Fatty acid metabolism disorder not found on prenatal testing

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ABSTRACT

Case Description: A 26 year old G3P2001 presented for amniocentesis due to a family history of carnitine palmitoyltransferase 2 (CPT II) deficiency. Her first child developed seizures and passed away soon after birth; CPT II deficiency was diagnosed on the newborn screen. Both parents were confirmed to be carriers. For her second pregnancy, she opted against invasive testing. The newborn was treated proactively. Testing confirmed the child was not affected, and treatment was halted. In the current pregnancy, she opted for amniocentesis, which revealed an affected male.

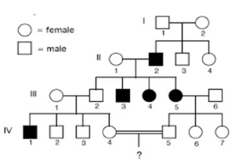
Background: CPT II deficiency is a rare autosomal recessive disease caused by a mutation in a gene encoding carnitine palmitoyltransferase 2, an essential enzyme in fatty acid oxidation. Affected patients are at risk for hypoketotic hypoglycemia, seizures, hepatomegaly, cardiomyopathy, arrhythmias, and other downstream issues. A postnatal diagnosis via the newborn screen does not confer the benefit of advanced awareness of the disease and allow for preemptive treatment. CPT II deficiency can be confirmed prenatally with diagnostic testing. Amniocentesis is an invasive test associated with a low but present risk of pregnancy loss, so some may opt against the test.

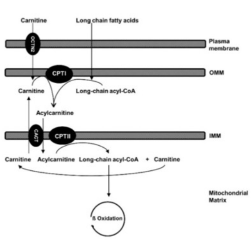
Conclusion: Carriers of CPT II mutations are counseled that future pregnancies confer a 25% risk of having an affected child. Prenatal diagnostic testing is recommended for prenatal diagnosis, which allows for planning of immediate treatment in the NICU. However, opting to forgo invasive testing and preemptively treat potentially affected child until newborn screening results return, as occurred in this patient's second pregnancy, is also an option.

Clinical Significance: CPT II deficiency is a rare disease that can have devastating effects in newborns without a known diagnosis. Parents with known carrier status must be extensively counseled on their options regarding prenatal and postnatal screening as well as immediate newborn care.

BACKGROUND

CPT II deficiency is inherited in an autosomal recessive pattern. This case is similar to what is seen in generation II, in which an affected child is born from two unaffected carrier parents.





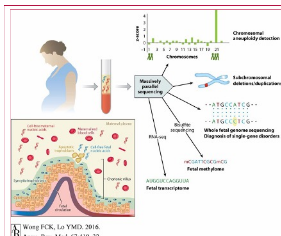
CPT II, located on the inner mitochondrial membrane, transfers long chain fatty acids attached to carnitine (acylcarnitine) into the mitochondrial matrix for oxidation.

CASE DESCRIPTION

- 26-year-old G3P2001 with amniocentesis confirmation of current pregnancy is fetus affected by CPT II deficiency
- Detailed pregnancy history in table below

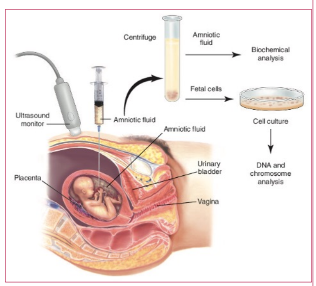
	Testing	Symptoms	Treatment	Outcome
First pregnancy	Prenatal: none Postnatal: newborn screen with +CPT II deficiency	Seizures, refractory hypoglycemia, autopsy with evidence of liver disease consistent with fatty acid oxidation defect	Supportive measures in NICU	Neonatal death
Second pregnancy	Prenatal: none Postnatal: newborn screen negative for CPT II deficiency		Proactive supportive treatment until negative genetic test	Healthy baby, carrier for CPT II deficiency
Third pregnancy	Prenatal: amniocentesis positive for CPT II deficiency		Plan for intensive postnatal treatment	

PRENATAL SCREENING



Noninvasive:
- Cell free DNA
- Particularly useful for diagnosing aneuploidies

Invasive:
- Amniocentesis
- Chorionic Villus Sampling
- Used to diagnose CPT II deficiency prenatally, among other diseases



TREATMENT FOR CHILD

- IV dextrose to maintain adequate glucose levels
- Frequent glucose monitoring

- IV levocarnitine

- Low fat, high carbohydrate diet
- G-tube placement often needed

COUNSELING

- CPT II deficiency is extremely rare → difficult to guide parents and their expectations
- Have been infants known to survive neonatal period
  - Little qualitative or quantitative data available
- Difficult to offer generalizations/numbers that might assist parents in planning for the birth of their baby

Information for parents:
- High mortality rate in severe CPT II deficiency
- Chance of survival with presymptomatic treatment
- Care team will follow mom and baby long-term and provide appropriate care
- Questions and open communication about the birth and treatment plans are encouraged

Making a neonatal plan:
- Some families may prefer to keep mom and baby in same hospital while mom is inpatient
- Consent should be obtained to transfer baby to a different hospital at/after birth if in baby's best interest
- Neonatal plan should be made with open communication between family, OBGYN team, NICU team, etc.

SUMMARY

- CPT II deficiency is a rare, autosomal recessive fatty acid oxidation disorder that prevents the proper use of long-chain fatty acids for energy.
- CPT II deficiency is associated with hypoketotic hypoglycemia, seizures, hepatomegaly, cardiomyopathy, and other symptoms depending on the severity. Some forms, particularly neonatal forms, can be lethal.
- CPT II deficiency can be tested for prenatally, via amniocentesis or CVS, if there is a known family history and the gene variants are able to be identified in an affected family member
- Since amniocentesis is an invasive procedure that carries risks, patient's must be carefully counseled
- It is optimal to begin treatment immediately after birth for infants diagnosed with CPT II deficiency prenatally
- If not fatal, treatment includes the administration of dextrose and Levocarnitine, imaging, possible G-tube placement, and long-term dietary treatment planning.

CONCLUSIONS

CPT II deficiency is a rare fatty acid metabolism disorder not found on standard prenatal testing, but one that confers great risk to infants affected by the disease. In this case, both parents were unknowing disease carriers, and their firstborn unfortunately died prior to diagnosis of the disease via newborn screening. For parents with known carrier status, extensive and careful counseling is necessary regarding prenatal and postnatal screening options and treatment plan following delivery. This patient presents a unique case study as she utilized different screening methods and treatment plans for each subsequent pregnancy.

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