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Case Report

Pregnancy combined with epilepsy and cerebral cavernous hemangioma: a case report and literature review

Yalan Xu, Yijun Song, Xiya Zhou, Qingwei Qi, Juntao Liu

Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing 100730, China

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Abstract: Background: The experience for the management of cerebral cavernous malformation (CCM) combined with epilepsyin pregnancy is limited, and little is known about the most appropriate means for it. We present a pregnant case of combined with epilepsy and cerebral cavernous hemangioma and to review the literature on the topic. Case presentation: A 31-year-old G1P1 woman presented to our department due to presentation of seizure at a gestational age of 36 weeks and 4 days. Slightly long T1 and slightly long T2 signs were identified using cranial MRI in left frontal lobe in which small punctiform low signal shadow was visualized and low signal band was noted at the border. Fluid attenuated inversion recovery (FLAIR) showed high signals, while diffusion-weighted imaging (DWI) showed isointensity. Finally, the patient was diagnosed with intracranial space-occupying lesions and cavernous hemangioma. Literature search was performed to identify all similar reports published available. Fourteen relevant articles including twenty-three patients were identified. Fourteen patients showed haemorrhage while 9 patients showed seizure. Nine patients received cesarean section, and eight patients received vaginal delivery. One patient chose termination of pregnancy. Hemorrhage occurred in 10 out of 15 patients. Method of delivery was by caesarean section in 10 cases. According to the literature, it seemed that the cesarean section was performed in the majority of pregnancies with intracranial haemorrhage and/or seizure. Conclusion: There is no increased risk of cranial haemorrhage associated with method of delivery in the pregnancy with CCM. In the presence of haemorrhage, intervention should be given according to the type of haemorrhage.

Keywords: Cerebral cavernous malformation, hemorrhage, delivery, pregnancy

Introduction

Cerebral cavernous malformation (CCM), also known as carvernousangiomas, is a common type of vascular malformation in the central nervous system. Pregnancy with blood pressure changes and endothelial cell proliferation has been reported as a risk factor for CCM [1, 2]. However, to date, only a few pregnant patients with CCM have been reported worldwide [3, 4]. In particular, pregnant women complicated with seizure and CCM is rare.

As the experience for the management of such condition in pregnancy is limited, little is known about the most appropriate means for it. In a previous study, Lynch et al reported CCM was responsible for the parental and fetal mortality of 20% and 30%, and the rates would be decreased after conservative therapy. Meanwhile, for the pregnant women received no treatment for CCM, it is hard to select the method of delivery (i.e. cesarean section or vaginal delivery) [5]. In this case, we present a case of pregnant women with CCM combined with and cerebral cavernous hemangioma. Besides, literature review was performed to select the useful information for the clinical management.

Case presentation

A 31-year-old G1P1 woman presented to our department due to presentation of seizure at a gestational age of 36 weeks and 4 days. For the clinical symptoms, she presented paroxysmal and abdominal seizure during sleep accompanied with white foam spat from the mouth and opisthotonos. She showed no response when

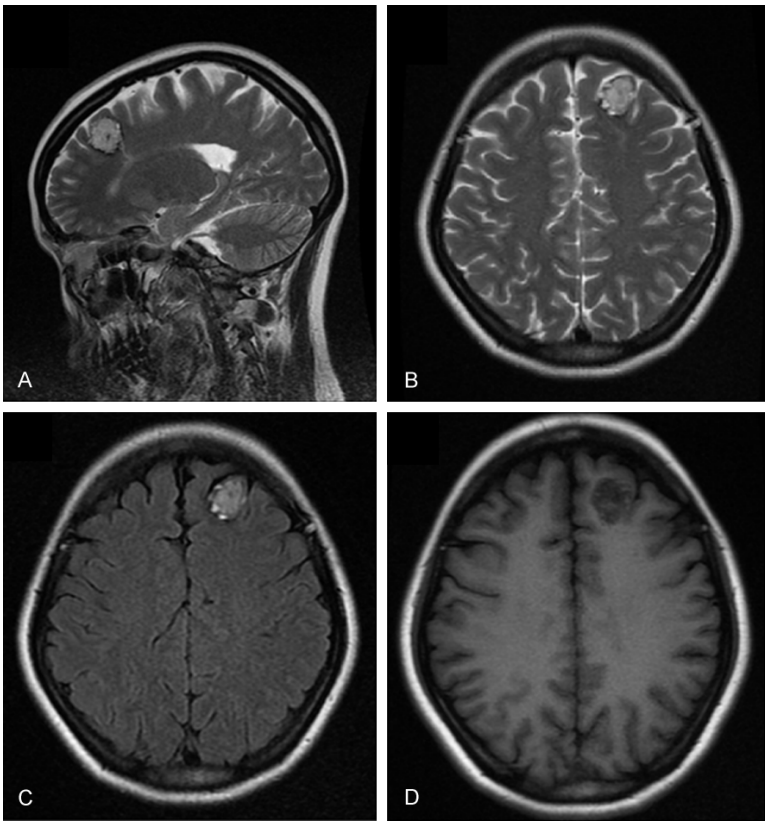

Figure 1. MRI findings on the pregnancy at the view of T2 sagittal plane (A), T2 coronary plane (B), T1 coronary plane (C) and diffuse weighing imaging coronary plane (D).

calling by others at that time. No obvious seizure was observed in the limbs, and the seizure was relieved 1-2 minutes later. The symptoms were presented again 3 hours later, which were manifested as consciousness disorders, no response to calling, as well as strong tremble of four limbs. No eyeball turnover, tongue bite, urinary and stool incontinence was accompanied. Ten minutes later, the patient was conscious and speech was normal. However, the patient complaint dizziness and headache after seizure.

On physical examination, no aberrant changes were noticed. Monitoring on the fetal heart and movement and uterine contraction was normal. Cranial MRI showed slightly long T1 and slightly long T2 signs in round-like pattern (size: 2.0 cm×2.1 cm×1.5 cm) in left frontal lobe in which small punctiform low signal shadow was visible and low signal band was noted at the border. Fluid attenuated inversion recovery (FLAIR) showed high signal and diffusion-weighted imaging (DWI) showed isointensity. Lower signal was visible. No obvious oedema was found in adjacent brain parenchyma. The adjacent cortical sulci was not significantly widened (**Figure 1**). The patient was finally diagnosed with intracranial space-occupying lesions and cavernous hemangioma. On this basis, the patient underwent uterine-incision delivery using combined spinal-epidural anesthesia on June 24, 2013 after signing the informed consent. The infant was healthy with an Apgar score of 10. After discharge, the patient was followed up, which indicated that no relapse of seizure and the infant was well developed. Intermittent seizure was present 2 years after the delivery. Therefore, surgical treatment was recommended by the neurosurgical physicians, but it was refused due to thyroid cancer one year after delivery.

Discussion

CCM was one of the important factors causing intracranial hemorrhage during gestational period [6]. To our best knowledge, the incidence of intracranial hemorrhage was increased together with increase of cerebral angioma size in the pregnancy. The possible mechanisms were as follows: the elevation of estrogen and progestogen resulted in high expression of growth factors (such as vascular endothelial growth factor) and placenta growth factor, as well as change of blood pressure and proliferation of endothelial cells [7, 8].

The risk of cavernous hemangioma rupture and intracranial hemorrhage was reported to be remarkably elevated in the pregnancy. In a previous study, 5 intracranial hemorrhage (2.98%) was reported among the 168 pregnancies in the 64 female cerebral cavernous malformation [9]. In addition, Witiw et al revealed the hemorrhage rate for pregnant women with cerebral cavernous malformation was 1.15% (95% confidence interval: 0.23-3.35) per person-year and 1.01% (95% confidence interval:

Table 1. Cases of cerebral cavernous malformations during pregnancy from the literature review

Authors	No. of cases	Site of CCM	Presence of haemorrhage	Presence of seizure	Method of delivery	Indications for CS	Surgery
Warner et al (1996)	1	Chiasm	√	-	Cesarean section	-	No
Pozzati et al (1996)	2	Brainstem	√	-	-	-	No
		Temporal lobe	-	√	-	-	After delivery
Awada et al (1997)	2	Temporal lobe	√	-	-	-	No
		Temporal lobe	√	-	-	-	No
Hoeldtke et al (1998)	1	Frontal lobe	-	√	Vaginal delivery	-	No
Flemming et al (2003)	1	Pons	√	-	Cesarean section	CCM	During pregnancy
Safavi-Abbasi et al (2006)	1	Intramedullary	√	-	Cesarean section	CCM	Two weeks after pregnancy
Aladdin et al (2008)	1	Frontal lobe	-	√	Termination of pregnancy	-	No
Cohen-Gadol et al (2009)	1	Pons	√	-	Cesarean section	-	The patient received surgery, but the time was not reported
Nossek et al (2011)	2	Brainstem	-	√	Cesarean section	-	No
		Frontal	-	√	Vaginal delivery	-	No
Burkhardt et al (2012)	3	Pontomesencephalic	√	-	-	-	At a gestation age of 12 weeks
		Thalamo-Mesencephalic	√	-	-	-	1 week after pregnancy
Witiw et al (2012)	3	Frontal lobe	√	-	Vaginal delivery	-	No
		Pons	√	-	Cesarean section	CCM	No
		Pons	√	-	Cesarean section	CCM	No
Kalani et al (2013)	1	Insula	√	√	Vaginal delivery	-	No
Simonazzi et al (2014)	5	Bulb	√	-	Cesarean section	CCM	No
		Bulb	√	-	Termination of pregnancy	-	No
		Corpus callosum	-	√	Cesarean section	CCM	No
		Pons	√	-	Cesarean section	Dystocia	No
		Pons	√	-	Cesarean section	-	No
This study	1	Frontal lobe	√	√	Cesarean section	CCM	No*

CCM, cerebral cavernous malformations; CS, cesarean section; *The patient was recommended to receive neurosurgery, but the surgery was postponed as the patient showed thyroid cancer

Table 2. Reported obstetric outcomes of the patients

Case/Literature	Site of CCM	Haemorrhage	Seizure	Method of delivery	Obstetric complications
Hoeldtke et al (1998)	Frontal lobe	-	√	Vaginal delivery	None
Flemming et al (2003)	Pons	√	-	Cesarean section	None
Aladdin et al (2008)	Frontal lobe	-	√	Termination of pregnancy	Preeclampsia
Cohen-Gadol et al (2009)	Pons	√	-	Cesarean section	None
Nossek et al (2011)	Brainstem	-	√	Cesarean section	None
Burkhardt et al (2012)	Ponto-mesencephalic	√	-	Vaginal delivery	None
Witiw et al (2012)	Frontal lobe	√	-	Vaginal delivery	None
	Pons	√	-	Cesarean section	None
	Pons	√	-	Cesarean section	None
Simonazzi et al (2014)	Bulb	√	-	Cesarean section	None
	Bulb	√	-	Termination of pregnancy	None
	Corpus callosum	-	√	Cesarean section	None
	Pons	√	-	Cesarean section	None
	Pons	√	-	Cesarean section	None
This study	Frontal lobe	√	√	Cesarean section	The patient showed thyroid cancer one year after delivery.

0.75-1.36) per person-year for nonpregnant women, which showed no statistical difference between these patients [10]. On this basis, it seemed that pregnancy, method of delivery and puerperium were not the risk factors for intracranial hemorrhage. Besides, the CCM was not the contraindications of pregnancy and vaginal delivery.

Currently, there is no consensus on the method of delivery in the pregnant with CCM [9]. No Cochrane evidence revealed the fact that cesarean delivery was related with reduced incidence of intracranial hemorrhage. Meanwhile, no evidence indicated that the method of delivery was associated with the risk of intracranial hemorrhage in CCM [10]. However, some researchers proposed that the incidence of hemorrhage in pregnancy with CCM was higher after receiving cesarean delivery or painless delivery at a gestational age of 32+ weeks (fetal weight > 2 kg). Therefore, inter-department cooperation is needed to select the delivery method and decide whether neurosurgical procedures are needed to ensure the safety of pregnant women and the fetus. In this case, the patient showed seizure twice, and was highly suspected with cavernous hemangioma after MRI and consultation. Considering the fetal age and the potential side effects of seizure on the child, cesarean delivery was given, and no relapse was noticed after delivery.

In this study, we also did a literature review using the following key words: “cavernous malformation” or “cavernous angiomas” or “cavernous haemangioma” and “cerebral and/or “pregnancy”. Additional sources were identified through cross-referencing. Only reports of cavernous malformations localized in the head were included in the literature research. Finally, a total of 12 relevant articles [4, 9-20] including 25 patients (including our case) were identified. Nineteen patients showed haemorrhage while eight patients showed seizure (**Table 1**). Twelve patients received cesarean section, and four patient received vaginal delivery. Two patients chose termination of pregnancy. **Table 2** listed the obstetric outcomes of our case and the previous cases. Hemorrhage occurred in 11 out of 15 patients. Method of delivery was by caesarean section in 10 cases. According to the literature, it seemed that the cesarean section was performed in the majority of pregnancies with intracranial haemorrhage and/or seizure.

Up to now, there is no consensus on the treatment of CCM combined with seizure in pregnancy. Administration of certain drugs such as nimodipine has been proposed to attenuate vasospasm, but it may induce deformity of fetus [21]. For the efficiency of surgery, there are still disputes. Lynch et al proposed that surgery was essential for the pregnancy with seizure or CCM [22]. Folkersma et al [23] revealed surgery together with removal of the tissues

affected by the seizure should be carried out for these patients. However, Kalani et al though that for the patients with mild or symptom-free CCM, conservative therapy may be an option [9]. Besides, the neurosurgery should be carried out according to the type of bleeding and severity of the conditions. In this study, the patient was recommended to receive surgery according to patient's conditions. However, the surgery was refused due to presence of thyroid cancer one year after delivery.

In conclusion, there is no increased risk of cranial haemorrhage associated with method of delivery in the pregnancy with CCM. In the presence of haemorrhage, intervention should be given according to the type of haemorrhage. Literature research indicated cesarean section was the mostly used delivery method of pregnancy with CCM, but its efficiency should be validated by the further clinical trials.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Juntao Liu, Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, No. 1, Shuaifu Garden, Dongcheng District, Beijing 100730, China. Tel: +86-10-6529-6228; E-mail: tao_aul@hotmail.com

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