SHORT REPORTS

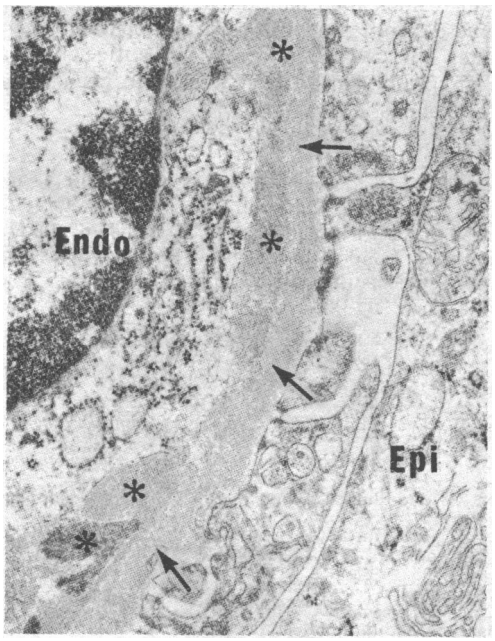
Glomerulonephritis in Agammaglobulinaemia

Most patients with glomerulonephritis develop glomerular injury through humoral mechanisms.[1] As patients with agammaglobulinaemia cannot show appreciable humoral response to an antigenic stimulus development of glomerulonephritis is unlikely to result from antibody-mediated injury. Glomerulonephritis which occurred in a patient with Bruton's agammaglobulinaemia prompted this report.

Case Report

A 3-year-old boy suffered from recurrent infections and was found to have persistently low serum gammaglobulins. Diagnosis was further confirmed by the absence of plasma cells in a lymph node biopsied after adequate antigenic challenge. Replacement with human gammaglobulins was started and continued until his death. Six months before death he developed proteinuria (1·0 to 2·0 g per day) and persistent microscopic haematuria. At no point during the illness had he had oedema or hypertension. He was last admitted for dyspnoea, cough, and fever. Repeated urine testing showed 4 + protein, 10-12 red blood cells, and 1-2 granular casts per high-power field. Concentration of blood glucose was 60 mg/100 ml; urea nitrogen 26 mg/100 ml; serum creatinine 0·6 mg/100 ml. The serum β_1C globulin level was 195 mg/100 ml (normal 125 $\pm^{40}$ mg/100 ml). Chest *x*-ray film showed diffuse pulmonary infiltrates with consolidation of both lower lobes. *Haemophilus influenzae* was recovered from cultures of sputum and blood. He died of respiratory failure and shock.

Necropsy findings included profound atrophy of central and peripheral lymphoid organs and absence of plasma cells. Macroscopically the kidneys were normal. On microscopic examination diffuse thickening of basement membranes with occasional splitting was found but the glomeruli were not hypercellular. Focal necrosis with fibrinoid deposition and hyaline capillary thrombosis was noted in some glomeruli. No amyloid deposition was seen with riboflavin-T staining. Electron microscopic examination confirmed that the glomerular basement membranes were thickened, and subendothelial electron dense deposits were present (fig.). No epimembranous deposits were found.



Electron micrograph of the renal glomerulus shows discrete electron dense deposits (*) on the endothelial (endo) side of the glomerular basement membrane (arrows). (Epi. = Epithelial Cells). (× 6982.)

Comment

Persistently low concentrations of gammaglobulins and the absence of plasma cells in regional lymph nodes after antigenic stimulation, which are the two major laboratory criteria for the diagnosis of agammaglobulinaemia,[2] were noted in our patient.

Aggregated gammaglobulins mimic biologic properties of immune complexes.[3] Aggregation and deposition of gammaglobulins administered for therapy could be implicated in starting glomerulonephritis. If this is so, renal lesions would be expected to occur frequently in patients with agammaglobulinaemia who receive long-term replacement therapy with gammaglobulins. We are unaware of any such report. In addition, attempts to induce renal lesions in mice by aggregated globulins have failed.[4] These observations lessen the likelihood that the aggregated immunoglobulins had a role in the pathogenesis of the renal lesion in our patient.

For recurrent infections, the child had intermittently received antibiotic treatment. Proteinuria and haematuria, however, were unchanged for six months, while no antimicrobials were given. Persistence of urinary abnormalities for such a long time after the drugs were withdrawn argues against an antibiotic-induced lesion.

Thickening of glomerular basement membranes and subendothelial electron dense deposits have been observed in experimental intravascular coagulation.[5] Our patient's renal lesion had similar morphological features, which suggests that repeated subclinical episodes of intravascular coagulation triggered by recurrent infections and septicemia may have caused the nephropathy. Though we cannot identify the pathogenetic mechanism, the development of glomerulonephritis in an agammaglobulinaemic individual is of interest.

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Vitamin D-resistant Rickets and 25-Hydroxycholecalciferol

Though patients with hypophosphataemic, vitamin D-resistant rickets (V.D.R.R.) have responded biochemically and clinically to 25-hydroxycholecalciferol (25-OHD_3) and 1,25-dihydroxycholecalciferol (1,25-$(OH)_2D_3$) in short-term trials,[1-4] few have received long-term treatment. It has been recommended that patients with pathological fractures of long bones should be treated with phosphate and vitamin D[4-5] since 25-OHD_3 and 1,25-$(OH)_2D_3$ do not correct the underlying metabolic defect. We treated a patient with 25-OHD_3 after vitamin D and phosphate had failed to heal his pathological fracture.

Case Report

Though the family of this 18-year-old man were normal in stature and metabolism, he began to limp when he was 6. The next year a brace was put on his left leg for his worsening limp. After five years with the brace he was referred for surgical correction of bilateral genu valgum in March 1968. He was in the 10th percentile for height and had secondary gait abnormalities. Blood urea nitrogen, sodium, potassium, chlorine, CO_2, protein-bound iodine, fasting blood sugar, and serum proteins were normal. Calcium,