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Case Report

Lethal fetal stroke *in utero*

Tzu-Hung Lin [a,b], Chien-Nan Lee [c], Yi-Ning Su [a,b,d,e,*]

[a] *Dianthus Maternal Fetal Medicine Clinic, Taipei City, Taiwan*
[b] *Sofiva Genomics, Taipei City, Taiwan*
[c] *Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei City, Taiwan*
[d] *Department of Obstetrics and Gynecology, Taipei Medical University Hospital, Taipei City, Taiwan*
[e] *Department of Obstetrics and Gynecology, China Medical University Hospital, Taichung, Taiwan*

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Abstract

Objective: Fetal intracranial hemorrhage (ICH) *in utero* is a rare complication of pregnancy associated with subsequent neurological sequelae or fetal death.
Case report: A 34-year-old woman with Crohn's disease presented at 36 weeks' gestation due to decreased fetal movement. Fetal heart-rate tracing indicated poor beat-to-beat variability. In addition, a Doppler ultrasonography suggested a prenatal stroke with evidences of ICH, reverse-end diastolic velocity of the middle cerebral artery, and a persistent distended bladder. A nonaggressive treatment option was chosen after counseling about the unfavorable prognosis. However, 22 hours after her admission, intrauterine fetal death occurred.
Conclusion: Fetal ICH *in utero* might be a rare yet lethal complication of Crohn's disease in pregnancy.

Keywords: Crohn's disease; fetal cerebral hemorrhage; fetal intracranial hemorrhage; fetal intraventricular hemorrhage; fetal stroke

Introduction

Fetal intracranial hemorrhage (ICH) occurs in approximately 25–45% of premature infants with a birth weight less than 1500 g [1]. However, fetal ICH (fetal stroke) is a rare complication in pregnancy and mostly occurs with predisposing factors [2–4]. Well-controlled Crohn's disease has little impact on pregnancy, and mostly involves fetal growth restriction and preterm delivery [5,6]. Herein, we present a case of Crohn's disease complicated with fetal cerebral hemorrhage diagnosed *in utero* with unfavorable outcome.

Case report

A 34-year-old, gravida 1, para 0, woman presented at 36 weeks' gestation with decreased fetal movements for 1 day. She received segmental ileal resection because of intussusception complicated with perforation 2 years before this admission. Crohn's disease was diagnosed postoperatively and she was treated with mesalamine (1.5 g/day) and prokinetic medications without clinical malnutrition. The postoperative course was uneventful and she conceived spontaneously. Results of prenatal examinations were uneventful until this episode. Fetal heart-rate tracing indicated poor beat-to-beat variability and a fetal ultrasonography showed a massive intracerebral hemorrhage, mainly in the right temporal lobe, with a midline shift to the left side. In addition, a duplex Doppler flow velocimetry showed reverse-end diastolic velocity (REDV) of the right middle cerebral artery (MCA), indicating increased intracranial pressure impairing cerebral blood flow. Persistent distended bladder indicated poor cortical function (Fig. 1). Fetal blood was obtained by cordocentesis and the level of fetal hemoglobin was found to be 2.3 g/dL, indicating severe anemia. Emergent fetal magnetic resonance imaging (MRI) also revealed a diffuse, but not a well-defined, hypointense mass in the right temporal lobe (Fig. 2A–C). Maternal alloimmune antiplatelet antibody, lupus

* Corresponding author. Dianthus Maternal Fetal Medicine Clinic, Taiwan, No. 78, Huaining St., Zhongzheng Dist., Taipei City, Taiwan.
E-mail address: ynsu@mfmclinic.com.tw (Y.-N. Su).

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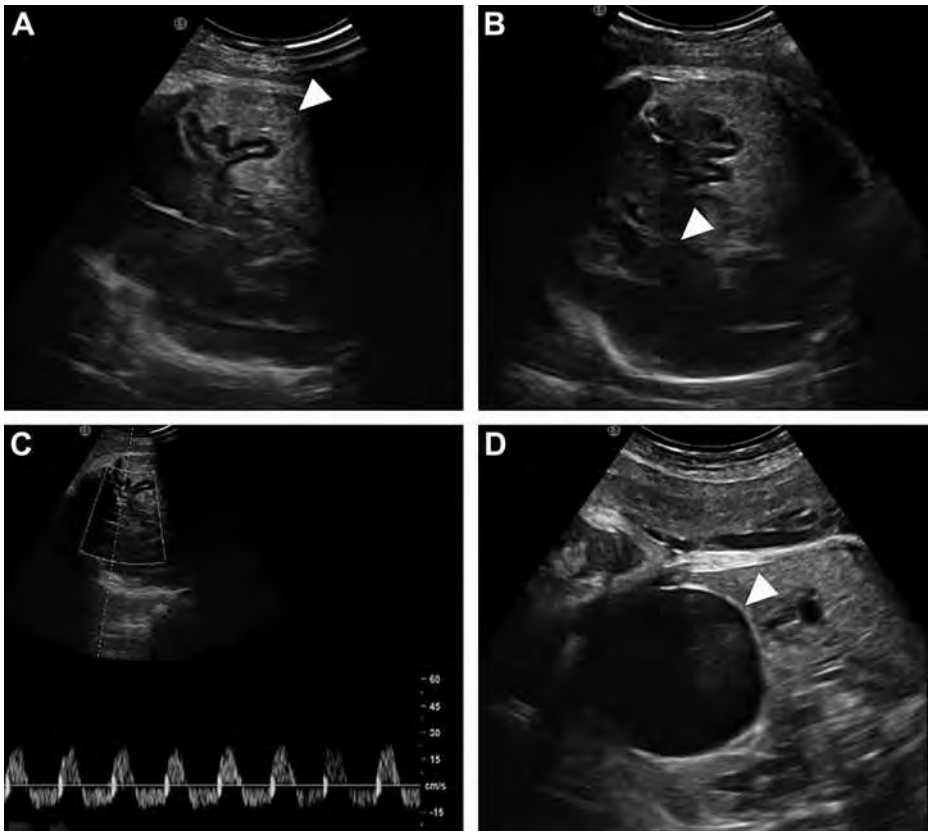

Fig. 1. Doppler ultrasonography showed a massive intracranial hemorrhage in the axial view of the fetal head and the distended bladder. (A) Diffuse, but not well-defined hyperechoic area (arrowhead) in the right temporal lobe, indicating cerebral hemorrhage. (B) The intracranial hemorrhage resulted in a midline shift to the left side (arrowhead). (C) Duplex Doppler flow velocimetry showed reverse-end diastolic velocity of the right middle cerebral artery, which indicates increased intracranial pressure. (D) Persistent distended bladder of the fetus (arrowhead).

anticoagulant, and antiphospholipid antibody were not detected. After discussing with patient and her family about the poor prognosis of fetus, a conservative (nonaggressive) treatment option was chosen. However, intrauterine fetal death occurred 22 hours after admission. A 2870-g dead girl was delivered by vaginal delivery after labor induction. Results of a fetal autopsy showed the evidence of fetal intracerebral, intraventricular hemorrhage (Fig. 2D) and a distended bladder, which were compatible with clinical manifestations. Other vital organs were unremarkable. Maternal Crohn's disease was continuously controlled by administering mesalamine (1.5 g/day) with minimal clinical signs and symptoms.

Discussion

The incidence of perinatal stroke is reported to be 1 in 4000 live births [7]. However, fetal ICH *in utero* is an extremely rare condition. One case series reported the incidence to be approximately 0.46/1000 deliveries in tertiary referral centers [2]. The predisposing factors are maternal, placental, fetal, or genetic aspect; however, no identifiable risk can be found in majority of the cases. Only one case had been reported in the literature indicating the association between active Crohn's disease and fetal ICH [8]. However, the antenatal ICH in our case cannot be explained by vitamin K deficiency because of lack of evidence of malnutrition [normal maternal albumin level, prothrombin time INR (PT INR), and adequate body mass index (22.4 kg/m^2)]. Mesalamine, a 5-amniosalicylic acid, crosses the placenta and is classified by the Food and Drug Administration as a category B/C depending on the actual product. Although its exact mechanism of action is not known, mesalamine is thought to reduce colonic inflammation. Unlike aspirin, an acetylsalicylic acid, mesalamine has not been demonstrated to have any antiplatelet effects though it may increase the risk for bleeding in patients on anticoagulant medications. In our case, the platelet count at the time of cordocentesis was normal, which eliminates a low platelet count as a possible source for bleeding. However, limited data are available on the prognosis of neurodevelopmental disorders if antenatal ICH occurs. Therefore, the MCA Doppler flow velocimetry study and fetal MRI may be the effective methods for diagnosing the severity of fetal ICH [9,10]. The intracerebral circulation is spared in conditions of fetal distress manifested by nonreactive fetal heart-rate tracing. If the fetal distress results from an intracranial episode, the elevated intracranial pressure impairs MCA-spared blood flow to A/REDV, causing the cortex under perfusion to destroy cortical function. Results of a fetal MRI not only clarify ventricular or parenchymal involvement, but also clarify grade III and IV ICH, which carries a high risk of postnatal neurological sequelae [2]. In our case, both massive temporal parenchymal hemorrhage and REDV of the MCA indicate the unfavorable

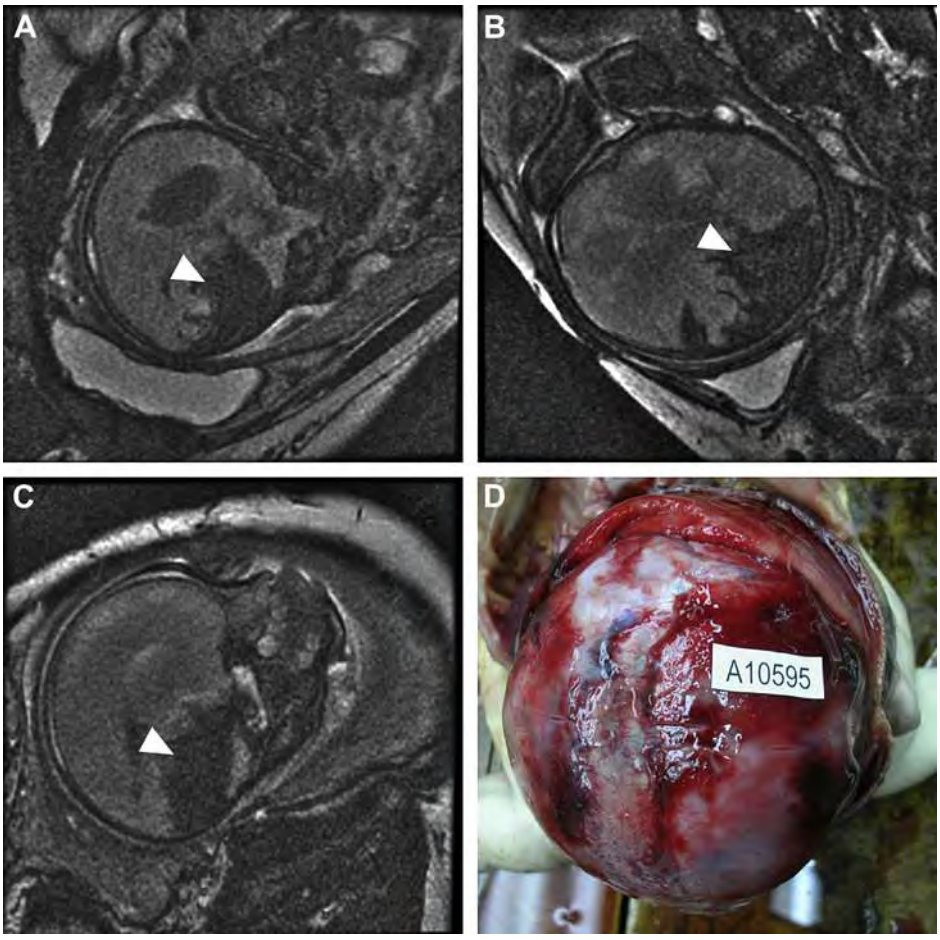

Fig. 2. Different views of magnetic resonance images and fast imaging employing steady-state acquisition images demonstrate the intracranial cerebral hemorrhage. (A) Coronal view, (B) axial view, (C) sagittal view, and (D) the fetal brain autopsy gross view.

prognosis described previously. In addition, a persistent distended urinary bladder provides another evidence of neurological deficiency, which has been reported for first time in the literature. No previous report showed that immediate delivery, either by cesarean section or by vaginal delivery, may ameliorate the fetal outcome [11].

In summary, fetal ICH diagnosed *in utero* might be a rare but lethal complication. The MCA Doppler flow velocimetry study, fetal urinary bladder evaluation, and fetal MRI are helpful for counseling about the fetal neurodevelopmental outcome.

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