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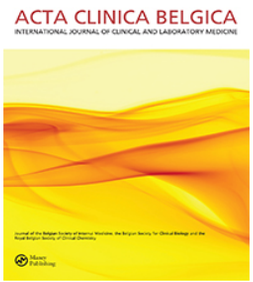

Acta Clinica Belgica
International Journal of Clinical and Laboratory Medicine

ISSN: 1784-3286 (Print) 2295-3337 (Online) Journal homepage: https://www.tandfonline.com/loi/yacb20

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**To cite this article:** Tülin Güngör, Fehime Kara Eroğlu, Evrim Kargın Çakıcı, Fatma Yazılıtaş, Gökçe Can, Evra Çelikkaya, Deniz Karakaya, Eda Didem Kurt Şükür, Fatih Özaltın, Beytullah Yağız & Mehmet Bülbül (2019): Gastric duplication cyst in an infant with Finnish-type congenital nephrotic syndrome: concurrence or coincidence?, Acta Clinica Belgica, DOI: 10.1080/17843286.2019.1675333

**To link to this article:** https://doi.org/10.1080/17843286.2019.1675333

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CASE REPORT



# Gastric duplication cyst in an infant with Finnish-type congenital nephrotic syndrome: concurrence or coincidence?

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**ABSTRACT**

Congenital nephrotic syndrome (CNS) is a rare disorder characterized by massive proteinuria and marked edema manifesting in utero or during the first 3 months of life. CNS can be caused by congenital infections, allo-immune maternal disease or due to the genetic defects of podocyte proteins most commonly NPHS1. Here we present a case of Finnish-type congenital nephrotic syndrome along with feeding problems and abdominal distention which was diagnosed during follow-up as a gastric-duplication cyst with a novel mutation in the nephrin gene. CNS feeding problems are attributed mainly to primary disease but in literature there are case reports of patients with CNS and hypertrophic pyloric stenosis. NPHS1 is also expressed in the stomach tissue. Physicians should be aware of this rare extra-renal manifestation or coincidence of this rare disease.

**KEYWORDS**

Congenital nephrotic syndrome; gastric duplication cyst; novel nephrin mutation

## Introduction

Congenital nephrotic syndrome (CNS) is a heterogeneous disorder that generally starts in utero or within the first 3 months of life and characterized by severe proteinuria, hypoalbuminemia and edema [1]. The majority of patients with CNS show mutations in genes encoding key podocyte proteins that constitute the slit diaphragm (NPHS1 and NPHS2); others are expressed in the podocyte membrane (PLCE1) or glomerular basement membrane (LAMB2), and other genes encode transcription factors (WT1, LMX1B) [2]. Mutations in genes coding structural and regulatory proteins of the glomerular filtration barrier are the main cause of congenital nephrotic syndrome. Autosomal recessive mutations in the NPHS1 gene are a common cause of congenital nephrotic syndrome. CNS is usually a single-organ disorder that is restricted to the kidneys, but it can manifest other extra-renal developmental abnormalities [3]. Progression to end-stage kidney disease (ESKD) occurs within a few years in most patients so the goals of therapy during infancy are the prevention and treatment of complications, such as infections and thrombosis, and the achievement of sufficient physical growth to allow for an adult kidney transplant. However, most infants with CNS exhibit a failure to thrive due to insufficient oral intake and/or frequent vomiting [1]. Here we present a case of Finnish-type congenital nephrotic syndrome along with feeding problems and abdominal distention which was diagnosed during follow-up as a gastric-duplication cyst with a novel mutation in the nephrin gene.

Gastrointestinal duplication cysts are a rare developmental anomalies characterized by an epithelial lining some part of the alimentary tract. Duplication cysts of the stomach are comprising 4% of all gastrointestinal duplications. The clinical presentation can be highly variable ranging from abdominal pain, vomiting, epigastric fullness, dysphagia, dyspepsia with abdominal tenderness and epigastric mass on physical examination. Gastrointestinal duplication cysts are diagnosed using computerized tomography and treated with surgical excision [4].

## Case report

A 2-month-old baby girl was admitted to our clinic with abdominal swelling since birth. The patient had been born prematurely (36 weeks) with a low birth weight. There was a degree of kinship between her parents but there was no history of kidney disease in the family. On examination, she was 25$^{th}$ percentile for height and weight (weight 5.3 kg; length 54 cm and head circumference 38 cm), and there were peripheral edema and abdominal distension. The urine dipstick resulted in 4 + for proteinuria, but with no signs of haematuria. Blood testing showed hypoalbuminaemia of 1.5 g/dL (reference interval 3,5–5,4 g/dL) indicating nephrotic syndrome. Her whole blood count revealed anaemia with haemoglobin of 9.4 g/L and there was thrombocytosis with 620 × 10$^9$/L. The plasmatic coagulation tests were found to be within normal range, as well as the liver

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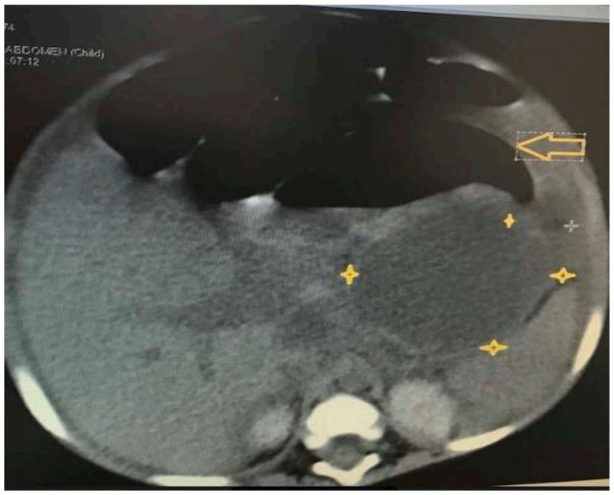

Figure 1. CT scan showing 9 × 7 × 7 cm gastric duplication cyst.

enzymes, renal function testing and electrolytes. The total- and LDL cholesterol levels were noticeably increased; TSH and PTH were also significantly elevated together with hypocalcaemia and hyperphosphatemia. Serologic testing for active infections including hepatitis, toxoplasmosis, anti-streptolysin-O titer, cytomegalo virus and syphilis gave negative results. A renal biopsy showed focal segmental glomerulosclerosis. Genetic testing revealed a novel homozygous mutation in the NPHS1 gene (Exon19: c.2663G>A (p.R888K) (Mutation taster: Disease causing; Polyphen2: Probably damaging (score 0.99). After establishing the diagnosis, optimal supportive treatment including intravenous albumin for twice a week, furosemid, high caloric and protein diet were provided along with thyroxine. However, on follow-up, the patient had abdominal distention with vomiting and nutritional problems. A gastric duplication cyst was detected based on the results of repeated ultrasound examinations and abdominal radiography. CT scans of the abdomen demonstrated the cystic lesion of the stomach large curvature to be 9 × 7 × 7 cm (Figure 1). During laparotomy, a gastric duplication cyst was confirmed and excised completely.

## Discussion

Mutations in the NPHS1 or NPHS2 gene cause most cases of congenital nephrotic syndrome. The disorder is characterized by massive proteinuria that occurs in utero or in the neonatal period during the first 3 months of life. NPHS1 encodes nephrin, a member of the immunoglobulin family of cell adhesion molecules and the main protein expressed in the renal slit diaphragm. Currently, there are approximately 250 mutations described in the NPHS1 gene distributed among all nephrin domains [5,6]. We present a case of Finnish-type congenital nephrotic syndrome with a novel mutation in the nephrin gene.

Gastrointestinal duplication cysts are rare congenital anomalies and affect the small intestine (45%) and esophagus (19%). The incidence of gastrointestinal duplication cysts among all gastrointestinal duplications is 4 %. Patients are mostly presented with vomiting and malnutrition. Half of all cases are diagnosed in the first year of life. A hypoechoic outer rim and hyperechoic inner rim also suggests the stomach as the etiologic origin of the cyst. No known associated genetic chromosomal anomalies are reported. CT is helpful in determining the size of the cyst and the relationship with the neighboring organs. Magnetic resonance imaging (MRI) may be performed in cases of difficulty in diagnosis. The treatment for a gastrointestinal duplication cyst is surgical excision. Simple cyst excision, gastroduodenostomy with cyst excision and pyloroantrectomy may be performed either conventionally or laparoscopically [7,8]. During follow-up, the patient had abdominal distention with vomiting and nutritional problems. A gastric duplication cyst was detected based on the results of repeated ultrasound examinations and abdominal radiography. During laparotomy, a gastric duplication cyst was confirmed and excised completely.

Most infants with CNS exhibit a failure to thrive due to insufficient oral intake and frequent vomiting. Any evaluation of vomiting by CNS infants should take into consideration the potential causes, such as increased nutritional requirement compared to healthy infants, hypo-peristalsis, edema of the gastrointestinal tract and uremia associated with chronic kidney failure [9]. Structural digestive disorders, such as hypertrophic pyloric stenosis, gastroesophagal reflux and intestinal malrotation, have to be considered. The etiology of hypertrophic pyloric stenosis is unknown but it is likely to be multifactorial, involving genetic predisposition and environmental factors. Pyloric stenosis appears to be associated with CNS. In one series, 12% of 41 infants with CNS presented pyloric stenosis. The reason for this association is not known [10]. A novel mutation in the nephrin gene was detected in our patient. Nephrin is expressed in the testis, central nervous system, pancreas, placenta, heart and lymphoid tissue; however, its expression in the digestive tract has not been clarified [11]. Perhaps the effects of the neprin gene on the gastrointestinal tract will be demonstrated as similar case samples increase in following years.

Feeding problems of CNS are attributed mainly to primary disease but in literature there are case reports of patients with CNS and hypertrophic pyloric stenosis. In particular, the mutation in the nephrin gene is presented as an important case in determining the relationship with the gastrointestinal system anomalies. Physicians should be aware of this rare extra-renal manifestation or coincidence of this rare disease.

As a result, we aimed to draw attention to the association of nephrin gene mutation and gastrointestinal system anomaly.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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