

Case Report

Skin amyloidosis and mesangial proliferation with focal segmental sclerosing glomerulonephritis: a case report

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Abstract: An old man presented to the clinic with nephrotic syndrome, and renal biopsy confirmed for glomerular mesangial proliferation with focal segmental sclerosis and skin amyloidosis. The final diagnosis was skin amyloidosis and mesangial proliferation with focal segmental sclerosing glomerulonephritis.

Keywords: Skin amyloidosis, mesangial proliferation, focal segmental sclerosing, renal biopsy, skin biopsy

Case summary

A sixty-eight years old man presented to the clinic in August 8, 2013 because of one week face and two lower limbs edema. The patient appeared the pitting edema of the face and lower limbs with no significant incentives before one week. The symptom was serious in the morning and mitigated daytime. The patient showed naked eye hematuria, bubble urine, urine volume reduction than usual (700-800 mL/day), no bladder irritation symptoms such as urinary frequency and urine pain without lumbago symptom and with dizziness, chest tightness and itching, no joint pain, hair loss and light allergic phenomenon, also no abdominal distension, abdominal pain, chills and fever symptoms. He was clinical in local hospital, which diagnosis with urine protein "3+" and nephrotic syndrome. The edema decreased slightly but still have dizzy giddy and weak after diuretic and detumescence treatment. He was in our hospital for further treatment. Since onset, the psychosis of patient was good, whose sleep and defecate was normal. The appetite of patient was normal and the weight was increase.

There was nasal polyp resection and no hypertension, diabetes mellitus, and hepatitis in past history of patient. The patient was smoking 20 cigarettes once day and no alcohol habits.

Physical examination

The temperature was 36.5°C, the pulse was 70/min, the heart rate was 20/min, the blood pressure was 140/80 mmHg. There was no yellowing of skin mucous membrane in the whole body. Part of body was eczema rashes, no subcutaneous hemorrhage, and local skin degeneration thickening. The patient was facial edema, slightly plentiful in jugular vein, no absence of tenderness of sternum, double lung breath sounds low but no dry wet sound, no upheaval in precordium. The apex beat was in the first V costal outside midline 1 cm of left collarbone. There was no shudder in pressure, the heart border expand left when percussion. The heart rate was 70/min and noise-free. The abdomen was flat and absence of tenderness and rebound tenderness. There was slight pitting edema in the two lower extremities pretibial, pachulosis and eczema rashes.

Laboratory examination

Urine

The urinary sediment was protein 3+. The 24-hour proteinuria was 6074.4 mg/24 h. The 24-hour urinary uric acid was 0.85 mmol/24 h. The 24-hour urine creatinine was 7.59 mmol/24 h. The 24-hour urine urea was 101.5 mmol/24 h. The 24-hour volume was 1200 mL.

Skin amyloidosis and mesangial proliferation with focal segmental sclerosis

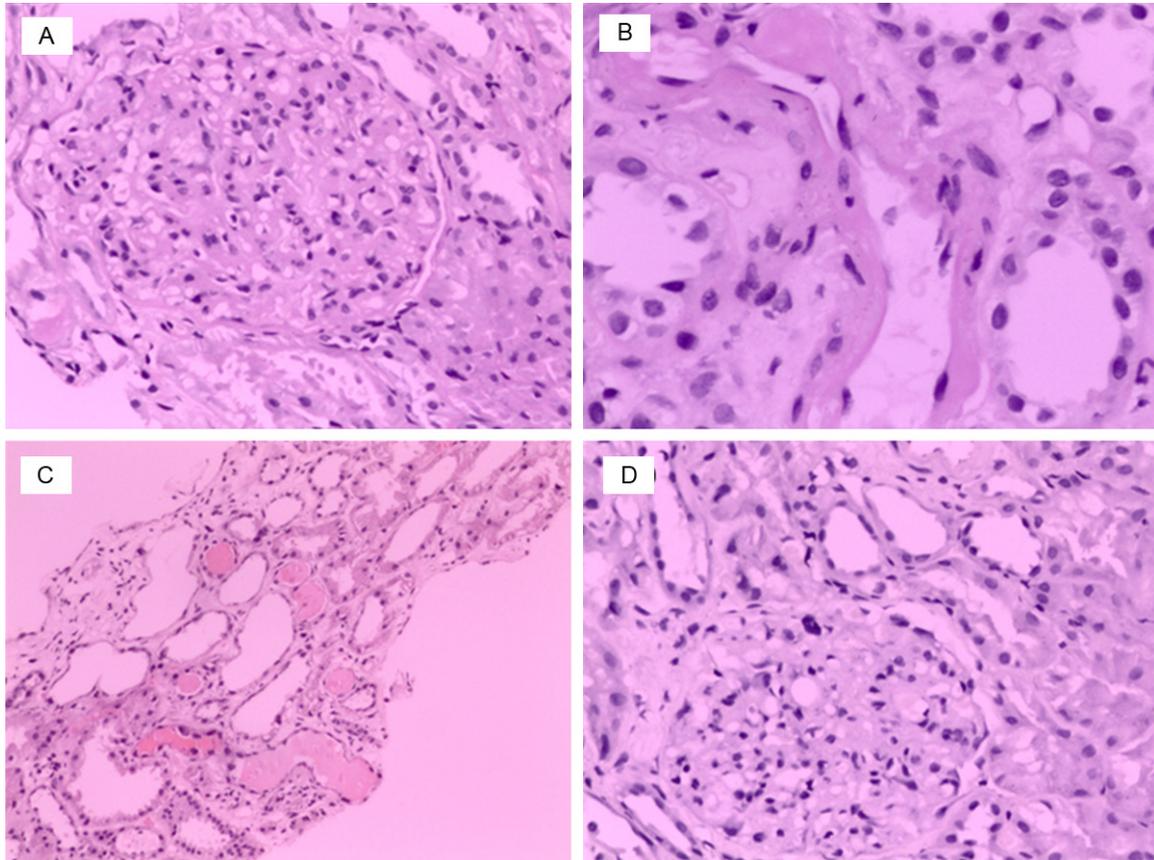


Figure 1. The results of light microscope of renal biopsy pathology. A-C were the results of immunohistochemistry. D was the result of congo red staining.

The urine λ light chain was 162.55 mg/L, k light chain was 248.88 mg/L, the NAG was 54 U/L, the retinol conjugated protein was 80.96 mg/L, α 1-microglobulin was 54.4 μ g/mL, microalbuminuria was 2434 mg/L, β 2-microglobulin was 1.35 μ g/mL, microtransferrin was 94800 ng/mL. The urine protein electrophoresis was 100% medium molecular substance.

Blood routine examination

The value of hemameba was 5.07×10^9 /L, red blood cell was 4.57×10^{12} /L, hemoglobin was 130 g/L, packed cell volume was 40.4%, blood platelet was 226×10^9 /L, neutrophilic granulocyte percentage was 70.7%.

Blood biochemistry

The value of total protein was 45.1 g/L, albumin was 23 g/L, and globulin was 22.1 g/L. The rate of albumin and globulin was 1. The value of urea was 7.47 mmol/L, creatinine was

129 μ mol/L, uric acid was 406 μ mol/L, triglyceride was 2.57 mmol/L, total cholesterol was 6.35 mmol/L, high density lipoprotein cholesterol was 0.93 mmol/L, low density lipoprotein cholesterol was 3.62 mmol/L. The oral glucose tolerance test was negative.

Immunology

The ANA, A-dsDNA and ENA polypeptide antibody repertoire were negative. The value of pre-albumin was 321.1 mg/L, serum λ light chain was 1.2 g/L, serum ferritin was 179.4 ng/mL, serum k light chain was 1.8 g/L, serum iron was 18 μ mol/L, serum transferrin was 3.9 g/L, α 1 microglobulin was 47.1 mg/L, cystatin C was 1.48 mg/L, β 2-microglobulin was 4 mg/L, retinol conjugated protein was 98.9 mg/L, ceruloplasmin was 218.5 mg/L, homocysteine was 21.4 μ mol/L, β -D-glucosaminidase was 40.3 U/L, erythrocyte sedimentation rate (ESR) was 68 mm/h, C reactive protein (CRP) was 23.8 mg/L.

Skin amyloidosis and mesangial proliferation with focal segmental sclerosis

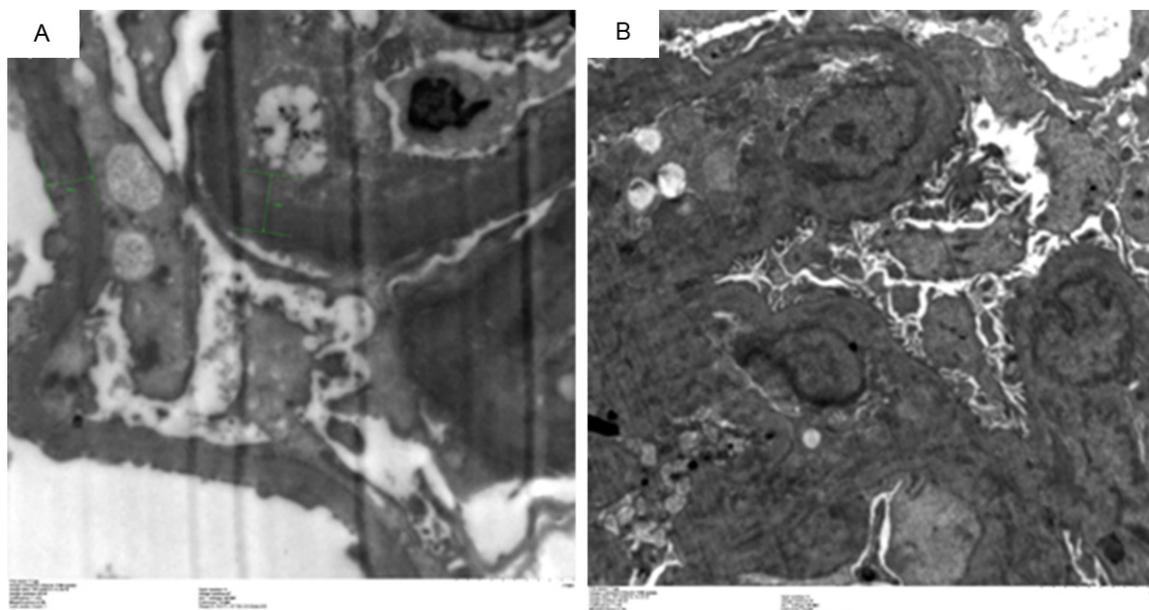


Figure 2. The results of electron microscope of renal biopsy pathology.

Assistant examination

Type-B ultrasonic of heart

The ventricular septal was thickening with slightly mitral regurgitation, slightly mitral valve and tricuspid backflow. The left ventricular diastolic function was decreased.

Type-B ultrasonic of renal

The size of left renal was 97×38 mm, the right renal was 100×40 mm. The morphological was rule and the outline was clear. The double renal parenchyma echo was slightly increased. There was no separation of the double renal collecting system observed. And there was no obvious calculus sound image. The color Doppler flow imaging showed the signal of double renal blood flow was rich.

Prostate sonography

The prostatic was hyperplasia and prostatomegaly.

Chest radiography

The cardiac was enlargement (majority of left ventricle) which resulted from hypertension considering the clinic.

Electrocardiogram

There was sinus bradycardia and T wave flatness.

The pathology of renal biopsy

Light microscope

There was one sphericity abandon and four focal segmental sclerosis among ten tested glomerulus. Other glomerulus was mesentery slightly and moderate broadening. The mesangial cell was proliferation. Rare capillary loops were adhesion with sacculus wall. The segment sacculus wall was increassation. Part of kidney tubule was observed protein cast, atrophy and accompanied interstitial fibrosis. The interstitial was observed a little mononuclear cell infiltrates and the arteriole was significantly hyaline degeneration. The immunohistochemical results showed the IgA+, IgG+, IgM+, C3+ and C4- (**Figure 1A-C**). The result of congo red staining was negative (**Figure 1D**).

Electron microscope

The mesangial matrix was moderate hyperplasia and amount of electron sediment. There was observed many capillary endotheliosis and hypertrophy which occupied the lumen near the mesentery. The mitochondria of the podocyte

Skin amyloidosis and mesangial proliferation with focal segmental sclerosis

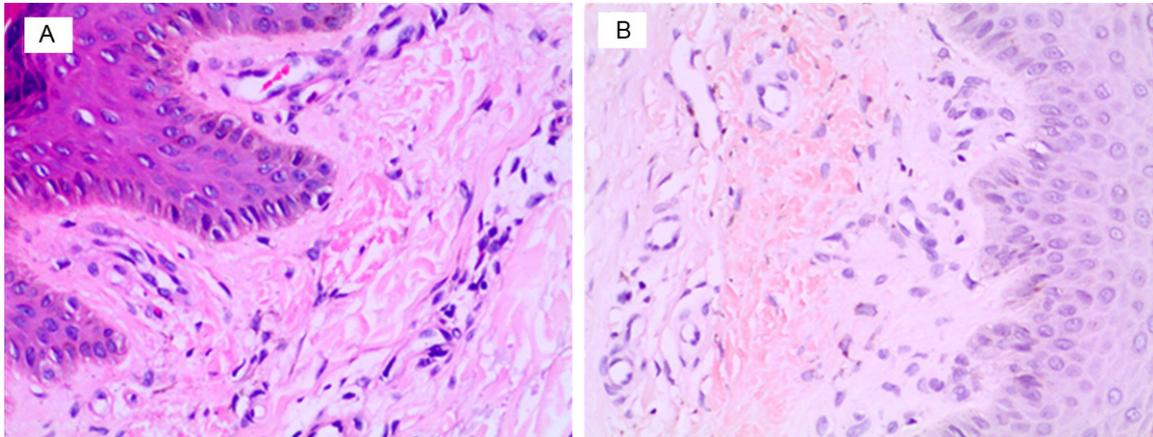


Figure 3. The results of congo red staining of skin biopsy pathology.

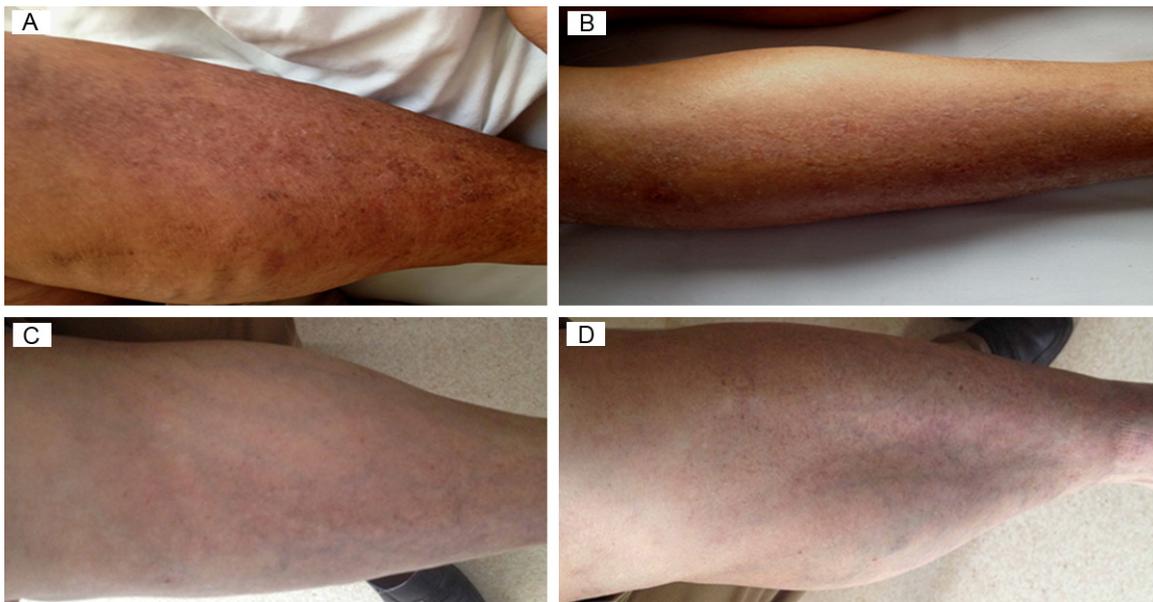


Figure 4. The results of treatment with hormone and immunosuppressor.

were edema and the podocyte was extensive fusion. The epithelium of kidney tubules was edema and mesenchyme fibroplasia (**Figure 2A, 2B**).

The pathology of skin biopsy

There was observed squamous epithelium hyperplasia, hyperkeratosis, dermis fiber and vascular hyperplasia and collagen. There was slightly homogeneity pink-dyeing lump deposition in the focal dermal papilla (**Figure 3A**). The result of congo red staining was shallow orange which suggested amyloid deposition (**Figure 3B**).

Final diagnosis

The final diagnosis was skin amyloidosis and mesangial proliferation with focal segmental sclerosing glomerulonephritis.

Treatment and follow-up visit

After treated with hormone, immunosuppressor, anticoagulation and ARB drug, the patient's subjective symptoms was significantly improved. The urine volume increased, edema degraded, skin color becoming white, proteinuria significantly decreased, blood albumin increased gradually, and the renal function

Skin amyloidosis and mesangial proliferation with focal segmental sclerosis

Table 1. The change of index during the treatment

Detection Inedx	Pre-treatment	2 weeks after treatment	1 month after treatment	Half a year after treatment	One year after treatment
HB (g/L)	120	118	124	138	126
24h-UP (mg/d)	6074.4	4678.2	2348.4	1647.0	589.9
ALB (g/L)	23.0	30.4	33.5	38.6	40.5
BUN (mmol/L)	7.47	8.15	7.75	7.85	6.23
CREA (umol/L)	129	120	119	117	102
UA (mmol/L)	406	504	437	420	320
TC (mmol/L)	6.35	6.74	5.98	4.96	5.36
TG (mmol/L)	2.57	2.37	2.19	1.89	1.42

HB: hemoglobin; 24h-UP: 24 hour urine protein; ALB: blood albumin; BUN: blood urea nitrogen; CREA: serum creatinine; UA: blood uric acid; TC: blood total cholesterol; TG: blood triglyceride.

improved. After one year follow-up visit, the patient showed no edema, the urine volume becoming normal with skin color recovered normal (**Figure 4A-D**). Laboratory examination showed trace urine protein, the blood albumin increased normal level, blood lipid and renal function recovered normal (**Table 1**).

Discussion

The characteristics of this case were: (1) elderly man; (2) nephrotic syndrome according to clinical manifestation without hypertension and diabetes mellitus; (3) eczema rashes in the whole body with part skin degeneration thickness and without subcutaneous hemorrhage; facial edema, double lower limbs slightly pitting edema, pachulosis and eczema rashes; (4) heavy proteinuria, serious edema, hyperlipemia and hypoproteinemia symptom according to laboratory examination. We excluded secondary nephropathy of diabetes mellitus, hepatitis B dependent nephritis, anaphylactic purpura nephritis, multiple myeloma, connective tissue diseases and other neoplastic diseases. There were much eczema rashes and pachulosis of the patient's body, which diagnosed skin amyloidosis by skin biopsy.

The definition of amyloidosis is that the disease caused by amyloid deposition in tissues or organs to result in inordinately dysfunction [1]. The amyloid deposition not only may violate many kinds of organs whole the body, but also be limited to skin. The amyloidosis could involve with not only kidney but also heart, lungs, skin, tongue, thyroid and intestinal tract, especially in respiratory tract and other organs showed localization lump [2]. There was no obvious

intestinal symptom and the patient refused more invasive examination so that it cannot be determination whether the amyloidosis involved with rectum without rectum mucosa biopsy. In addition, the liver, spleen and heart of the patient B ultrasonic examination showed no obvious increase and without liver function damage and cardiac function abnormal, which suggested that amyloidosis uninvolved with liver. However, it needed liver tissue biopsy to make a definite diagnosis.

The renal biopsy of the patient showed not typical and prospective glomerulus amyloidosis, but glomerular mesangial proliferation with focal segmental sclerosis. Considering the skin amyloidosis under the skin biopsy, the congo red staining was used for patient's renal tissue which the result was negative. In all, the patient was diagnosed for primary glomerulonephritis and the pathological pattern was mesangial proliferation with focal segmental sclerosing glomerulonephritis.

Traditional opinion considered that the cause of primary glomerulonephritis may be related with heredity [3], environment susceptibility [4, 5], friction factor [6], virus infection [7, 8] and so on. The mechanism was the malpighian cell apoptosis first and then filamentous degeneration, which entered into the derma through basilar membrane and was formation amyloid protein with amyloid protein P (AP), elastic fibers, collagenous fiber and/or other component under some unknown mechanism. The emphasis of this theory was the source of amyloid protein, but it cannot explain the phenomenon of derma slightly lymphocytes infiltration and without neutral lymphocytes infiltration.

Skin amyloidosis and mesangial proliferation with focal segmental sclerosis

Recently, researchers at home and abroad begin to realize that there is immunology abnormal during the primary skin amyloidosis. Schultz [9] studied the acute phase serum of patient and showed that the pathogenesis of amyloidosis was related with dysimmunity. Chen et al. [10] found that the levels of serum IL-4 and IgE of skim amyloidosis was significantly increased compared with the control group. Other studies showed that the T cell was increased in injured skin, CD8+T cell increased, CD4+T cell decreased and the rate of CD4+ T cell and CD8+T cell was decreased [11]. There was C1q deposition in the skin amyloid protein [12]. Noren et al. [13] investigated immunology of skim amyloidosis with IgG, IgA, IgM and C3 antibody and found that the IgM and C3 deposition inside the amyloid protein and IgM deposition in the basement membrane, which suggested that immune factors participated in the formation of skim amyloid protein.

Above studies evidenced that immunologic derangement was the predisposing factor of skim amyloidosis and the glomerulonephritis was the immune-mediated inflammation disease. Under the focal segmental glomerulosclerosis glomerulonephritis patient, the infiltrative cytotoxic T cell of the glomerulus may direct attack glomerulus inherent cell and CD4+T cell could aggravate glomerulus tissue damage with inflammatory factor secretion. There was mass T cell infiltration in the renal interstitium which may play an important role in prognosis and progress of glomerular disease. Other studies [15, 16] confirmed that circulation factor played an important role in pathogenesis of FSGS. Especially IL-13 and IL-4, the two cell cytokines could activate the sertoli cell receptor and alter permeability of glomerular filtration membrane [17-19].

The renal pathology of this patient showed mesangial proliferation with focal segmental sclerosis, which was different with the pathology characteristic of renal amyloidosis. After treatment with hormone and immunosuppressor, the nephropathy and skim amyloidosis was improved. The authors suggested that skim amyloidosis may induce immunoreaction in vivo and mediate focal segmental glomerulonephritis. Currently there was rare report about skim amyloidosis combined with mesangial proliferation with focal segmental glomerulone-

phritis. Further studies need to confirm these suppose.

In conclusion, present article reported one case of skim amyloidosis and mesangial proliferation with focal segmental sclerosing glomerulonephritis. After treatment with hormone and immunosuppressor, the skim amyloidosis and glomerulonephritis was improved. The patient proceeded skin and renal biopsy meanwhile played critical role in diagnosis, which suggested the important role of biopsy in clinical diagnosis.

Disclosure of conflict of interest

None.

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