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Three consecutive pregnancies in a woman with Crigler–Najjar syndrome type II with good maternal and neonatal outcomes

Sir,

Crigler–Najjar syndrome (CNS) is a rare autosomal recessive condition associated with complete deficiency (type I) or severely reduced activity (type II) of the hepatic microsomal bilirubin-uridine 5′-diphosphate-glucuronosyltransferase (UDPG-T). Both manifestations result in congenital unconjugated hyperbilirubinaemia being significantly higher in CNS type I than in type II [1]. Pregnancy in women with CNS is a therapeutic challenge due to the risk of bilirubin encephalopathy with serious neurological damages as life-threatening complications for the foetus. To date, only two pregnancies in women with CNS type I and six in women with CNS type II have been reported [2,3]. Thus, there is limited experience handling CNS in pregnancy.

Previously, we described a woman with CNS type II and her first healthy pregnancy [4]. This daughter of Nepalese and Tibetan parents is a double homozygous carrier of a glycine (GGA)-to-arginine (AGA) substitution at amino acid position 71, encoded by exon 1, and of a tyrosine (TAC)-to-asparagine (GAC) replacement at residue 486, encoded by exon 5. Meanwhile the currently 41-year-old woman has become twofold pregnant again. As all three pregnancies were successfully approached in the same manner we would like to share and communicate our experiences in this unique case.

To reduce the initial serum bilirubin of 9.9–11.8 mg/dl, in each pregnancy we initially performed a phototherapy for a total of 48–60 h between the 8th and 12th weeks of gestation. After bilirubin decreased to 4.0–7.0 mg/dl, induction of enzyme activity with low-dose phenobarbital was initiated after completion of embryogenesis (adapted doses of 1×25 mg up to a maximum of 2×50 mg), thereby maintaining bilirubin levels in the range between 4.2 mg/dl and 5.5 mg/dl until delivery. Daily doses of 75–100 mg phenobarbital were not well tolerated as the pregnant complained about dizziness and tiredness. Maternal bilirubin serum levels were monitored in 2-week intervals. Regular foetal ultrasonic investigations were performed according to the guidelines of the German society of Ultrasound in Medicine—Level II. In the last two pregnancies (16th week of gestation) amniocentesis was performed for the exclusion of aneuploidy. Detailed ultrasound screening included foetal echocardiography in the 21st week of gestation. In the 3rd trimester we performed regular and Doppler ultrasound to monitor foetal growth and well being. As we observed increasing foetal macrosomia and polyhydramnion in each pregnancy, gestational diabetes was excluded through 75 g oral glucose tolerance test. The three pregnancies progressed without any other complications.

Due to a narrow pelvic inlet in the very slender woman we indicated Caesarean delivery in the 40th, 36th and 36th week respectively. The corresponding weights and lengths of the three healthy newborns were 3800 g and 52 cm, 3440 g and 51 cm, and 3420 g and 49 cm. Apart from increased serum levels of unconjugated bilirubin with a maximal of 6.4 mg/dl, the postpartal periods were unremarkable showing normal echocardiographic and ultrasonic findings of the encephalon, abdomen and hips. The currently 5- and 3-year- and 6-month-old boys are normally developed, and their serum bilirubin levels are normal. Since family planning is complete, the last Caesarean section was followed by tubal sterilisation.

Experiences from our patient and a comparable maternal therapy in two pregnancies in a further woman with CNS type II [5] suggest that dual treatment consisting of phototherapy during embryogenesis and phenobarbital during the rest of the pregnancy are safe and effective options avoiding foetal and neonatal sequelae. Furthermore, close interdisciplinary care in a perinatology centre with cooperation of internists, obstetricians and paediatricians is considered to be indispensable in these high-risk pregnancies. Provided appropriate medical care CNS type II should be no reason to resign pregnancy.

Conflict of interest statement

None declared.

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