Membranoproliferative Glomerulonephritis in a Young Cat

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ABSTRACT. A 9-month-old male Japanese domestic cat showed pleural effusion, ascites, azotemia, hypoproteinemia and severe proteinuria. Histopathology of the percutaneous renal biopsy specimen revealed that all glomeruli showed intense mesangial hypercellularity with an increased mesangial matrix and thickening of the capillary walls, resulting in lobular accentuation of the glomerular tufts. Frequent duplication of the capillary walls was also observed. Immunostaining for α-smooth muscle actin distinctly revealed mesangial interposition. Diffuse global and linear deposition of C3 and IgG was observed mostly along the peripheral capillary loops. Electron microscopy confirmed frequent circumferential mesangial interposition and subendothelial dense-deposits in the glomerulus. The glomerular lesion was consistent with human membranoproliferative glomerulonephritis type I, and might be a rare case that developed at young age.

KEY WORDS: feline, glomerulus, pathology.

Membranoproliferative glomerulonephritis (MPGN) is a chronic and progressive renal disease characterized by intense glomerular hypercellularity and diffuse thickening of the glomerular basement membrane with the appearance of “double contours”. According to the World Health Organization classifications of human glomerular diseases, MPGN can be divided into three subtypes based on morphologic appearance [2]. Spontaneous MPGN has been reported in cats, dogs, horses, pigs, and lambs [7, 9]. Most of these cases have corresponded to types I or II, and type III MPGN of domestic animals has been reported only in a cat [6]. There have been no reports on the distinct cases of feline MPGN type I. In this report, we describe a young feline case comparable to MPGN type I with typical lobular accentuation of the capillary tufts that might be a rare case that developed at a young age.

A 9-month-old male Japanese domestic cat was reported to have shown signs of anorexia, appendicular edema, and diarrhea 1 month before examination. At the first examination, pleural effusion, ascites, and bilateral renal swelling were revealed by X-ray examination. The results of a blood test showed non-regenerative anemia (PCV: 20%), thrombocytopenia (26,000/μl), azotemia (blood urea nitrogen: 79 mg/dl, creatinine: 1.8 mg/dl), and hypoproteinemia (total protein: 3.0 g/dl), indicative of a renal glomerular disorder. Proteinuria (1,583 mg/dl) and a high urine protein:creatinine ratio (25.7) were observed by urinalysis. The laboratory test for feline leukemia virus (FeLV) was positive and that for feline infectious peritonitis virus (FIPV) was negative.

A percutaneous renal biopsy was performed to confirm diagnosis, and the specimen was fixed in 10% formalin. The paraffin-embedded sections were made and stained with hematoxylin and eosin (HE) or periodic acid-Schiff (PAS). Immunohistochemical staining by the streptavidin-biotin peroxidase method (Histofine kit, Nichirei, Tokyo or VECTASTAIN ABC kit, Vector Laboratories, Burlingame, CA, U.S.A.) was carried out on the paraffin sections using primary antibodies against α-smooth muscle actin (α-SMA, clone 1A4, 1:50, DAKO, Glostrup, Denmark), proliferating cell nuclear antigen (PCNA, PC10, 1:100, DAKO), cat IgG (1:200, Kirkegaard & Perry Laboratories, Gaithersburg, MD, U.S.A.), or cat complement component 3 (C3) (1:200, Biogenesisi, Poole, UK). Antigen retrieval for PCNA was performed by heating sections in 10 mM citrate buffer pH 6 for 10 min using microwave oven. For IgG and C3 staining, the sections were pretreated by 0.1% trypsin at 37°C for 30 min. Antigen retrieval was not required for α-SMA staining. The immunoreaction was visualized by a dianimobenzidine-hydrogen peroxide solution, and the sections were counterstained with hematoxylin. Electron microscopy was carried out using a formalin-fixed biopsy specimen.

Microscopically, there were ten glomeruli in the section of biopsy specimen. All glomeruli in the specimen showed severe mesangial hypercellularity with an increased mesangial matrix and prominent thickening of the capillary walls, resulting in lobular accentuation of the glomerular tufts (Fig. 1). Adhesion between glomerular capillary tufts and the Bowman’s capsules often developed. Also, proteinaceous substances were frequently observed in the Bowman’s spaces. PAS and PAM stains revealed frequent duplication or splitting of the capillary walls. Unusual cellular localization was seen in the peripheral capillary walls of the glomeruli, indicating mesangial interposition between endothelial cells and glomerular basement membrane. Mild inflammation and fibrosis were seen in the interstitium. Some proximal tubular epithelium showed swelling due to...
hydropic degeneration.

Immunohistochemically, α-SMA expression was intense in the capillary walls and the mesangial areas, suggesting mesangial interposition and activation or a phenotypic change in the mesangial cells (Fig. 2). In the mesangial areas, PCNA-positive cells were frequently observed. Diffuse global and linear deposition of C3 and IgG was observed along the peripheral capillary loops by immunohistochemistry (Fig. 3). Less intense deposition of these substances was also seen in the mesangium with granular appearance.

Electron microscopy revealed prominent mesangial hypercellularity and circumferential mesangial interposition resulting in narrowing of the glomerular capillary lumens (Fig. 4). Further, irregular thickening of the glomerular basement with frequent wrinkling, and dense-deposits in the subendothelial (Fig. 5) and occasionally in mesangial areas were detected in the glomerulus. The cat died one week after the biopsy. Necropsy revealed bilateral renal swelling, subcutaneous edema, pleural effusion, ascites, and pulmonary edema.

Spontaneous immune complex-mediated glomerulonephritis has been well-reported in cats and membranous nephropathy is the most frequent type of feline glomerulonephritis [1]. On the other hand, the clinical and pathological features of MPGN in cats have not been well documented. The clinical, pathological, and immunohistochemical findings of the glomerulopathy in the present case were consistent with those of human MPGN type I. Circumferential mesangial interposition in the glomeruli is one of characteristic morphological features of MPGN [2], however sometimes it may be difficult to detect this glomerular lesion by routine HE stain or PAS reaction. In the present case, immunostaining for α-SMA clearly proved this characteristic lesion. Therefore, α-SMA immunostaining is preferable as a routine diagnostic method to evaluate the expansion of the mesangial cells into the glomerular capillary walls.

The clinical presentation of this cat was characteristic of so-called “protein-losing nephropathy”, therefore the cat was readily suspected to have a certain glomerular disease. However, the type of glomerular disease could not be confirmed without detail histopathological and immunopathological examinations on the biopsy specimen. Even though the relationship between the types of feline glomerular diseases and the efficacy of treatments has not been clarified yet, a renal biopsy is fairly important to evaluate the inten-
Nephrotic syndrome and macroscopic or microscopic hematuria is often associated with MPGN in human cases. The most characteristic clinical finding in humans is hypocomplementemia, especially with decreased C3 levels. The primary causes of human MPGN have not been elucidated, but nephritic factors are involved in complement activation and hypocomplementemia in this type of glomerular disease [2]. In animal cases of MPGN, congenital or hereditary abnormalities of the complement system have been also suggested to be involved in MPGN of some cases in which the disease develops in early life [3, 5, 7]. However, we could not evaluate complement system in this case and could not trace the family history. In immune-mediated glomerulonephritis in cats, infection with FeLV [1], FIPV [4] or feline immunodeficiency virus [8] is frequently complicated, although typical MPGN as seen in the present case has not been reported in these infectious diseases.

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