Sonographic Findings in Two Consecutive Pregnancies Affected with Fetuses of Congenital Nephrotic Syndrome of Finnish Type

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Dear Editor,

Congenital nephrotic syndrome (CNS) is a kidney disorder that begins in infancy and typically leads to end-stage renal disease by early childhood. The CNS of Finnish type (CNF) refers to that caused by *NPHS1* defects.[1] We, here, report two consecutive pregnancies affected with fetuses of CNF.

A 28-year-old G2P1 female was referred to our unit at her third trimester of pregnancy because of abnormal fetal ultrasound. The couple were nonconsanguineous, and both were healthy without significant family history. During her first pregnancy two years previously, the third-trimester ultrasound showed breech presentation, bilateral renal enlargement with hyperechogenicity, and normal amniotic fluid volume. The pregnancy continued to 32 weeks when preterm labor occurred spontaneously. The female infant died two weeks after birth. The clinical diagnosis was CNS.

During the present pregnancy, both 12-week and 22-week scans had no significant findings. The ultrasound at 28 weeks showed breech presentation, a slight increase in renal size (the left kidney measured 42 mm and the right 43 mm) as well as in echogenicity and normal amniotic fluid [Figure 1]. There was no hydronephrosis and cystic changes. Genetic amniocentesis reported a normal microarray, but trio exome sequencing (ES) detected a pathogenic homozygous *NPHS1* (NM_004646) variant c.2443C>T (p.Gln815Ter) with parental inheritance [Figure 1]. Again preterm labor occurred at 34 weeks, and a girl was born with birth weight of 2290 g and height of 41 cm. Apgar score was 7 and 8 in the 1st and 5th minute, respectively. The postnatal course was uneventful until two weeks after birth when periorbital and lower extremities edema, abdominal distension, fever, and failure to thrive occurred. Abdominal ultrasound

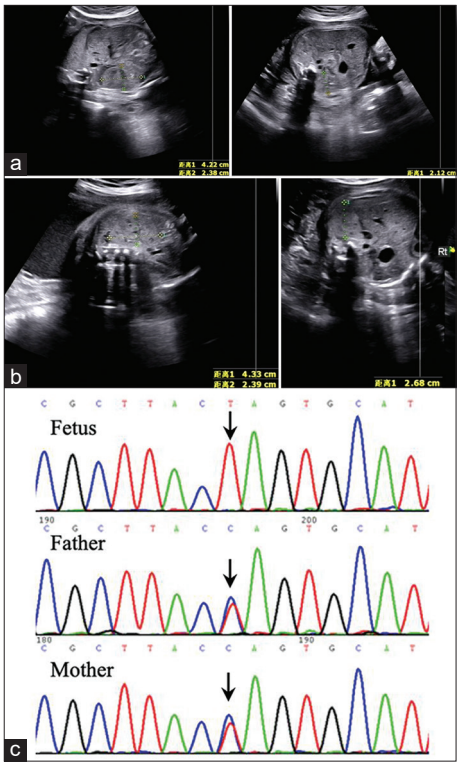

Figure 1: Prenatal ultrasound of a fetus with congenital nephrotic syndrome of Finnish type caused by a homozygous *NPHS1* variant c.2443C>T. Fetal ultrasound at 28 weeks of gestation shows a slight increase in size and echogenicity of the kidneys, with the left measuring 4.2 cm × 2.3 cm × 2.1 cm in length (a), the right 4.3 cm × 2.3 cm × 2.6 cm (b). DNA sequencing shows a homozygous *NPHS1* c.2443C>T variant in the fetus, a heterozygous state in both parents (c)

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showed enlarged hyperechogenic kidneys with abnormal corticomedular differentiation (CMD). Urinalysis revealed massive proteinuria (4+). Renal biopsy confirmed CNS. The girl died at 4 weeks old because of pneumonia.

In CNF children, the kidneys are enlarged with hyperechogenic renal cortex and preserved CMD during the first 2 months of life.[2] Between the age of 2 and 12 months, renal echogenicity enlargement persists, but CMD disappears. The disease develops *in utero*, and prenatal diagnosis would be important for CNF because the treatment is very challenging. A high level of serum α-fetoprotein in the second trimester of pregnancy,[3] which is usually detected by routine Down screening test, used to be a clue to the suspension of CNF. However, this second-trimester screening approach is now replaced by NT-based first-trimester screening or cell-free DNA screening. Prematurity was common in CNF patients.[4] The sonogram of the fetal kidneys may show normal or echogenic parenchyma and normal or enlarged renal size.[5] We report two affected pregnancies with fetal CNF, which presented with breech presentation, preterm labor, and a mild increase in renal size and echogenicity. Our study further indicates that some affected fetuses do have subtle renal features on ultrasound although they are nonspecific. These fetal renal characteristics cannot provide an accurate etiological diagnosis. Our report suggests that clinicians should be alerted to the possibility of CNF. ES testing should be considered to accelerating discovery of pathogenic variants related to rare genetic disorders.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent form. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her names and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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