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(CASE REPORT)

Early diagnosis and management of finish type congenital nephrotic syndrome in a 3-year-old child: A case report

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Abstract

This study describes a 3-year-old non Finnish girl who was diagnosed with Finnish-type nephrotic syndrome (FTNS), a rare kidney illness brought on by NPHS1 gene abnormalities. Even though she had low protein levels and severe swelling when she was three months old, her case of congenital nephrotic syndrome (CNS) was incorrectly identified as minimal change disease (MCD). The standard MCD treatments, cyclosporine and steroids, did not affect her. A genetic test and a kidney sample confirmed the diagnosis of FTNS, a condition that necessitates an early renal transplant for survival. She is awaiting a kidney transplant and was treated with drugs that save proteins to lessen her edema. The study emphasizes the significance of FTNS early and correct diagnosis as well as the requirement for alternate treatments for this difficult illness.

Keywords; Finnish-type nephrotic syndrome (FTNS); NPHS1 gene; Congenital nephrotic syndrome (CNS); Minimal change disease (MCD); Cyclosporine; Steroids; Renal transplant

1. Introduction

During the first three months of life, babies are susceptible to an uncommon kidney condition called congenital nephrotic syndrome (CNS). Severe bodily edema and a significant loss of protein in the urine are its defining features. Complications from CNS include reduced renal function, recurring infections, and decreased development. Mutations in the genes encoding proteins associated in the development and upkeep of the glomerular filtration barrier—the structure responsible for filtering blood in the kidneys—are the primary cause of CNS. A recent research found that around 75% of cases are caused by mutations in the NPHS1 and NPHS2 genes, which code for podocin and nephrin, respectively [1]. The slit diaphragm, the portion of the glomerular filtration barrier that stops proteins from seeping into the urine, is formed by the synthesis of nephrin and podocin. Proteinuria and nephrotic syndrome are brought on by mutations in these genes that affect the slit diaphragm's shape and functionality.

Because of a founder effect caused by two distinct NPHS1 mutations, CNS is more frequent in Finland, affecting around 1 in 8,200 infants [2]. With varying kinds and frequencies of mutations, it can also happen in different ethnic groups around the world [3]. The majority of newborns with CNS die during the first year of life due to end-stage renal failure, making their prognosis dismal. To increase their chances of survival and quality of life, there are therapies available. The management of complications like thrombosis and hypertension, the use of specialized intravenous fluids to correct

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fluid and electrolyte imbalances, dietary changes to prevent malnutrition and infection, renal replacement therapy with dialysis or transplantation, and genetic counseling for the families are a few of these [4].

This is a significant case in our country - the first baby with a reported CNS diagnosis by tissue and genetic analysis. The pathologists used a combination of pathological examination, pathological postmortem examination, and microscopic tissue analysis to piece together what had transpired. This demonstrates how crucial it is to continue studying. Finding novel approaches to comprehend and manage an extremely uncommon issue might be aided by it.

2. Case presentation

The patient was a 3-year-old non-Finnish girl who had a typical vaginal delivery and was born at full term. Neither maternal TORCH infections nor birth asphyxia affected her during the pregnancy. The parents were related by cousins. Her developmental milestones were typical. Her parents ignored her periorbital edema initially, which began at three months of age. Over time, the edema became more severe and affected the entire body. At the age of twelve months, her CNS of suspected minimal change disease type (MCD) was identified based on urine protein +++ and serum albumin levels of 0.8 g/dL (normal range; 3.5-5.5 g/dL). After using steroids for two months, she went into remission. But her recurrent relapses were brought on by eating too much salt. For 1.5 years after being switched to cyclosporine, she did not have remission. The patient arrived with a distended abdomen, edematous lower limbs, and severe widespread edema including periorbital edema as shown in Figure 1.

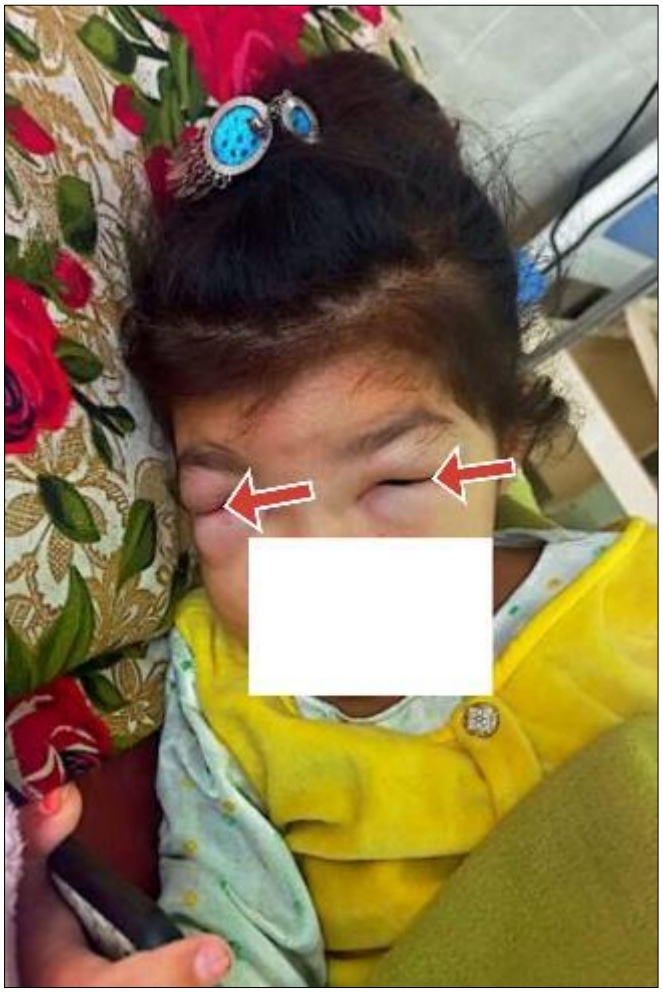

Figure 1 The red arrows in the image showing periorbital swelling

Vitals including pulse, respiratory rate, saturation and temprature were all normal. Baseline investigations showed normal white blood cells (WBCs) count,normal hemoglbin (Hb) concentration as well as normal platelets. Her renal function tests including creatinine and blood urea nitrogen were normal through out her course of illness. Despite receiving many albumin transfusions, her serum albumin level was low (1.2 g/dL). Her liver function tests, bowel,

cardiac profile, coagulation profile, lipid profile, and virology screening were all within normal. On ultrasonography, she showed large kidneys with enhanced echogenicity in the renal parenchyma but normal corticomedullary junction (CMD). She required a conclusive diagnosis as well as medical care. We performed a kidney biopsy to try and determine what was the underlying cause of her proteinuria. The biopsy revealed focal glomerular hypercellularity and young glomeruli, which are indicative of Finnish-type nephrotic syndrome. To further confirm our suspicion, we also conducted a genetic analysis, which revealed two heterozygous pathogenic variants of the NPHS1 gene: II. c.1048 T.C. (protein: Ser 350Pro) in exon 9 and I. c.248 dupA (protein: Tyr 83*) in exon 2. In autosomal recessive inheritance, these mutations are known to cause FTNS. Other genes in the panel (CD2AP, ACTN4, INF2, TRPC6, NPHS2, WT1) did not show any harmful mutations in the sequencing analysis. This is a unique case in the sense that our patient has survived for 3 years while most of the patients with Finnish-type nephrotic syndrome don't survive this long.

We began her on protein-sparing drugs, such as Qsartan, alpha D drops, Sodamint pills, ACE inhibitors (enalapril), NSAIDs (indomethacin), and so on. As the last resort, we intended to use renal transplantation. The protein-sparing drugs caused the patient's edema to somewhat improve. Throughout her illness, her renal function tests stayed normal. She has now been scheduled for a renal transplant for which she has been referred to another hospital with more advanced facilities.

3. Discussion

The unusual and severe congenital nephrotic syndrome (FTNS), which is brought on by mutations in the NPHS1 gene, is demonstrated in this case along with its clinical manifestation, diagnosis, and course of treatment. Since she was two weeks old, the patient has experienced the usual symptoms of CNS, including edema, failure to thrive, and abdominal distension. Through the identification of two heterozygous pathogenic mutations of the NPHS1 gene, I. c.248 dupA (protein: Tyr 83*) in exon 2 and II. c.1048 T.C (protein: Ser 350Pro) in exon 9, a genetic investigation was able to validate the diagnosis of FTNS.It has been previously documented that these mutations cause FTNS illness [5,6]. Nephrin is a transmembrane protein that the NPHS1 gene encodes and is necessary for the glomerular filtration barrier. The rate at which this gene is mutated varies according on the ethnic group; it is greater in Finnish children with CNS [7] than with other cultures. NPHS1 gene mutations have been found in 80% of CNS patients from North America, Europe, and North Africa, according to Lenkkeri et al. [6]. Additionally, a another research found that 39% of Finish types were found in Europe alone [1]. The CNS is extremely difficult to treat.

Treatment for CNS is extremely difficult and involves dialysis, renal transplantation, early bilateral nephrectomy, dietary and vitamin supplements, and intense therapy with regular albumin infusions [2]. Thyroxine supplements are necessary for individuals who develop hypothyroidism, which wasn't the case in our instance [8]. Hypothyroidism develops as a result of loss of thyroid binding globulin, thyroid hormone, and iodine.

It has been demonstrated that protein-sparing drugs, such as angiotensin II type-1 receptor blockers (ARB) and angiotensin-converting enzyme inhibitors (ACEi), can postpone the development of chronic renal disorders [9]. Moreover, using ACEi or ARB reduced the amount of urine protein excreted in children with nephrotic syndrome and other glomerular disorders [10,11]. In fact, unilateral nephrectomy combined with captopril and indomethacin was shown to be a beneficial treatment strategy for CNS by Kovacevic et al. [12]. This might potentially act as a substitute medication, delaying transplantation until the third year of life or beyond. In this instance, the patient had treatment with a unilateral nephrectomy combined with captopril and indomethacin, which may act as a substitute medication and postpone the transplant until the patient is three years old or older.

However, the patient had to be sent to a more specialized facility for ongoing care because our setup did not allow for dialysis for newborns. This case report aims to draw attention to the challenges of diagnosing and treating uncommon congenital conditions in underdeveloped nations, as well as to doctors who may be contemplating prenatal diagnosis based on higher maternal blood alpha fetoprotein and big placental size [13].

4. Conclusion

A 3-year-old girl with Finnish type nephrotic syndrome (FTNS), a severe variant of congenital nephrotic syndrome (CNS) brought on by NPHS1 gene abnormalities, was the subject of a unique case that we recently described. The most prevalent kind of CNS illness, minimal change disease (MCD), did not improve in her with standard therapies. Renal biopsies and genetic testing were used to diagnose her, and protein-sparing drugs were used to treat her condition. The best course of action for her is a kidney transplant. This example emphasizes the need of a correct and timely diagnosis of FTNS as well as the requirement for alternate treatments for this difficult illness.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work is a retrospective case study and does not require ethical approval form Institutional Review Board (IRB) or ethics committee.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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