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Carta al Director

Fibronectin glomerulopathy: A case report and literature review

Glomerulopatía por fibronectina: informe de un caso y revisión de la literatura

Dear Editor,

Fibronectin glomerulopathy (FNG) is an uncommon autosomal dominant disease with age-related penetrance. Burgin¹ first reported the disease in 1980. Strøm² verified fibronectin glomerulopathy – a newly recognized autosomal dominant kidney disease. It has been distinguished from these other disease entities by the presence of glomerular fibrillary deposits that show strong immune reactivity to fibronectin (Fn).

Here we report a case of FNG 2017 in our hospital. A 45-year-old Chinese female was hospitalized because of edema for 7 days. She denied history of hair loss, oral ulceration, alopecia, oliguria, joint pain, rashes and menstrual irregularities. She had medical history of malignant hydatidiform mole 8-years ago which had been cured. Her sister had nephritic syndrome for ten years with no biopsy performed. Physical examination showed mild hypertension (158/119 mmHg) and leg edema. The laboratory examination showed her daily urinary protein, serum albumin, blood urea nitrogen and creatinine were 4.21 g/day, 40.9 g/L, 4.39 mmol/L, 53 μmol/L. The blood tests of liver function, lipid, immunoglobulin, complement, antinuclear antibody spectrum, antineutrophil cytoplasmic antibody, hepatitis B and C serology were all negative. The renal and gynecologic ultrasound was normal. The kidney biopsy was showed in Fig. 1. Light microscopy showed one of 25 glomeruli was sclerotic glomeruli, others showed moderate to severe mesangial hypercellularity with a lobular appearance with cellular mesangial nodules that were expanded by matrix. Capillary walls showed stenosis, occlusion and basement membrane thickening. Segmental mesangial insertion and double track formation could be seen. Immunofluorescence only showed faint staining for IgM deposits in a band pattern in the subendothelial spaces and testing of IgG, IgA, C3, Cq1, fibrinogen, albumin completely negative. There was

no evidence of amyloid deposits on Congo Red stain. Diffuse strong granular-smudgy staining was observed in mesangial and subendothelial locations with fibronectin. Electron microscopy showed 2 glomeruli that the capillary loops were lobulated, and focal endothelial cells proliferated. The wall of renal capsule is thickened and stratified. Extensive fine granular deposits in the mesangium and in the subendothelial spaces could be seen with a diameter of 10–12 nm fibrils.

A PubMed and CNKI searching using the terms “fibronectin glomerulopathy” yielded 35 English and 6 Chinese articles reports of patients with clinical and (or) biopsy characteristics until January 31, 2018. This allowed us to compare the disease clinical features and biopsy features. A total of 86 patients, 52 male, 34 female, aged 3–88³ years were reported in these literatures. 25% of patients receive renal replacement therapy.² 42 patients among 78 patients observed with nephritic range proteinuria (more than 3.5 g/day). 53 patients among 85 patients suffered from hypertension. 23 of 43 cases which were available Urine Analysis had microhematuria. 23 cases' serum creatinine (normal values 0.6–1.3 mg/dl) was abnormal except for 18 patients who did not provide renal function. Family history was noted in 61 patients. 57 patients of the literatures were provided with renal biopsy. 47 patients were tested intense staining for the serum fibronectin by immunohistochemistry which was the basis for the diagnosis. The Congo red staining is negative.

FNG is a newly recognized autosomal dominant hereditary renal disease. The deposition of Fn in the glomeruli is the key to FNG. The increasing Fn leads to some glomerular diseases. FNG is considered to be a hereditary disease and associated with mutations in the Fn1 gene.^{4,5} By haplotype analysis, p.Pro1472del and p.Leu1974Pro are fundamental mutations.⁶ FNG is considered an unimmune glomerulopathy. Diagnosis of FNG is made only by renal biopsy. Light microscopy has no diagnostic value for FNG.

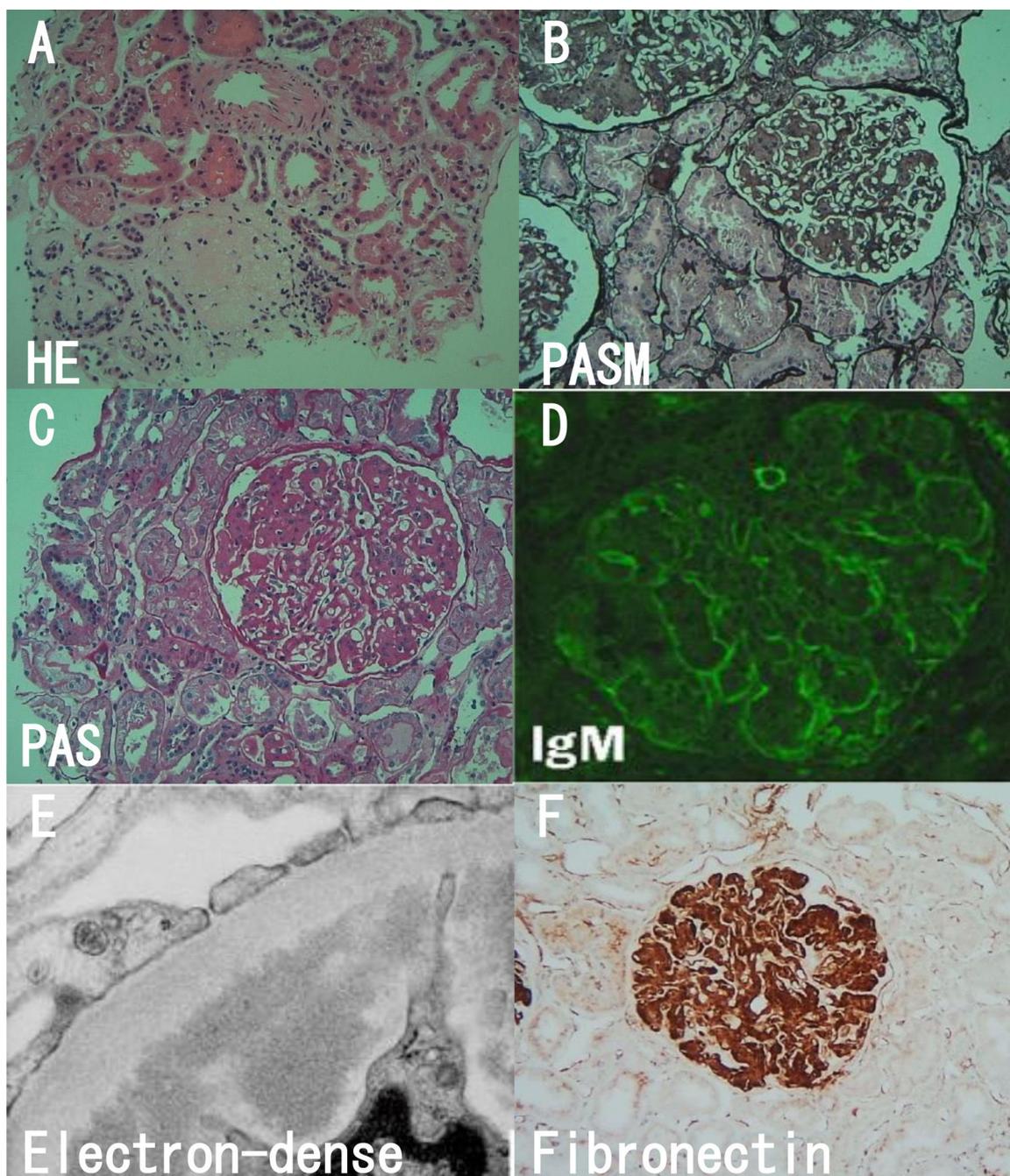


Fig. 1 – Light microscopic, immunofluorescence and electron studies. (A) Sclerotic glomeruli (HE). (B) Lobular appearance with cellular mesangial nodules (PASM). (C) Moderate to severe mesangial hypercellularity (PAS). (D) Faint staining for IgM (Immunofluorescence). (E) Massive electron-dense deposits. (F) Fibronectin was strongly positive (immunohistochemistry).

The diameter of the special deposits is important to diagnose in electron microscope. Fn staining of immunofluorescence can make a definite diagnosis. The disease is characterized by proteinuria, microscopic hematuria, hypertension and slow progression to end-stage renal failure. Some treatments such as glucocorticoid,⁷ immunosuppressant,⁸ ACEI, ARB⁹ et al. have used for the disease, but none of them is effective. There is still a risk of recurrence after renal transplantation.¹⁰

Our patient had the distinguishing feature of the disease on the basis of clinical symptoms: hypertension, proteinuria, microhematuria, family history and pathological manifestation: intense staining for the serum fibronectin, Congo red staining negative. At present, there are no specific treatments for FNG. Our patient had received angiotensin receptor blocker (ARB) and Shenyanshu tablets. After 3 months of follow-up, the urine protein was 2.85 g/day. The proteinuria became less. However, further observation was needed to the proteinuria and renal function.

Conflict of interest

The authors declare that they have no conflict of interest.

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Carta al Director

Tratamiento con alirocumab en paciente en diálisis peritoneal con intolerancia a estatinas

Treatment with alirocumab in a patient on peritoneal dialysis with statin intolerance

Sr. Director:

La intolerancia a las estatinas afecta a un 10-20% de los pacientes que inician tratamiento con estos fármacos¹. La interrupción del fármaco se debe fundamentalmente a los efectos secundarios musculares asociados al mismo².

En los últimos años, se han realizado estudios con anticuerpos monoclonales inhibidores de la proproteína convertasa subtilisina/kexina tipo 9 (iPCSK9)³, demostrando ser eficaces a la hora de disminuir los niveles de colesterol unido a lipoproteínas de baja densidad (cLDL) y una alternativa segura para aquellos pacientes en los que el uso de estatinas está contraindicado.

Además, tanto en el ensayo ODYSSEY⁴ (alirocumab) como en el FOURIER⁵ (evolucumab) se puso de manifiesto una reducción del infarto no fatal, el ictus isquémico y la hospitalización por angina estable y una disminución del 15% de eventos cardiovasculares sin reducción de la mortalidad. Con todo ello,

en septiembre de 2015, la comunidad europea autorizó el uso de alirocumab⁶ como tratamiento hipolipemiente.

En estos dos ensayos, solamente se incluyeron pacientes con un filtrado glomerular (FG) ≥ 30 mL/min/1,73 m² y ≥ 20 mL/min/1,73 m², respectivamente. Además, en el estudio con alirocumab⁷, se realizó un análisis por subgrupos según su estadio de enfermedad renal crónica (ERC)⁸, observándose una reducción de cifras cLDL similar en ambos grupos, sin modificaciones en la progresión de la enfermedad renal y con buena tolerancia y seguridad del fármaco. En ninguno de los ensayos fueron incluidos pacientes en terapia renal sustitutiva⁸.

Presentamos el caso de un paciente de 58 años con antecedentes personales de hipertensión arterial en tratamiento con 3 fármacos, entre ellos un antagonista del receptor de angiotensina II y un diurético; diabetes mellitus tipo 2 insulino dependiente con afectación micro- y macrovascular; índice de masa corporal de 31,1 kg/m²; cardiopatía isquémico- valvular con afectación de la descendente anterior revascularizada y recambio valvular aórtico quirúrgico en 2012, fracción de eyección de ventrículo izquierdo conservada