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Case report

Oligomeganephronic renal hypoplasia with tapetoretinal degeneration

Report of one case with ultrastructural study of the renal biopsy

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Summary. Bilateral renal hypoplasia with oligomeganephronia, associated with bilateral tapetoretinal degeneration was observed in a child; this association has been reported only once before. Light, ultrastructural and immunofluorescent microscopic studies of the renal tissue were performed. The glomeruli were few and hypertrophic, with numerous mesangial cells, mesangial deposits, focal glomerular sclerosis and prominent thickened basement membrane. Two types of tubular changes were observed: focal necrosis of proximal tubules and focal atrophy of tubules surrounded by a thickened basement membrane. Mild fibrosis with few lymphocytes could be observed in the interstitium. A congenital reduction in the number of nephrons, related to a yet unknown pathological process may explain these morphological changes in part.

Key words: Oligomeganephronic renal hypoplasia – Tapetoretinal degeneration – Ultrastructure – Focal glomerular sclerosis – Nephronic reduction

Introduction

Oligomeganephronia was described by Royer and Habib (1962) as a form of congenital bilateral renal hypoplasia with few and markedly hypertrophied glomeruli. An ultrastructural description was reported in 4 cases of

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this disease (Scheinman and Abelson 1970; Morita et al. 1973; Elfenbein et al. 1974; Waldherr et al. 1975). We report the ultrastructural features of a case of oligomeganephronia associated with tapetoretinal degeneration, an association described only once before by Hirooka et al. (1969). We have compared our observations with the results of recent experiments on partial five-sixths nephrectomized rats (Shimamura and Morrison 1975; Salusky et al. 1981; Brenner 1984).

Case report

A 11-year-old male was admitted for blindness associated with polyuria, polydipsia and proteinuria. No family history could be ascertained.

On physical examination, he showed stunted growth (24.5 kg and 126 cm) and normal blood pressure. He had no mental retardation.

Ocular examination revealed a bilateral tapetoretinal degeneration: fundal changes included pale papillae and bilateral retinal atrophy with pigment dusting in some areas; the ERG showed no response to stimuli. Furthermore, a mild hearing loss was found on the audiogramm and diffuse spikes were observed on EEG though the child never had seizures.

Urinanalysis showed proteinuria (4 cg per kg per 24 h) without erythrocytes in the urine sediment. In the blood, urea nitrogen level was 22 mmoles/l, creatinine concentration 220 μmoles/l and potassium level was normal. The maximum concentrating ability was 512 mosm/kg of water.

On intravenous pyelogram, both kidneys appeared very small (within 4 standard deviations on nomogram for kidney length – Eklof and Ringertz 1976), with regular shape. No abnormality of the urinary tract was associated. Renal biopsy was performed. The glomerular filtration rate progressively declined. A haemodialysis program was started 2 years after the first examination and successful kidney transplantation was subsequently performed. After two years follow-up the patient is well.

Morphological results

On light microscopy of the 10 glomeruli observed 2 were totally sclerotic. All the other ones appeared enlarged, with a mean diameter of 300 μ. The Bowman's capsule was not thickened. Lesions of focal glomerular sclerosis (FGS) were found in every glomerulus involving one or two thirds of the glomerular tuft and included increased cellularity of the mesangium with hypertrophy of the mesangial matrix, capillary wall wrinkling and collapse, intraluminal eosinophilic deposits and adherence of the injured glomerular part to the capsule (Fig. 1). Tubules were irregularly dilated (Fig. 2). Some of them had an epithelium of proximal type but without brush border; their basement membrane was not thickened. Other tubules had a flat dedifferentiated epithelium and a very thick basement membrane. No interstitial fibrosis was observed. Blood vessels appeared normal. No dysplastic lesion was present.

By immunofluorescence mesangial deposits of IgM and C_3 were observed.

On electron microscopy glomerular epithelial cells showed cytoplasmic signs of intense synthetic activity. Their food processes were normal. The basement membranes appeared either normal or focally split into 2 laminae.

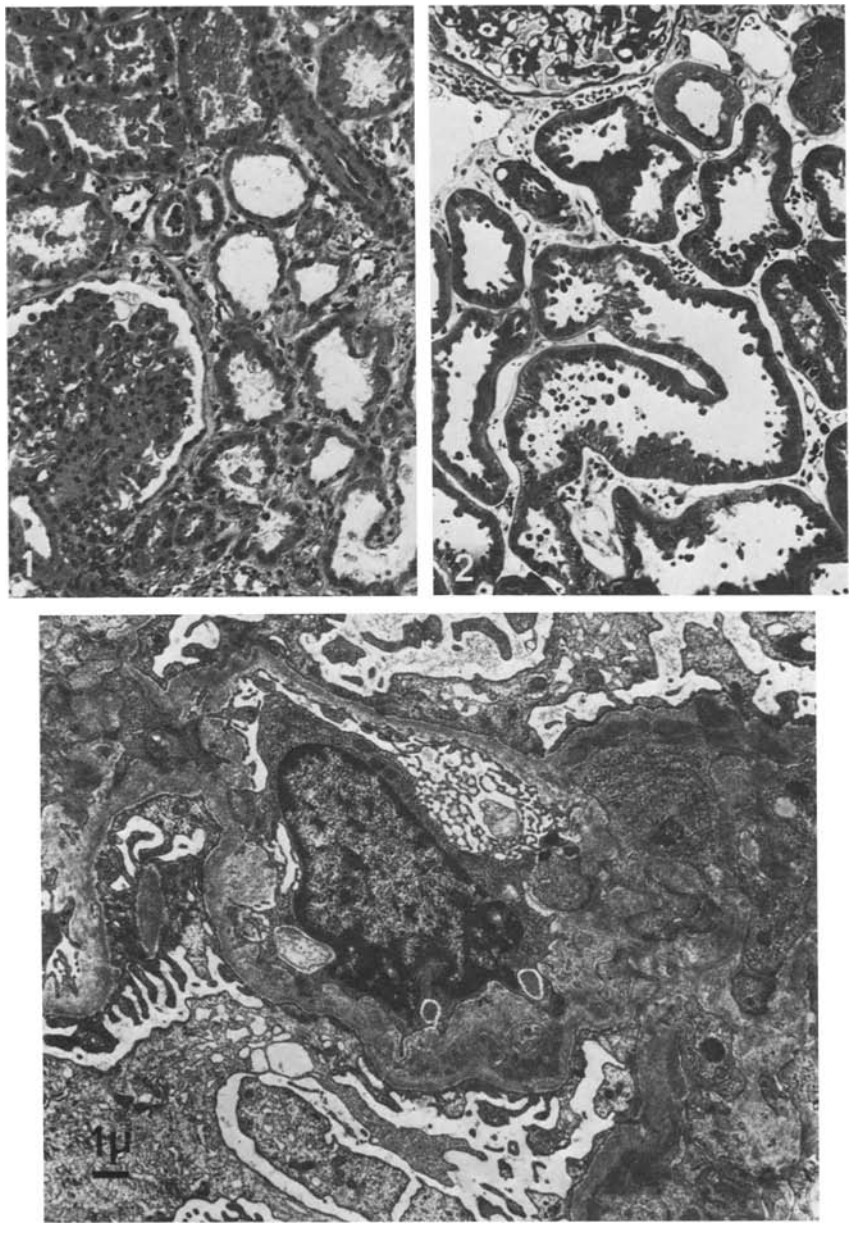

Fig. 1. Enlarged glomerulus with proliferative lesions and irregularly dilated tubules. HES $\times 80$

Fig. 2. Dilated tubules with epithelial alterations. Semi thin section stained with toluidine blue $\times 80$

Fig. 3. Thickened mesangium with electron-dense deposits within the mesangium and the basement membrane

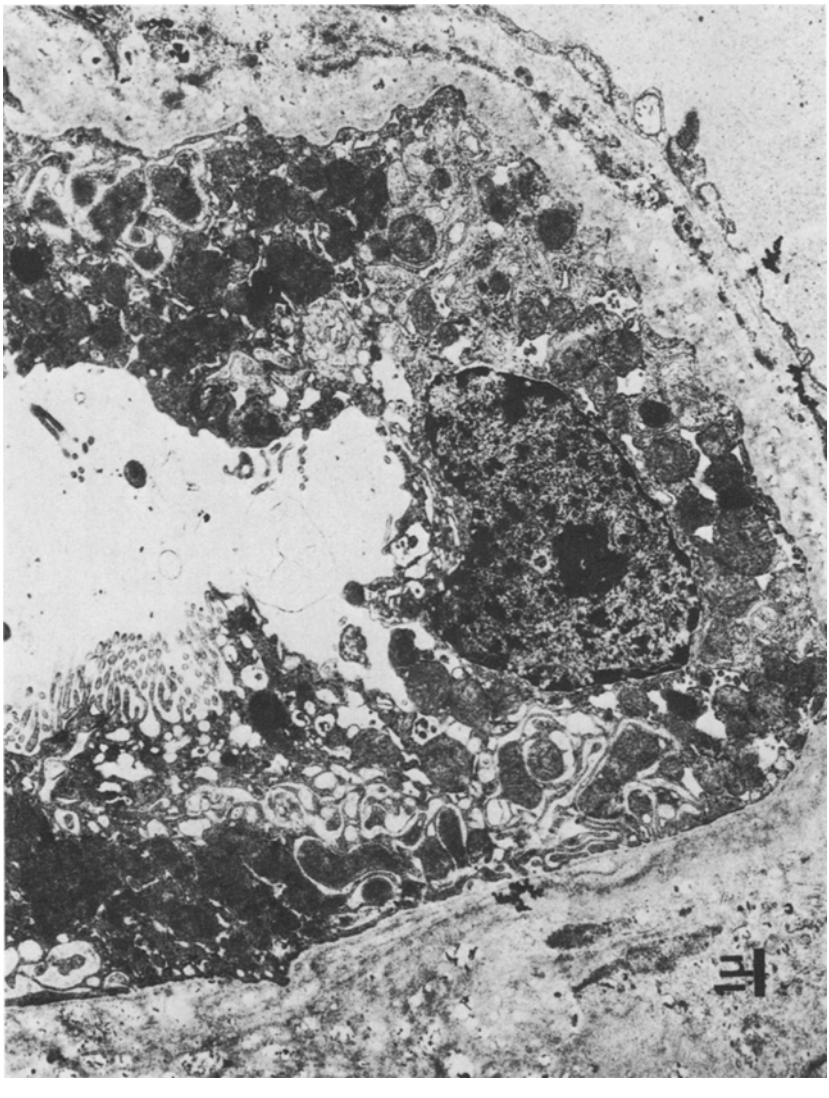

Fig. 4. Tubule with necrotic epithelial cell and thickened basal membrane

In FGS, the mesangium was thickened by hypertrophic membranous matrix and by finely granular electron-dense deposits (Fig. 3). The endothelial cells had an abundant cytoplasm with consequent encroachment on capillary lumina. In proximal tubules, intact and necrotic cells were mixed. The basal membrane was not thickened, except underneath the necrotic cells. Tubules with a flat epithelium had poorly-differentiated cells without basal folds or mitochondria. Their basal membrane was heavily thickened and contained many cell fragments and vacuoles with dense osmiophilic material (Fig. 4).

In conclusion, morphological features were those of FGS in oligomeganephronia associated with degenerative changes in tubules.

Discussion

The discussion will focus on three points, the clinical features, the nephron hypertrophy, and the degenerative lesions.

The clinical association of characteristic oligomeganephronia and tapetoretinal degeneration has been reported only once before by Hirooka et al. (1969). Tapetoretinal degeneration is more frequently associated with nephronophtisis and was observed in 8 of the 13 series of cases published by Waldherr et al. 1982 and designed as renal-retinal dysplasia or dystrophy. In addition to this association of oligomeganephronia and tapetoretinal degeneration, which might be an autonomous syndrome, our patient – like Hirooka's – had hearing impairment and an abnormal EEG. However, he had neither mental retardation nor seizures.

The nephron hypertrophy was fully demonstrated in our case; the few glomeruli were voluminous with enlarged diameter (mean diameter: 300 μ), and the tubules were dilated with various epithelial injuries and thickened basal membranes. Fetterman and Habib (1969) using a microdissection technique, have shown that the proximal tubules are greatly elongated and contain small diverticuli.

Renal hypoplasia with oligomeganephronia is a congenital disorder resulting in the development of a restricted number of nephrons. Nephron hypertrophy may thus be a compensatory mechanism, the nephrons increasing their size to balance the deficit of filtration induced by the embryonic lesions. Subtotal nephrectomy in experimental models (Shimamura and Morrison 1975; Salusky et al. 1981) leads to marked enlargement of glomeruli and tubules with increase in mesangial matrix. Recently, Brenner (1984) has suggested that nephronic reduction results in an increase of renal plasma flow and filtration pressure. Subsequently proteinuria and azotaemia appear and histopathological studies show sclerotic lesions in the glomeruli.

Focal glomerular sclerosis (FGS) was observed in our case as in others (Cruveiller et al. 1966; Royer et al. 1967; Callis et al. 1970; van Acker et al. 1971). Ultrastructurally thickening of glomerular basement membranes with occasional folds, hypertrophy of mesangial matrix, hypertrophy of endothelial and epithelial cells were all features of FGS observed in oligomeganephronia (Scheinman and Abelson 1970; Morita et al. 1973; Elfenbein et al. 1974; Waldherr et al. 1975). It happens in various kinds of human nephropathies (Gubler et al. 1978) as well as in experimental models: in the aging, heavily proteinuric Sprague Dawley rat (Couser and Stilmant 1975), in Wistar rats after 5/6 nephrectomy (Shimamura and Morrison 1975), in nephrectomized rats receiving a protein-rich diet (Salusky et al. 1975) and in Münich-Wistar rats after 5/6 nephrectomy (Hostetter et al. 1981). In all these conditions proteinuria preceded FGS. In oligomeganephronia similar mechanisms may affect the remaining hypertrophic nephrons which are functionally overloaded as suggested by McGraw et al. (1984).

The thickening of the basement membrane of Bowman's capsule reported by Callis et al. 1970; Royer et al. 1966; and in the ultrastructural studies of Scheinman (1970) and Waldherr et al. (1975) was constantly associated with extensive interstitial fibrosis. It was not observed in our case where interstitial fibrosis was absent.

Tubular lesions are well-illustrated in our case; all kinds of cellular injury from mild cytoplasmic vacuolisation to total necrosis with subsequent regenerative changes were observed in proximal tubules. As in Elfenbein's (1974) and Waldherr's (1975) cases, the most marked thickening of the basement membranes was located under the most severely-injured epithelial cells or under regenerative cells. In our case, there was a sharp contrast between the absence of interstitial lesions and the severe tubular injuries.

Experimentally tubular atrophy was parallel to glomerular damage in $9/10^{th}$ nephrectomized (Salusky et al. 1981) or aging rats (Bolton et al. 1976).

In our patient the renal lesions of oligomeganephronia were similar to those of experimental nephronic reduction but the exceptional association of oligomeganephronia and tapetoretinal degeneration have, so far, no physiological explanation.

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