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Fetal intracranial hemorrhage associated with maternal coagulopathy and vitamin K deficiency after biliary drain placement: A case report and literature review

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ABSTRACT

Introduction: Fetal intracranial hemorrhage (ICH) is a rare but serious prenatal diagnosis. Predisposing factors include maternal trauma and fetal coagulation dysfunction. Maternal vitamin K deficiency has been described as an etiology. We present a case of maternal vitamin K deficiency associated with fetal ICH after percutaneous biliary drain (PBD) placement in a complicated cholecystectomy with injury to the common bile duct.
Case presentation: A 21-year-old woman, G2P1, presented at 23 weeks and 3 days of gestation with epigastric pain, nausea and vomiting. Right upper quadrant ultrasound diagnosed cholelithiasis. The patient was managed conservatively and discharged. She returned four days later, at 24 weeks of gestation, with worsening symptoms and ultrasound showing acute cholecystitis. She underwent laparoscopic cholecystectomy. Increasing bilirubin and imaging showed a transected biliary duct that required percutaneous biliary drain (PBD) placement. The patient was discharged and followed up at a high-risk obstetric clinic. Prenatal ultrasound showed bilateral ventriculomegaly with features of ICH. Maternal vitamin K deficiency was confirmed with PIVKA-II testing. The patient received vitamin K supplementation with normalization of the coagulopathy. Delivery occurred at 36 weeks of gestation via cesarean delivery after preterm premature rupture of membranes for fetal macrocrania. The neonate was discharged to a hospice.
Discussion: Maternal and neonatal etiologies for ICH include malabsorption and coagulopathy. Maternal vitamin K deficiency should be considered when coagulopathy is present. This case highlights that maternal vitamin K deficiency due to biliary diversion and malabsorption increases the risk of fetal ICH, which impacts pregnancy and neonatal outcomes.

1. Introduction

Fetal intracranial hemorrhage (ICH) is a rare occurrence [1]. Predisposing factors for in utero ICH are maternal trauma and fetal coagulation dysfunction [2]. Maternal warfarin use and enzyme-inducing antiepileptic medications have been implicated in fetal ICH [3]. Maternal vitamin K deficiency is a rare cause of fetal ICH, with eight reported cases; malabsorption or other gastrointestinal etiology was a component in all these cases [3–10].

Vitamin K supplementation for the newborn has become standard practice in pediatrics and has led to a reduction in neonatal morbidity and mortality secondary to vitamin K deficiency [3,11,12].

We present the first case report of maternal vitamin K deficiency leading to fetal ICH after percutaneous biliary drain (PBD) placement in a complicated cholecystectomy with injury to the common bile duct.

2. Case Presentation

A 21-year-old woman, gravida 2 para 1, presented at 23 weeks 3 days of gestation with epigastric pain, nausea and vomiting. Her pregnancy was complicated at 22 weeks of gestation by a low-speed motor vehicle crash in which she was the restrained driver. A right upper quadrant ultrasound scan diagnosed cholelithiasis without evidence of cholecystitis. She was discharged home after intravenous hydration and supportive treatment.

She returned four days later with worsening upper abdominal pain, nausea and vomiting. Repeat ultrasound confirmed cholelithiasis, cholecystitis and a dilated common bile duct. The patient was started on

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intravenous piperacillin and sulbactam for biliary flora coverage and acute cystitis based on urinalysis.

The patient underwent laparoscopic cholecystectomy; the gallbladder was inflamed and filled with purulent bile and gallstones. Fetal heart tones were obtained pre- and postoperatively.

Postoperatively, the patient developed a transaminitis and total bilirubin increased from 0.2 mg/dL on admission to 2.3 mg/dL. Magnetic resonance cholangiopancreatography (MRCP) was performed and demonstrated an abrupt truncation of the common bile duct 1.9 cm distal to the hepatic confluence, confirming transection of the common bile duct. There was also a 3.2 × 5.1 × 7.5 cm fluid collection in the gallbladder fossa, raising concerns regarding a seroma. Interventional radiology placed a percutaneous biliary drain without complication, and interval repair of the duct was planned for the postpartum period. A single course of betamethasone for fetal lung maturity was administered on postoperative day 1 due to an increased risk of preterm labor or preterm delivery with acute maternal illness. The patient was discharged home on postoperative day 3 with resolution of fever and leukocytosis.

The patient was followed up in the high-risk obstetrics clinic one week postoperatively, when it was noted that her nausea, vomiting and abdominal pain had improved. Follow-up prenatal ultrasound was performed at 27 weeks of gestation to assess interval growth. Imaging showed bilateral ventriculomegaly (19.4 mm on the right and 18 mm on the left), increased echogenicity of the right choroid plexus, and variable opacification of the cerebrospinal fluid suggestive of intracranial hemorrhage (Figs. 1–3). Of note, the fetal anatomy at 19 weeks and 23 weeks was normal. Fetal MRI confirmed bilateral severe ventriculomegaly, with dilatation of the lateral third and fourth ventricles; intraventricular, choroid plexus and intraparenchymal hemorrhage; small subdural left frontoparietal collection; and abnormal gray-white matter differentiation in the cerebral parenchyma. These findings suggested evolving encephalomalacia or gliosis (Figs. 4 and 5).

Investigation of potential etiologies of fetal intracranial hemorrhage included evaluation for neonatal alloimmune thrombocytopenia (NAIT) with negative antiplatelet antibodies and inconsequential incompatibilities in the HPA-3b and HPA-15 s. Evaluation of maternal coagulation profile revealed a prolonged prothrombin time (PT) and international normalized ratio (INR). This led to evaluation for vitamin K deficiency and measurements of Des-gamma-carboxy prothrombin, a protein induced by vitamin K absence or antagonist II PIVKA-II, which was elevated to 200 ng/mL (reference < 7.5 ng/mL). This was diagnostic for maternal vitamin K deficiency.

Maternal coagulation profile was normal after three doses of 10 mg vitamin K. Maintenance dose of weekly 10 mg vitamin K injections and 5 mg oral vitamin K daily were given. Vitamin D deficiency was also noted and treated.

The patient met with the neonatology department at 32 weeks of gestation to discuss postnatal care options as well as possible outcomes, including severe neurodevelopmental delay, palliative shunt placement and palliation if life-limiting. The patient desired postnatal evaluation with MRI after birth. Follow-up fetal ultrasound at 35 weeks 5 days of gestation revealed worsening of the hydrocephalous, further decline

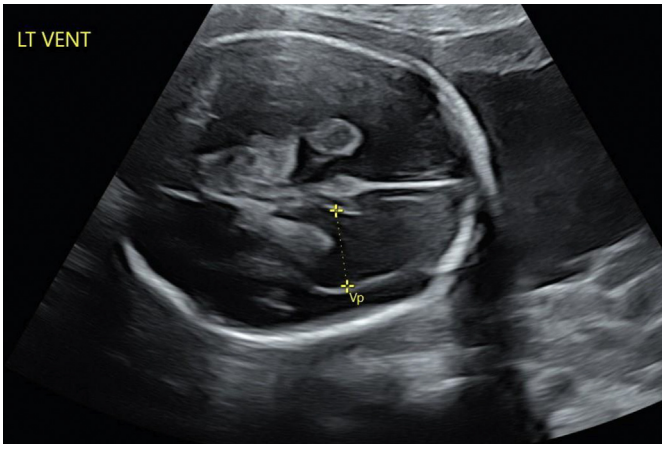

Fig. 1. Prenatal ultrasound scan at 27 weeks demonstrating bilateral ventriculomegaly (left ventricle).

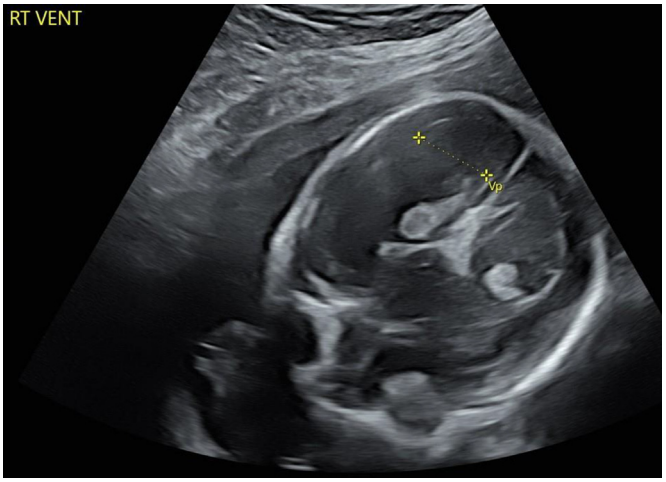

Fig. 2. Prenatal ultrasound scan at 27 weeks demonstrating bilateral ventriculomegaly (right ventricle).

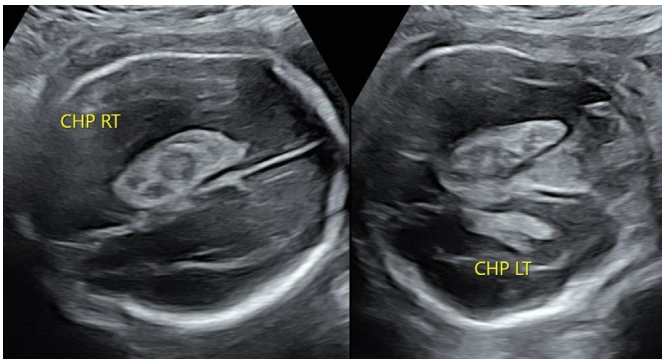

Fig. 3. Prenatal ultrasound scan at 27 weeks demonstrating bilateral ventriculomegaly (right choroid plexus, left choroid plexus).

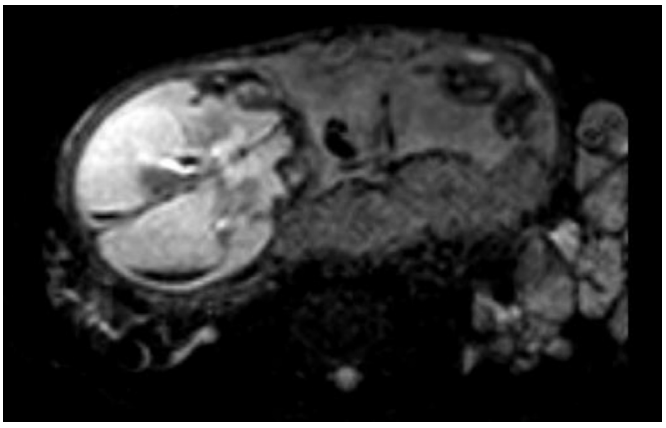

Fig. 4. T1-weighted sagittal magnetic resonance image of fetus at 27 weeks 2 days.

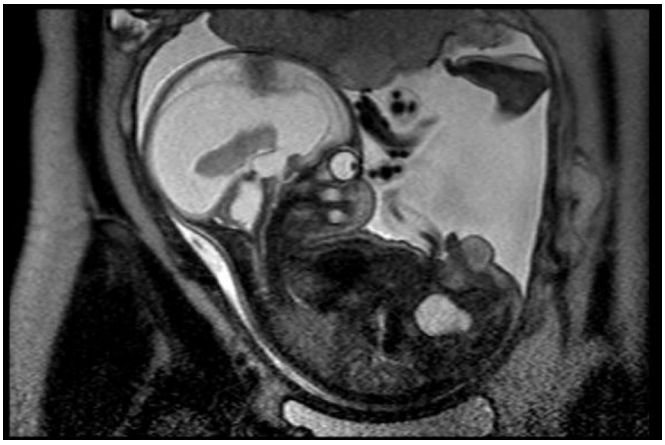

Fig. 5. T2-weighted coronal magnetic resonance image of fetus MRI at 27 weeks 2 days.

in identifiable normal brain tissue, and macrocrania, with head measurements exceeding the 99th percentile.

At 36 weeks 1 days of gestation, the patient presented with preterm prelabor rupture of membranes. She was given another dose of vitamin K and underwent an uncomplicated primary low transverse cesarean section due to fetal macrocrania. She delivered a vigorous male infant weighing 2790 g with Apgar scores of 8 and 9.

The neonate was transferred to the children's hospital where MRI showed severe hydrocephalus with obstruction at the level of the foramen of Luschka and Magendie, with evidence of prior intraventricular and subarachnoid hemorrhage. Pediatric neurology suspected significant neurodevelopmental effects due to timing in which the intracranial hemorrhage (ICH) occurred, limiting brain tissue development. Neurosurgery remarked that a palliative shunt may control head growth but would not improve the neurologic outcome. Genetic testing was not performed as syndromic etiologies of ventriculomegaly were not suspected after delivery. At five weeks of age, the neonate developed cyanosis, hyponatremia, and hypoxia. Due to the poor prognosis, the family elected to transition to comfort care and he died shortly thereafter.

The patient eventually underwent bile duct reconstruction with Roux-en-y side-to-side choledochojejunostomy 8 weeks postpartum and with an uncomplicated course at the time this report was written.

3. Discussion

Though fetal ICH is rare, it is a life-threatening condition with potential for persistent neurological sequelae among survivors [5]. Both maternal and fetal etiologies have been implicated [1,5]. Fetal etiologies of ICH include neonatal alloimmune thrombocytopenia (NAIT), vascular malformations, congenital coagulation factor deficiency, genetic mutations associated with hereditary parenchymal hemorrhage or porencephaly, and complicated monochorionic twin gestation [1,5]. Maternal etiologies include infection, anticoagulant use or coagulopathy, medication side-effects, substance misuse, seizure disorders, trauma, cholestasis and febrile illness [1]. Placental and umbilical cord abnormalities have also been implicated [1].

Humans rely on dietary intake and bacterial synthesis as vitamin K sources, and storage in the liver lasts one week in adults [6,8,13]. While vitamin K crosses the placenta, the umbilical cord vitamin K concentration is estimated to be approximately 1/30 of the maternal plasma concentration [5,8,11,14]. Therefore, maternal vitamin K deficiency predisposes the fetus to symptomatic deficiency as well.

Antibiotic therapy may decrease vitamin K stores due to alterations of colonic bacterial flora with subsequent decreased absorption, warfarin-like effects, or inhibition of enzymatic reuptake in the liver [15,16]. Deficiency can also be caused by inflammatory bowel disease, cystic fibrosis, pancreatic disease and chronic liver disease [4,17–20]. The eight reported cases of fetal intracranial hemorrhage related to maternal vitamin K deficiency have a common theme of poor maternal nutritional intake or absorption. Three cases were attributed to eating disorders, two due to hyperemesis gravidarum, one to Crohn's disease, one to esophageal hiatal hernia and total parenteral nutrition administration, and one to prolonged vomiting after slippage of a gastric restrictive band [3,5–10].

We confirmed the diagnosis with PIVKA-II testing, which is a functional marker useful for quantifying vitamin K levels. [5] Prolongation of the PT with normal platelets and fibrinogen is suggestive of vitamin K deficiency [5]. Prolongation of the PT due to vitamin K deficiency lacks sensitivity, especially in sub-clinical deficiency, because it requires at least a 50% decline in prothrombin concentration for prolongation to occur [5]. Normalization of the PT after vitamin K administration is a simple confirmatory test of deficiency diagnosis, as exemplified in our patient [5]. Baseline PT was not evaluated in the patient until fetal ICH was noted. However, the temporal occurrence of the fetal ICH after PBD placement and the short duration of antibiotic therapy suggest that the PBD combined with antibiotic therapy contributed to fat-soluble vitamin deficiencies.

Fetal coagulation status at the time of the maternal trauma and ICH is unknown, as cordocentesis was not performed. It is expected that a fetal vitamin K deficiency and coagulopathy would improve with correction of the maternal deficiency, therefore limiting the ability for postnatal diagnosis. It is the authors' opinion that the low-speed motor vehicle crash with minimal damage would have sufficient force to cause the severe ICH in this case and that maternal vitamin K deficiency related to fat-soluble losses was the most likely etiology.

This case reinforces the recommendations from the American College of Obstetrics and Gynecology (ACOG) that non-obstetric surgery during pregnancy should not be delayed due to pregnancy alone [21]. Conservative management in surgical intervention when maternal infection is present may lead to more advanced infection, increasing the risk of morbidity and adverse outcomes [22,23]. In the above case, initial management was conservative when only cholelithiasis was present; surgical management was performed when progression to cholecystitis occurred.

This case highlights that subclinical maternal vitamin K deficiency due to biliary diversion and malabsorption may increase the risk of fetal ICH, which may impact pregnancy and neonatal outcomes, particularly if severe hemorrhage occurs. Monitoring maternal coagulation may aid in the diagnosis of maternal vitamin K deficiency. Additional research is needed to determine if vitamin K supplementation in pregnant patients with fat-soluble vitamin malabsorption decreases the risk of fetal ICH.

Contributors

Muhammad Abu-Rmaileh contributed to acquisition and analysis of data, and drafting the article or revising it critically for important intellectual content.

Abigail Ramseyer contributed to acquisition and analysis of data, and drafting the article or revising it critically for important intellectual content, and was involved in patient care.

Lyle Burdine contributed to acquisition and analysis of data, and was involved in patient care.

Nafisa K. Dajani contributed to acquisition and analysis of data, and was involved in patient care.

All authors gave final approval of the version to be submitted.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Patient Consent

Verbal patient consent was obtained with use of medical translator services.

Provenance and Peer Review

This case report was peer reviewed.

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