Effect of Low-Protein Diet on Glomerular Changes in ddY Mice; A Spontaneous Animal Model of IgA Nephropathy

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Dear Sir,

Long-term dietary protein restriction is generally considered to reduce the levels of urinary protein and ameliorate the glomerular injuries in patients with various glomerulonephritides. We usually start dietary protein restriction after the definite diagnosis, although restriction from an early stage might show a good prognosis in such diseases. The authors reported that the ddY mouse strain can serve as a spontaneous animal model for IgA nephropathy [1, 2].

Marked depositions of IgA and C3 in glomeruli and glomerular mesangial expansion were observed in the ddY mice after 40 weeks of age [1]. We attempted to compare the glomerular changes between the low-protein and the high-protein diets in ddY mice. Twenty ddY mice were fed a standard diet containing 22% protein until 40 weeks of age. These ddY mice were divided into two diet groups, i.e. low protein (6%) and high protein (50%). ddY mice of both groups were sacrificed at 70 weeks of age. Urinary protein was measured every 2 weeks according to the method of Knight et al. [3]. Renal sections stained with hematoxylin and eosin, and periodic acid-Schiff were examined by light microscopy. Renal cryostat sections were stained with FITC-labelled goat anti-mouse IgA, IgG, IgM and C3 antisera at room temperature for 45 min. Type IV and I collagens, fibronectin and laminin were also stained. The sections were examined using a

Fig. 1. a Glomerular enlargement and mesangial expansion were observed in the high-protein diet ddY mouse. PAS. $\times 400$. b These light-microscopic findings were improved in the low-protein diet mouse. PAS. $\times 400$. c Glomerular deposition of IgA was marked in the high-protein diet ddY mouse. $\times 400$. d The intensity of glomerular IgA deposition was decreased in the low-protein diet mouse. $\times 400$.

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Zeiss universal microscope (Carl Zeiss, New York, N.Y., USA). At each time after 50 weeks of age, the levels of urinary protein in the low-protein diet mice were significantly decreased compared with those in the high-protein diet mice ($p < 0.01$). Glomerular enlargement and mesangial expansion were observed in the high-protein diet ddY mice (fig. 1a). These findings were improved in the low-protein diet ddY mice (fig. 1b). The intensity of IgA, IgG, IgM and C3 in glomeruli of the low-protein diet mice was significantly lower than that of the high-protein diet mice (fig. 1c, d). However, there was no significant difference in the intensity of type IV and I collagens, fibronectin and laminin staining in glomeruli between the two groups. We demonstrated that dietary protein restriction ameliorates glomerular expansion and depositions of immunoglobulins and complement in glomeruli. It appears that the dietary protein restriction is useful for the prevention of glomerular injuries, even when such a therapy is started after the appearance of IgA nephropathy in ddY mice.

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