Early Development of Spontaneous Glomerular Lesion in Syrian Hamsters of APA Strain
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In a pathological survey of a Syrian hamster colony of APA strain which has been developed in Japan [13] and maintained as a closed colony by random breeding in our laboratory, Doi et al. [3] demonstrated that APA hamsters developed focal segmental glomerulosclerosis (FSG) after 6 months of age instead of glomerular amyloidosis, the most common feature of renal lesions in aged Syrian hamsters of other strains [5, 9]. Nowadays, it is said that FSG is a pathologic diagnosis that describes a distribution of glomerular scarring [2, 4, 7, 11, 16], but its pathogenesis is still unclear [8].

The purpose of this study is to clarify the early glomerular alteration prior to the onset of FSG in APA hamsters.

Forty-five male (mean body weight: 64 g) and 45 female (mean body weight: 63 g) 4-week-old Syrian hamsters of APA strain were used. They were weaned at 4 weeks of age and thereafter kept in stainless steel cages with sterilized wood shavings for bedding in groups of 5 of the same sex under controlled conditions (temperature, 24±2°C; humidity, 60±5%). The animals were fed a commercial pelleted diet, CMF (27.7% protein, 8.8% fat; Oriental Yeast Co., Ltd., Tokyo) and tap water ad libitum.

Fifteen animals of each sex were weighed and killed by exsanguination under ether anesthesia at 4, 8 and 12 weeks of age, respectively. Urine samples collected at necropsy by urinary bladder puncture were examined for urinary total protein and glucose using uropaper (Eiken Chemical Co., Tokyo). Three male and 3 female 12-week-old hamsters of Std: golden strain (mean body weight: 125 g) purchased from Japan SLC (Shizuoka) were also used as histological controls. The kidneys of each animal were weighed and fixed in 10% neutral buffered formalin. Two to 4 μm-paraffin sections were made and stained with hematoxylin and eosin (HE), periodic acid-Schiff (PAS) or periodic acid-methenamine-silver (PAM). Small pieces of the renal cortex were fixed in 2.5% glutaraldehyde and 2.0% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4), postfixed in 1.0% osmic acid in the same buffer, dehydrated through graded alcohol and embedded in Quetol 812 (Nisshin EM Co., Ltd., Tokyo). Ultrathin

Fig. 1. Glomerulus of a 4-week-old male hamster. Slight focal expansion of mesangial region (arrowheads). (PAS, × 500).

Fig. 2. Glomerulus of a 12-week-old male APA hamster. Apparent expansion of mesangial region is seen. (PAS, × 500).

Fig. 3. Glomerulus of a 12-week-old male Std: golden hamster. No significant changes are seen in glomerulus. (PAS, × 500).
sections were double-stained with uranyl acetate and lead citrate and observed under a JEM-100S electron microscope (JEOL Ltd., Tokyo).

All animals showed normal body weight gain and were negative for urinary glucose throughout the experimental period. Proteinuria (30 to 100 mg/dl) was recorded in some APA hamsters at 4 weeks and in all animals at 12 weeks of age, and it accompanied histologically a slight increase of proteinaceous cast in a small number of atrophic and/or dilated tubules in the kidney with glomerular changes. Proteinuria in young APA hamsters might be related to a glomerular epithelial cell injury [14, 15] and to an alteration of charges or size selectivity barrier in the glomerular basement membrane [6, 10]. At 4 weeks of age, most APA hamsters showed slight enlargement of some glomeruli with slightly expanded mesangial region especially in the juxtamedullary cortex (Fig. 1). These changes progressed with advancing age, and focal but apparent expansion of glomerular mesangial region due to increase of matrix material and mesangial cells was commonly observed at 12 weeks of age (Fig. 2). The incidence and severity of such renal changes were similar between males and females. On the other hand, 12-week-old Std: golden hamsters showed no changes

Fig. 4. A part of glomerulus of a 4-week-old female APA hamster. Slight focal expansion of mesangial region. × 6,000.

Fig. 5. A part of glomerulus of a 12-week-old male APA hamster. Apparent expansion of mesangial region due to an increase of basement membrane-like material and mesangial cells. Collagen fiber-like fragments (arrowhead) are found. × 4,000.
both in glomeruli and in uriniferous tubules (Fig. 3).

Electron microscopic examination revealed that slight focal expansion of mesangial region (Fig. 4) and focal effacement of foot processes of podocytes had already developed at 4 weeks of age in the renal glomeruli of APA hamsters. These changes progressed with advancing age (Fig. 5) and accompanied segmental thickening of glomerular basement membrane (Fig. 6) at 12 weeks of age. In addition to an increase of basement membrane-like material, appearance of collagen fiber-like fragments in expanded mesangial matrix may suggest an existence of abnormality in matrix material metabolism, because collagen fibers are not found in the normal glomerulus [13]. On the other hand, these changes were not detected even in 12-week-old Std: golden hamsters in the present study and they also have not been reported in young Syrian hamsters of other strains [1, 5]. Therefore, such an early appearance of glomerular alterations of spontaneous nature is considered to be a characteristics of APA hamsters.

In conclusion, it was clarified in the present study that APA hamsters developed glomerular lesions from their early stage of life, and these early glomerular alterations were considered to result in the later FSG reported in this strain of Syrian hamsters [3]. Immuno- and lectin-histochemical investigations are now in progress to find out the trigger of the early glomerular changes in APA hamsters.

REFERENCES