Case Report

Congenital nephrotic syndrome associated with congenital cytomegalovirus infection

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Congenital nephrotic syndrome (CNS) is a rare disorder characterized by heavy proteinuria, hypoalbuminaemia and oedema in first 3 months of life. The majority of cases are caused by genetic defect in the components of the glomerular filtration barrier, specially nephrin and podocin. Other causes of congenital nephrotic syndrome include congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus (CMV), HIV and hepatitis B. We are reporting a case of CNS in a 2 months old male child associated with CMV infection. On routine urine analysis, the patient had heavy (++++) proteinuria without hematuria or pyuria. In 24 hours protein excretion was 12.5 gm/24 hrs, serum total protein 4 gm/dl, serum albumin 2.0 gm/dl,total cholesterol 347.0mg/dl, urinary creatinine 41.0mg%, urinary protein 500mg/dl, protein to creatinine ratio was 12.1:1 and TSH was normal. IgM & IgG antibodies for CMV were raised and maternal IgG for CMV was strongly positive. PCR for CMV in urine was sent and it was positive, which is strongly suggestive of active CMV infection.

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Key words **: Cytomelovirus(CMV), Congenital Nephrotic Syndrome(CNS), Proteinuria, Ganciclovir.**

Congenital nephrotic syndrome (CNS) is a rare disorder characterized by heavy proteinuria, hypoalbuminaemia and oedema in first 3 months of life[1]. CNS seems to be primarily associated with defect in the structure and function of podocyte foot processes but can be associated in rare cases, with malformation syndromes, infections or systemic diseases. The prototype and probably the most severe form of CNS is the finnish type nephrotic syndrome[2]. Other causes of congenital nephrotic syndrome include congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus (CMV), HIV and hepatitis B[3]. CMV infection has been reported as a cause of CNS in few studies[2-4]. We are presenting a case of CNS in 2 months old child due to congenital cytomegalovirus. To the best of our knowledge perhaps this is first case of PCR (Polymerase chain reaction) proved CMV infection associated with CNS.

Case Report

A 2 months old male child presented with history of developing generalized oedema since 1 month of life. The child was full term appropriate for gestation age hospital delivered, without any significant antenatal and family history and born from non-consanguineous marriage. On examination his weight and height were 4.5 kg and 55.5 cm respectively, pitting oedema was present all over body, with presence of ascites. His BP was 60/40 mm Hg, liver was 2 cm below right costal margin and spleen was not palpable. The kidney were not ballotable and renal angle was not tender, other system examination and fundus revealed no abnormality.

On routine urine analysis, the patient had heavy (++++) proteinuria without hematuria or pyuria. His complete blood count (CBC) revealed Haemoglobin 10.6 gm/dl, total leucocyte count 10,560/cmm with diffrential leucocyte count N26%, L69%. SGOT, SGPT, BUN, serum creatinine were in normal range. USG abdomen revealed mildly enlarged kidney with bilateral brightness, suggestive of medical renal disease, with massive ascites. In view of persistent heavy proteinuria and anasarca, a provisional diagnosis of congenital nephrotic syndrome was made. In 24 hours protein excretion was 12.5 gm/24 hours, serum total protein 4 gm/dl, serum albumin 2.0 gm/dl, total lipid 1398.0mg/dl, triglycerides 690.0gm/dl, phospholipid 310.0 mg/dl, total cholesterol 347.0mg/dl, urinary protein to creatinine ratio was 12.1:1 and TSH was normal. Tuberculin test was negative and chest and skull skiagram, and stool examination were normal.

Other biochemical investigation included serum VDRL, HbsAg, HIV and IgM & IgG titre against toxoplasmosis and rubella were negative. IgM & IgG antibodies for CMV were raised (levels 1.356 & 0.613 respectively) and maternal IgG for CMV was strongly positive. PCR for CMV in urine was positive, which is strongly suggestive of active CMV infection. Parents refused for renal biopsy. A final diagnosis of CNS with congenital cytomegalovirus infection was made and patient was put on IV Ganciclovir (5 mg/kg/dose BD) for 14 days followed by oral Valganciclovir (15mg/kg/dose BD). Initially child improved and urinary albumin came to one + only. Later on the child succumbed to infection and died on 36 day of treatment.

Discussion

CNS comprises a heterogenic group of renal diseases that results in increased postnatal glomerular permeability and is manifested by massive proteinuria[2]. The majority of cases are caused by genetic defect in the components of the glomerular filtration barrier, specially nephrin and podocin. Commonest type is finnish type CNS which is caused by mutation in NPHS1 gene which encodes for nephrin. Mutation in the NPHS2 gene, encoding for a podocyte

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protein podocin is another common cause. Few cases of CNS are described in literature due to mutation Wilms tumor suppressor gene (WT1) & in the Laminin-ß2 (LAMB2) gene. Congenital CMV, syphilis, toxoplasmosis, congenital rubella, hepatitis B virus and HIV infection may also cause CNS[3-5].

In severe form of CNS, generalized oedema, massive proteinuria and hypoalbuminaemia can be detected in newborn period. Renal biopsy does not reveal the aetiology of CNS. Genetic analysis is the method of choice for precise CNS diagnosis[5].

There is no specific therapy for CNS and death usually occurs within the first two years of life. The cause of death is usually secondary infection particularly Gram negative septicaemia but if they survive long enough they may die due to renal failure[6]. The goal of medical therapy is to provide good nutrition, to control oedema by parenteral protein supplementation, and to prevent infections and thrombosis. Few medical centers advocate unilateral nephrectomy or percutaneous renal ablation. Most institutions now recommend early bilateral nephrectomy in CNF patients, followed by dialysis, adequate nutritional support, and transplantation[7].

CMV infection has been associated with congenital & infantile NS. However, only few cases have been reported in literature[2,4,8,9].

VP Dange *et al* reported a case of CNS in 1993 with isolated mesangioproliferative histology, and strong serological evidences of CMV infection, but PCR/Culture was not done[4]. We are presenting the first case of serologically as well as PCR proved congenital CMV infection associated with CNS from India.

In present case positive IgM & IgG and urine PCR for CMV in child and positive IgG for CMV in mother, together with clinical and biochemical evidence of CNS, suggest a causal relationship. This child also had anasarca and anaemia. This case did not have other evidences of CMV infection such as hepato-splenomegaly, thrombocytopenia, rashes, growth retardation & retinal abnormalities.

Currently, Ganciclovir and Valganciclovir are employed in the treatment of congenital CMV infection[10].

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