Congenital Nephrotic Syndrome

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Congenital nephrotic syndrome is a kidney condition that begins in infancy and typically leads to irreversible kidney failure (end-stage renal disease) by early childhood. Children with congenital nephrotic syndrome begin to have symptoms of the condition between birth and 3 months.

Keywords: genetic conditions

1. Introduction

The features of congenital nephrotic syndrome are caused by failure of the kidneys to filter waste products from the blood and remove them in urine. Signs and symptoms of this condition are excessive protein in the urine (proteinuria), increased cholesterol in the blood (hypercholesterolemia), an abnormal buildup of fluid in the abdominal cavity (ascites), and swelling (edema). Affected individuals may also have blood in the urine (hematuria), which can lead to a reduced number of red blood cells (anemia) in the body, abnormal blood clotting, or reduced amounts of certain white blood cells. Low white blood cell counts can lead to a weakened immune system and frequent infections in people with congenital nephrotic syndrome.

Children with congenital nephrotic syndrome typically develop end-stage renal disease between ages 2 and 8, although with treatment, some may not have kidney failure until adolescence or early adulthood.

2. Frequency

Congenital nephrotic syndrome affects 1 to 3 per 100,000 children worldwide. In Finland, where this condition is particularly common, congenital nephrotic syndrome is estimated to affect 1 in 10,000 children.

3. Causes

Mutations in the *NPHS1* or *NPHS2* gene cause most cases of congenital nephrotic syndrome. These genes provide instructions for making proteins that are found in the kidneys. Specifically, the proteins produced from the *NPHS1* and *NPHS2* genes are found in cells called podocytes, which are located in specialized kidney structures, called glomeruli, that filter the blood. The proteins are found at the podocyte cell surface in the area between two podocytes called the slit diaphragm. The slit diaphragm is known as a filtration barrier because it captures proteins from blood so that they remain in the body while allowing other molecules like sugars and salts to be excreted in urine. The proteins produced from the *NPHS1* and *NPHS2* genes also help relay cell signals.

Mutations in the *NPHS1* or *NPHS2* gene result in a decrease or absence of functional protein, which impairs the formation of normal slit diaphragms. Without a functional slit diaphragm, more molecules pass through the kidneys abnormally and get excreted in urine, including proteins and blood cells. The filtering ability of the kidneys worsens from birth, eventually leading to end-stage renal disease.

NPHS1 gene mutations cause all cases of congenital nephrotic syndrome of the Finnish type. This form of the condition is found in people of Finnish ancestry. *NPHS1* gene mutations can cause congenital nephrotic syndrome in non-Finnish individuals, but they are a less common cause than *NPHS2* gene mutations, which appear to be the most frequent cause of all cases.

Mutations in other genes cause a small number of cases of congenital nephrotic syndrome. Fifteen to 20 percent of individuals with congenital nephrotic syndrome do not have an identified mutation in one of the genes associated with this condition. In these cases, the cause of the condition may be environmental, including infections such as congenital syphilis or toxoplasmosis, or it may be caused by mutations in unidentified genes.

3.1. The Genes Associated with Congenital Nephrotic Syndrome

- NPHS1
- NPHS2
- WT1

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- familial nephrotic syndrome

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