Nephrotic and Nephritic Syndrome in the Newborn

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KEYWORDS

• Proteinuria • Hematuria • Congenital nephrotic syndrome
• Diffuse mesangial sclerosis • Nephritis • Hemolytic uremic syndrome
• Neonatal lupus

KEY POINTS

- Congenital nephrotic syndrome (CNS) presents within the first 3 months of life with massive proteinuria, hypoalbuminemia, and edema.
- Elevated maternal serum α-fetoprotein, enlarged placenta (>25% of birth weight), and prematurity are suggestive of CNS.
- CNS is most often caused by single gene mutations affecting kidney podocyte structural or signaling proteins.
- Infants with CNS are at risk for infection and thromboembolism, which may be the initial clinical manifestation.
- Nephritic syndrome in the newborn is rare, and presenting features may include hematuria, proteinuria, hypertension, acute kidney injury, oliguria, and edema.

INTRODUCTION

Glomerular disorders in infancy are rare, and can include both nephrotic and nephritic syndromes. These syndromes can be idiopathic, or due to primary genetic disorders, congenital infections, or maternal antibody transfer. Regardless of etiology, dysfunction of the glomerular filtration barrier is evident in these conditions. The kidney glomerular filtration barrier is a size-selective and charge-selective filter that prevents the passage of red blood cells and plasma proteins into the urine while allowing the passage of water and small solutes. It is composed of 3 layers: an endothelium, a glomerular basement membrane (GBM), and epithelial cells, also known as podocytes. Podocytes are highly differentiated cells that have a complex cellular architecture consisting of a cell body, major processes, and foot processes. Adjacent foot processes are connected by a slit diaphragm, which comprises the main size-selective filtration

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barrier in the kidney (Fig. 1).[1–3] Dysfunction in any of the 3 components of the glomerular filtration barrier can lead to loss of red blood cells and plasma proteins in the urine, and clinical nephrotic or nephritic syndromes. The presence of these syndromes in the neonate can cause significant morbidity and mortality; therefore, urgent diagnosis and treatment are necessary.

DIAGNOSIS OF CONGENITAL NEPHROTIC SYNDROME

Nephrotic syndrome (NS) is defined as massive leakage of plasma proteins into the urine caused by dysfunction of the glomerular filtration barrier, leading to hypoalbuminemia and edema. NS can be further classified by age at presentation as congenital NS (CNS, age at presentation <3 months), infantile NS (age at presentation 3–12 months), or childhood NS (age at presentation >1 year). As the genetics of NS have started to be unraveled over the past 15 years, it has become clear that different mutations in the same gene can manifest at various ages, making the classification by age somewhat arbitrary (*NPHS1*- and *NPHS2*-related disease can present in infancy, childhood, or rarely in adulthood, for example).[4,5] Nonetheless, the designation of "congenital nephrotic syndrome" still guides diagnosis, management, and prognosis, and this terminology has been retained by the pediatric nephrology community.

Prenatal diagnosis of CNS is suggested by elevated maternal serum α-fetoprotein (MSAFP) obtained in routine second-trimester screening. Fetal serum contains high concentrations of α-fetoprotein (AFP) that is lost into the urine/amniotic fluid during the nephrotic state. Elevated MSAFP is common and is found in approximately 1% of all pregnancies using a cutoff of greater than 2.5 multiples of the mean (MoM). Elevated MSAFP can be seen in pregnancies complicated by neural tube defects, gastroschisis, or chromosomal abnormalities as well as CNS.[6,7] CNS is a rare cause of elevated MSAFP, with one retrospective study identifying only 5 infants with CNS among 658 women with elevated MSAFP (<1%).[7] Most patients with pregnancies affected by CNS have persistently elevated MSAFP on follow up screens in addition to elevated AFP in amniotic fluid obtained by amniocentesis.[7] Median MSAFP concentrations were 8.3 MoM in pregnancies affected with CNS attributable to *NPHS1*

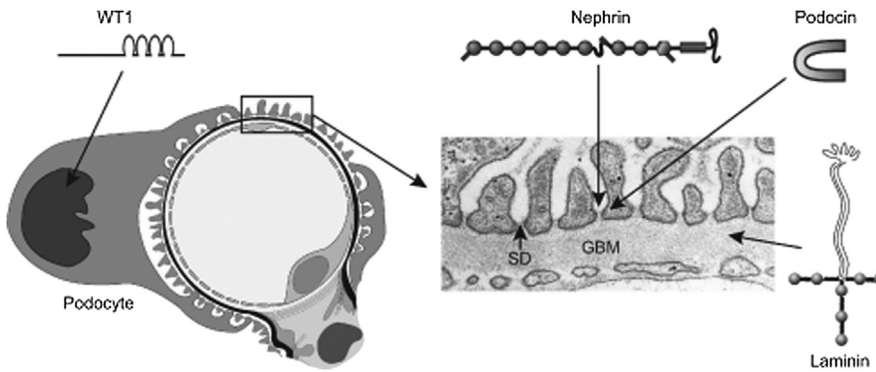

Fig. 1. The glomerular filtration barrier. Cross section of a glomerular capillary (*left*) and electron microscopy image of a normal capillary wall (*right*). WT1 is a transcription factor important for podocyte function. Nephrin is a major component of the slit diaphragm (SD) connecting podocyte foot processes. Podocin is an adapter protein located intracellularly in the SD area. Laminin is a major structural protein of the glomerular basement membrane (GBM). Genetic mutations in these proteins lead to congenital nephrotic syndrome. (*From* Jalanko H. Congenital nephrotic syndrome. Pediatr Nephrol 2009; 24(11):2121–8.)