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Research Paper

Membranous Lupus Nephritis in A 50-Year-Old Male

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CASE SUMMARY
The patient was a 50-year-old businessman who presented with bilateral leg swelling and generalized joint pains for about 4 weeks. Following clinical and biochemical evaluation, he was found to have renal impairment, with positive serology results for lupus nephritis and histologic features of membranous glomerulopathy. He was diagnosed as case of lupus nephritis. His initial treatment was with anangiotensin converting enzyme inhibitor,however due to non-regression of proteinuria, immunosuppressive therapy was instituted. His condition improved remarkably and he is currently on routine follow-up in the renal clinic.

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I. CASE PRESENTATION

Mr. DU a 50-year-old business man was in his usual state of health until four weeks prior to presentation when he observed bilateral leg swelling which was insidious in onset, initially at the level of the ankle but gradually progressed to the mid shin. There was associated facial puffiness however he had no history of abdominal swelling, oliguria, hematurianor dysuria.

About a week later, he developed severe joint pains and swelling involving the ankle and knee joints bilaterally. The pain was continuous andof moderate to severe intensity with no known aggravating factor, but occasionally relieved by analgesic.There was associated low grade fever. He had a history of fatigue, malaise with some weight gain. He also observed some erythematous rash on his upper chest wall, however there was no oral ulcer, sore throat nor hair loss.

He had no history of indiscriminate use of non-steroidal anti-inflammatory drugs, neither any use of herbal remedies nor mercury containing soaps or creams. There was no history of blood transfusion. He was neither a known diabetic nor hypertensive.

In the course of this illness, he was treated for malaria and typhoid fever in various peripheral hospitals all to no avail. He was also managed for early osteoarthritis in the general outpatient clinic of this hospital but was later referred to us following worsening of symptoms.He wasnot on any long term medication and not allergic to any known drug.

He was the first of six siblings, with a history of hypertension and long term osteoarthritis in his father but no family history of diabetes. He is married in a monogamous setting with four children, he neither used tobacco in any form nor consumed alcoholic beverages.

At presentation, general physical examination revealed an acutely ill looking middle aged man, not in any distress. He was afebrile, not cyanosed, anicteric and moderately pale. He had no finger clubbing and the peripheral lymph nodes were not palpably enlarged. He had bilateral pitting pedal edema up to the mid shin. He weighed 65kg with a body mass index of 25.4kg/m^2.

The pulse rate was 86 beats/minute, normal volume and regular.There was no thickened arterial wallnor locomotor brachialis. His blood pressure was 150/90mmHg and his jugular venous pressure not elevated. The apex beat was localized to the 5th left intercostal space mid clavicular line and was not heaving. His heart sounds were 1st and 2nd only and there were no murmurs.
The clinical findings on examination of respiratory system were essentially normal.

The abdomen was full and moved with respiration. There was no tenderness and no palpable organ enlargement. He had no ascites. His bowel sounds were present, normoactive and there were no renal or hepatic bruits.

There was diffused swelling of both knee joints, but no change in color nor differential warmth. He had marked tenderness of both knee and ankle jointswith mild crepitus and limitation of movement.There were no malar rash, discoid rash or non-scarring alopecia but he had few erythematous macular rashes on the upper chest wall mostly around the sun exposed areas.

There were no abnormalities in the examination of central nervous system.
A working diagnosis ofbilateral effusive osteoarthritis of the knees to rule out Rheumatoid arthritis was made. He wasadmitted into the medical ward, subsequently investigated and the following results wereobtained;
Urinalysis revealed a pH of 5.0, specific gravity of 1.015, proteinuria of 300mg/dl (+++) and blood (++). Other parameters were normal. Urine microscopy showed red blood cells of 2-4 per high power field (HPF), pus cell of 1-2/HPF, bacteria (+) and epithelial cell 0-2/HPF, granular cast (++). Culture yielded no growth after 48hours of incubation.24 hours urine protein was 3.2g/24hours and urine protein creatinine ratio (uPCR) was 300mg/mmol.
The hematological and biochemical indices are as shown in table 1.

Table 1: Hematological and biochemical results at presentation

Investigations	Results	Reference range
Hematology		
Hemoglobin(g/dl)	9.0*	12-16
White blood cell(L^{-1})	4.5 x 10^9	4-11 x 10^9
Platelet (L^{-1})	220 x 10^9	140-400 x 10^9
Neutrophil (%)	78*	40-75
Lymphocyte (%)	21	20-45
Eosinophil (%)	1	1-6
ESR (MM/HR)	120*	5-7
Biochemistry		
Serum Urea (mmol/l)	10.2*	2.4-6.0
Serum creatinine(mmol/l)	200*	60-120
Sodium (mmol/l)	136	135-145
Potassium(mmol/l)	3.8	3.5-5.0
Bicarbonate (mmol/l)	21*	24-30
Serum calcium(mmol/l)	2.2	2.2-2.6
Phosphate (mmol/l)	1.2	1.1-1.7
Uric acid (mmol/l)	341	120-420
Total protein(g/l)	74	62-80
Serum albumin(g/l)	24*	36-50
Total cholesterol(mmol/l)	5.5*	<5.2
Triglyceride (mmol/l)	2.0*	0.3-1.7
HDL (mmol/l)	0.8*	>1.12
LDL(mmol/l)	3.76*	<2.6

Abnormal results *
The eGFR calculated was 33.5ml/min/1.73m^2 using Modified diet in renal disease (MDRD) formular.

Serology test for Viral disease research laboratory (VDRL) was negative, rheumatoid factor was 12IU/mL (negative), antinuclear antibody (ANA) using ELISA was 10 IU/mL(≥6IU/ml)) and the titervalue was 1:160 using indirect immunofluorescence assay (positive) and anti-double stranded DNA (dsDNA) was 106IU/mL (≥75IU/ml))(positive).

Serological screening for Human immunodeficiency virus (HIV), Hepatitis B surface antigens and Hepatitis C antibody were all negative.

Abdominal ultrasound scan showed normal size kidneys of 12.1 x6.4 and 12.3 x6.0 for the right and left kidneys respectively with slightly increased echogenicity but good corticomedullary differentiation. No cyst, calculi or calyceal dilatation was seen. The gall bladder, spleen, pancreas and bowel loops were normal on ultrasound scan.

The liver was normal in size. It had normal echo texture. No focal mass lesion was seen. The intrahepatic ducts were not dilated.

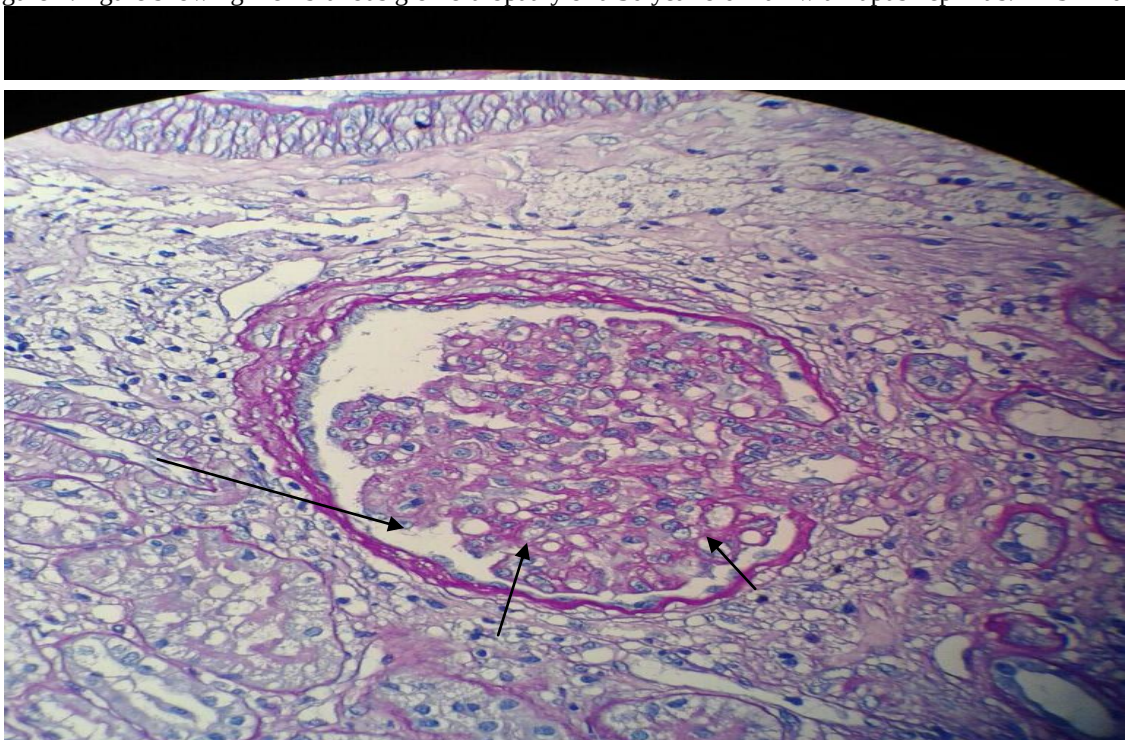
Renal biopsy was done and the biopsied tissue was examined under light microscopy with Periodic Acid Schiff (PAS) stain. There was no facility for electron microscopy or immunofluorescence. On light microscopy histology, normal sized glomeruli with thickening and prominence of glomerular capillary wall were noted. There was no increase in cellularity. The interstitium and tubules were unremarkable. The features were in keeping with membranous glomerulopathy (figure 1).

Based on the urinary protein, hematuria, positive ANA and anti-dsDNA as well as his histological findings, a final diagnosis ofMembranous lupus nephritis (ISN/RPS CLASS V) was made.

He was admitted into the medical ward and was placed on low dietary salt (<5g/day) and protein (0.8/kg/day) restriction in view of edema, proteinuria and renal impairment. He also received loop diuretics (Intravenous furosemide 80mg daily) for edema mobilization. He was also commenced on tablet Paracetamol for relief of joint pains and fever, tablet Lisinopril 20mg daily as well as tablet Amlodipine 10mg daily for blood pressure control including reduction of proteinuria, and tablet Atorvastatin for his abnormal lipid profile. Iron deficit was calculated and corrected using intravenous 200mg of Iron sucrose weekly for four doses. He also received subcutaneous erythropoietin (Recormon) 4000 IU weekly following correction of iron deficit.

While in the ward, he had daily monitoring of his proteinuria with dip stick urinalysis semi-quantitative assay which revealed persistent heavy proteinuria of (+++), 24 hours urine estimation remained at 3.2g/day and uPCR was 300mg/mmol after two weeks of treatment with Angiotensin converting enzyme inhibitor, warranting the commencement of immunosuppressive agents.He had an initial remission with induction therapy of intravenous pulse Methyl prednisolone 1g daily for 3 days followed by maintenance therapy of tablet Prednisolone 1mg/kg (60mg) daily and tablet Mycophenolate sodium (Myfortic) 360mg twice daily. The prednisolone was tapered to 45mg after one month and subsequently to 30mg.

Figure 1: figure showing membranous glomerulopathy of a 50 year old man with lupus nephritis. PAS x 100



Arrows showing thickening and prominence of the glomerular capillary wall.

He responded well to immunosuppressive therapy and achieved some clinical improvement. Malaise and fatigue improved, joint pains subsided with regression of joint swelling. Proteinuria subsided and he had gradual normalization of serum creatinine. Repeated hemoglobin levels was 11g/dl and erythrocyte sedimentation rate had dropped to 28mm/hr. He was discharged following 4 weeks of therapy on admission to be followed-up in the Nephrology subspecialty clinic.He is currently on maintenance oral Prednisolone 25mg daily and monthly monitoring of his renal indices and uPCR. The results of his monthly renal functions and uPCR are highlighted in table 2.

Table 2: Result of follow up monthly renal function test and uPCR.

Paramters	**1st month**	**2nd month**	**3rd month**	**4th month**	**5th month**
uPCR	200mg/mmol	200mg/mmol	100mg/mmol	50mg/mmol	50mg/mmol
Creatinine	200umol/l	180umol/l	180umol/l	160umol/l	158umol/L
Urea	10mmol/l	10mmol/l	8.5mmol/l	8.0mm/l	7.5mmol/L
Potassium	3.8mmol/l	3.8mmol/l	3.5mmol/l	4.0mmol/l	3.9mmol/L

II. DISCUSSION

Systemic lupus erythematosus (SLE) is a chronic autoimmune diseaseaffecting almost any organ system with protean manifestations,ranging from an indolent to a fulminant disease exhibiting a relapsing and remitting course. It is characterized by an autoantibody response to nuclear and cytoplasmic antigens. Although the specific cause of SLE remains unknown, multiple factors are associated with the development of the disease, including genetic, epigenetic, ethnic, immunoregulatory, drugs, hormonal, and environmental factors.[1]

About 90% of patients with lupus are female, thus a role for female hormonesseems likely, but a protective role for male hormones or an effect of genes on the X chromosome is also possible.[1] As have been observed lately, hormone-replacement therapycontaining conjugated estrogens and progesterone had a risk of a mild-to-moderate disease flare up to 1.34 times, however, trials of hormonal treatments for lupus, such as

dehydroepiandrosterone (DHEA), have been disappointing.[1]The incidence of Systemic lupus erythematosus in females to males occur at a rate of 11:1 during child bearing years[7] with prevalence highest in women aged 14-64 years. SLE does not have age predilection in males however, this ratio reduces as women age due to loss of estrogen effect in older women.

Male SLE patients may have more severe disease than females.[2] Several inconsistent reports suggests a distinct type of lupus in males and the possibility of more severe disease forms and less mucocutaneous presentation in males however due to paucity of male patients with SLE, there has been difficulty in analyzing the disease course in males. Despite the aforementioned, few studies have suggested that approximately 4% to 22% of SLE patients in reported series are males[3] with more severe skin lesions, serositis, renal disease, thrombotic events and seizure been reported by several authors, Interestingly, our patient was a middle aged man presenting for the first time with features suggestive of Lupus Nephritis, arthritis and photodermatitis.

The criteria for SLE itself have undergone changes in recent years. The generally accepted 1997 ACR classification criteria for SLE, which was a non-validated update of the 1982 ACR criteria, was found lacking in certain cutaneous criteria and exclusion of newer immunological markers for SLE.[4]According to the American Rheumatology Association (ARA) criteria for the diagnosis of SLE, the presence of at least 4 out of the 11 criteria yields a sensitivity of 85% and specificity of 95% for SLE.[4-5] These criteria are malar rash, discoid rash, photo sensitivity, non-erosive arthritis, oral ulcer, pleurisy or pericarditis, neurological, renal, hematological and immunological disorders and presence of antinuclear antibody (ANA).[4-5]

Ultimately, the Systemic Lupus International Collaborating Clinics (SLICC) [6] group convened to produce a more definitive revision of the SLE criteria. The SLICC criteria, published in 2012, expands the total number of criteria from 11 to 17 which requires the fulfillment of four criteria, at least one of which must be clinical and one of which must be immunologic; it also permits patients with biopsy-proven lupus nephritis in the presence of ANA or anti-dsDNA antibodies to meet criteria for SLE on this basis alone.[6]Our index patient presented with non-erosive arthritis, photosensitive rash with renal and serological evidence of SLE in keeping with the SLICC criterion.

The prevalence of lupus nephritis worldwide varies between different regions, races and ethnicities. The APOL1 gene, which has been implicated in the development of ESRD in black patients, has also been associated with progression and development of ESRD in the lupus nephritis population.[7]An HLA-DR2 subtype (HLA-DRB181503), characteristic of black populations, was linked to worsening proteinuria. Black individuals are also more likely to have positive anti-Ro, anti-Sm, and anti-RNP antibodies, which have a high association with LN.Approximately 35% of adults with SLE have clinical evidence of nephritis at the time of diagnosis with an estimated total of 50-60% developing nephritis during the first 10years of disease.[8]

In a 3 year prospective study of patients with renal diseases who were admitted to the rheumatology and nephrology unit of Lagos State University Teaching Hospital, all the 12 patients studied had serological evidence of lupus[9]this is in agreement with previous studies suggesting an increased prevalence of renal involvement in SLE.LN is a major risk factor for morbidity and mortality, with 10% of patients with LN developing end stage renal disease (ESRD) requiring dialysis or transplant.The risk of ESRD is higher in class IV LN to about 44% over 15 years. Patients with LN also die earlier than SLE patients without LN. Importantly, 10-year survival improves from 46% to 95% if disease remission can be achieved.[7]

Multiple factors including male sex, black race, presence of anti-phospholipid antibodies, and increased creatinine at the time of diagnosis, anemia, frequent nephritic flares, hypertension and excessive proteinuria are all considered risk factor for increased progression to end-stage renal disease.[3]Our patient presented with some of these factors predisposing him to declining renal functions. Several studies reports gender-associated differences in SLE and LN. Males had higher prevalence, poorer renal outcome and poor overall survival amongst males,[10] despite these, comparative long term renal outcome in both gender still remains controversial.

Several studies from experimental models suggests an autoantibody pathogenesis in LN, but the mechanisms leading to the formation of immune deposits and the development of renal lesions are not clarified.Three categories of autoantibodies constitute the basis for any pathologic and/or clinical consideration.[11] The first category targets implanted antigens (DNA, histones, and nucleosomes), mainly derived from breakdown of apoptotic cells. The second category of antibodies binds C1q, which is a component of the complement cascade accumulating in the kidney in LN. The third category includes several podocyte antigens, mainly α-enolase and annexin AI, that have been only recently identified as well as other glomerular antigens.

Evidence from the literature suggests that it is the combination of all auto-antibodies that produces stable renal lesions in LN and that different subsets have specific implications.[11]Experimental studies support the role of anti-DNA antibodies in starting the process, while anti-podocyte antibodies plays a role in its maintenance.In the case of antibodies versus DNA and/or DNA components (*i.e.*, histones and nucleosomes),the binding is directed to basement membrane and mesangial matrix and seems propaedeutic to further immune complex deposition.Antibodies versus podocyte antigens induce lupus-like renal lesions in mice, and the same antigens (*i.e.*, *α*-enolase) are targets of nephrogenic antibodies.[11]

Rezende *et al*[12]further describedstructural podocyte damage in proliferative forms of LN, whereas in the pure membranous forms, the predominant preserved pattern suggests a dysfunctional podocyte lesion that may account for the better long-term prognosis of proteinuria outcome. This finding may explain the clinical improvement observed with treatment in our index patient.

Renal pathologists and nephrologists have currently evaluated the degree of histological damage to establish therapeutic plans for lupus nephritis. Therefore, all patients with clinical evidence of active lupus nephritis are advised to mandatorily undergo renal biopsy in a bid to classify glomerular disease by the current ISN/RPS classification and treatment tailored accordingly.

In order to standardize definitions, emphasize clinically relevant lesions, and thus improve inter-observer reproducibility, the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification was proposed and developed in 2004, termed the ISN/RPS pathologic classification.[13]

INTERNATIONAL SOCIETY OF NEPHROLOGY/RENAL PATHOLOGY SOCIETY 2004 CLASSIFICATION OF LUPUS NEPHRITIS.[13]

Class I: Minimal mesangial lupus nephritis
Class II: Mesangial proliferative lupus nephritis
Class III: Focal lupus nephritis (<50% of glomeruli)
Active or inactive focal, segmental or global endo or extracapillary glomerulonephritis involving <50% of all glomeruli, typically with focal subendothelial immune deposit with or without mesangial alterations.
Class III(A): Active lesions-focal proliferative lupus nephritis
Class III(A/C): Active and chronic lesions-focal proliferative and sclerosing lupus nephritis.
Class III(C): Chronic inactive lesions with glomerular scars-focal sclerosing lupus nephritis.
Class IV: Diffuse lupus nephritis(>50% of the glomeruli)
Active or inactive diffuse, segmental or global endo or extracapillary glomerulonephritis involving 50% of all glomeruli, typically diffuse subendothelial immune deposit with or without mesangial alterations. This class is divided into diffuse segmental (IV-S) lupus nephritis when 50% of the involved glomeruli have segmental lesion and diffuse global (IV-G) when 50% of the involved glomeruli have global lesions.
Class IV-S (A): Active lesions-diffuse segmental proliferative lupus nephritis
Class IV-G (A): Active lesions-diffuse global proliferative lupus nephritis
Class IV-S (A/C): Active and chronic lesions-diffuse segmental proliferative and sclerosing lupus nephritis.
Class IV-G (A/C): Active and chronic lesions-diffuse global proliferative and sclerosing lupus nephritis.
Class IV-S (C): Chronic inactive lesions with scars-diffuse segmental sclerosing lupus nephritis.
Class IV-G (C): Chronic inactive lesions with scar-diffuse global sclerosing lupus nephritis.
Class V: Membranous lupus nephritis
Class VI: Advance sclerosing lupus nephritis
(≥90% of glomeruli globally sclerosed without residual activity)
Class II constitutes about 10-25% of all biopsies, class III constitutes 20-35%, class IV 35-60%, class V 10-15% while class I and VI constitutes about 1-2%

Recently, several retrospective validation studies concerning the utility of the ISN/RPS classification, especially among class IV, were performed. In these reports, reproducibility is improved by the definition of each diagnostic term, but the clinical outcome related with classification, especially in class IV, remains controversial. Sada *et al*[13] reports that the class IV-G group tended to exhibit a worse renal outcome, but the difference compared with IV-S was not significant, furthermore, in a Cox proportional hazards models, independent histological predictors of poor renal outcome were extra capillary proliferation, glomerular sclerosis and fibrous crescents, while hyaline thrombi and fibrous adhesions were of favorable renal outcome. Both were similarly observed in IV-G and IV-S. A more qualitative categorization by the response to standard treatment may be needed to emphasize clinically relevant lesion related to renal outcome

Membranous lupus nephritis (MLN) accounts forapproximately 10-20% of lupus nephritis (LN).[14]The clinicalpresentation of MLN is variable, ranging from isolated subnephroticproteinuria to nephrotic syndrome with reduced glomerular filtration rate (GFR), with or without extra renalmanifestations of SLE, positive lupus serology or hypocomplementemia. Although associated with a betterprognosis than proliferative LN, MLN can lead to significantmorbidity, including thrombosis and infection associated withthe nephrotic syndrome, transition to a proliferative LN inapproximately one-third of patients[14] and progression to endstagekidney disease (ESKD) in approximately 10% of patients after 10 years.

The treatment of LN is based largely on the classification of LN by the ISN/RPS criteria.[13] Class I and II usually presents as mild renal disease, such as microscopic haematuria or proteinuria that do not usually warrant specific therapy. Aggressive immunosuppressive therapy is required in patients with class III and IV. Patient with class V lupus nephritis who have normal renal function and sub-nephrotic proteinuria may not warrant aggressive immunosuppressive therapy and may be adequately managed with angiotensin converting enzyme inhibitors/angiotensin receptor blockers and statin as needed for hyperlipidemia.All patients with LN

should receive treatment withhydroxychloroquine,[15] unless there is a contraindication. Renin-angiotensin-aldosterone system blockade shouldbe introduced if there is proteinuria >0.5g/day[14] and/or ifanti-hypertensive medication is required to achieve blood pressure control <130/80mmHg.

Immunosuppression is typically indicated for persistent nephrotic-range proteinuria or declining renal function unlike primary membranousnephropathy, the likelihood of spontaneous remission in MLN is low. Steroid monotherapy[16] has been associatedwith high remission rates and excellent renal survival, however, combination immunotherapy may be superior ininducing remission in MLN with nephrotic range proteinuria.There is presently no consensus on which patients may besuitable for a trial of steroid monotherapy from onset of disease.

Clinical practice guidelines have highlighted the need forfurther investigation into the role of steroid monotherapy in LN. [16]Those with high grade nephrotic range proteinuria like our patient, particularly if unimproved by angiotensin antagonists, should be treated with similar but less intense regimens of corticosteroids[14] plus cyclophosphamide or mycophenolate mofetil. When class V is combined with class III and IV, it should be treated in the same manner as class III and IV. Class VI generally requires preparation for renal replacement therapy.

Cyclophosphamide (CYC) remains a reliable and effective treatment for inducing remission in lupus nephritis. There are two regimens of intravenous CYC as recommended by an expert Task force panel[17] which includes: 1) low dose "Eurolupus" CYC (500 mg IV once every 2 weeks for a total of 6 doses), followed by maintenance therapy with daily oral azathioprine (AZA) or daily oral MMF, and 2) high dose CYC (500–1000 mg/m^2 IV once a month for 6 doses), followed by maintenance treatment with MMF or AZA. Previous studies suggested that 30 months of high-dose intravenous CYC (the "NIH" regimen) in which CYC was given monthly for 6 doses, then quarterly for an additional 2 years, was more effective in preventing renal flare than the shorter "eurolupus" regimen.However, the more current 3-to-6-month regimens followed by AZA or MMF maintenance are showing good long-term results.

Members of the Expert Panel[17] recommended intravenous CYC at the low "Eurolupus" dose for European patients, since the low and high dose regimens were equivalent in efficacy. The Euro-lupus group (ELNT)[18] in a trial aimed to reduce the risk of side effects of cyclophosphamide without jeopardizing its efficacy used a shorter treatment courseand serious infections and leucopenia were less frequent with the lower doses. The low and high dose regimens have not been compared in non-Caucasian racial groups.[17] Ten years of follow-up comparing low and high dose regimens showed similar rates of LN flares, end-stage renal disease, and doubling of the serum creatinineNevertheless side effects were significant and this included infection, haemorrhagic cystitis, gonadal toxicity and malignancies.[18]

Several controlled trials such as the Aspreva Lupus Management Study (ALMS)[19] induction trial and subsequent meta-analysis established mycophenolate mofetil (MMF) as one of the recommended choice regimens for inducing remission in severe active proliferative lupus nephritis in all races.The Task Force Panel[17]similarly recommended that patients with pure Class V lupus nephritis and with nephrotic range proteinuria be started on prednisone (0.5 mg/kg/day) plus mycophenolate mofetil (MMF) 2–3 g total daily dose for 6 months.Retrospective studies[20] suggests improvement similar to that with cyclophosphamide (CYC) (0.5–1.0 mg/kg i.v. monthly × 6) plus prednisone, with zero to 30% of patients having nephrotic range proteinuria after 6 months.

In similar manner, it was observedin a controlled trial that for post-induction maintenance therapy, both oral mycophenolate mofetil (MMF) and oral azathioprine were superior in efficacy and had reduced toxicity than a regimen of continued quarterly intravenous cyclophosphamide. Recently, both Aspreva Lupus Management Study (ALMS) [19] maintenance and MAINTAIN[19] nephritis trials have provided important information regarding the comparative efficacy and safety of MMF and azathioprine as well as information on the effect of dosage and duration of treatment with these agents as maintenance therapies.

The use of calcineurin inhibitors in the treatment of MLN have also been studied with remissions occurring more rapidly with cyclosporine[16] with a cumulative probability of remission of 83%.[16] Similar data are available from small number of patients treated with Tacrolimus monotherapy.

The optimal treatment for pure membranous lupus nephritis (MLN) remains undetermined. In a retrospective study[21] of SLE patients with biopsyproven pure MLN suggested that Rituximab (a chimeric monoclonal anti-CD20 antibody) as monotherapy may represent an effective treatment for pure MLN with an excellent tolerance profile if repeated courses are given.[17]However this may seem, recent trials have disagreed with Rituximab use as monotherapy in the treatment of MLN. The EXPLORER trial[22] did not observe any significant difference between the Rituximab arm and the placebo arm. Similarly the LUNAR trial[23] observed decrease anti-DNA antibody titres and increase in complement levels, but no significant difference was observed in all renal endpoints at 1 year.

Further studies on treatment of severe lupus nephritis with plasmapheresis[24] plus a standard regimen of prednisone and cyclophosphamide therapy did not improve the clinical outcome in patients with systemic lupus erythematosus and severe nephritis, as compared with the standard regimen alone.

All lupus nephritis patients with proteinuria ≥0.5g/24hours should have blockade of the renin-angiotensin system which drives intraglomerular pressure and delays the occurrence of renal involvement and progression to end stage renal disease.[25]Careful attention should be paid to control of hypertension with target of ≤130/80mmHg. We were able to achieve this target blood pressure in our patient. Although our patient received adequate angiotensin receptor blocker, he did not achieve significant reduction of proteinuria warranting the commencement of immunosuppressive agents.Every Patientwith features of SLE should have a thorough laboratory assessment for lupus nephritis, whether male or female and those with abnormal result should have renal biopsy to determine the ISN/RPS class. Early detection and commencement of therapy will delay the progression to end stage renal disease.

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