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Case Report

Lupus Nephritis Emerging During Remission of Minimal Change Disease

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Abstract

Introduction: Rare cases of association between lupus nephritis (LN) and minimal changes nephrotic syndrome (MCNS) were described. Some authors suggest that this association, taking into account the low prevalence of both diseases, may not be a simple coincidence. Several pathophysiological hypotheses have been proposed to explain this association, including a potential central role of T lymphocytes.

Case Report: We describe the case of a 21 years-old female patient who initially presented with isolated nephrotic range proteinuria. She had no evidence of systemic involvement and Immunological tests were negative, including anti-neutrophil antibodies (ANA) and anti-double-stranded DNA antibodies (Anti-dsDNA). Renal biopsy showed normal glomeruli under light microscopy and no significant deposits were found in immunofluorescence studies. She was diagnosed to have MCNS and responded to a short course of steroids. She remained in remission for three years, after which she presented again with nephrotic-range proteinuria accompanied by clinical signs of systemic involvement. During her second presentation, she fulfilled the diagnostic criteria of systemic lupus erythematosus (SLE) and another kidney biopsy showed class-V lupus nephritis. She was treated with pulse steroids followed by oral prednisolone and mycophenolate mofetil, with good clinical response.

Conclusion: This case indicates that relapses of MCNS should be carefully investigated in the right setting to avoid missing a systemic disease such as SLE.

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Introduction

Minimal change nephrotic syndrome (MCNS) is a clinical and pathological entity defined by selective proteinuria and hypoalbuminemia that occurs in the absence of cellular glomerular infiltrates or immunoglobulin deposits. The pathogenesis of MCNS is yet unknown [1]. Systemic lupus erythematosus (SLE) is a multi-organ systemic autoimmune disease with numerous immunological and clinical manifestations. It is characterized by an autoantibody response to nuclear and cytoplasmic antigens [2].

Few cases of association between these two diseases have been described previously [3-16]. However, in the majority of these cases, MCNS occurred in patients known to have SLE or occurred simultaneously with the onset of SLE. In very rare cases, MCNS preceded the diagnosis of SLE [4, 13].

Case Report

A 21 years-old white female, with no significant past medical history, presented during her first pregnancy at 16 weeks of gestation with isolated proteinuria. Her 24 hour protein excretion was 3.6 g/day. She had no history of non-steroidal anti-inflammatory drugs (NSAIDs) intake. Immunological tests were negative, including anti-double-stranded DNA (anti-ds DNA), anti-neutrophil antibodies (ANA), anti-Smith antibodies (anti-Sm) and anti-ribonucleoprtoein antibodies (anti-RNP). A renal biopsy was taken and examined by an experienced nephropathologist, showing normal glomeruli under light microscopy (Figure-1). No significant deposits were found in immunofluorescence studies. These histological finding were consistent with the diagnosis of MCNS. Electron microscopy was not performed. Prednisolone

Figure 1: First renal biopsy showing normal glomeruli in light microscopy

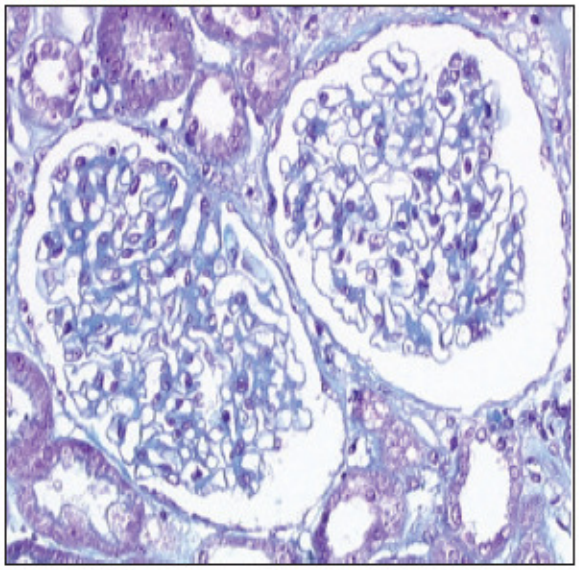
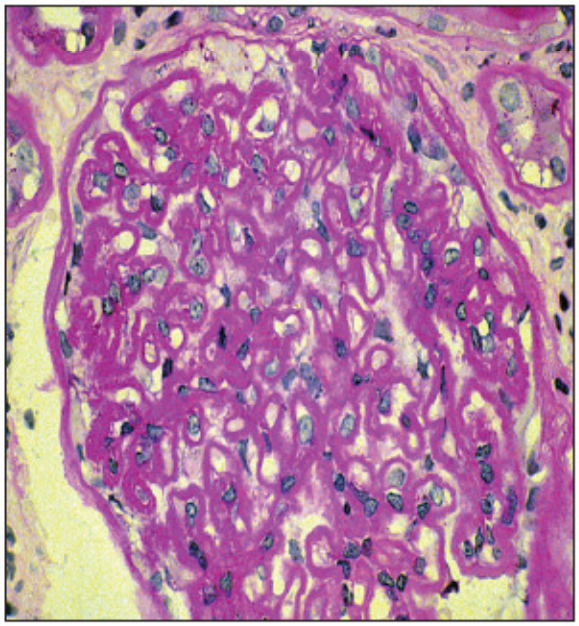


Figure 2: Second renal biopsy under light microscopy, showing irregular thickening of glomerular capillary walls and mesangial expansion without cell proliferation



was started at a dose of 1mg/kg/day. The fetus died started at a dose of 1mg/kg/day. The fetus died in-utero at 24 weeks of gestation. Complete remission was obtained one week after fetal expulsion and nine weeks after starting prednisolone. Steroids were gradually tapered and then stopped. The patient became pregnant again six months later; her second pregnancy progressed to term without fetal or maternal complications.

The same patient was readmitted to hospital three years later complaining of irritability, poly-arthralgia, bilateral malar rash, photosensitivity, hair loss and cheilitis. Laboratory investigations revealed the following findings: urine was positive for blood (2+) and protein (4+) with daily protein excretion of 5 g. Renal function tests were normal with serum creatinine at 0.6 mg/dL. The serum was positive for ANA (1/320), anti-dsDNA antibodies (1/320) and rheumatoid factor. Complements C3 and C4 levels were low (values at 0.12 g/L and 0.03 g/L respectively). Anti-Sm, anti-Scl 70 and anti-RNP antibodies were also positive. Anticardiolipin, antiphospholipid and anti-B2-glycoprotein-1 antibodies were negative. She also had polyclonal hypergamma-globuminemia and pericarditis. Thus, she had eight of the eleven SLE diagnostic criteria of the American College of Rheumatology.

A second renal biopsy was performed (Figure-2) revealing features of lupus nephritis (ISN class V). Light microscopy showed irregular thickening of the glomerular capillary wall and discrete mesangial matrix expansion without cell proliferation. No capillary thrombi or necrosis was noted. The interstitium, the tubules and the blood vessels showed no significant anomalies. Immunofluorescence showed granular extra-membranous deposits of IgG along the capillary walls with glomerular granular deposits of IgA, IgM, C3 and C1q.

The patient was treated by intravenous methylprednisolone (600 mg/day for 3 days) followed by oral prednisolone (60 mg/day tapered after one month) along with mycophenolate mofetil (3 g/day). Remission was induced and maintained. After one year of follow-up, her proteinuria was only 150 mg/day and renal function tests remained normal.

Discussion

Rare cases of association between SLE and MCNS have been described in the literature. In most of these cases, nephrotic syndrome developed in patients known to have SLE. Hertig et al estimated the probability of MCNS occurring in a patient with SLE to be less than 1 in 10,000. The observed prevalence of concurrent idiopathic MCNS in the SLE patient population is much higher than expected by chance alone. Hertig et al reported MCNS occurring in two out of 132 SLE patients in one center. These authors suggest that this association may not be a coincidence [11]. Patients diagnosed to have concomitant SLE and MCNS presented with nephrotic syndrome and had either minimal glomerulopathy or focal segmental glomerulosclerosis without evidence of glomerular immune complex deposition or endocapillary proliferation. They also had complete or near-complete podocyte foot process effacement [8, 11, 17].

Despite arguments suggesting a dysfunction of the immune system, the pathogenesis of MCNS is yet unknown [1]. There is no clear evidence to suggest that complement and immune complexes play a role in the pathogenesis of MCNS. It has been proposed that MCNS reflects a disorder of T lymphocyte function. T cells are thought to release a cytokine (permeability factor) that injures the glomerular epithelial cells. The identity of this permeability factor is still uncertain. Epithelial cell damage may lead to albuminuria in MCNS by altering the metabolism of poly anions that constitute most of the normal charge barrier to the glomerular filtration of macromolecules [1].

There is ample evidence of the important role played by T cell in the pathogenesis of SLE. T cells exert their effect at multiple levels; they help B cells to produce autoantibodies potentially pathogenic to the kidney, they regulate the response of dendritic cells, they exert a direct potentially cytotoxic effect on affected organs and promote the recruitment and activation of other cell types [18]. Quantitative and functional abnormalities of regulatory T cells have been described in SLE [19]. An over activation of effector properties of these cells was also found [20]. A common genetic basis between the two pathologies cannot be excluded. Susceptibility genes in SLE and some forms of MCNS have been identified [21, 22].

Conclusion

This case is interesting not only because of the rarity of the association between SLE and MCNS, but also because the diagnosis of SLE was made three years after remission from MCNS. We need to look for evidence of systemic involvement during relapse in patients diagnosed to have MCNS, with due consideration to obtaining another renal biopsy. In addition, there may be immunological basis to the association between SLE and MCNS.

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