Glomerular Expression of α-Smooth Muscle Actin (α-SMA) in Idiopathic Mesangiocapillary Glomerulonephritis Type I. A Quantitative Study

M. Danilewicz, M. Wągrow ska-Danilewicz
Department of Pathology (Morphometry Division), Medical University in Łódź, Poland

Eighteen renal biopsy specimens from patients with mesangiocapillary glomerulonephritis type I (MCGN-I) evaluated by both light and electron microscopy as well as immunofluorescence microscopy and whose full clinical data were available were examined quantitatively. As control 10 biopsy specimens of kidneys removed because of trauma were used. Morphometric investigations were performed by means of a computer image analysis system to evaluate the glomerular expression of α-SMA in MCGN-I, as well as to determine whether this parameter could correlate with quantitatively analysed glomerular cells and mesangial areas. Another purpose of this study was to verify if the expression of α-SMA correlated with the intensity of glomerular leukocyte infiltrates in this glomerulopathy. The morphometric study revealed that mean values of the expression of α-SMA, total glomerular cells per total glomerular area, mesangium (% of total glomerular area), CD 45RB+ , CD 43+, CD 20+ and CD 68+ cells were in MCGN-I patients increased in comparison with normal controls. Moreover, in the MCGN-I group, but not in controls, significant positive correlation existed between the glomerular expression of α-SMA and total glomerular cells per total glomerular area, mesangium (% of total glomerular area), as well as CD 45RB+ cells and CD 68+ cells. Significant positive correlation between α-SMA staining and total glomerular cells and mesangial areas suggested that increased α-SMA expression might be in MCGN-I an indicator of mesangial cell activation and mesangial matrix production. The significant positive correlation between the glomerular expression of α-SMA and glomerular CD 68+ cells requires further investigations to elucidate whether monocytes/macrophages play a role in the process of inducing myofibroblast phenotype in mesangial cells.

Introduction

Mesangiocapillary glomerulonephritis type I (MCGN-I) is a form of proliferative glomerulonephritis, which occurs in older children and young adults. Prognosis in this glomerulopathy is rather poor and pathogenesis is incompletely understood [2, 3, 4, 11, 17].

In MCGN-I mediation by an immune complex is suggested, in which the classic complement pathway is activated, but the antigen responsible for idiopathic disease is unknown [19]. Structurally, there is marked mesangial expansion, with a tendency to glomerular lobulation. Mesangial interposition between the endothelial layer and the glomerular basement membrane leads to
thickening of the capillary walls [8]. Recent studies in animal models [12] and in human glomerulonephritis [1] have shown that injury producing mesangial cell proliferation also results in increased expression of α-smooth muscle actin (α-SMA) by mesangial cells. Such phenotypic changes in the mesangial cells are assumed to be associated with mesangial cell activation and with mesangial synthesis of cytokines and extracellular matrices, which cause glomerulosclerosis [6, 10, 14]. However, insufficient attention has been paid to the local mechanisms leading to these phenotypic changes.

Therefore, the present investigations were undertaken to evaluate the glomerular expression of α-SMA in MCGN-I, and to determine whether this parameter correlated with quantitatively analysed glomerular cells and mesangial areas. Another purpose of this study was to verify if the expression of α-SMA was associated with the intensity of glomerular leukocyte infiltrates in this glomerulopathy.

Material and methods

Patients

Eighteen renal biopsy specimens from patients with MCGN-I were examined by percutaneous renal biopsy. Morphological diagnosis of MCGN-I was established independently by two experienced nephropathologists on the basis of light microscopy, immunofluorescence and electron microscopy. For the present study only patients with normal blood pressure at the time of biopsy were selected. As control 10 biopsy specimens of the kidney were used. All biopsy specimens were taken from kidneys removed because of trauma. None of the persons from whom renal tissue originated were known to have had previous or current renal disease. All control specimens were histologically examined by an experienced nephropathologist and found to be normal renal tissue before quantitative examinations were carried out.

Light microscopy

Tissue specimens were embedded in paraffin, sections cut precisely at 4 μm, and stained with haematoxylin and eosin, periodic acid-Schiff (PAS)-alcian blue, trichrome light green (Masson), and with silver impregnation (Jones). Thickness of each section was controlled according to the method described by Weibel [20].

Immunofluorescence microscopy

Tissue was snap frozen, sectioned at 5 μm and fixed in 95% alcohol for 10 min. Sections incubated with FITC-antisera (Hoechst) to human IgG, IgA, IgM and complement (C3) were viewed on a Carl Zeiss (Jena) NU-2 microscope, using an HBO 200 lamp and proper filters.