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CASE REPORT

Hidden maternal autoimmune thrombocytopenia complicated by fetal subdural hematoma—case report and review of the literature

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Introduction

Fetal intracranial hemorrhage (IH) is a quite rare event, with an incidence of 1 in 10,000 pregnancies and may present in five different types: intraventricular, cerebellar, miscellaneous intraparenchymal, subdural, and primary subarachnoid hemorrhages [1, 2]. Whereas neonatal hemorrhage is relatively common and affects especially infants delivered before 32 gestational weeks, the majority of prenatally detected cases of IH occur during the third trimester of gestation.

Subdural hemorrhages (SDH) are the less frequent type of fetal IH and usually occur due to the tearing of loose bridging subdural veins that drain the brain blood flow to the dural sinuses [3]. Fetal SDH generally have an unfavorable prognosis, but may resolve spontaneously, with varying long-term outcomes reported in the literature [2, 4].

Fetal subdural hematomas may be diagnosed by ultrasound and magnetic resonance imaging and are seen mainly in the supratentorial region [5]. The most frequent etiology is intrauterine or birth trauma. Deficiency of coagulation factors and alloimune thrombocytopenia are frequent causes of spontaneous intraventricular and intraparenchymatous hemorrhages, although rarely related to SDH [6]. We report a case of subdural hematoma related to fetal autoimmune thrombocytopenia with a good outcome, along with a review of the sparse literature available on this issue.

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Case report

A 35-year-old primigravida was referred to our institution for routine scan at 34 gestational weeks (GW). Previous personal and family history was unremarkable. She denied trauma or recent symptomatic infection. Two previous scans at 12 and 24 GW revealed appropriate fetal biometry and development. Maternal serology was within normal limits. A right temporal–parietal–occipital extra-axial mass was observed, measuring 54×27 mm (Fig. 1a). The predominantly cystic, wedge-shaped lesion occupied the space between the brain and the skull, presenting irregular thick echogenic walls with rough debris in its interior. Brain parenchyma and the midline were displaced leftwards, suggesting a subdural hematoma. Color Doppler showed no flow at the topography of the mass. No additional anomalies were seen. One week later, a follow-up scan was performed depicting the same findings, although the mass size had increased to 68.7×31 mm, suggesting a new bleeding event (Fig. 1b). The parents were properly counseled about the meaning of the findings and the possibility of a hematologic disturbance leading to the intracranial bleeding. Nonetheless, due to the advanced gestational age and the possible risks, the family refused to perform a cordocentesis. Maternal platelet levels were assessed during pregnancy and delivery and were always normal.

A full-term boy was delivered by cesarean section at 39 GW, appropriate for the gestational age (3,315 kg). Physical

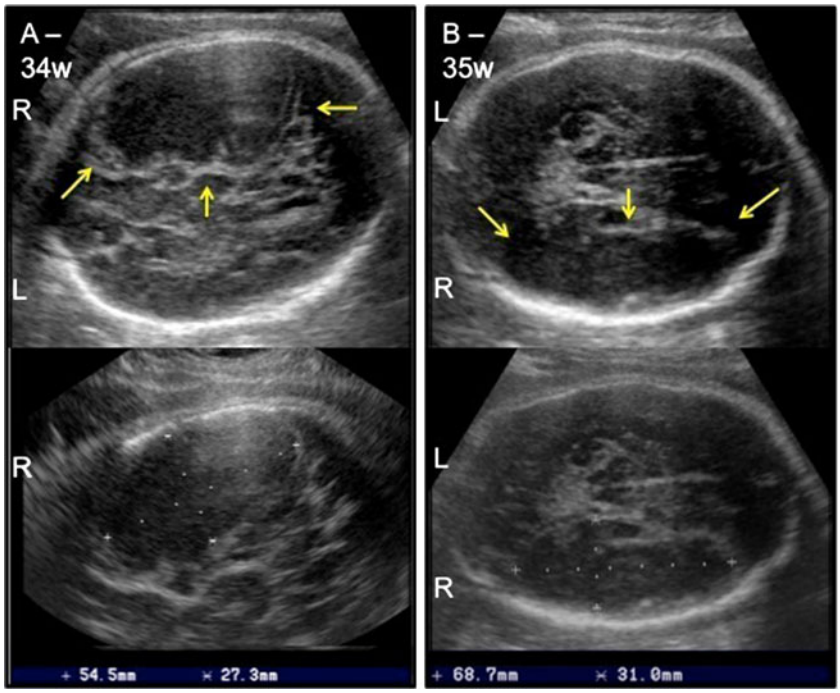

Fig. 1 Right side fetal subdural hemorrhage; **a** 34 weeks. A wedge-shaped irregular cystic lesion may be seen (*arrows*), displacing leftwards the brain parenchyma. Note the irregular echogenic borders and the presence of internal debris. **b** Same lesion at 35 weeks, showing increase in size. (*R* right, *L* left)

exam of the newborn detected a generalized petechial rash and ecchymoses (Fig. 2). There were no clinical or laboratorial signs of infection. A platelet count showed a severe thrombocytopenia and the newborn received platelet transfusions. Brain sonography confirmed the presence of a right subdural hematoma that was managed surgically with success. The images matched perfectly the characteristics of the lesion and the measurements were performed prenatally, suggesting no further bleeding (Fig. 3). There were no signs of hydrocephalus or other associated brain anomalies. The diagnosis of hidden maternal autoimmune thrombocytopenia was suggested. Follow-up at 5 years was normal, regarding cognitive and neuropsychomotor function.

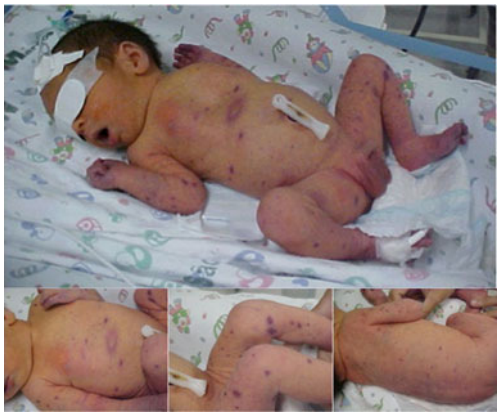

Fig. 2 Eight-hour newborn presenting a generalized petechial rash and ecchymoses

Discussion

Fetal hemorrhagic and hypoxic–ischemic insults are processes that lead to antenatal brain damage and fetal stroke and are associated with seizure disorders, mental retardation, psychomotor delays, and cerebral palsy [5]. Unfortunately, maternal or fetal medical conditions that may alert the attending physician to the risk of significant fetal brain lesions are present in only 45% of the cases.

Maternal risk factors for fetal IH include oscillations in blood pressure and conditions such as platelet or coagulation disorders, seizures, trauma, placental abruption, viral or bacterial infection, febrile disease, amniocentesis, medications such as warfarin or cholestyramine, and drugs such as cocaine [7–9]. Fetal predisposing conditions include invasive procedures (fetal trauma), congenital coagulopathy with factor V and factor X deficiency, congenital tumors, twin–twin transfusion syndrome, demise of a co-twin, fetomaternal hemorrhages, and fetal thrombocytopenias [10, 11].

We hereby have described a case of a spontaneous SDH related to a very rare etiology of fetal thrombocytopenia, hidden maternal autoimmunity, which evolved very well despite all previsions. Nevertheless, the pathogenesis of intrauterine spontaneous SDH still remains unclear. It has been postulated that those lesions may occur due to the presence of intermittent aqueductal obstruction, which results in intermittent decompression. This can result in tearing of bridging veins and subsequent bleeding [12]. Coagulation deficiencies and fetal alloimmune thrombocytopenia were also reported.

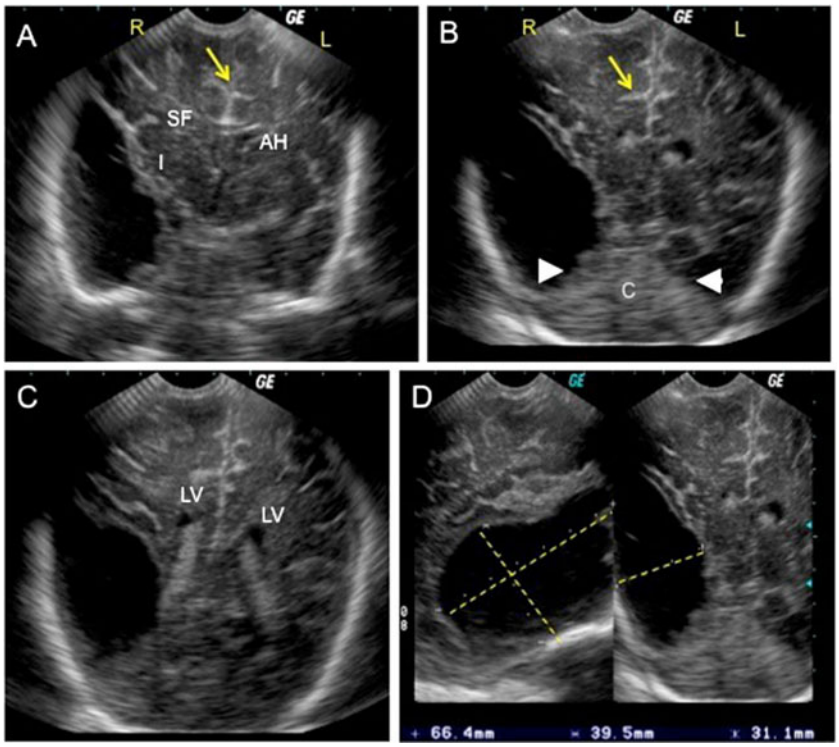

Fig. 3 Neonatal brain sonography. **a**, **b** Coronal views of the brain confirm the prenatal findings of a supratentorial subdural hematoma, at the level of the Sylvian fissure (*SF*) and the insula (*I*). The midline is displaced leftwards (*thin arrow*). The brain parenchyma seems to be preserved, with sulci and gyri compatible to the gestational age and normal anterior horns. No focal lesions are seen. The posterior fossa is not affected (*C* cerebellum; *arrow heads*). **c** Axial view showing normal-sized lateral ventricles (*LV*). **d** The size of the lesion is the same as measured during the 35th week, suggesting no new bleeding events. (*R* right, *L* left)

SDH generally presents with fetal macrocephaly on imaging studies. On sonography, a collection of heterogeneous material (echodense and echolucent) outlining the cortex and separating the brain from the inner table of the skull may be seen, and the presence of cerebral edema may lead to acoustic enhancement of brain gyri and sulci [13]. Catanzarite et al. [9] recommended imaging the fetal head in the axial or coronal plane at one level of the Sylvian fissure. In normal cases, the separation between the cortex and the inner table of the skull should be less than 4 mm. Expected postnatal brain function still cannot be predicted sonographically, except in the most severe cases. However, the absence of hydrocephalus, the amount of preserved brain parenchyma, and the behavior of the hematoma throughout the pregnancy seem to be short-term protective factors, as seen in the present case. Cardiac function alterations were also described related to SDH, with abnormal fetal heart rate patterns, nonreactive nonstress test, fetal tachycardia, or a positive oxytocin challenge test related to fetal anemia. No relationship, however, has been demonstrated between the umbilical and cerebral artery pulsatility index and severe intracranial hemorrhage [14].

Differential diagnosis depends on the location of the lesion and includes arachnoid cysts with intracystic hemorrhage, intracranial tumor hemorrhage, and true malformation of the dural sinuses [15]. Regarding treatment, there is no standard management for SDH. Treatment of the underlying disorder, when recognized, is paramount.

Hidden maternal autoimmune thrombocytopenia (HMAT) is a borderline entity described first in 1993 by Tchernia et al. [16], related to a pathophysiological process that stands between alloimmunity and autoimmunity. It may be as severe as alloimmune-induced thrombocytopenia, presenting with severe fetal and/or neonatal thrombocytopenia associated to SDH in approximately 20% of the cases and mucosal hemorrhages (urinary, gastrointestinal), without maternal thrombocytopenia. Affected mothers showed high levels of antiplatelet autoantibodies that have increased affinity for fetal platelet epitopes only, which explains the normal maternal platelet count [17].

HMAT has a 100% risk of recurrence after a first affected child, which implies in important questions regarding parental counseling. De Spirlet et al. [17] recommend aggressive management if a new pregnancy occurs, starting obtaining fetal blood sampling at 20 weeks to guide the need of platelet transfusion. Transfusion must be made immediately in when the count is less than 50,000 platelets/mm^3. If the thrombocytopenia persists despite all in utero transfusions, corticosteroids for pulmonary maturation are recommended previously to a cesarean section scheduled for 32–34 weeks. Gammaglobulin and corticosteroids are not routinely indicated for fetal treatment since they appear to have no effect on fetal platelets in autoimmune thrombocytopenia cases.

Once a SDH is diagnosed, repeated sonography is indicated to monitor the evolution of the bleeding, the development of hydrocephalus, and to check for the presence of hydrops fetalis secondary to fetal anemia. Daily nonstress tests and contraction stress tests along with daily biophysical profiles must be considered [18]. Despite the aggressive treatment of fetal thrombocytopenia and dedicated sonographic follow-up, there is always the risk of new bleeding episodes, which may be lethal

[13]. In the presence of stable, mild lesions, delaying delivery to attain pulmonary maturity is feasible. Vaginal delivery does not appear to be contraindicated if there is no other obstetric contraindication, although most of the reported cases were delivered by cesarean section [17].

Prognosis and long-term sequelae of the surviving child are still difficult to be predicted prenatally but are poorer compared to prenatal intraventricular hemorrhage. Complications related to poor prognosis include secondary ventricular obstruction with progressive hydrocephalus, cerebral infarction, and diffuse cerebral atrophy leading to microcephaly [19]. Vergani et al. reported a 43% demise rate (intrauterine and neonatal), and among the survivors, 57% presented severe sequelae (developmental delay, speech delay, optic nerve atrophy, and spastic diplegia or quadriplegia). Only 30% of the cases were normal after 2 years of follow-up [2].

In summary, hidden maternal autoimmunity is a very rare cause of fetal thrombocytopenia and may lead to many complications, including subdural hemorrhage. Fetal SDH have usually poor prognosis with a high rate of demise and long-term sequelae. The absence of secondary hydrocephalus and brain parenchyma lesions is related to a good prognosis, though, as shown in this case. Parents must be carefully counseled about the 100% rate of recurrence of this entity in further gestations, and aggressive management of the fetal thrombocytopenia is highly recommended in order to prevent fetal damage.

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