Coexpression of Vimentin and Cytokeratin in Damaged Tubular Epithelia of Kidney in Balkan Nephropathy

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Dear Sir,

Balkan nephropathy is now recognized as a chronic tubulointerstitial kidney disease of unknown etiology [1]. Renal histology in the early clinical stages of the disease have been described; however, although peculiar, it resembles that of aging with pronounced renal vascular changes [2-4]. Since the histological examination of kidney in Balkan nephropathy could be misleading we have previously studied distribution of laminin, the major noncollagenous basement membrane protein. Evidence was presented that major changes in Balkan nephropathy occur in interstitial capillaries and proximal tubules [5]. The aim of this study was to investigate expression of two intermediate filament proteins, cytokeratin and vimentin, in the kidney of patients in different stages of Balkan nephropathy.

Renal biopsy specimens were obtained in 12 patients with Balkan nephropathy diagnosed according to the criteria previously described [1]. The mean age of patients was 53.8 years (range 49-58). Renal failure was demonstrated in all but 3, with a mean serum creatinine of 113 μ mol/l (range 75-142). Glomerular filtration rate (GFR) estimated by 99m Tc-DTPA clearance was 74.3 ml/min (range 28-122). Arterial blood pressure was normal (8 patients) or moderately increased. The mean systolic pressure was 138.3, diastolic 90.8 mm Hg. Ten kidney specimens of apparently healthy accident victims, obtained at autopsy 6-10 h after the death, served as controls. For light microscopy study, biopsy specimens were fixed in alcoholic Bouin's fixative for 12-24 h followed by routine processing and embedding in paraffin. For immunocytochemical analysis, monoclonal antibodies against cytokeratin 18 and vimentin (Sigma Chemical Co., St. Louis, Mo., USA) were used. Frozen sections of biopsy specimens were first incubated with the monoclonal antibody. Subsequently, avidin-biotin complexed specific anti-rabbit antibody was used as a secondary antibody. The avidin-biotin complexes of the secondary antibodies were visualized with aminoethylcarbazole, and sections were evaluated by routine light microscopy.

Normal kidney: Cytokeratin 18 was demonstrated in various parts of renal tubules, proximal, distal and collecting ducts. Positive staining was obtained also for the parietal cells of Bowman's capsule. Vimentin-positive filaments were demonstrated in glomeruli and in interstitial cells, in particular in blood vessels. No vimentin staining was obtained in tubular epithelium of the adult kidney.

Balkan nephropathy: Cytokeratin 18 was overexpressed in tubular epithelium, most intense on atrophic proximal tubules of the outer cortex, where also light microscopic changes were the most pronounced. Marked apical localization of cytokeratin in tubular epithelium is evident (fig. 1a). Vimentin expression in glomeruli was slightly increased, segmental and mostly in mesangium. Extra-glomerular localization was marked, especially in atrophic tubules (fig. 1b). Proximal

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Fig. 1. a Focal cytokeratin 18 expression in atrophic tubules. b Increased focal expression of vimentin in atrophic tubules.

tubular overexpression of vimentin corresponded to the degree of proximal tubule damage. Some peritubular blood vessels were also vimentin positive. Very intense vimentin staining was found in the areas of marked interstitial sclerosis. The observed overexpression of vimentin was much pronounced in the outer cortex. Distal tubules were vimentin negative. The present results show that vimentin is not detectable in tubular epithelium of the adult kidney, as previously described [6]. In Balkan nephropathy, however, the prominent finding was coexpression of vimentin and cytokeratin 18 in proximal tubular epithelial cells. The coexpression of vimentin with cytokeratins was also demonstrated during development. In fetal kidneys, the coexpression of cytokeratins and vimentin was detected in the visceral and parietal epithelium of the glomerulus, the proximal tubules, the thin loops of Henle, and the collecting ducts [7,8]. In contrast, in the tubules of normal adult kidney, the presence of vimentin and cytokeratins was nearly always mutually exclusive. Damage to the tubular epithelium has been followed by the coexpression of vimentin and cytokeratin [7, 8]. In the present study, further evidence on the tubulointerstitial lesions in the early stages of Balkan nephropathy is presented.

References

Stefanovic V, Polenakovic M: Balkan nephropathy. Kidney disease beyond the Balkans? Am J Nephrol 1991;1:1-11. Dojcinov D, Strahinjac S, Stefanovic V: Pathohistology of the kidney in the early phases of endemic (Balkan) nephropathy; in Strahinjac S, Stefanovic V (eds): Endemic (Balkan) Nephropathy. Nis, University Press, 1979, pp 91-104.

Mandal AK, Sindjic M, Sommers SC: Kidney pathology in endemic nephropathy. *Clin Nephrol* 1987;27:304-308.

Ferluga D, Hvala A, Vizjak A, Trnacevic S, Halilbasic A: Renal function, protein excretion and pathology of Balkan endemic nephropathy. III. Light and electron microscopic studies. *Kidney Int* 1991;40(suppl 34):S57-S67.

Cukuranovic R, Savic V, Dojcinov D, Stefanovic V: Immunohistochemical localization of laminin in renal lesions of Balkan nephropathy. *Nephron* 1995;70:504-505. Holthofer H, Miettinen A, Lehto VP, Lehtonen E, Virtanen I: Expression of vimentin and cytokeratin types of intermediate filament proteins in developing and adult human kidneys. *Lab Invest* 1984;50:552-559. Gröne HJ, Weber K, Gröne E, Helmchen U, Osborn M: Coexpression of keratin and vimentin in damaged and regenerating tubular epithelia of the kidney. *Am J Pathol* 1987;129:1-8.

Moll R, Hage C, Thoenes W: Expression of intermediate filament proteins in fetal and adult human kidney: Modulations of intermediate filament patterns during development and in damaged tissue. *Lab Invest* 1991;65:74-

120

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