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Letter to the Editor

LETTER TO THE EDITOR

Type VI collagen-related nephropathy

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Glomerular diseases with organized deposits are classified as amyloidosis, diabetic fibrillosis, fibrillary glomerulopathy, immunotactoid glomerulopathy, fibronectin glomerulopathy, collagenofibrotic glomerulopathy, cryoglobulinemic glomerulonephritis and various advanced kidney diseases [1]. We herein report a case of glomerular disease with unusual, organized deposits.

An 84-year-old man with a 4-year history of microhematuria and proteinuria was referred to our hospital because of the exacerbation of hypertension and nephrotic-range proteinuria. He had developed left glaucoma 11 years previously and suffered a cerebral lacunar infarction 2 years previously. His medications included clopidogrel (75 mg/day) for stroke prevention; amlodipine (5 mg/day), enalapril (5 mg/day), and azosemide (30 mg/day) for hypertension; atorvastatin (5 mg/day) for hyperlipidemia; and naftopidil (50 mg/day) for benign prostatic hypertrophy. He had also been diagnosed with prostate cancer, which had not shown progression at regular outpatient visits. He was admitted to our hospital for further evaluation.

His blood pressure was 189/95 mmHg. Pitting edema was found on his bilateral lower legs, without any purpura.

A urinalysis revealed microhematuria and proteinuria (the urinary protein:creatinine ratio was 5.67 g/g Cr; Supplementary data, Table S1). His cystatin C–based estimated glomerular filtration rate (eGFR) was 53.4 mL/min/1.73 m^2. His serum albumin level was decreased and his serum total cholesterol level was increased. Antinuclear antibody, cryoglobulin and cryofibrinogen were all negative with normal complement levels. Serum and urine immunoelectrophoresis showed negative results. Chest computed tomography (CT) showed bilateral pleural effusions and pericardial fluid and abdominal CT showed several simple cysts in both kidneys without atrophy.

A kidney biopsy showed lobulated glomeruli with thickening and duplication of the glomerular basement membranes (GBMs), mesangial hypercellularity and mild endocapillary hypercellularity (Supplementary data, Figure S1). An immunofluorescence study revealed granular deposition of immunoglobulin M (IgM) and complement 3 (C3) along the glomerular capillary wall and in the mesangial area (Supplementary data, Figure S2). There was a light chain restriction for κ. Direct fast scarlet staining was negative under polarized light microscopy. Electron-dense deposits were observed in the subepithelial, intramembranous and subendothelial area under transmission electron microscopy (Figure 1A). A high-magnification view of the deposits revealed fibrillary structures of 8–14 nm in width that were associated with ladder formation, with a periodicity of 25–30 nm (Figure 1B). Glomeruli on paraffin sections were analyzed with laser-capture microdissection followed by liquid chromatography–tandem mass spectrometry. The results identified an increase in collagen α1 (VI), α2 (VI) and α3 (VI) chains; IgM; C3; κ light chain; fibrinogen α, β and γ chains and apolipoprotein B-100 (Supplementary data, Figure S3). An immunofluorescence study using rabbit polyclonal antibody against collagen α1 (VI) chain showed positive findings on capillary wall segments (Supplementary data, Figure S4).

Intravenous methylprednisolone (500 mg/day) was administered for 3 consecutive days, as proteinuria did not improve with azilsartan and the urinary protein:creatinine ratio and serum albumin value were 0.73 g/g Cr and 3.2 g/dl, respectively, under treatment with prednisolone at a dose of 7.5 mg/day.

While the present case resembled cryofibrinogen-associated glomerulonephritis [2–4], cryofibrinogen was not identified in the plasma. There have been two similar cases with unusual, organized deposits [5, 6]. However, a proteomic analysis was

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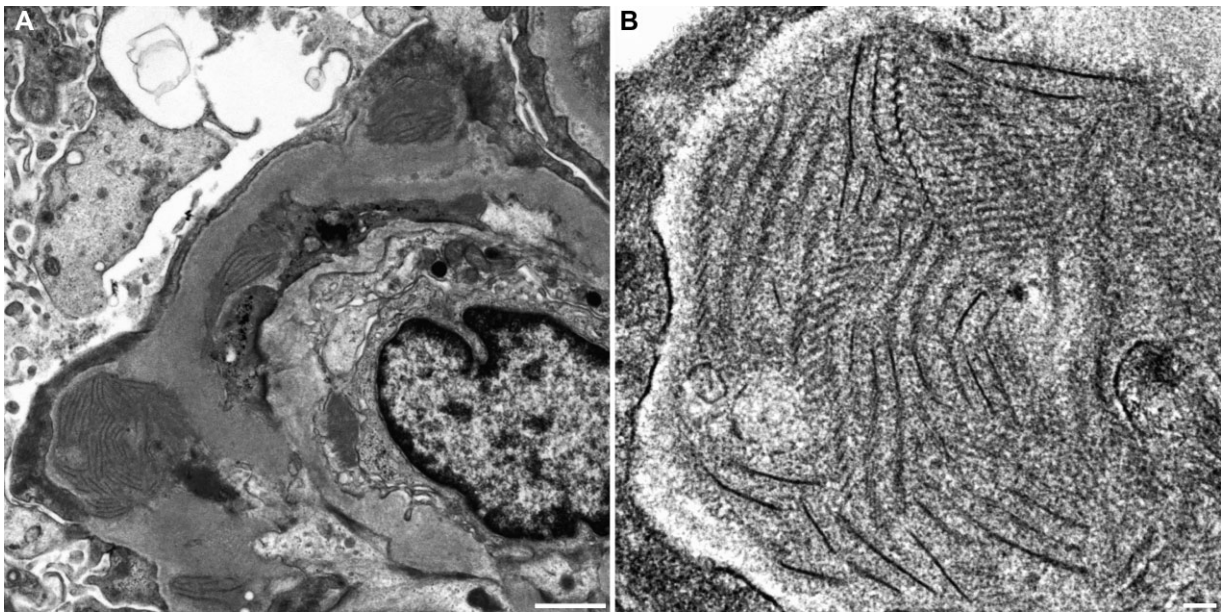

FIGURE 1: (A) Electron-dense deposits were observed in the subepithelial, intramembranous and subendothelial areas of the GBM under transmission electron microscopy. Extensive foot process effacement of the podocytes and mesangial interposition were also observed. Bar = 1 µm. (B) The deposits at high magnification revealed fibrillary structures with a width of 8–14 nm associated with ladder formation with a periodicity of 25–30 nm. Bar = 100 nm.

not performed in one report [5] and immunohistochemical staining of type VI collagen was negative in the other report [6]. In contrast, a proteomic analysis in the case of cryofibrinogen-associated glomerulonephritis identified collagen α3 (VI) chain [4]. Although the details concerning the mechanism underlying the glomerular deposition of type VI collagen are unclear, the diagnosis in the present case was type VI collagen-related nephropathy.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests in association with the present study. The results presented in this article have not been published previously in whole or part. Written informed consent was obtained from the patient. A proteomic analysis of glomeruli was approved by Mie University (H2020-184).

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