ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 4, Issue – 5, September – October - 2021, Page No. : 213 – 217

Congenital Nephrotic Syndrome: A Case report

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How to citation this article: Praveen Unki, Ankitha Chamanna, Tazeem Fatima Ansari, "Congenital Nephrotic Syndrome: A Case report", IJMACR- September – October - 2021, Vol – 4, Issue - 5, P. No. 213 – 217.

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Congenital Nephrotic Syndrome (CNS) presents within 3 months of life, most common cause being NPHS 1 mutation. The early diagnosis and management can increase the survival rates up to 60%. The largest reported series on CNS from India revealed suboptimal management with poor outcome as well as low number of CNS being subjected to genetic evaluation. We describe a case of CNS in a 2-month-old prematurely born baby, who presented with refractory edema and proteinuria. Genetic testing revealed mutation in NPHS1 gene, the most common genetic defect in CNS. The child was treated symptomatically with albumin infusion and discharged with follow up advice. Children with CNS have varied presentations and should be considered a first line differential in any case presenting with edema in first 3 months of life. Early genetic testing is mandatory and helps in individualized treatment of the case. Regular follow-ups and early definitive treatment decreases mortality.

Keywords: Congenital Nephrotic Syndrome, Proteinuria, Nephrin.

Introduction

CNS is the triad of nephrotic range proteinuria (>40mg/m^2/hr), hypoalbuminemia and clinically detectable edema, occurring in the first three months of life (1). Majority of it is caused by genetic defects in the podocyte-associated genes (podocytopathy) especially nephrin and podocin and less commonly it has been correlated to congenital infections such as syphilis, toxoplasmosis, rubella, and cytomegalovirus (CMV) (2). Patients with CNS are prone to severe complications such as hemodynamic instability, recurrent infections, thrombosis and impaired growth. Most children with CNS progress to kidney failure within a few years (5). The incidence of CNS is 1–3 per 100,000 live births with

mode of inheritance being autosomal recessive. Mutations in NPHS1 are the commonest cause and are particularly prevalent in Finland ("Finnish-type" CNS) where the incidence of CNS rises to 1 in 10,000 [4]. The early diagnosis and management of CNS is imperial for the survival. The limitations of accessibility to genetic testing, poor adherence to treatment and increased risk of infections challenge the management of children with CNS. Bilateral nephrectomies followed by dialysis and transplantation are followed in most centers, but conservative treatment may also be effective in resource poor developing countries (5). The largest reported series on CNS from India shows suboptimal management and poor outcome as well as low number of CNS being subjected to genetic evaluation (2).

Case presentation

A 42 days old female child born of Non consanguineous marriage to Primi mother at 30 weeks gestation through vaginal route. Birth weight of the baby was 1.2 kg (Appropriate for Gestational Age) admitted in NICU in view of prematurity. The baby was started on bubble CPAP and 2 doses of surfactant were given by InSurE technique for RDS. Maintained in Thermoregulatory environment and was started on maintenance intravenous fluids and prophylactic antibiotics. Minimal enteral feeds initiated for gut maturity, non-nutritive sucking tried and gradually breast feeding established. Routine Retinopathy of Prematurity (ROP) screening was done prior to discharge which showed ROP stage 2 in zone 2. Intravitreal bevacizumab was tried as first line of treatment. Discharged on day of life 22 after baby started gaining weight. Baby followed with ophthalmology department for treatment of ROP and noticed progress in ROP from stage 2 to stage3 in zone 2 with stage 2 changes in zone 1. Patient was admitted and laser coagulation planned as a definitive treatment. Routine investigation done and found out to be having anemia (Hb - 6.4gm/dl) and referred for pediatric opinion. Baby had anasarca with pallor and persistent tachycardia. Diagnosis of Anemia in congestive cardiac failure (CCF) was made and baby was transfused with PCV (5cc/kg followed by 10cc/kg). After 2 transfusion baby hemoglobin (Hb) increased to 9.8g/dl (table 1). Edema persisted and cause for edema investigated thoroughly. Liver pathology has been ruled out. Urine examination which was done showed proteinuria in nephrotic range and increased protein creatinine ratio >0.2 (0.54) (table 1). Serum cholesterol levels were elevated with low total protein and albumin (2.1g/dl) with reversal of albumin globulin ratio. Provisional diagnosis of congenital nephrotic syndrome made and sent for genetic workup, which showed mutation in NPHS 1 gene which codes Nephrin. Patient was transfused albumin (in view of decreased urine output), discharged and advised follow up and nephrectomies in future. Baby died at 2 and half month of age at residency.

Table 1: Investigations.

	On admission		At discharge
Hemoglobin	6.4 g/dl	7.2 g/dl	9.8 g/dl
Urea	14 mg/dl	8 mg/dl	12 mg/dl
Creatinine	0.2 mg/dl	0.1 mg/dl	0.3 mg/dl
Calcium	8.3 mg/dl		
Serum Albumin	2.1g/dl		3.4g/dl

Serum cholesterol	250mg/dl		
Immune profiling (Complement, Anti dS DNA, ANA, ANCA, Immunoglobulins, Hepatitis B & Varicella Serology)	Negative		
Syphilis serology	Negative		
Genetic mutational analysis	NPHS 1 mutation		
Urine analysis	Within normal limit		
Urinary protein: creatinine ratio	0.54		
Ultrasonography- Abdomen and pelvis	Within normal limit		

Discussion

Congenital Nephrotic Syndrome most often presents in the initial period of infancy. NPHS1 mutation is the most common genetic etiology for CNS, as found out after rigorous analysis of published research data (3). NPHS 1 encodes the production of Nephrin which is the major structural component of the slit diaphragm (3,12). Mutation in NPHS1 causes loss of Nephrin expression and resultant damage to the podocyte cytoskeleton (3). The detection of massive nephrotic range proteinuria strongly suggests the diagnosis of CNS. Usually present with clinically evident edema, decreased urine output, poor feeding and lethargy (4). The early genetic testing helps in confirmation of diagnosis and guides further management. The main stay of therapy is optimization of nutrition, fluid management, Albumin infusions, prevention of Thrombosis and treatment of infections and minimization of complications (5, 6). Definitive treatment is renal transplantation.[6] High energy (130 kcal/kg per day) and protein content (4 g/kg per day) but low salt content diet is recommended. Regular albumin infusions are recommended in children with severe hypovolemia and failure to thrive (6). Furosemide (with caution to prevent thrombosis), RAS inhibitors (ACE inhibitors and ARDS) or NSAIDS have considerably beneficial effects in the treatment of CNS (6,7). Children are monitored for and prevention of complications of CNS, including acute complications (such as hypovolemic and hypervolemic crisis, intermittent hypertensive and thromboembolic events, and bacterial and viral infections) and chronic consequences of the disease (including hypertension, dyslipidemia, hypothyroidism, hypomagnesaemia, hypocalcemia, vitamin D deficiency, bone disease, growth failure and progressive CKD) as well as adverse effects of medications and complications of prematurity (e.g. Hyperbilirubinemia) (7-9). Infections are a major concern and the primary cause of death (7). Other therapies include IVIG to treat infections in children. The children should be vaccinated against Hib, pneumococcal and varicella zoster. Supplementation with Vitamin D, Calcium and iron is essential for optimal growth (7-11). Dialysis is initiated in children with CNS with kidney failure. The mortality of those infants on dialysis is low (6–11%). Bilateral nephrectomy is advised, and dialysis initiated when the infant weighs around 7–9 kg (6–12 months of age) followed by kidney transplantation a few months later (upon attainment of 10 kg body weight) (6). Renal transplantation is curative for majority of cases of congenital nephrotic syndrome. Delayed presentations, high rates of sepsis, poor follow-up, low uptake of aggressive therapy options, low rates of genetic testing,

and high mortality are the contributors of mortality and morbidity among CNS children.

Conclusion

Congenital Nephrotic syndrome should be considered a first line differential in any case presenting with edema within 3 months of age. A simple biochemical screening for proteinuria may hint towards diagnosis. A thorough investigation for the same with genetic testing for the early detection of mutated gene helps in individualized management of the case. The survival rate is as low as 47% (2). Therapeutic management should be based on clinical severity, aimed at intravascular euvolemia, adequate nutrition and prevention of complications. A strict regular follow-up is the key for the management, without which mortality is inevitable. CNS has 25% recurrence risk in future pregnancies and hence prompt genetic testing of parents and offspring should be advised (12).

References

1. E. Erkan, 'Congenital Nephrotic Syndrome', In Kleigman, R.M., Stanton, B.F., St Geme III, J.W. (ed.) Nelson Textbook of Pediatrics, 21ed, Philadelphia, Elsevier,2020,pp2760.
2. Sinha, R., Vasudevan, A., Agarwal, I., Siddharth, K.S., Abhijeet, S., Subal, P., Sudha, E., Nilam, T. and Manoj,M.,2019. Congenital Nephrotic Syndrome in India in the Current Era: A Multicenter Case Series. Nephron,144(1),pp21-29.
3. Kestila, M., Lenkkeri, U., Mannikko, M., Lamerdin, J., McCready, P., Putaala, H., Ruotsalainen, V., Morita, T., Nissinen, M., Herva, R., Kashtan, C.E., Peltonen, L., Holmberg, C., Olsen, Anne. and Tryggvason, K.,1998. Positionally Cloned Gene for a Novel Glomerular Protein—Nephrin—Is Mutated in Congenital Nephrotic Syndrome. Molecular Cell,1(4),pp575-582.
4. Reynolds, B.C. and Oswald, R.J., 2019. Diagnostic and management challenges in congenital nephrotic syndrome. Pediatric Health, Medicine and Therapeutics,10,pp157-167.
5. Dufek, S., Holtta, T., Trautmann, A., Trautmann, A., Webb, H., Pasini, A., Ariceta, G. and Shroff, R,2018. Management of children with congenital nephrotic syndrome: challenging treatment paradigms. Nephrology Dialysis Transplantation,34(8),pp 1369-1377.
6. Boyer, O., Schaefer, F., Haffner, D., Bockenhauer, D., Holtta, T., Berody, S., Webb, H., Heselden, M., Beata, S., Tkiewicz, L., Ozaltin, F., Levtchenko, E. and Vivarelli, M,2021. Management of congenital nephrotic syndrome: consensus recommendations of the ERKNet-ESPN Working Group. Nature Reviews Nephrology,17(4),pp277-289.
7. Jalanko, H.,2007. Congenital nephrotic syndrome. Pediatric Nephrology,24(11),pp2121-2128.
8. Patrakka, J., Kestila, M., Wartiovaara, J., Ruotsalainen, V., Tissari, P., Lenkkeri, U., Mannikko, M., Visapaa, I., Holmberg, C., Rapola, J., Truggvason, K. and Jalanko, H, 2000. Congenital nephrotic syndrome (NPHS1): Features resulting from different mutations in Finnish patients. Kidney International, 58(3),pp972-980.
9. Holmberg, C., Antikainen, M., Ronnholm, K., Ala-Houhala, M. and Jalanko, H,1995. Management of congenital nephrotic syndrome of the Finnish type. Pediatric Nephrology,9(1),pp87-93.
10. Berody, S., Heidet, L., Gribouval, O., Harambat, J., Niaudet, P., Baudouin, V., Bacchetta, J., Boudaillez, B. and Dehennault, M,2018. Treatment and outcome

of congenital nephrotic syndrome. Nephrology Dialysis Transplantation,34(3),pp458-467.

11. Kovacevic, L., Reid, C. and Rigden, S,2003. Management of congenital nephrotic syndrome. Pediatric Nephrology,18(5),pp426-430.
12. Lipska-Ziętkiewicz, B., Ozaltin, F., Holtta, T., Bockenhauer, D., Berody, S., Levtchenko, E., Vivarelli, M., Webb, H., Haffner, D., Schaefer, F. and Boyer, O,2020. Genetic aspects of congenital nephrotic syndrome: a consensus statement from the ERKNet–ESPN inherited glomerulopathy working group. European Journal of Human Genetics,28(10),pp1368-1378.