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Genetic hyperinsulinism as a rare cause of fetal macrosomia and shoulder dystocia: A case report

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Abstract
Congenital hyperinsulinism (CHI) is a rare genetic disorder of pancreatic β-cell function and the leading cause of persistent hypoglycemia in infancy. While most cases present postnatally, in utero hyperinsulinism can promote excessive fetal growth, even in the absence of maternal diabetes.
We report a case of a 23-year-old primigravida with an uncomplicated pregnancy who delivered a macrosomic infant (6175 g) complicated by severe shoulder dystocia following vacuum assisted delivery (VAD). The infant was stillborn after failed maneuvers and surgical extraction. Histopathological examination revealed islet cell hypertrophy and hyperplasia, and genetic testing identified an *ABCC8* mutation shared by both the mother and the fetus.
This case illustrates autosomal dominant *ABCC8*-related CHI manifesting as fetal macrosomia in nondiabetic pregnancies. The findings highlight the potential for monogenic hyperinsulinism to drive fetal overgrowth and obstetric complications, such as shoulder dystocia. Recognition of genetic causes of fetal macrosomia is essential for individualized obstetric management, anticipatory delivery planning, and genetic counselling.

Keywords: Genetic hyperinsulinism, macrosomia, shoulder dystocia

Introduction
Fetal macrosomia, often defined as a birth weight exceeding 4000-4500 g, is a significant obstetric concern associated with labor dystocia, cesarean delivery, and neonatal morbidity. Although maternal diabetes remains the most common cause, a subset (ca 8%) of macrosomic infants are born to nondiabetic mothers [1], suggesting alternative metabolic or genetic mechanisms of overgrowth.
CHI represents a rare but important cause of fetal and neonatal hyperinsulinemia [2]. The disorder is characterized by dysregulated insulin secretion from pancreatic β-cells, most often resulting from mutations in the *ABCC8* or *KCNJ11* genes [3, 4]. This leads to persistent β-cell depolarization and uncontrolled insulin release, driving hypoglycemia postnatally and, in utero, promoting excessive anabolic growth.
While CHI typically presents after birth with hypoglycemia, in utero manifestations may include disproportionate fetal growth and increased adiposity, which may manifest as an enlarged abdominal circumference or excess subcutaneous tissue on ultrasound. Recognition of this mechanism is crucial when evaluating macrosomia in the absence of maternal diabetes.
We report a case of severe fetal macrosomia and shoulder dystocia in a nondiabetic pregnancy, in which both the mother and fetus were found to carry a heterozygous *ABCC8* mutation. This case underscores the relevance of monogenic hyperinsulinism in obstetric outcomes.

Case Report
Background
A 23-year-old primigravida at 40 weeks of gestation presented to the labor and delivery ward with irregular uterine contractions. The pregnancy had been uncomplicated, with normal fetal growth and a symphysis-fundal height slightly below +2 SD at 38 weeks of gestation. Her BMI was 23 kg/m², and she had no medical or obstetric comorbidities, including hypertension, diabetes, or bleeding disorders. She was a nonsmoker and had attended all routine prenatal visits from early pregnancy.

Admission

On admission at 10:00, the patient was in the latent phase of labor. Fetal heart rate monitoring showed a reassuring pattern. The following morning at 06:00, spontaneous rupture of membranes occurred, releasing meconium-stained amniotic fluid. The cervix was 0.5 cm thick and dilated to 6 cm.

Labor Course

At 11:00, epidural analgesia was administered and an oxytocin infusion was initiated due to slow progress. At 14:00, the cervix had swollen edges and was dilated to 7-8 cm. The fetal head had descended slightly further into the pelvis. A mild increase in baseline fetal heart rate was noted, and the maternal temperature was 37.9 °C.

At 22:00, the cervix was fully dilated (10 cm), and the maternal temperature had risen to 38.0 °C. Intravenous antibiotics was administered as prophylaxis against group B streptococcal infection due to prolonged rupture of membranes.

Because of slow progress, ultrasound examination was performed to assess fetal position, confirming an anterior cephalic presentation.

At 07:00 the next morning, the cervix was fully retracted, and the fetal head was just below the ischial spines, at a mid-station. The maternal temperature had increased to 38.6 °C. Blood cultures were obtained, and broad-spectrum intravenous antibiotics was administered.

Given the lack of fetal descent despite an hour of spontaneous pushing and emerging signs of maternal exhaustion, the obstetric team decided to proceed with VAD.

Delivery

At 08:00, VAD was performed after completion of the institutional protocol and obtaining informed consent. The indication was labor dystocia and maternal exhaustion. Contractions were short and ineffective, and oxytocin infusion was maintained at 225 mL/h.

Extraction was described as moderately difficult. The vacuum cup detached on the fourth pull, and a total of six pulls were required. The fetal head was delivered at 08:17, but the rest of the body did not follow. Upon assessment, shoulder dystocia was suspected, and the according protocol was promptly activated. Sequential maneuvers were performed at 30-second intervals: McRoberts, suprapubic pressure (Rubin I), internal rotational maneuvers (Rubin II, Woods corkscrew and reverse Woods) followed by the Gaskin maneuver. Additional obstetric specialists were summoned for assistance. When all standard maneuvers failed, the patient was transferred to the operating theatre 18 minutes after the delivery of the head.

Surgery commenced under general anesthesia. After gaining access to the fetus via a cesarean incision, attempts were made to dislodge the anterior shoulder with downward traction. When this failed, the shoulder was manipulated in the opposite direction. The team rotated duties multiple times, administering muscle relaxants and Nitroglycerin. Zavanelli maneuver was performed followed by repeat extraction attempts. Despite these measures, delivery remained difficult until extraction was ultimately achieved using a destructive procedure due to confirmed intrauterine demise. The head-to-body delivery interval was 1 hour and 13 minutes. The infant was born with Apgar score of 0-0-0 and a birth weight of 6175 g. Figure 1 shows a schematic diagram of the labor course.

Postpartum Course

Following delivery, the abdominal surgical procedure was completed. During a subsequent surgical session, a complex vaginal laceration was repaired, including bilateral levator muscle injuries, a urethral lesion, and a third-degree perineal tear.

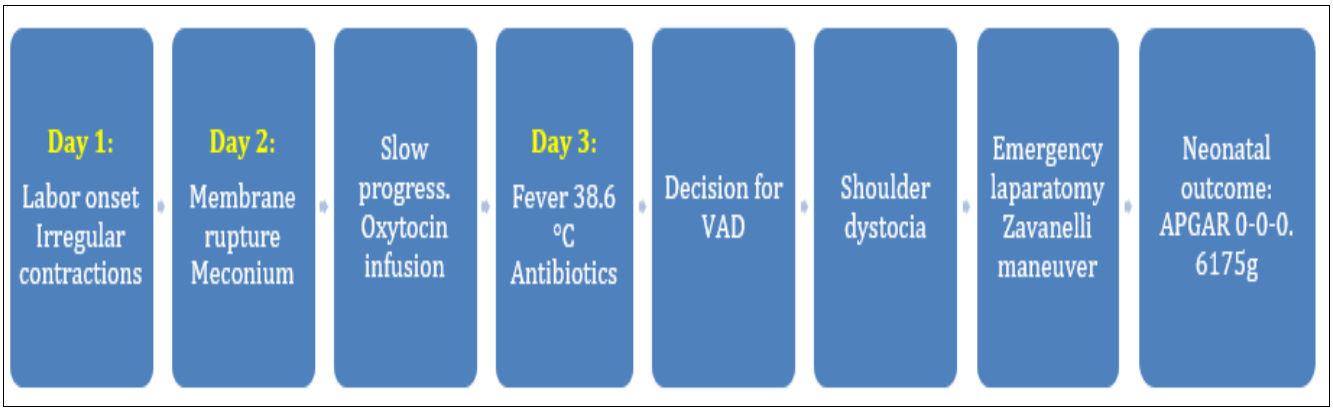

Fig 1: Clinical timeline of labor and delivery

Discussion

The newborn exhibited pronounced macrosomia and histopathological evidence of islet cell hypertrophy and hyperplasia. Genetic analysis revealed a pathogenic mutation in the hyperinsulinism-associated gene *ABCC8*, which was also present in the mother.

These findings align with previous reports describing fetal overgrowth and pancreatic β-cell proliferation secondary to in utero hyperinsulinism, even in the absence of maternal diabetes [5]. The presence of increased visceral and subcutaneous fat and hepatic erythropoiesis further supports chronic metabolic stimulation. Congenital hyperinsulinism (CHI) represents the leading cause of persistent hypoglycemia in infancy and results from dysregulated insulin secretion due to genetic defects in the pancreatic β-cell [6]. The majority of cases arise from mutations in the *ABCC8* or *KCNJ11* genes, which encode the SUR1 and Kir6.2 subunits, respectively [4]. Together, they link cellular metabolism to insulin secretion. Loss-of-function mutations in *ABCC8* disrupt this mechanism by preventing channel opening. This results in continuous depolarization and unregulated insulin release characteristic of congenital hyperinsulinism, and consequently hypoglycaemia [2]. The *ABCC8* gene exhibits both recessive and dominant modes of inheritance, the latter typically associated with heterogeneous clinical expression and reduced disease severity [3]. In this case, genetic testing revealed a heterozygous *ABCC8* mutation shared by both the mother and

the neonate, supporting an autosomal dominant form with variable expressivity (Figure 2). The mother remained asymptomatic, while the fetus demonstrated pronounced macrosomia and histological evidence of islet cell hyperplasia and hypertrophy. Fetal hyperinsulinemia promotes anabolic growth, excessive glycogen deposition, and increased adiposity, mechanisms well described in diabetic and hyperinsulinemic pregnancies. Notably, the macrosomia in this case occurred in the absence of maternal diabetes or clinical metabolic abnormalities, underscoring the pathogenic potential of monogenic hyperinsulinism as an underrecognized cause of fetal overgrowth.

The obstetric course was complicated by protracted labor, chorioamnionitis, and ultimately shoulder dystocia following VAD. Shoulder dystocia is an unusual but serious complication that can occur unpredictably, even in the absence of classical risk factors such as maternal diabetes or estimated fetal weight >5000 g [7]. Predicting shoulder dystocia at the time of operative vaginal delivery remains challenging, and no robust predictive model has yet been established [8].

When VAD fails to achieve descent after the first few pulls, prompt reassessment and readiness for alternative delivery methods, including cesarean section, are critical. Current guidelines recommend strict adherence to extraction limits and early team communication to prevent escalation to severe dystocia or maternal/fetal trauma [9]. In this case, the VAD was performed according to protocol, with steady descent of the fetal head observed during the initial pulls. However, the very slow labor progress leading to VAD was not fully appreciated. Considering the minimal progress over the preceding ten hours, short and ineffective contractions despite oxytocin augmentation, and an hour of active pushing without descent, proceeding with VAD carried inherent risks, though not absolute contraindications. The subsequent operative sequence, including attempted Zavanelli maneuver and cesarean extraction under general anesthesia, was consistent with established stepwise management of intractable shoulder dystocia [10].

From a multidisciplinary perspective, this case demonstrates the importance of integrating genetic insights into obstetric risk assessment. Familial *ABCC8* mutations should be considered when unexplained fetal overgrowth occurs in a nondiabetic pregnancy. Early recognition allows targeted perinatal monitoring, delivery planning with readiness for shoulder dystocia, and postnatal metabolic evaluation of both mother and infant. Precision medicine is increasingly bridging the gap between perinatal medicine and clinical management, improving outcomes for rare disorders.

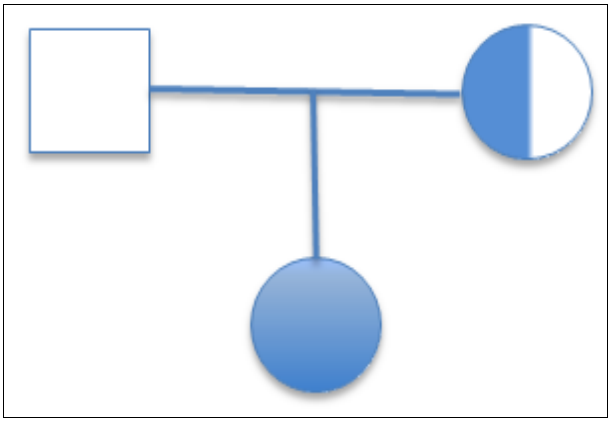

Fig 2: Pedigree Showing Inheritance of the ABCC8 Mutation

Pedigree chart illustrating autosomal dominant inheritance with variable expressivity. The mother is a heterozygous ABCC8 mutation carrier (clinically unaffected), the father is unaffected, and the daughter is heterozygous with clinical congenital hyperinsulinism

Conclusion

This report describes a rare instance of maternal and fetal *ABCC8*-related congenital hyperinsulinism presenting as severe macrosomia and complicated delivery. The case illustrates how fetal hyperinsulinism, independent of maternal diabetes, can lead to excessive growth and shoulder dystocia. It also underscores the value of early multidisciplinary collaboration, adherence to operative delivery protocols, and genetic evaluation when disproportionate fetal size arises without maternal metabolic disease. Recognition of monogenic causes of macrosomia has important implications for obstetric management, neonatal care, and for genetic counselling and reproductive planning, including preimplantation genetic testing (PGT).

Conflict of Interest

Not available

Financial Support

Not available

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