Congenital Mesangioproliferative Nephrotic Syndrome Associated with Cytomegalovirus Infection

V.P. Dandge
V.R. Dharnidharka
W. Dalwai
B.N. Kandalkar
M. Agrawal
A.M. Phatak

The presence of extensive mesangial proliferation in renal tissue, without any other histological abnormality, in Congenital Nephrotic Syndrome (CoNS) is an extremely rare situation, with only few cases reported in the world literature(1) and possibly none from India.

Further, though CoNS is not uncommonly associated with intra uterine infections such as syphilis and toxoplasmosis, only three case reports could be traced revealing evidence of cytomegalovirus infection in association with cogenital nephrotic syndrome(2-4).

We are reporting herewith a case of CoNS with isolated mesangioproliferative histology, and strong serological evidences of CMV infection which we came across recently. This is perhaps the first report of non-Finnish type of congenital nephrotic syndrome with CMV infection from India.

From the Departments of Pediatrics and Pathology, T.N. Medical College and B.Y.L. Nair Charitable Hospital, Dr. A.L. Nair Road, Bombay 400 008.
Reprint requests: Dr. Vikas Dharnidharka, 124, Basant, Cuffe Parade, Bombay 400 005.
Received for publication: September 9, 1992
Accepted : November 13, 1992.

Case Report

A 3-month-old girl presented with the history of developing sudden onset generalized edema since 3 days. The edema was preceded by loose motions for 1 day. The child was full term normal weight hospital delivery, born of non consanguinous parents, without any significant antenatal or family history. Her weight and height were 6.75 kg and 59 cm, respectively. On general examination, pitting edema was present all over the body, with presence of ascites and abdominal wall edema. Her BP was 80/54 mm. Hg. Liver and spleen were 2 and 1 cm palpable below the costal margin, respectively. The kidneys were nonballotable and renal angle was normal. Other systems, including fundus examination revealed no abnormality. On routine urine analysis, the patient had severe (+++) proteinuria, without associated hematuria or pyuria. In view of consistent heavy proteinuria a provisional diagnosis of nephrotic syndrome was made.

Further investigations revealed 24 hour urinary protein excretion of 1.3 g/m^2/24 h, total serum proteins 4.6 g/m^2/dl with serum albumin 1.6 g/m^2/dl, and serum cholesterol of 260 mg/dl. Her Hb was 8.9 g/m^2/dl, with TLC 8000/cu mm ($P_{30}L_{66}E_4$), and microcytic hypochromic anemia. Tuberculin test, chest and skull skiagrams, and stool examination were negative. Other biochemical investigations included BUN 10 mg/dl, serum creatinine 0.5 mg/dl, Na 132 mEQ/L, K 4.7 mEQ/L and uric acid 5.4 mg/dl. Serum complement level was normal, *i.e.*, 62.8 μg/L. Serum VDRL and IgG titres against toxoplasmosis were negative. Initial anti-CMV IgG titre was raised, 128 EIU/ml,

and the titre rose further to 197 EIU/ml after 2 months, but anti-CMV IgM titre could not be done initially. Anti-CMV IgM titre was positive (R 1.2) at the age of 7 months. Anti-CMV IgG titre in the mother was strongly positive, *i.e.,* 216 EIU/ml. These serological evidences were strongly suggestive of active CMV infection.

Renal sonography revealed mildly enlarged kidneys with loss of corticomedullary differentiation. The child was subjected to renal biopsy which showed hypercellular glomeruli, thickened mesangium, and increased matrix (*Fig.*) features suggesting extensive mesangial proliferation. Cytomegalic inclusion bodies were absent. Immunoflorescent and electron microscopic studies were not possible.

Considering the above observations, a final diagnosis of congenital mesangioproliferative nephrotic syndrome with CMV infection was made, and the patient was put on steriods, *i.e.,* prednisolone as per ISKDC schedule. There was no response after 8 weeks of steroid therapy and thereafter cyclophosphamide (2.5 mg/kg/day) was added. Still the proteinuria perisited till the patient left the hospital against medical advice after a further 3 weeks.

Discussion

CoNS is a rare condition denoting onset of proteinuria in the first three months of life. Till now, approxmiately 200 cases have been reported in world literature, mainly from the Scandinavian countries (1,5). Most of them are of the Finnish type, *i.e.,* an autosomal recessive disease with cystic dilatation of the proximal convoluted tubules, mild mesangial proliferation and sclerosis. Approximately ten cases of CoNS, all of the Finnish type, have been

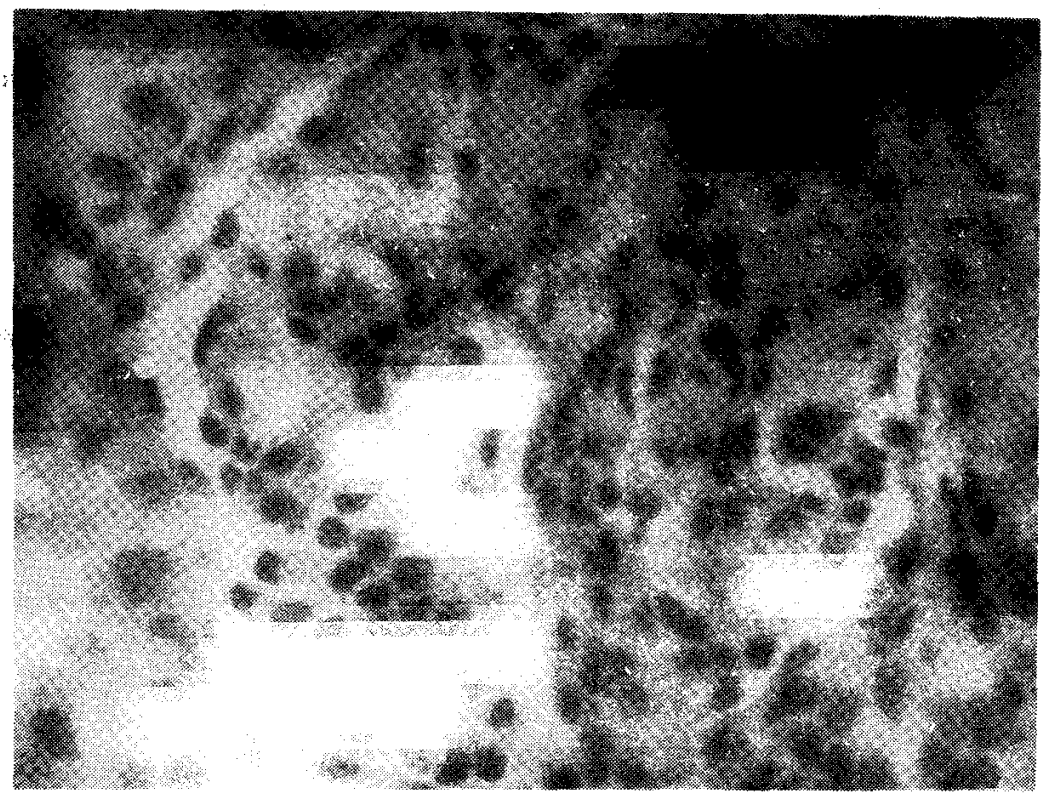

Fig. Ultrastructure of glomerulus showing extensive mesangial proliferation.

reported from India(6,7). The presence of extensive mesangial proliferation without additional abnormalities as seen in this case, is extremely rare. In a study by Sibley *at al.*(1) of 48 cases of CoNS, only 10 cases of mesangioproliferative CoNS were observed over a period of 28 years.

So far, CMV infection has been described in only 3 cases of CoNS(2-4) with as yet questionable etiological relationship. In the present case, rising titres of anti-CMV IgG, positive anti-CMV IgM even at 7 months of age, and strongly positive anti-CMV IgG in the mother, together with clinicopathological evidence of CoNS, strongly suggests a causal relationship. This case did not have any other evidence of CMV infection such as hepatosplenomegaly, anemia, thrombocytopenia, IUGR and retinal abnormalities.

The usefulness of steroid and cytotoxic therapy is doubtful, in these cases and most of them run a downhill course to end stage renal failure. However, as a previous study observed clinical response to steroids in a case of congenital toxoplasmosis associated nephrosis, it was thought worthwhile to use steroids and cytotoxic agents in this case. None of these therapies proved useful. Renal transplantation is the only hope in CoNS as shown by Mahan *et al.*(8) with a 2-year-patient survival of 82%. In CMV related infections Gancyclovir has been reported to give promising results but it was not available(9).

In summary, this case illustrates the significance of CMV infection in CoNS, and the need for doing detailed work up in non Finnish type of cases.

Acknowledgements

The authors wish to thank Dr. K.D. Nihalani, Dean, T.N. Medical College and B.Y.L. Nair Charitable Hospital for giving permission to publish this article and Dr. James D Costa, Pathologist, St. Elizabeth Hospital, for carrying out the CMV and Toxopmma antibody titres.

REFERENCES

1. Sibley RK, Moahan JD, Mauer SM, Vernier RL. A Clinicopathological study of 48 infants with nephrotic syndrome. Kidney Int 1985, 27: 544-552.
2. Hoyer JR, Anderson CE. Congenital nephrotic syndrome Clin Perinatol 1981, 8: 333-339.
3. Werthen HG, Vernier RL, Good RA. Infantile nephrosis–Clinical, biochemical, and morphologic studies of the syndrome Am J, Dis Child 1959, 98: 731-748.
4. Giles HM, Pugh RCB, Darmady EM, Stranack F, Woolf LI. The nephrotic syndrome of early infancy: A report of 3 cases. Arch Dis Child 1957, 32: 167-180.
5. Huttonen NP. Congenital nephrotic syndrome of Finnish type. Study of 75 cases. Arch Dis Child 1976, 51: 344-348.
6. Arya LS, Aram GN, Goel RG, Singh M. Congenital nephrotic syndrome of Finnish type in Afghanistan. Indian Pediatr 1982, 19: 1027-1029.
7. Udani RH, Parikh PH, Pai PM, Kandalkar BM. Congenital nephrotic syndrome. Indian Pediatr 1987, 24: 1157-1158.
8. Mahan JD, Mauer SM, Sibley RK, Vernier RL. Congenital nephrotic syndrome –The evaluation of medical management and results of renal transplantation. J Pediatr 1984, 105: 548-557.
9. Shepp DH, Dandliker RN, de Miranda, P, *et al.* Activity of ganciclovir in the treatment of cytomegalovirus pneumonia. Ann Intern Med 1985, 103: 368-373