Unusual Case of Crescentic Lupus Nephritis, A Management Challenge

Shaikha Salman Aldoseri, Bsc, MD* Ahmed Fathi MBBH, Msc, MRCP(UK)**

ABSTRACT

Lupus nephritis is a serious complication of systemic lupus erythematosus (SLE) and it is suspected in SLE patients with abnormal urine analysis or kidney function test found during routine lab investigations. Despite the improvement of management plans, up to 10 percent of the patients end up to have end stage renal disease (ESRD). We report a case of a 47-year-old female known case of SLE who had severe form of lupus nephritis though she had mild deterioration in kidney function. In spite of having multiple risk factors for renal failure, she showed a significant improvement with early detection and immunosuppressive therapy.

Keywords: Lupus nephritis, Systemic lupus erythematosus, Immunosuppressive therapy

INTRODUCTION

Systemic lupus erythematous (SLE) is an immunological chronic disease that affects multiple organs and produces an array of clinical presentations. Among the multiple presentations is lupus nephritis (LN), which affects about 40% of adults with SLE[1]. LN is characterised by glomerular deposition of immune complexes followed by an inflammatory response. The clinical features varies from asymptomatic hematuria or proteinuria to nephrotic or nephritic syndrome and end-stage renal disease[1,2].

The vast majority of SLE patients develop lupus nephritis within three to five years of the diagnosis, while others do so subsequently (15%)[3], which may carry a worse prognosis than lupus nephritis present earlier. Other risk factors for poor prognosis include male gender, Black and Hispanic ethnicity, long-term hypertension, nephrotic range proteinuria, and onset of lupus at a young age[1,4].

The aim of this report is to present a case of unusual presentation of lupus nephritis that showed significant improvement because of early detection and immunosuppressive therapy.

CASE

A 47-year-old Bahraini female, G9P7L7A2 known case of hypertension on coveram 10 mg, diagnosed with SLE in 2013, prednisolone 5mg prescribed for her and she was noncompliant, presented with a one-week history of progressive left upper limb swelling and pain. She denies any history of fever, recent trauma or weakness. Physical examination revealed mild left upper limb swelling compared to the right side, associated with tenderness on palpation. On CT angiogram, occlusive thrombi in the left jugular, axillary, and innominate veins reported. The patient admitted for heparin infusion and transluminal balloon veinoplasty.

After a successful vienoplasty, the patient had persistent high blood pressure. Her systolic blood pressure ranged from 190 to 150 mmHg. Although the patient started multiple antihypertensive medications to control her blood pressure, there was no response. Lab results showed a significant rise in serum creatinine of 103µol/L (base line of 45.2); estimated glomerular filtration rate (EGFR) was 50 mmol/L, and Urinalysis done for further evaluation, the twenty-four urine proteins were 2.5 g/dl and the urine microscope showed no casts. However, the urine RBS was 11–20. The WBC was 11-20. Urine culture was negative. Her ESR was 94 mm/1hr. A complete blood count showed hemoglobin of $8.9x10^{12}$/L, platelets of $343x10^{9}$/L and a white cell count of $5.04x10^{9}$/L. Electrolyte levels were normal, urea was 10.7 mmol/L, the international normalized ratio (INR) was 1.7, and prothrombin time was 15.5 seconds. She had positive ANA, anti-DNA, and anti-Ro antibodies. The echocardiogram revealed normal left ventricle size with an ejection fraction of 60% and normal diastolic filling pressure.

On previous findings, she diagnosed with lupus nephritis. The renal biopsy done urgently after stabilizing the blood pressure while the patient was on a heparin infusion, which temporarily withheld.

Renal biopsy under a light microscope (Figure 1) revealed eight perfused glomeruli, seven of which had segmental to global endocapillary hypercelullarity, a focal necrotizing lesion, and wire loops. Three cellular crescents seen. The glomera basement membranes are focally and segmentally split. Chronic tubulointerstitial damage accounts for less than 5% of all cases. Acute tubular injury and cytoplasmic vocalization observed in the proximal tubular epithelium. Four small arteries observed with mild fibro intimal thickening. Thrombotic microangiopathy is present.

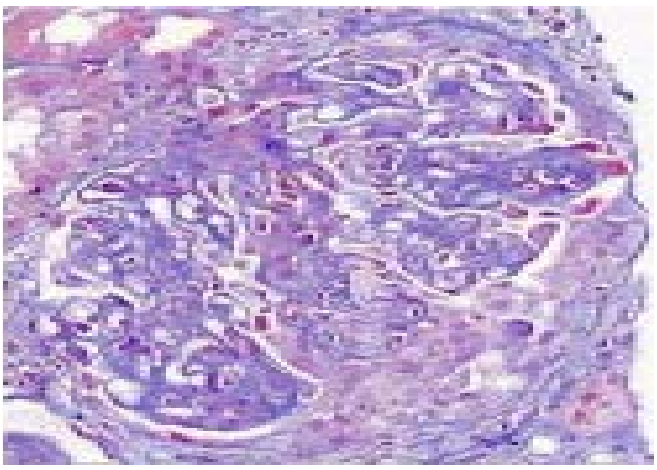

Figure 1: Endocappillary hypercellurity celluluar carsents under light microscopy stained with H&E, PAS, Trichorome and Jones

Renal biopsy under an immunofluorescence microscope (Figure 2) revealed that frozen sections stained for IgG, IgM, IgA, C3, C1q, fibrinogen, kappa and lambda light chains. There was mesangial and interrupted wall capillary positivity for IgG, IgA, C3, C1q, fibrinogen, kappa and lambda light chains, and a trace of mesangial IGM.

* General practice resident
Bahrain defence force hospital
Kingdom of Bahrain Email: shai5aagu@gmail.com
**Fellowship Adult nephrology
Kingdom of Bahrain Email: afame73@gmail.com

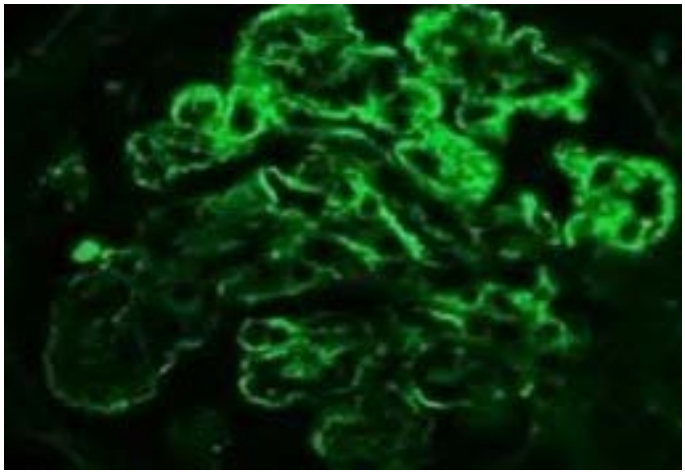

Figure 2: Frozen section in Immunofluorescence showing trace of IgG

Renal biopsy under electron microscope (Figure 3) reveled three perfused glomeruli, the podocyte were enlarge with microvillation and cytoplasmic voclation, approximately 10% of the podocyte foot process were effaced , Electron cell deposit were seen in subendothelial and mesangial areas.

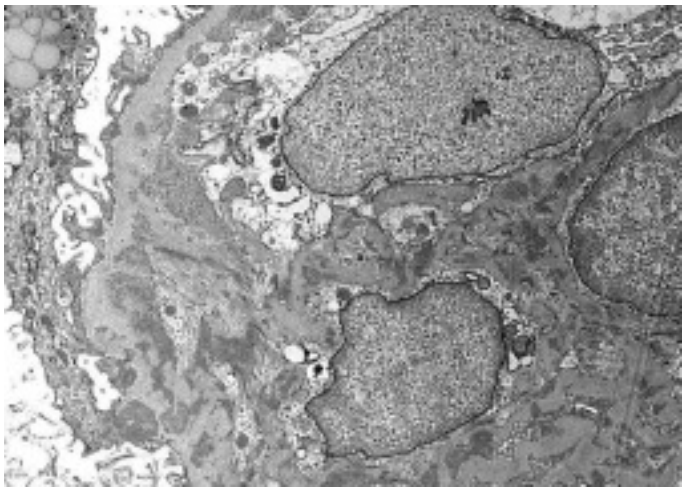

Figure 3: Electron microscope showing protein deposits

The patient diagnosed with diffuse global nephritis, membranoproliferative glomerulonephritis with active crescents with a high activity index of up to 38%. International society of nephrology and renal pathology classification IV –GA, national institute of health (NIH) activity index 13/24, chronicity index 2/12.

After discussing the treatment plan and ensured that the patient completed her family, she initially received 1g of methylprednisolone for three days and a dose of cyclophosphamide 500 mg, which repeated every two weeks for six cycles (Euro lupus protocol), with a tapering dose of prednisolone starting at 60 mg orally. For maintenance immunosuppression, Mycophenate Mofetil 1g prescribed. After the course of treatment, the patient had normal blood pressure and restored her renal function; the last EGFR was 60.

DISCUSSION

According to the American College of Rheumatology (ACR), lupus nephritis defined as persistent proteinuria of more than 0.5g per day or greater than three by dipstick or cellular casts, including red cell, hemoglobin, granular, tubular, or mixed[5].

Renal biopsy is fundamental for the diagnosis and management of lupus nephritis. It is indicated in SLE patients with proteinuria more than 500mg/24h, hematuria in the presence of any level of proteinuria, active sediment casts[6]. A proper glomeruli sample, containing at least ten glomeruli should be taken during the procedure to ensure an accurate assessment and to avoid any confusion regarding the result[7].

The 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) classification system classifies lupus nephritis into six classes according to the histological pattern (Table 1)[8]. Among the six classes, class four has the highest risk of progression to end-stage renal disease. Class IV LN is sub-classified into two categories. LN IV-S (segmental) shows more than 50% segmental endocaplliry proliferation, and LN IV-G (glomerular) shows more than 50% glomerular lesion, which is diffuse endocapillary, extracappliray, mesanagiocappillary proliferation or wire loop deposit[8].

Cellular crescents, which are formed when immune complexes disrupt the glomerular capillary wall basement membrane, allowing macrophages and T cells to enter the bowman capsule and cause severe destruction, are a significant histological finding most commonly found in Class IV LN and represent a severe disease.[9]

Table 1: Abbreviated international society of Nephrology/Renal pathology society (ISN/RPS) classification of lupus nephritis (2003)

Class I	Minimal mesangial lupus nephritis
Class II	Mesangial proliferative lupus nephritis
Class III	Focal lupus nephritis[a]
Class IV	Diffuse segmental (IV-S) or global (IV-G) lupus nephritis[b]
Class V	Membranous lupus nephritis[c]
Class VI	Advanced sclerosing lupus nephritis

Indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, severity of arteriosclerosis or other vascular lesions.
[a]Indicate the proportion of glomeruli with active and with sclerotic lesions.
[b]Indicate the proportion of glomeruli with fibrinoid necrosis and cellular crescents.
[c]Class V may occur in combination with class III or IV, in which case both will be diagnosed.

Double strand Anti-dsDNA antibodies are one of the most important analysis, which rises and falls in relation to disease activity. Anti-dsDNA levels are higher in proliferative LN (Class III or IV) than other classes[2,10].

The ultimate goal of therapy in LN patients is to prevent nephron loss and reduce the risk of deterioration into end stage renal disease (ESRD). The management plan is determined according to ISN/RSP histological classification[11]. Class I and II generally do not requires immunosuppressive therapy as both classes have excellent long-term outcome, unless there are features of transformation to more aggressive type of LN or minimal change disease[12,13].

For proliferative LN (Class III and IV) the treatment divided into two phases: a short-term induction phase to treat the acute disease, and a long-term maintenance phase to avoid any relapse and to suppress the disease with minimum therapeutic side effects[2,12].

All current treatment regimens for the induction phase include a high dose of IV pulse methylprednisolone and either IV CYC or Mycophenolate mofetil (MMF) as immunosuppressive therapy[5]. There are two regimens for CYC therapy: a high-dose regimen characterized

by IV CYC 0.5 to 1g/m2 monthly for six months (National institute of health protocol), and a low-dose regimen characterized by IV CYC 500mg every two weeks for six doses (Euro lupus protocol). Clinical studies done on European people showed that a low-dose regimen had the same efficacy as a high-dose regimen with fewer side effects. More multiracial clinical trials need to be done to test the applicability of the low dose regimen on other races[5,12].

In the maintenance phase, low dose oral prednisone along with MMF one to two g or AZA 1-2.5 mg/daily is used studies showed superiority of MMF over AZA[12,13].

The optimal time to withdraw the immunosuppressive therapy in the maintenance phase is undefined. However, most renal flares occur within 5 to 6 years following the induction phase. For that reason, it is recommended not to discontinue the immunosuppressive therapy at that time[13].

Corticosteroids in combination with an immunosuppressive agent such as CYC, MMF, AZA is used for pure class V LN with nephrotic range proteinuria. MMF is preferred over the rest of the immunosuppressive for both the induction and maintenance phase of class V yet larger clinical studies should be done to prove the fact. If kidney biopsy reveals features of class III and IV along with class V, it should be treated as class III and IV [5,12].

Moreover, strict control of blood pressure by renin angiotensin inhibitors and hydroxyquinoline is highly recommended in all classes of LN as it's proved that it decreases the risk of renal flares and ESRD[5,13].

CONCLUSION

Despite the improvement in treatment plans, LN remains a devastating complication among SLE patients. Our case proved that early detection and treatment with immunosuppressing therapy showed a notable improvement in her renal function.

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Competing Interest: None

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