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ORIGINAL ARTICLE

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Infantile nephrotic syndrome and congenital glaucoma

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Abstract A case of infantile nephrotic syndrome (NS) with advanced membranoproliferative glomerulonephritis (MPGN), type I, and bilateral congenital glaucoma, is presented. The patient also had persistent thrombocytopenia and subclinical hypothyroidism. The parents were second-degree cousins and the affected infant had a sibling who was born with congenital glaucoma. His mother had an aunt and uncle on the maternal side who were born with congenital glaucoma. In addition, there was a history of infantile death in five family members of unknown causes (pedigree). To the best of our knowledge, the association of congenital glaucoma and infantile NS due to MPGN has not been reported previously.

Keywords Infantile nephrotic syndrome · Congenital glaucoma · Thrombocytopenia

Introduction

Congenital nephrotic syndrome (NS) presenting in the first 3 months of life [1] and infantile NS presenting during the 1st year of life [2] are usually secondary to microcystic disease (Finnish NS) or diffuse mesangial sclerosis. However, other histopathological lesions can occur with infantile NS, including minimal change histopathology [3], and infrequently children presenting with infantile NS can go into complete remission [4]. However, membranoproliferative glomerulonephritis has not been reported as a cause of congenital or infantile NS [5–7].

Different associations between congenital/infantile NS and ocular lesions have been reported previously [8–10]. We report a case of infantile NS secondary to membranoproliferative glomerulonephritis (MPGN), type I, and congenital glaucoma.

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Case report

A full-term baby boy was born with bilateral congenital glaucoma and thrombocytopenia. The patient did not have any dysmorphic features, developmental delay or abnormal genitalia. He had a normal head circumference and the rest of the systemic examination was unremarkable. Intrauterine infection (TORCH syndrome) was excluded and bone marrow aspirate showed increased megakaryocytes, suggesting peripheral destruction of the platelet. He was diagnosed with isoimmune thrombocytopenia; however, his platelets remained low despite a slow improvement without specific treatment. At 8 months of age investigations showed a low serum albumin [20–22 g/dl (normal values: 35–50 g/dl)], normal serum creatinine [30 μmol/l (normal values: 18–35 μmol/l)], high serum cholesterol [7.23 mmol/l(normal <5.2 mmol/l)] and high triglycerides (TG) [13.39 mmol/l (normal <1.7 mmol/l)]. No records of his urine proteins were available and he was not reported to be edematous at that stage. At the age of 23 months, he presented with carpopedal spasm, tachypnea and irritability. He was found to be hypocalcemic with a total Ca of 0.52 mmol/l (normal: 2.1–2.6 mmol/l), hypertensive and in renal failure, with elevated serum creatinine (196 μmol/l) and elevated blood urea nitrogen [11.3 mmol/l (normal 1.8–6.4 mmol/l)]. There was no evidence of hemolytic uremic syndrome (HUS) as there was no evidence of microangiopathic hemolytic anemia (normal blood film) or worsening of his thrombocytopenia. He was edematous with low serum albumin [22 g/dl (normal 35–50 g/dl)] and his urine was 4+ positive for protein. His urine continued to show a nephrotic range proteinuria with a high protein/creatinine ratio (2.4–5.3). His plasma C3 and C4 components of complement were normal. Renal biopsy contained 18 glomeruli, most of which revealed enlarged glomerular tufts filling the Bowman's space. Many of the glomeruli showed lobular patterns associated with markedly expanded mesangium due to increased mesangial matrix and mesangial hy-

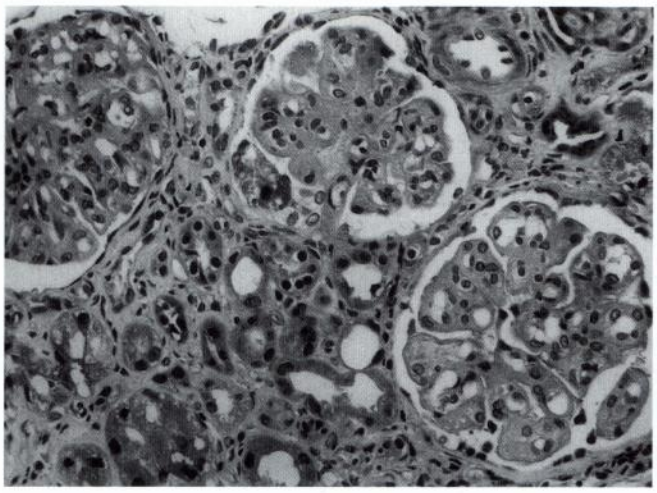

Fig. 1 Photomicrograph from the renal biopsy showing three glomeruli, all of which reveal expanded mesangium and thickened capillary wall. Hematoxylin and eosin, ×87

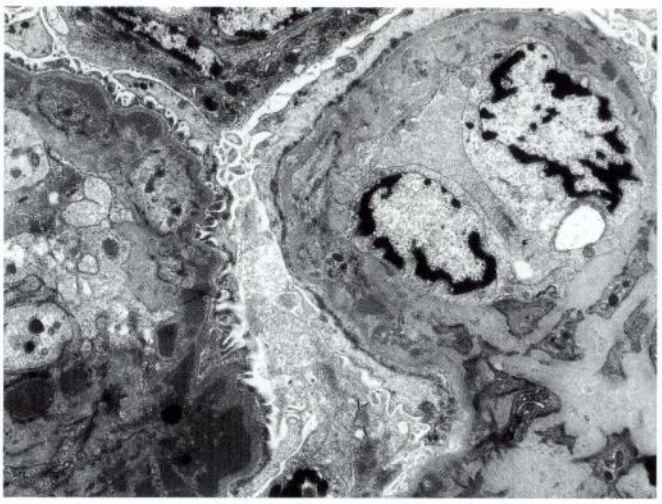

Fig. 3 Electron micrograph showing mesangial interposition and duplication of basement membranes. Several subendothelial electron-dense deposits are also seen. ×2240

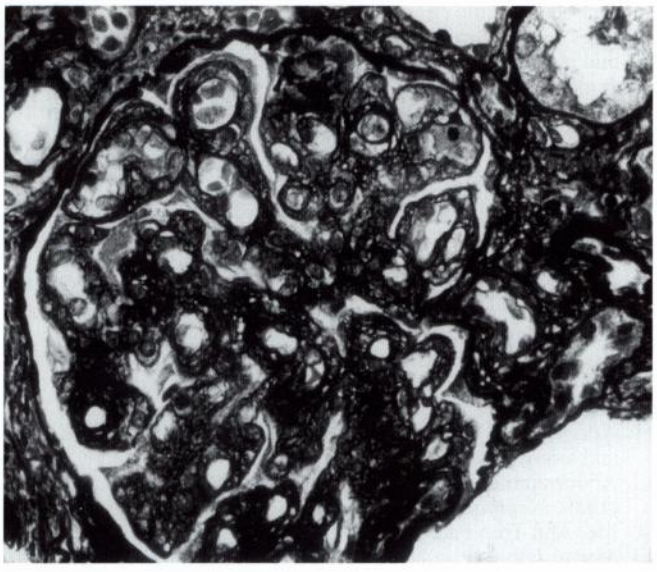

Fig. 2 A glomerulus after silver staining, showing prominent duplication of glomerular capillary basement membrane

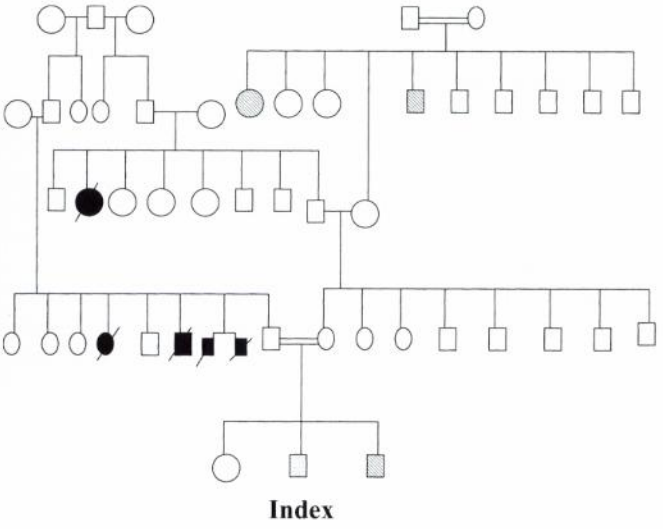

Fig. 4 Pedigree (*open circles, open squares* affected with congenital glaucoma, *solid circles, solid squares* patients who died in infancy, *dotted square* affected with congenital glaucoma and infantile NS)

percellularity (Fig. 1). The capillary walls were thickened and on silver stain revealed a prominent double contour of basement membrane (Fig. 2). There was focal tubular loss replaced by mild fibrosis. Occasional small blood vessels showed focal intimal thickening. Electron microscopic examination revealed numerous subendothelial electron-dense deposits with mesangial interposition and duplication of basement membranes and mesangial interposition. Marked mesangial expansion with obliteration of many of the capillaries was seen (Fig. 3). The renal biopsy was compatible with advanced membranoproliferative glomerulonephritis type I.

His kidneys had normal shape and size on ultrasound and there were no iliac horns on the X-rays. His thyroid function test showed high TSH and therefore he was started on thyroxin replacement therapy.

The parents were second-degree cousins and his younger sibling was born with bilateral congenital glaucoma, as was an aunt and uncle of his mother on the maternal side (Fig. 4). However, they did not have other known ocular abnormalities or renal diseases. The affected sibling has not had thrombocytopenia or proteinuria so far (6 months old). There was a history of infantile deaths of unknown cause in five family members.

Discussion

The association of membranoproliferative glomerulonephritis presenting in infancy and congenital glaucoma has not been reported before. Membranoproliferative glomerulonephritis usually presents in older children and young adults [5, 6], although it has been described in an infant aged 15 months [7]. Our case presented at 8 months of age. This is in contrast to mesangial prolif-

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LITERATURE ABSTRACTS

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Heat shock protein-70 repairs proximal tubule structure after renal ischemia

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Background Recent studies have suggested a role of heat shock protein (HSP)-70 in cytoskeletal repair during cellular recovery from renal ischemia. The aim of this study was to test the hypothesis that HSP-70 interacts in vitro with cytoskeletal elements obtained from rat renal cortex during early reflow after renal ischemia.
Methods Cellular proteins were fractionated into cytoskeletal pellets and noncytoskeletal supernatants by Triton X-100 extraction of rat renal cortex obtained after 15 minutes or 18 hours of reflow after 45 minutes of renal ischemia, or from controls. Aliquots of isolated pellets were coincubated with aliquots of isolated supernatants in different combinations. A repeat Triton extraction was performed, and differential distribution of Na, K-ATPase or HSP-70 was assessed by Western blots and densitometric analysis.
Results Coincubation of cytoskeletal pellets obtained during early reflow after renal ischemia (exhibiting severe injury of the cytoskeletal anchorage of Na,K-ATPase) and noncytoskeletal supernatant obtained during later reflow (showing high HSP expression) resulted in specific translocation of HSP-70 from the supernatant into the pellet, functionally associated with dose-dependent stabilization of Na,K-ATPase within this cytoskeletal fraction. These effects could be reproduced by incubation with purified HSP-70 and were abolished by the addition of anti-HSP-70 antibodies.
Conclusion These data support the hypothesis that HSP-70 interacts with cytoskeletal elements during the restoration of proximal tubule cell structure and polarity after renal ischemia. This experimental approach represents a new in vitro assay to study further the role of HSP in cellular repair.

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Albuminuria in nondiabetic relatives of IDDM patients with and without diabetic nephropathy

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Background In non-insulin-dependent diabetes mellitus (NIDDM), there is a clustering of an elevated urinary albumin excretion rate (U-AER) in nondiabetic relatives of albuminuric patients. Whether this is also the case in insulin-dependent diabetes mellitus (IDDM) is unknown.
Methods Overnight U-AER was measured in 186 nondiabetic first-degree relatives of 80 IDDM patients with diabetic nephropathy (U-AER >200 μg/min or 300 mg/24 hours; DN+) and in 52 relatives of 25 IDDM patients without nephropathy (U-AER <20 μg/min; DN-). The two groups of relatives were comparable regarding gender distribution, age, obesity, blood pressure, prevalence of antihypertensive therapy, and smoking habits.
Results No difference was found in overnight U-AER between relatives of patients with DN+ and DN– [median (range), 3.4 (0.1 to 372) vs. 4.0 (0.2 to 62) μg/min, respectively, P=NS]. The proportion of relatives with a U-AER=10 μg/min was 12% in DN+ compared with 8% in DN– (P=NS). Among relatives of DN+, those with antihypertensive treatment (AHT+) had higher U-AER compared with those without [AHT+ vs. AHT–, 5.0 (0.5 to 372) vs. 3.4 (0.1 to 26.5) μg/min, P<0.01], a phenomenon that was not seen among relatives of DN-[AHT+vs. AHT–, 3.6 (2.1 to 24.3) vs. 4.0 (0.2 to 61.5) μg/min, P=NS]. However, this analysis was impaired by the small number of relatives of DN- with hypertension (n=7).
Conclusions In IDDM, we found no clustering of elevated U-AER in nondiabetic relatives of patients with nephropathy. This is different from what has been reported in NIDDM, and suggests heterogeneity in the genesis of albuminuria in diabetes.