Case report

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병리조직검사에서 "Full-house" 패턴의 면역 복합체 침착이 발견된 비루푸스 신염

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A Case of "Full-house" Nephropathy in a Non-lupus Patient

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Histopathologic evidence of "full-house" immune complex deposits is a pathognomonic feature of lupus nephritis. This report presents the case of a 12-year-old boy with persistent microscopic hematuria and proteinuria. He was diagnosed with "full-house" nephropathy based on a renal biopsy. However, there was no other clinical or biological evidence of systemic lupus erythematosus (SLE). Although the potential for isolated "full-house" nephropathy preceding SLE is unclear, such patients should be followed for clinical signs and autoantibodies of SLE. In most cases, microscopic hematuria has a good prognosis, and follow-up usually requires only regular urinalysis. However, we should be aware of isolated "full-house" nephropathy that remains asymptomatic for a long time, as few patients with no clinical signs and negative serology ultimately develop SLE.

Key words: Lupus nephritis, Immunofluorescence, Systemic lupus erythematosus, Biopsy

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect any part of the body. The diagnosis of SLE is based on the clinical and laboratory findings. Anti-nuclear antibody (ANA) is an important serologic marker for SLE, found in more than 95% of SLE patients [1]. However, negative serology does not exclude SLE. Occasionally, renal disease is the only clinical manifestation. The histopathology of lupus nephritis can vary markedly. However, some histopathological features are pathognomonic for lupus nephritis. One such finding characteristic of lupus nephritis is immunofluorescence staining for immunoglobulin G (IgG), IgA, IgM, complement (C3), and C1q in glomerular immune

deposits, known as the full-house staining pattern [2]. Here, we report a patient who presented with "full-house" nephropathy, but with no serologic or extrarenal findings associated with SLE. Our patient had only persistent microscopic hematuria and proteinuria. Therefore, clinicians must remember that microscopic hematuria or proteinuria can be an early isolated sign of "full-house" nephropathy.

Case report

A 12-year-old boy was admitted to hospital with a 2-year history of microscopic hematuria and proteinuria. He had no family history of kidney disease. On physical examination, he was a well-developed boy, with a weight of 58.5 kg (75-90th percentile), height of 170.2 cm (97th percentile), and blood pressure of 114/69 mmHg. His physical examination was unremarkable. The laboratory examination showed the following: hemoglobin 14.9 g/dL, hematocrit 42.6%, white blood cell count 6.890/μL, platelets 259,000/μL, blood urea nitrogen 10.5 mg/dL, creatinine 0.6 mg/dL, sodium 137 mmol/L, potassium 4.4 mmol/L, chloride 105 mmol/L, total CO_2 19 mmol/L, and anion gap 16 mmol/L. The prothrombin and activated partial thromboplastin times were normal. The C3 level was 126 mg/dL (reference range 83-177), C4 30 mg/dL (reference range 15-45), and CH50 46.1 U/mL. Serum ANA was weakly positive (1:40), while anti-dsDNA antibody, p-antinuclear cytoplasmic antibodies (ANCA) and c-ANCA were negative. Urinalysis showed protein 1+, blood 3+ (RBCs 10-19/HPF), and 70% dysmorphic red blood cells (RBCs); urine cultures were negative. The daily urinary protein excretion was 3.1 mg/m^2/hour and the glomerular filtration rate (GFR) was 129.2 mL/min/1.73m^2. Abdominal ultrasound was normal. A renal biopsy showed normal-looking glomeruli in terms of cellularity and size on light microscopy (Fig. 1A). Immunofluorescent microscopy revealed the "full-house" pattern of IgG, IgA, IgM, C3, C1q, kappa and lamda positive deposition in the glomerular area (Fig. 1B-H). Electron microscopy showed variable sized subendothelial and subepithelial deposition and some mesangial deposition in the glomeruli (Fig. 2 A and B). No cytoplasmic tubuloreticular inclusions were identified in the current case.

The renal biopsy pathology was suggestive of lupus nephritis as an underlying disease, but the patient had no symptoms or immunological evidence of lupus. After the renal biopsy he was discharged and followed as an outpatient. After 18 months, the ANA became negative, and C3 and C4 were normal. However, microscopic hematuria was still present (5-9 RBCs/HPF), but he showed no extrarenal manifestations of SLE.

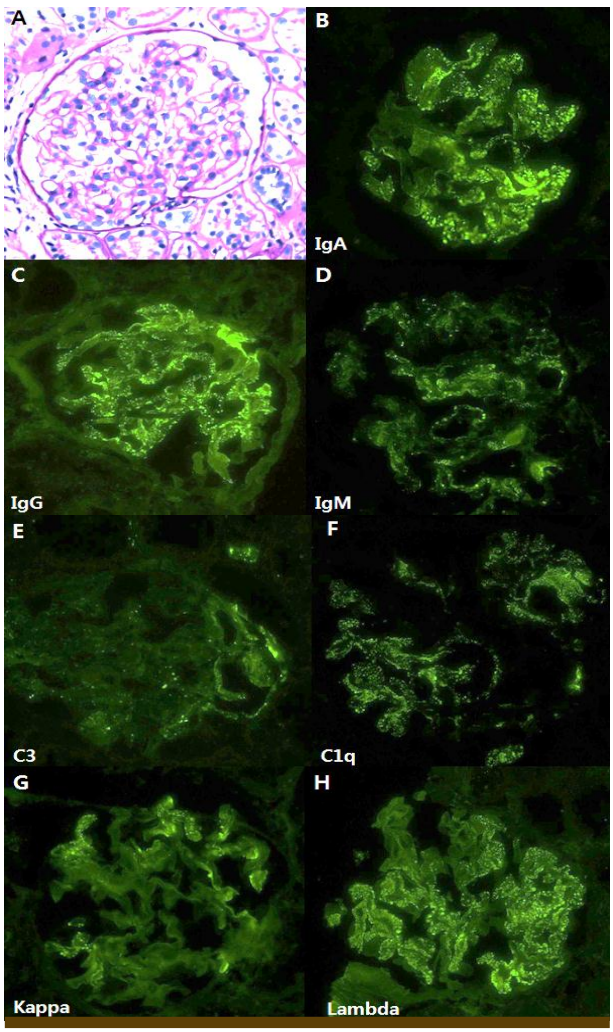

Fig. 1. (A) The glomeruli appear normal in terms of cellularity and size. There is no crescent formation, tubular atrophy, interstitial fibrosis, or interstitial inflammation (Light microscopic examination, PAS, ×400). (B-H) The tubular basement membrane shows focal granular staining (IgA, IgG, IgM, C3, C1q, kappa, and lambda immunofluorescence) (Immunofluorescence staining, ×400).

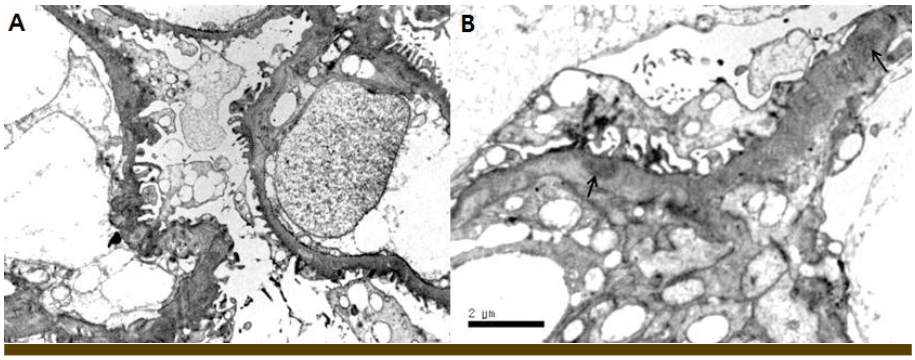

Fig. 2. The glomerular basement membrane shows evenly distributed subepithelial and subendothelial deposits (arrows) and some mesangial deposits (Electron microscopic examination, ×6,000).

Discussion

SLE is a chronic, inflammatory, multisystem disease characterized by the existence of circulating autoantibodies. The cause of SLE remains unclear, but probable causative factors include a genetic predisposition, complement deficiencies, antigen persistence, drugs, and environmental factors [3]. Renal involvement is typical in SLE. An abnormal urinalysis and elevated plasma creatinine level are frequent in lupus nephritis. Presenting signs of lupus nephritis include hematuria in 79%, proteinuria in 55%, decreased GFR in 50%, hypertension in 40%, and acute renal failure in 1.4% [4].

Our patient had weakly positive ANA, but this normalized during follow-up. Other serologic markers were normal, including anti-dsDNA antibody and serum complement. Although ANA is positive in more than 90% of SLE cases and is the best indicator of SLE, ANA positivity is not essential to the diagnosis [5]. The rate of ANA negative SLE is about 1-5% [6]. ANA negativity in lupus patients might result from technical failure or entrapment of ANA in circulating immune complexes. In addition, low C3 levels are also not diagnostic. However, ANA positivity and low C3 level are valuable signs of the recurrence of illness and for evaluating the treatment response [7]. Clinicians should be aware of the possibility of "full-house" nephropathy in a seronegative patient with asymptomatic urine abnormalities.

"Full-house" immunofluorescence shows glomerular staining for IgG, IgA, IgM, C1q, and C3 deposits in the renal biopsy and implies lupus nephropathy, so the patient should be evaluated for clinical and serological proof of SLE [6]. In our case, the histopathological findings were prominent and suggested WHO class I lupus nephritis on electron microscopy and full-house nephropathy on immunofluorescence. Nevertheless, he had only microscopic hematuria and proteinuria with no other manifestations of SLE. The histopathological findings of lupus nephritis can be found months before the detection of an abnormal urinalysis [7].

It is controversial whether "full-house" nephropathy precedes the development of overt lupus [8]. Approximately 12-45% of patients met the criteria of "full-house" nephropathy SLE based on autoantibodies and symptoms during follow-up over 1-10 years [9-11]. However, none of the patients with "full-house" nephropathy in Jones and Magmil [10] and Enriquez et al. [12] showed worsening clinical or serological evidence of SLE during the follow-up period, though the follow-up durations were as short as 0.1-4.8 years. Gianviti et al. [13] found that 3 of 31 children with full-house nephropathy had negative serologic markers for SLE or autoantibody appearance during follow-up; 14 of them remained seronegative and showed no clinical evidence of SLE except full-house nephropathy. These data reveal that patients with isolated "full-house" immunofluorescence can become seropositive and develop extrarenal symptoms of SLE.

Patients with "full-house" nephropathy must be observed closely because the emergence of autoantibodies and clinical signs can be delayed for several years. Clinical suspicion and the renal biopsy findings improve earlier

intervention, which increases the possibility of renal preservation [14]. Close observation of these patients for abnormal urine microscopic findings and a decreased GFR is necessary. Nevertheless, some might never become seropositive or manifest extrarenal findings of SLE, and may be part of another group of patients with an unidentified clinical entity [7].

In conclusion, there is a broad spectrum of histopathological findings in non-lupus "full-house" nephropathy. Although it is not certain whether isolated "full-house" nephropathy precedes SLE, the patients who remain seronegative and show no extrarenal manifestations of SLE during follow-up appear to constitute an unconfirmed clinical entity. Furthermore, although this "full- house" pattern is relevant to lupus nephropathy, it can be also rarely detected in IgA nephropathy, membranoproliferative glomerulonephritis, and postinfectious glomerulonephritis [8]. Nevertheless, those with "full-house" nephropathy should still be monitored for the occurrence of autoantibodies and clinical signs suggestive of SLE.

한글요약

"full-house" 면역 복합체 침착은 루푸스 신병증의 진단적인 조직 소견이다. 이 증례 보고에서 12세 남자 환아는 지속적인 현미경적 혈뇨와 단백뇨를 주소로 내원하였다. 그는 신장 조직 검사에서 "full-house" 신병증을 진단받았으나 전신성 홍반성 낭창과 관련한 어떠한 임상적 징후나 혈청학적인 결과를 보이지 않았다. 비록 "full-house" 신병증이 전신성 홍반성 낭창에 선행하는 질병인지에 대해서는 명확히 밝혀진 바는 없으나, 루푸스와 관련된 증상이나 혈청학적인 자가 항체가 출현할 수 있으므로, 추적 관찰을 요한다. 대부분의 현미경적 혈뇨는 좋은 예후를 가지고 있고, 보통은 소변검사를 정기적으로 검사하며 관찰한다. 그러나 이 증례에서 보듯이 소변검사 이상이 발견 되었을 때 오랫동안 무증상으로 잠복하는 "full-house" 신병증 또한 고려되어야 하며, 이는 몇몇의 임상적인 증상 및 혈청학적 소견이 음성이었던 환자가 전신성 홍반성 낭창으로 진행할 수 있기 때문이다.

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