Cystic kidneys in a neonate: do not forget to examine pupils

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DESCRIPTION

A male infant was born out of third-degree consanguineous marriage at 36-week gestation with a birth weight of 2340 g. The antenatal ultrasound at 23 weeks of gestation showed enlarged, hyperechoic kidneys with normal liquor. On physical examination, he had generalised oedema, prominent eyes, axial hypotonia and fixed contractures at bilateral knee joints ([figure 1](#)). The prominent eyes prompted us to do an ophthalmological examination. We noticed that his pupils were small, constricted and non-responsive to light. The pupils remained miotic even after instillation of tropicamide and atropine ([figure 2](#)). Refractory microcoria, along with cystic kidney disease in the neonatal period, raised the possibility of Pierson syndrome and directed further evaluation. The postnatal ultrasound showed enlarged (right kidney 6.3 cm, left kidney 6.8 cm), globular hyperechoic kidneys, with poor corticomedullary differentiation. Laboratory evaluation revealed nephrotic range proteinuria (urine protein 3.9 g/dL, urine dipstick 3+), hypoalbuminemia (albumin 1.9 g/dL) and hyperlipidemia (serum cholesterol 277 mg/dL, serum triglyceride 628 mg/dL) consistent with the diagnosis of congenital nephrotic syndrome. It further strengthened our suspicion of Pierson syndrome; therefore, genetic analysis by targeted gene sequencing was done.

Figure 1 Generalised oedema and contractures at bilateral knee joints.

Figure 2 Pupil is miotic and refractory to atropine ointment.

A homozygous non-sense variation in exon 23 of the LAMB2 gene (chr3:g.49161965G>A) that results in a stop codon and premature truncation of the protein at codon 1064 (p.Gln1064Ter) was detected. This is a novel mutation and has not been reported until in 1000 Genomes Project and ExAC database.¹²

He worsened with oliguria and anasarca leading, to pulmonary oedema, and respiratory distress for which continuous positive airway pressure support, albumin infusion and diuretics were given. The anasarca was refractory to diuretics and albumin infusions. Because of poor prognosis, parents decided to discontinue treatment and he died at the age of 17 days.

Pierson syndrome is caused by mutations in $\beta 2$ -laminin encoded by the LAMB2 gene and is clinically characterised by congenital nephrotic syndrome and bilateral microcoria.³ Presence of characteristic eye findings helps in clinically differentiating this entity from other causes of congenital nephrotic syndrome.⁴ It exhibits good genotype–phenotype correlation. The patients with milder forms of Pierson syndrome have at

Patient's perspective

It was painful to us when we came to know that our baby is having such a severe medical condition. Despite the best efforts of the doctors, the fate of our child cannot be changed.

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least one missense or non-truncating deletion mutation, while those with more severe phenotype have two truncating mutations.⁵ Our patient had a homozygous non-sense mutation resulting in premature truncation of the protein leading to severe phenotype.

Renal involvement is universal and is associated with ocular and neuromuscular abnormalities. The ocular manifestations are microcoria (the most common and characteristic), megalocornea, glaucoma, microphthalmia, posterior lenticonus, cataract, persistent fetal vasculature and retinal detachment.⁴ Owing to the expression of LAMB2 gene in the neuromuscular system, neurological manifestations, such as muscle hypotonia, contractures and neurodevelopmental abnormalities are also seen.⁶ The

overall prognosis is poor and most of the affected individuals die in infancy only.

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Learning points

- ▶ Pierson syndrome is a rare cause of congenital nephrotic syndrome.
- ▶ Early renal impairment in the neonatal age group and characteristic eye findings helps in clinically differentiating Pierson syndrome from other causes of congenital nephrotic syndrome.
- ▶ Mutational analysis of LAMB2 gene is considered diagnostic for this entity.

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