen activator (rtPA) or urokinase was used successfully in recanalization in some case studies.^{14,15} Some CVST patients with severe headache and papilledema may have increased intracranial pressure (ICP), which can be reduced by diuretics and osmotherapy. If syndromes of ICP significantly progress, such as herniation, decompressive surgery should be considered as a life-saving procedure.¹⁶ There are evidences showing that CVST alone, pregnancy-related or puerperium-related CVST are not a contraindication for future pregnancies.^{1,17}

In conclusion, CVST, although rare, can occur in early pregnancy. The clinical manifestations are divers and non-specific. MRI and MRV are recommended for a suspected CVST in pregnancy. Anticoagulation treatment with heparin or LMWH is safe and efficient for pregnant patients. CVST in early pregnant patients may have a good prognosis.

Consent

Written informed consent was obtained from the patient for publishing this case report.

Conflict of interests statement

The authors declared no conflict of interests.

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