CYCLOPHOSPHAMIDE IN THE TREATMENT OF STEROID-RESISTANT MINIMAL-CHANGE NEPHROTIC SYNDROME. Norman J. Siegel, Ayfer Gur, Leonard S. Krassner and Michael Kashgarian, (Intro. by C.D. Cook). Yale Univ.Sch. of Med., Depts. of Ped. and Path., New Haven.

Although cyclophosphamide is effective in the treatment of steroid-sensitive, frequently-relapsing nephrotic syndrome, little data are available on the use of this agent in the treatment of children with steroid-resistant nephrotic syndrome. Six children who had a minimal change lesion on both light and electron microscopy and who had failed to respond to an initial 8-10 week course of prednisone (2 mg/kg/d) were studied. All 6 children had a complete remission during treatment with cyclophosphamide (2 mg/kg/d for 12 weeks) and prednisone (0.5-1.0 mg/kg/d for the first 6 weeks). Three of these children have subsequently relapsed 6-18 months after treatment with cyclophosphamide, and, because of the potential gonadal toxicity of this drug, treatment was reinstituted with prednisone alone. All 3 patients sustained a complete remission within 2 weeks after restarting only steroid therapy.

These observations suggest: a) cyclophosphamide may be effective in the treatment of steroid-resistant minimal-change nephrotic syndrome; b) patients who are initially steroid resistant prior to treatment with cyclophosphamide may become steroid sensitive following such therapy; and, therefore, c) initial treatment of relapses which occur after a course of cyclophosphamide should be glucosteroids alone.

HYPERTENSION AND UNILATERAL PARENCHYMAL RENAL DISEASE (UPRD). Alan R. Sinaiko, Bernard L. Mirkin and Robert L. Vernier, Dept. Ped. and Pharm., Div. Clin. Pharm., University of Minnesota, Minneapolis, Minnesota 55455

The management of hypertension associated with UPRD in children constitutes a major therapeutic dilemma. the decision to nephrectomize a patient must be made on the basis of clinical judgment since available diagnostic procedures have not proven useful.

11 patients less than 20 years of age have been studied at the Univ. of Minn. hospital with UPRD. 8 were 15 years or less. Hypertension was found in 8 subjects at routine physical examination; 2 had recurrent urinary tract infections; and 1 had seizures 2 months following a motor accident. All had diastolic pressures greater than 100 mmHg as well as normal renal function. Radiographic studies revealed non-visualization of 1 kidney in 3 patients, unilaterally small kidneys in 7 (5 of which had evidence of scar formation) and a small cortical defect in the upper pole of 1 kidney in 1 patient. Selective renal vein renin determinations were obtained in 6 patients but lateralization to the affected side was noted in only 2 patients.

Surgery appears to have been effective in the majority of patients. 9 are considered cured, 1 is improved on antihypertensive therapy (Aldomet) and 1 has shown no improvement. These results suggest that nephrectomy in cases of hypertension with UPRD offers a better prognosis in young patients than that reported in adults.

UTILIZATION OF PROPERDIN BY C3 NEPHRITIC FACTOR IN PATIENTS WITH MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS. R. Spitzer, A. Stitzel. State University of New York, Upstate Medical Center, Dept. of Pediatrics, Syracuse, New York 13210.

When zymosan is added to normal human serum, it interacts directly with properdin convertase converting this enzyme to its active form. This interaction requires no other factors and can be demonstrated in vitro using purified properdin convertase. Thereafter, properdin convertase can activate purified native properdin in the fluid phase so that it now has the ability to cleave C3 and thereby mediate the conversion of C3PA or properdin factor B. In the sera of patients with membranoproliferative glomerulonephritis (MPGN), a complement reactive material, C3 nephritic factor (C3NeF), has been shown to interact with C3 through the utilization of C3PA. Quantitative studies by radial diffusion and immunoelectrophoresis of the sera of several patients with MPGN demonstrate that levels of properdin convertase are often markedly decreased. In addition, it can be shown that C3NeF containing sera require properdin convertase to consume specific C3 hemolytic activity. Hence, sera depleted of properdin convertase by antibody adsorption will not interact with C3NeF to effect consumption of C3 hemolytic activity. It, therefore, appears that C3NeF functions as a complex polysaccharide like zymosan with the cleavage of C3PA and the subsequent consumption of C3-C9 being dependent upon the initial activation of properdin convertase. (Supported in part by NIAMD grant AM 17376 and N.Y.S. Kidney Disease Inst.)

CRYOPRECIPITABLE PATHOGENIC IMMUNE COMPLEXES IN THE NEPHROPATHY ASSOCIATED WITH SICKLE CELL DISEASE. Jose Strauss, Michael N. Koss*, Victor Pardo*, William Griswold* and Rawle M. McIntosh, Depts. of Ped. and Pathol., Univ. of Miami, Miami, Fla., Depts. of Ped. and Pathol., Columbia Univ., N.Y., N.Y. and Depts. of Ped. and Med., Univ. of Colorado, Denver, Colo.

In previous communications we have demonstrated the presence of cryoprecipitable complexes of antigen and specific antibody in the sera of patients and experimental animals with immune complex disease. Recently we have reported localization of renal tubular epithelial antigen (RTE) and specific antibody in the glomeruli of a patient with sickle cell disease and immune complex nephritis and demonstrated an autologous immune complex pathogenesis for the renal lesion. This study describes the isolation of cryoprecipitable complexes of RTE and anti-RTE in this disease. Cryoprecipitates were isolated from the serum as previously described. The cryoprecipitate was dissolved in 3MKI at 37°C and fractions eluted from Sepharose 6B and Sephadex G200 column with 0.2M acetate buffer pH 5. The fractions obtained contained IgG antibody to RTE as demonstrated by immunofluorescent and absorption studies; immunoreactive RTE antigen and IgM antibody to RTE as well as to IgG. No other proteins were detected. These studies support the hypothesis that RTE-anti-RTE complexes are of immunopathogenic significance in the autologous immune complex nephropathy associated with sickle cell disease.

IMMUNE COMPLEX NEPHRITIS ASSOCIATED WITH CHRONIC BACTEREMIA (SHUNT NEPHRITIS). C. Frederic Strife, A. James McAdams and Clark D. West. University of Cincinnati College of Medicine and Children's Hospital, Department of Pediatrics, Cincinnati.

Although the evidence to date suggests that, as in lupus nephritis, the diffuse proliferative nephritis associated with chronic bacteremia from infected ventriculo-atrial shunts is produced by circulating immune complexes, the antigen in the complexes has not been demonstrated. A complement reactive cryoglobulin composed of IgG, IgM, C3 and C4 was isolated from a patient with shunt nephritis due to staphylococcal epidermidis. Antibody produced in rabbits to the patient's washed cryoglobulin reacted by double diffusion in agarose to the techoic acid isolated from the infecting Staphylococcal epidermidis. In vitro, the cryoglobulin activated complement by the classical pathway. Both the patient's serum and the cryoglobulin contained heat stable C1q precipitins (Agnello, et.al., JEM 134:228s, 1971). Serum C3, C4 and properdin levels were initially depressed while C5 and C3 proactivator levels were normal. Following removal of the infected shunt, the C3 level rose into the normal range in 10 days while the C4 and properdin levels became normal after 3 weeks.

These observations support the concept that, as in lupus nephritis and experimental immune complex nephritis, circulating complement reactive antigen-antibody complexes manifested in vitro as cryoglobulins are responsible for the nephritis.

NEUROLOGY

FAMILIAL GROWTH RETARDATION ASSOCIATED WITH GENETICALLY DETERMINED BRAIN DYSFUNCTION. Faika Abaci and Salvador Castells, Jewish Hospital and Downstate Med. Ctr., Depts. Ped., Brooklyn, New York

Three brothers, ages 12,7 and 6 years with a striking similar history of psychomotor retardation, developmental defects in speech and reading, low I.Q.'s, behavioral disabilities and hyperactivity were found to be retarded in growth and skeletal maturation. There was a positive family history of short stature and mental retardation. The oldest sibling had panhypopituitarism as indicated by lack of increase in serum HGH during insulin, arginine and deep sleep, low PBI and T_4, low 24 hr. urinary 17KGS and lack of response to metyrapone. Administration of 25U of ACTH produced an increase in plasma cortisol levels from 3.2 mcg/100 ml to 19.4. The other two had normal increases in serum HGH and normal thyroid and adrenal functions. A normal increase in serum TSH after administration of 7 μg/kg of TRF in the three indicated an intact pituitary gland. The increase in nitrogen balance, plasma FFA, insulin release, and the marked calciuria and hydroxyprolinuria produced by administration of HGH ruled out peripheral unresponsiveness to HGH. It is possible that a genetically determined brain lesion affected the hypothalamic centers controlling the anterior pituitary gland, resulting in a multiple deficiency of releasing factors in the oldest and a decreased secretion of an unknown hypothalamic factor involved in promoting growth in the other two.
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