

# A Case of Full-House Nephropathy with Anti-Nuclear Antibody Negative Lupus

## *Anti-Nükleer Antikor Negatif Lupus ile Birlikte Görülen 'Full-House Nefropati' Olgusu*

### ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the development of antibodies against a variety of nuclear and cytoplasmic antigens. SLE renal involvement is referred to as 'lupus nephritis' and is generally associated with anti-nuclear antibody (ANA) positivity. ANA is negative in approximately 5% of patients diagnosed with SLE. Existence of full-house nephropathy is generally associated with lupus nephritis. Herein, we present a case of full-house nephropathy in a 48-year-old male patient with negative serology for SLE. The patient had signs of lupus such as oral aphthae, symmetrical polyarthritis, and diffuse proliferative glomerulonephritis.

**KEY WORDS:** ANA negative SLE, Full-house nephropathy, Lupus nephritis

### ÖZ

Sistemik lupus eritematozus (SLE), çeşitli nükleer ve sitoplazmik antijenlere karşı antikor gelişimi ile karakterize otoimmün bir hastalıktır. SLE renal tutulumu 'lupus nefriti' olarak adlandırılır ve genellikle anti-nükleer antikor (ANA) pozitifliği ile ilişkilidir. SLE tanısı konmuş hastaların yaklaşık %5'inde ANA negatiftir. Renal biyopside 'full-house nefropati' varlığı genellikle lupus nefriti ile ilişkilidir. Bu yazıda, 'full-house nefropatisi' olan ve SLE serolojisi negatif olmakla birlikte oral aft, simetrik poliartrit ve diffüz proliferatif glomerülonefrit gibi lupus belirtileri olan 48 yaşındaki bir erkek olgu sunulmuştur.

**ANAHTAR SÖZCÜKLER:** ANA negatif SLE, Full-house nefropati, Lupus nefriti

### INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the development of antibodies against a variety of nuclear and cytoplasmic antigens. SLE renal involvement is referred to as 'lupus nephritis' and is generally associated with anti-nuclear antibody (ANA) positivity. ANA is negative in approximately 5% of patients diagnosed with SLE. Existence of full-house nephropathy is generally associated with lupus nephritis. Herein, we present a case of full-house nephropathy with ANA-negative SLE clinic.

### CASE REPORT

A 48-year-old male patient was referred to our clinic because of proteinuria (900 mg/day) and microscopic hematuria. He

complained of widespread joint pain, fatigue and weight loss (5 kg in 3 months). He experienced recurrent oral aphthae more than 10 times a year. He denied having any fever, diarrhea, vomiting, cough, dyspnea, nocturia, or bloody urination. His medical history revealed being admitted to a health facility due to bilateral swelling and pain of small hand joints (proximal interphalangeal), wrists, ankles and knee joints three years ago. He also had diarrhea. The upper and lower gastrointestinal endoscopy findings were normal. Duodenal and terminal ileum biopsy showed normal findings on histopathological examination. ANA, anti-double stranded DNA antibody (anti-dsDNA), rheumatoid factor (RF), anti-CCP (Anti-Cyclic Citrullinated Peptide) were negative. The first tests revealed normal

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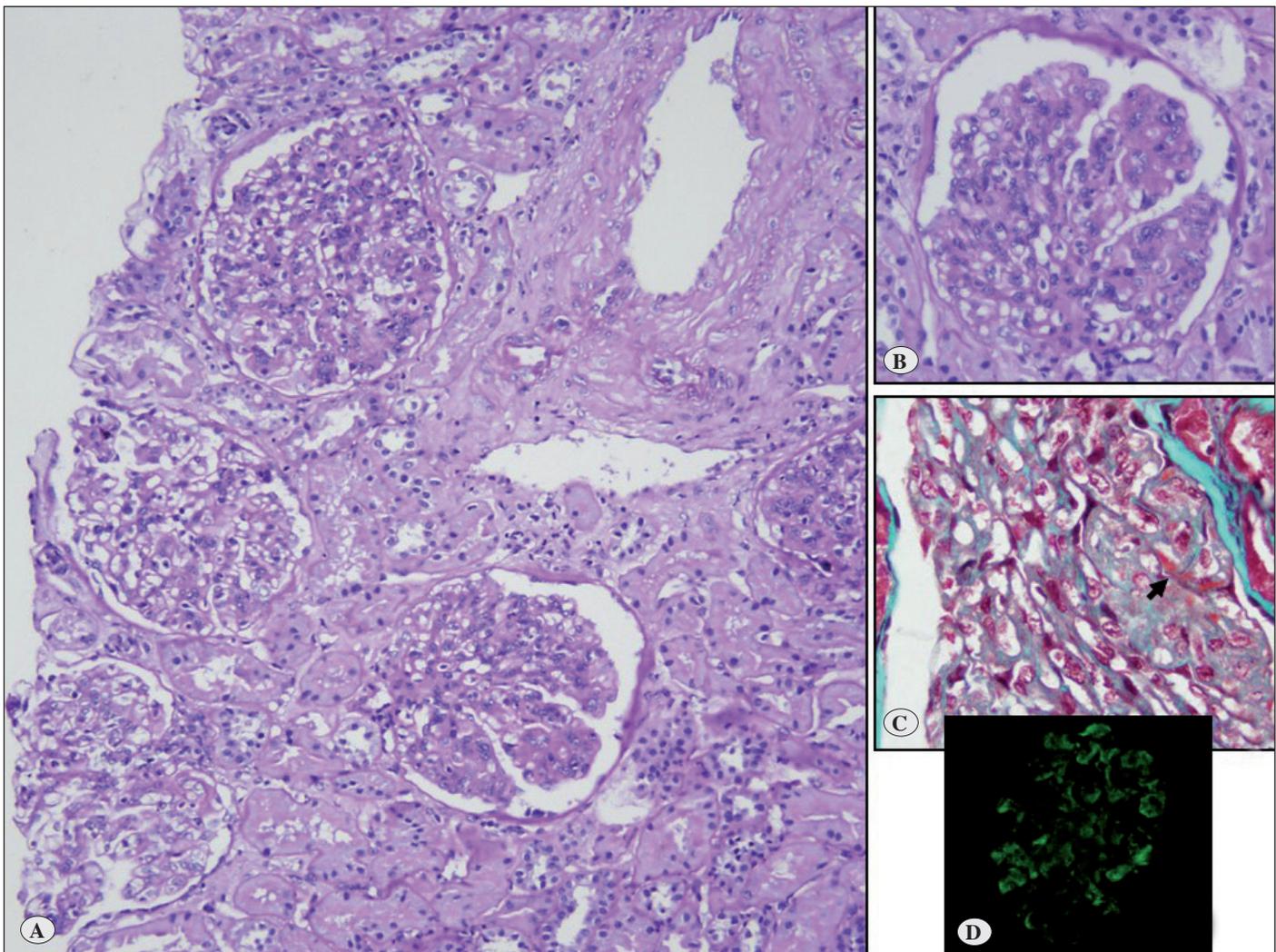
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creatinine level (0.9 mg/dL) and urine tests. Salazopyrin and methyl-prednisolone treatment had been started with a diagnosis of seronegative rheumatoid arthritis in another hospital. We do not know why he had been diagnosed with seronegative rheumatoid arthritis. He had stopped the treatment after eight months when his symptoms did not fully improve. He had not continued outpatient follow-ups.

Examination of the joints revealed mild pain and swelling at the metacarpal-phalangeal joints, wrists, knees, and ankles bilaterally. The rest of the physical examination was unremarkable. There were no pathological findings on the ophthalmic examination. Laboratory analysis revealed a creatinine level of 1 mg/dL, an erythrocyte sedimentation rate of 47 mm/hr, and a C-reactive protein (CRP) level of 1.7 mg/dL. Thin coarse granular casts, 14 leukocytes and 10 erythrocytes

(60% dysmorphic) were observed in every area in the urine microscopy. Urine culture was sterile. 24-hour urine proteinuria was 0.8 g. Serological examinations revealed that ANA, anti-dsDNA, ANCAs, anti-RNP antibodies, anti-SSA antibody, anti-SSB antibody, anti-sm antibody ve anti-cardiolipin antibodies were negative. Hepatitis markers were negative for hepatitis B and C. Other laboratory parameters including liver-cardiac markers were all normal. Ultrasonography revealed normal kidneys. Renal biopsy was performed because of an active urinary sediment and proteinuria and was consistent with diffuse proliferative glomerulonephritis (Class-IV, GA) with activity index 9 (Figure 1A-D). In the immunofluorescence (IF) examination, immune deposits, such as IgA (+++), IgG (++), IgM (+), C1q (++) and C3 (+++), were detected in accordance with 'full house nephropathy'.



**Figure 1:** Renal biopsy showed increase in glomerular mesangial matrix and cellularity, capillary obliteration and thickened basement membranes. A) PAS x100, B) PAS x400). There are subendothelial deposits lining along the capillary loops, C) MT x1000). Immunofluorescence microscopy revealed positivity both in the mesangium and along capillary loops in a coarsely granular pattern, D) Anti IgG FITC x400).

Our patient was diagnosed with type-IV lupus nephritis despite the negative serology for SLE, due to the three positive findings of American College of Rheumatology Association (ARA) criteria. Hydroxychloroquine 400 mg/day was started first. One g of methyl-prednisolone per day pulse therapy for three days and one g of cyclophosphamide per day pulse therapy for one day were administered. Methyl-prednisolone treatment was continued with 48 mg/day in maintenance therapy and was going to be continued at an outpatient clinic. After two months of treatment his symptoms disappeared, and the acute phase values and urinary sediment returned to normal range.

### DISCUSSION

SLE is an autoimmune disease characterized by the development of antibodies against a variety of nuclear and cytoplasmic antigens (1). SLE renal involvement is referred to as 'lupus nephritis' and is generally associated with ANA positivity (2). ANA is negative in approximately 5% of patients diagnosed with SLE according to ARA criteria (3). Existence of 'full-house nephropathy' defined as the presence of IgG, IgA, IgM, C1q and C3 deposits at the same time on the IF examination is generally associated with lupus nephritis (4,5). Full-house nephropathy can be seen in clinical conditions such as lupus nephritis, posthepatic cirrhosis, diabetic nephropathy, membranous nephropathy, membranoproliferative glomerulonephritis and C1q nephropathy (3). At least four criteria must be present for the diagnosis of SLE according to ARA criteria (6). However, the diagnosis of SLE cannot be excluded in the presence of the 'full-house' IF pattern even in the presence of only two criteria (7). Our patient had negative serology but he had signs of lupus such as oral aphthae, symmetrical polyarthritis and diffuse proliferative glomerulonephritis. In addition, our patient did not have another finding consistent with other possible etiologies. Distinction between seronegative lupus nephritis and C1q nephropathy is difficult. There is just one specific finding - hematoxylin bodies - for lupus nephritis on light microscopy (8). However it is rare and unprecedented in our case. Tubulo-reticular inclusions are seen in electron microscopic examination of lupus nephritis, but not seen in C1q nephropathy. Our patient was not investigated with electron microscopy. Nevertheless, he was compatible with lupus nephritis clinically. C1q nephropathy does not respond well to immunosuppressive therapy. Lupus nephritis responds well to treatment. In addition, C1q infiltration should be much greater than the other components of complement and immunoglobulin in the IF examination for the diagnosis of C1q nephropathy (9). Circulating immune complexes (CIC) may be the best indicators of the clinical activity of lupus. CIC could be measured by the fluid phase (FC1q) and solid phase (SC1q) C1q binding assays. Elevations of the SC1q results are related with the presence of manifestations of SLE, including active renal disease and arthritis (10). However, it was not possible to measure the CIC in our hospital.

In conclusion, serology may be negative in 5% of patients with SLE. We wish to alert all colleagues about that this knowledge should be kept in mind while dealing with these conditions. When renal biopsy is performed in a patient with clinical SLE and negative serology, a renal biopsy sample should also be taken for electron microscopic examination.

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