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A 70-year-old patient with seronegative lupus nephritis: Rare case

Yetmiş yaşında seronegatif lupus nefritli hasta: Nadir olgu

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease known to be associated with various kinds of autoantibodies such as Antinuclear antibodies (ANA). ANA is found to be positive in most of the SLE patients. In fact, ANA positivity in serum is one of the diagnostic criteria of SLE. However, a minority of SLE patients may present with ANA negativity. We report a 70-year-old female who presented with massive edema and 10-gram/day proteinuria. Her serum antibodies for SLE were all negative and the renal biopsy showed a class V lupus nephritis. This case was unusual type of SLE due to multiple reasons namely the patient was an elderly woman, with isolated lupus nephritis and negative serology including ANA negativity.

Keywords: *Systemic lupus erythematosus, lupus nephritis, antinuclear antibody*

ÖZ

Sistemik lupus eritematozus (SLE), antinükleer antikor (ANA) gibi çeşitli antikorlar ile ilişkili olduğu bilinen otoimmun bir hastalıktır. SLE hastalarının çoğunda ANA pozitif olarak bulunmaktadır. Aslında ANA pozitifliği SLE'nin tanı kriterlerinden biridir. Fakat, SLE hastalarının çok az bir kısmı ANA negatifliği gösterebilir. Masif ödemi ve 10 g/gün proteinürisi olan 70 yaşındaki kadın hastayı rapor yayınladık. Hastanın SLE serum antikorlarının hepsi negatifti ve böbrek biyopsisi lupus nefriti sınıf 5 olduğunu gösterdi. Bu olgu, birden fazla nedenden dolayı SLE'nin alışılmadık bir şeklidir. Bu hasta yaşlı bir kadın olup, izole lupus nefriti ve ANA negativiteyi de içeren negatif seroloji ile beraberdi.

Anahtar kelimeler: *Sistemik lupus eritemetozus, lupus nefriti, antinükleer antikor*

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease with multiple system involvement. Although it has a variety of presentations due to involvement of different systems. There are certain antibodies which are found to be associated with SLE including Antinuclear antibodies (ANA), anti-double stranded DNA antibody (anti-dsDNA) antiplasma membrane antibodies and Anti-Smith antibodies (Anti-Sm). Though less specific, many other antibodies such as Anti-Ro or Anti-La can also be found in SLE patients[1]. Of all the antibodies, ANA is the diagnostic hallmark for SLE and it is found to be positive in 95% of SLE patients[2]. However, ANA-negative SLE patients have also been reported[3]. These patients were described to have a high incidence of photosensitivity and a low incidence of nephritis or neuropsychiatric manifestations[4,5]. Lupus nephritis, being one of the most common and serious complications of SLE, can be detected clinically in 23-60% of SLE patients, mostly within the first 3 years of diagnosis[6,7]. Moreover, lupus nephritis also has different presentations and it is classified into 6 subgroups based on the histological evaluation, thus necessitating renal biopsy for diagnosis. Renal biopsy determines the type of lupus nephritis as well as its management and prognosis. Early diagnosis is especially important for the prompt management of kidney involvement in SLE patients[8]. Furthermore, although unusual, lupus nephritis was also reported in patients with ANA-negative SLE[9]. In this case report, we present a case of seronegative lupus nephritis in an elderly patient with a full-house nephropathy pattern.

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CASE

A 70-year-old female with hypertension presented with shortness of breath and massive, anasarca-like diffuse edema. She reported 15 kg weight gain in 3 months and recent difficulty in breathing. A review of systems was found to be remarkable for arthralgia and multiple oral ulcers, but she denied the presence of a recent infection, fever, rash, headache, finger discoloration, joint swelling, or bloody urination. Her past medical history was remarkable for renal artery stenting one year ago in addition to her 20-year-history of hypertension and hyperlipidemia controlled with antihypertensives and statins. She also reported seafood and metamizole allergy as well as a 13 pack-year smoking history. At presentation, her vitals were within normal limits except the presence of 90% oxygen saturation and mild tachypnea. On physical examination, the patient was alert and oriented, but she could not walk owing to her massive edema. She was found to be in mild respiratory distress with bibasilar rales. She had diffuse edema, most notably around pretibial and sacral areas. Her skin examination was unremarkable as well as her neurological, cardiovascular and abdominal examination. She had multiple gingival and mucosal ulcers detected during her oral inspection. She also had mild tenderness in her metacarpophalangeal joints during palpation. Some remarkable laboratory parametres at presentation were as follows: white blood cell count, 12 300 g/L; hemoglobin, 12.1 g/dl; hematocrit, 34.3%; platelet count, 256 000 g/L; serum sodium, 133 mmol/L; potassium, 4.2 mmol/L; calcium, 8.1 mg/dL; blood urea nitrogen, 46 mg/dL; creatinine, 0.8 mg/dl; ALT, 37.3 U/L (N<33 U/L); AST, 13.4 (N<32 U/L); serum albumin, 2.5 g/dL; total protein, 4.2 g/dL; thyroid stimulating hormone, 1.32 µIU/mL; CRP, 6.9 mg/L (N<5 mg/L); LDL, 184 mg/dL; triglycerides, 436.5 mg/dL; HDL. 57 mg/dL , and total cholesterol, 301 mg/dL. Her urinalysis was remarkable for hematuria, proteinuria, and hyaline casts. Her spot urine protein/creatinine ratio was 9.9 g/day. Her hepatitis serology was negative for HBV and HCV. Her serum complement C4 and C3c levels were within normal limits. We have done a serologic investigation for the following antibodies: ANA, Anti-dsDNA, Anti-nRNP/Sm, Anti-Sm, Anti-SS A, Anti-Ro52, Anti-SS B, Anti-Scl70, Anti-PM Scl, Anti-Jo1, Anti-centromere B, Anti-PCNA, Anti-nucleosome, Anti-histone, and Anti-ribosomal protein. All serology tests yielded negative results including ANA, which was repeated twice. Because of this atypical presentation, we have also checked for some tumor markers such as CEA, CA19-9, CA125, CA 15-3 and AFP, which all came back as normal. We also ordered a mammography and evaluated her recent Pap smear results.

At presentation, the patient had +4 diffuse edema and 9.9 g/day proteinuria. She was managed with a high dose of furosemide for her edema while she received 1 mg/kg/day methylprednisolone and 500 mg/day cyclophosphamide pulse therapy intravenously. After ten days of treatment, her diffuse edema almost completely resolved with residual minimal pretibial edema. She had daily weight measurements and in ten days, her weight reduced from 86 kg at presentation down to 72 kg at discharge. Her proteinuria also declined to 3.8 g/day with an albumin of 2.9 g/dl. Her difficulty in mobilization because of the massive edema and weight gain have also resolved. After the treatment course, she was mobilized easily with no shortness of breath and an increase in her exertional capacity.

The kidney biopsy revealed membranous glomerulonephritis with full-house pattern suggestive of class V lupus nephritis. The histology was remarkable for global sclerosis, basal membrane thickening, mesangial proliferation, mild interstitial fibrosis and tubular atrophy. There was IgA, IgG, IgM, C1q and C3 positivity on immunofluorescence while no fibrin deposition was noted. There were no vasculitic changes in the biopsy specimen.

DISCUSSION

Lupus nephritis is an important cause of morbidity and mortality in SLE patients, especially if left untreated. If lupus nephritis in an elderly patient was seronegative, it can be difficult to diagnose because

of the rareness of such patients. ANA negativity in lupus is seen only in a minority of patients and in fact, lupus nephritis in seronegative SLE patients is less likely to be encountered, but it should not be disregarded[2,3,8]. These patients may be underdiagnosed or misdiagnosed due to lack of clinical experience with these unusual presentations, resulting in an increased morbidity and mortality rate especially in elderly patients.

ANA and Anti-dsDNA are frequently positive in lupus nephritis. Seronegative lupus nephritis is rarely reported in the literature. Simmons et al. reported that there are multiple reports of seronegative lupus nephritis in the literature. In addition ANA and Anti-dsDNA may become positive during the follow up[10]. In contrast, in our patient none of these serological markers became positive. The ''full-house'' glomerulopathy may be the only finding which may delay the early diagnosis of the lupus nephritis. The mechanism of seronegative lupus nephritis involves loss of circulating antigens via urinary loss due to the nephrotic range proteinuria (Simmons ref[11]). The ages of the reported patients are younger than 50 years while our patient was a 70-year-old female. The manifestations of the seronegative lupus nephritis patients are not usually seen alone and it is accompanied by skin, joint or other system involvements. Our patient, on the other hand, had minimal other system findings, but rather demonstrated isolated kidney involvement causing nephrotic range proteinuria and massive edema.

Despite a low incidence of seronegative lupus nephritis, clinicians should keep in mind the possibility of ANA-negativity in SLE patients, particularly with kidney involvement. Regardless of the age of the patient or ANA-negativity, lupus nephritis should be entertained in the differential diagnosis of a nephropathy.

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