International Journal of Public Health Excellence (IJPHE)
Vol. 3, No. 2, January-May 2024, pp. 617~623
Journal Homepage: https://ejournal.ipinternasional.com/index.php/ijphe
ISSN: 2809-9826, DOI: 10.55299/ijphe.v3i2.779

Case Report: 18 Year Old Male Patient with Lupus Nephritis

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Article Info

Article history:

Received February 05, 2024
Revised February 12, 2024
Accepted February 13, 2024

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ABSTRACT

Systemic Lupus Erythematosus is a chronic autoimmune disease that can affect various organs of the body, one of the most commonly affected complications is the kidneys and results in lupus nephritis, the percentage of disease occurrence is more than 50% of patients in the first 5 years. Male patients tend to have more aggressive disease with renal, vascular, and cardiac involvement. Based on the criteria of Systemic Lupus International Collaborating Clinics in 2012 defines lupus nephritis if there is proteinuria in 24 hours ≥ 0.5 g / day, there is urine sediment, and there is a decrease in renal filtration function. Although the disease can be diagnosed based on these three things kidney biopsy remains the gold standard of diagnosis. In this case report, an 18-year-old male with lupus history came to the emergency room with the main complaint of fever accompanied by shortness of breath, from the results of supporting examinations obtained anemia, thrombocytopenia, high creatinine, and eGFR of 4 mL/minute, complete urine showed proteinuria, cylinders, and erythrocytes, AP thorax photo showed cardiomegaly, bronchopneumonia, and bilateral pleural effusions. Based on history, physical examination, lab, and imaging, the patient was diagnosed with systemic lupus erythematosus, lupus nephritis, chronic kidney disease, normocytic normochromic anemia, and community acquired pneumonia. The patient received glucocorticoids, immunosuppressants, diuretic, antihypertensives, antibiotics, and other supportive therapy, this patient also received renal replacement therapy in the form of hemodialysis and a kidney biopsy will be done after the condition improves.

Keywords:

Lupus Nephritis, Systemic Lupus Erythematosus, Autoimmune

1. INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune systemic disease that have a diverse impact on the body's organs affected, SLE has a variety of clinical symptoms, one kind of disease condition that can occur is Lupus Nephritis (LN) [1]. Lupus Nephritis is one of more severe SLE complications, incident of LN often happen on period time of first 5 years, which patients diagnosed with SLE have a percentage of > 50% to develop this complication[2]. Patients who experience SLE with LN complications are frequent to found on younger age rather than patient whose only suffer from SLE without accompanied by kidney damage [2]. Development of this disease generally rapidly progressive , often happen in period from 6 months up to 1 year or more, in some cases can appear more early after diagnosis of the disease have been made [3]. There are lots of possible risk factors that influence the occurrence of LN in SLE patients like male gender, younger age, and different races like on Non-Caucasian descent for example Negro and Hispanic race who have higher risk to develop kidney damage in SLE [4].

If seen on a global scale SLE patients mostly can be found on the Continent of North America with amount as many as 241 patients per 100,000 residents, in Asia-Pacific countries the number between 4.3 to 45.3 each 100,000 residents, the situation in Indonesia based on data taken from various outpatient hospital polyclinics in 2015 were 17.9% to 27.2%, then in 2016 18.7% to 31.5%, and in 2017 it was recorded around to 30.3% to 58% patients, this phenomenon show uptrend of SLE cases every year [5]. Ratio between patient's gender manifold in man than woman i.e. 15:1 to 22:1, also onset of the first manifestation of apparent SLE symptoms can be found in young age between

9 years old to the oldest recorded at 58 years old [5]. Based on data from hospitals in Indonesia there are various type of symptoms of which appear on SLE patients i.e. arthritis by 32.9% to 75.5%; abnormality of skin, mucosa, and hair by 13.2% to 86.3%; abnormality on kidney like lupus nephritis by 10.8 to 65.5%, then other constitutional symptoms such as fatigue and fever [6].

The American College of Rheumatology define LN disease If on a SLE patients are found to have persistent proteinuria amount of 0.5 g/24 hours or > +3 at urine dipstick or found cylinder cellular, including erythrocytes, hemoglobin, granular, tubular, or mix on urine [7]. Classification criteria for Systemic Lupus International Collaborating Clinics 2012 define involvement of kidney if the protein-creatinine ratio urine or urinary protein excretion within 24 hours in the amount of 0.5 g / day or found red blood cell in urine sediment [8]. Kidney biopsy is gold standard for diagnostic also recommended on patient which suspected to experience kidney damage [9].

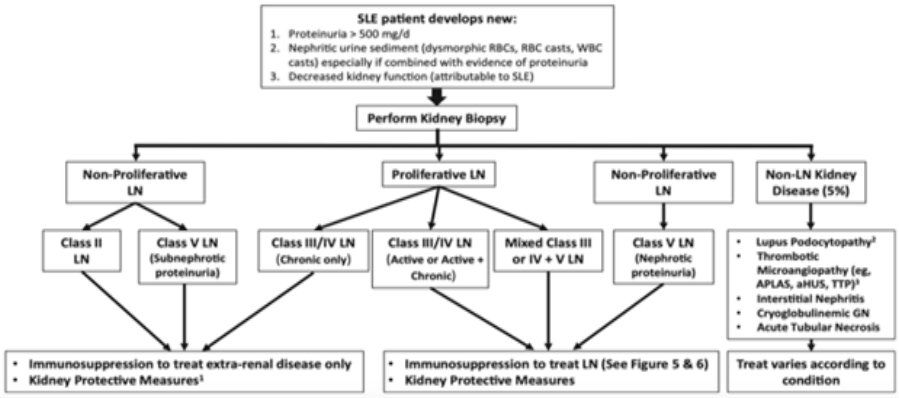

Figure 1. Algorithm to diagnose kidney disease associated with Systemic Lupus Erythematosus (SLE) [4]

The pathogenesis of LN are highly associated with formation of immune complex antibody such as anti-dsDNA or anti-DNA that later attach and deposit within kidney glomerular basement membrane as well as mesangium from the glomerulus, immune deposits which are formed will trigger disturbance of leukocytes as well as anti- inflammatory mediators for cleaning immune complex along with debris where this caused by decreasing affinity of Fcγ receptor as well as development of C1q and C3b autoantibodies [10]. Adherence of immune deposit complex on mesangium and in subendothelial gap of kidney will activate classic complement pathway causing increase production of C3a complement that will activate chemoattractant C5a so inflammation happen as consequence from leukocytes activation, such as neutrophils and macrophages, later this will injure kidney in a direct way through release of free radical and proteolytic enzyme [4]. This circumstances will give rise to proliferative, focal, or diffuse mesangial glomerulonephritis on SLE patients, which are marked by the results on urine inspection that found red blood cell, white blood cell, granular cylinders, as well as proteinuria accompanied with rapidly progressive declining of kidney function [11].

Classification based on the 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) states that kidney biopsy has to be done if patients with existing SLE and have signs on kidney involvement such as: hematuria, and/or formation granular casts, proteinuria > 0.5 g/24 hours, or urine protein-creatine ratio > 500mg/g, and declining rate of glomerular filtration (GFR) without any other suspicious found by other causes [4,12]. All of that conditions have to properly watch out because their tightly connection with significant inflammatory processes of kidney and needed further inspection i.e. biopsy so it can be confirmed that the process happen due to LN or by other similar conditions [12]. Repetition of biopsy proven can give more accurate information to managing disease as well as avoid giving drug excessively, there is not a certain agreement related to time and duration when repetition of biopsy have to be done, however patient must in full remission condition at least 1 year before it can be done [13].

Class	Definition	Description
I	Minimal mesangial LN	Normal glomeruli by LM,[a] but mesangial immune deposits on IF[b] or EM.[c]
II	Mesangial proliferative LN	Purely mesangial hypercellularity of any degree or mesangial matrix expansion by LM, with mesangial immune deposits. A few isolated subepithelial or subendothelial deposits may be visible by IF or EM, but not by LM.
III	Focal LN	Active or inactive focal, segmental or global endocapillary or extra-capillary glomerulonephritis involving <50% of all glomeruli:
		III (A)[d]: Active lesions
		III (A/C)[e]: Active and chronic lesions
		III (C)[f]: Chronic inactive lesions
IV	Diffuse LN	Active or inactive diffuse, S[g] or G[h] endocapillary or extracapillary glomerulonephritis involving ≥50% of all glomeruli:
		IV-S: ≥50% glomeruli with segmental lesions
		IV-G: ≥50% glomeruli with global lesions
		IV-S(A), IV-G(A): active lesions
		IV-S(A/C), IV-G(A/C): active and chronic lesions
		IV-S(C), IV-G(C): chronic inactive lesions
V	Membranous LN	G or S subepithelial immune deposits or their morphological sequelae by LM and by IF or EM, with or without mesangial alterations. May occur in combination with class III or IV, in which case both classes are diagnosed. May show advanced sclerosis.
VI	Advanced sclerotic LN	≥90% of glomeruli globally sclerosed without residual activity.

Figure 2. Classification of lupus nephritis histopathology ISN/RPS 2003 [4]

Guidelines from European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association EULAR/ERA-EDTA 2019 recommend treatment of active class III or IV LN with induction therapy consisting from mycophenolate mofetil (MMF) dose 2-3 grams/day, mycophenolic acid (MPA) dose 1440–2160 mg/day or intravenous cyclophosphamide (CYC) with dose 500 mg every 2 weeks for a total of 6 doses as first line agent together witch glucocorticoids (GC) [14]. Administration of high dose GC at dose 0.5-1 mg/kg/day has generally become induction therapy used on LN class III-V patients, however recent research proven that with low dose glucocorticoids also have own potency comparable with higher dose, so GC can be given as methylprednisolone (MP) intravenous of 500–2500 mg followed with oral prednisone 0.3–0.5 mg/kg per day and later can be lowered to ≤7.5 mg/day in 3–6 months [4,14]. For therapy on LN in maintenance phase, EULAR 2019 recommends MMF on previous patient get MMF as therapy in induction phase, and MMF or azathioprine (AZA) on patients who are on induction phase received intravenous CYC [15]. Similar thing showed in KDIGO 2021 guidelines that patient with active class III or IV LN can receive therapy of low dose intravenous CYC or MMF together with GC as induction therapy. For class V LN, KDIGO 2021 recommend medicine that blocks renin-angiotensin system such as ACEI/ARB for all patients and immunosuppressive therapy for patients with symptom indicating nephrotic syndrome, extrarenal manifestations of SLE, or complications of proteinuria such as thrombosis, edema, or dyslipidemia [14]. If on pregnancy condition and patient contraindicated to get ACEI/ARB then inhibitor channel calcium (CCB) can be used especially non- dihydropyridine group because its potential effect on reducing proteinuria and hinder progressivity of damaged kidney [16]. Patients with LN that condition reach renal failure is a candidate for all modalities of Kidney Replacement Therapy (KRT) like kidney transplant or dialysis [17].

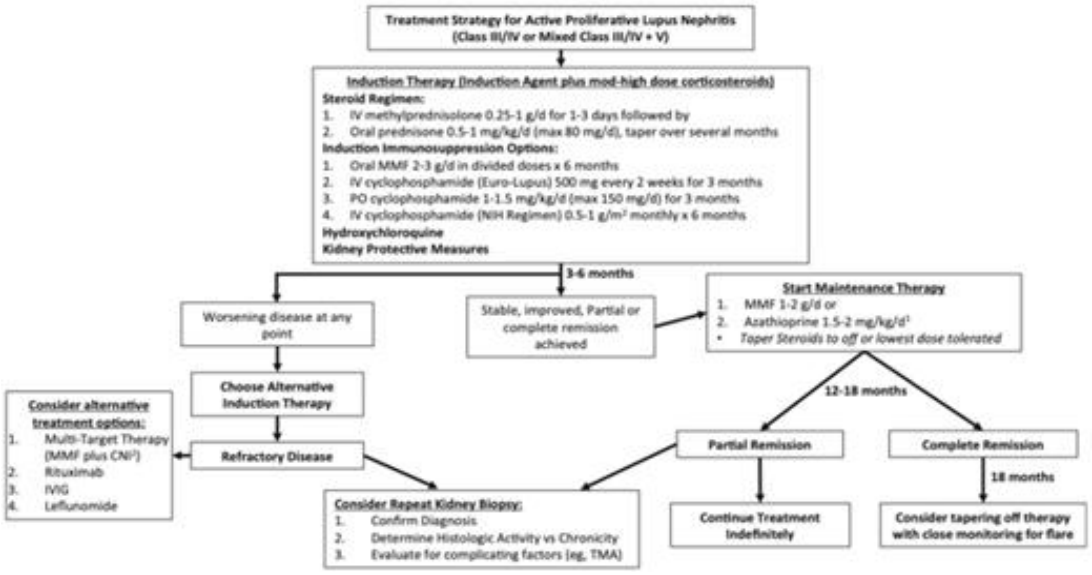

Figure 3. Algorithm for management of active proliferative lupus nephritis [4]

2. CASE

An 18 year old male patient came to the emergency room at Santo Vincentius General Hospital, Singkawang (12/10/2023) with complaints of fever that did not go down and had been felt since 6 days before he come to the hospital, especially at night the fever get higher, so the patient's mother has given him fever-reducing medication but the complaints have not improved, apart from fever the patient has also complained shortness of breath since 2 days before hospitalization, where the patient said that he felt heavy breathing and accompanied by pain in both chests [18]. The patient also complained of a productive cough with thick white phlegm, an amount of approximately ¼ tablespoon each time he coughed, without any spots, also there is no blood in his phlegm.

Patient felt tired and have no appetite, this feeling of tiredness happens since fever appear and not reduce by rest, the patient described as felt like having heavy activity, during this condition patient only bedridden and sleep. Patient also complaint of having a painful headache since yesterday that felt like throbbing on all over head, but get better if he consuming paracetamol. Based on patient's information he is not experiencing lose weight.

On upper and lower lip appear ulcer wounds, spontaneously since yesterday also accompanied by reddish and swelling gum, when patient have to eat he will feel intense painful on mouth so that he only can consuming porridge or soft food, another complaint on skin, hair, and mucous membrane in any part of bodies are denied by patient. Painful stomachache on the epigastric part also accompanied with nauseous and vomiting for 3 times, each vomiting containing food at of ±200 cc each time he vomited, no fresh blood or dark color vomit was found.

Patient then hospitalized, as his stay in second day his condition become weaker, patient also can only urinate 1 time in a day, with amount as much ±100 cc, the color yellow with concentrated brownish also accompanied with foam, complaints of painful when urinating is denied. Patient only defecate once a day with yellow brownish color, solid consistency, and not found any mucus nor blood [19].

Patient Already diagnosed SLE since a year ago and has done laboratory examination in form of profile anti-nuclear antibody (ANA) with results pattern speckled with a titer >1:1000 and strongly positive RNP/Sm and Sm antigens as well as positive PM100. Patient previously have received treatment for the disease such as: methylprednisolone 2x16 mg, azathioprine 2x50 mg, and candesartan 1x8 mg, however during this past 4 months he didn't consume his routine medicine, any other history of disease like another autoimmune disease, high blood pressure, diabetes, heart disease, kidney disease, are denied. History of similar disease in family also denied [20].

Figure 4. Results of the patient's ANA profile

Based on the results from the physical examination, patient appeared to be in moderate pain with compos mentis consciousness (GCS E4 V5 M6), visual analogue score at 5/10, patient's blood pressure 140/80 mmHg, pulse 86 times/minute, respiration rate 25 times/minute, O_2 saturation 98 % with nasal canule at 5 lpm, temperature 38.2ºC, patient's BMI 19.3 kg/m^2. On eye examination, it was found that the palpebral conjunctiva was pale, lip mucosa was dry, accompanied by mouth ulcers on the patient's upper and lower lip, and the gums were visibly erythematous, on examination of the skin and hair there were no visible abnormalities, there was no enlargement of the lymph nodes, on examination of the thorax it was found to be symmetrical, with basal crackles in both lung fields, and there was no wheezing. On abdominal examination was found supple in palpation, intestines sound normal, at percussion sound tympanic, also no shifting dullness and fluid waves nor hepatosplenomegaly found. Inspection of extremity that there

is no edema appears and there is painful sensation at both elbow and knee. Inspection of neurological didn't found any abnormality [21].

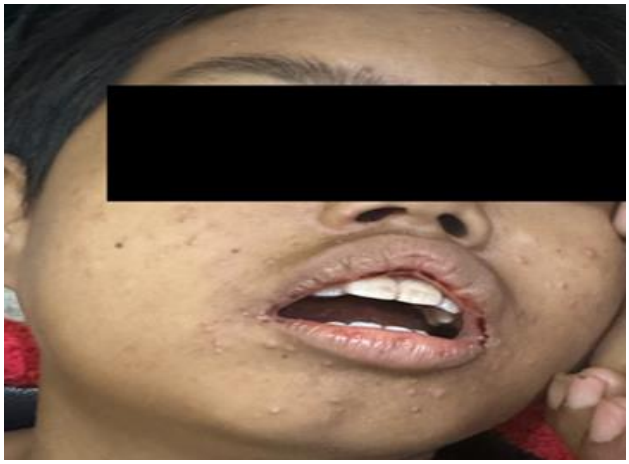

Figure 5. Ulcer on patient's lip

During hospitalization patient also get laboratory examination and the result in routine hematology decline amount erythrocytes at 2.96 10^6/uL, leukocytosis amounting to 11,400/uL. On inspection clinical chemistry, found enhancement of creatinine at 17.1 mg/dl with eGFR of 4 mL/ minute. On inspection urine in a macroscopic obtained glucose by +1 and protein by +3, and on results of urine microscopic obtained leukocytes as many as 4-6/Large field of view, full of erythrocytes, flat epithelial 10-12/Large field of view, round epithelial 2-4/Large field of view, and granular cylinder 1-2/Large field of view. On immunology obtained Anti-HIV and HBsAg nonreactive. Inspection on radiologist also done in the form AP chest radiograph with impression cardiomegaly (LV, LA), suspected pulmonary edema, bronchopneumonia, and minimal both lungs pleural effusion [22].

This patient was diagnosed as SLE, lupus nephritis, chronic kidney disease, normocytic normochromic anemia, and community-acquired pneumonia (CAP), patient then treated with Infusion of RL 10 drops per minute, MP 3 x 125 mg intravenously, ceftriaxone 2 x 1 gram intravenously, paracetamol 3 x 500 mg intravenously, furosemide 2 x 20 mg intravenously, pantoprazole 1x40 mg intravenously, candesartan 1x8 mg orally, MMF 500 mg 2 x 2 tablets orally, and given nystatin drops 4 x 1 ml orally, patient Also planned for hemodialysis and will be referred for kidney biopsy after condition improved.

3. RESULTS AND DISCUSSION

An 18 years old male patient came to the emergency room with the main complaint of fever accompanied by other complaints such as shortness of breath, weakness, pain all over the body, and vomiting. Physical examination showed pale on palpebral conjunctiva, ulcer on the upper and lower lip, and on lung examination there are crackles in both basal lung fields. In laboratory examination results Hb 9.1 g/dL, platelets 98,800/µL, leukocytes 11,400/µL, creatinine 17.1 mg/dl and eGFR 4mL/minute, from urine examination obtained protein +3, leukocytes 4-6/Large field of view, erythrocytes full, and exists epithelium as well as granular cylinder 1-2/Large field of view. On patient 's ANA profile 1 year ago, ANA titer >1:1000 was obtained with strong positive RNP/Sm and Sm antigens as well as positive PM100 results. Based on criteria from ACR/EULAR 2019 this patient can be classified as entry criteria in the form of ANA titer >1:1000, speckled pattern, then addition criteria in form of fever with 2 point, thrombocytopenia 4 point, ulcer on mouth 2 point, pleural effusion 5 point, proteinuria > 0.5 grams/24 hours 4 point, and Anti-Smith antibodies 6 point, in total points for clinical criteria as many ≥10, which in this patient at 17 points so that this patients were diagnosed with SLE. However in the last 4 months, patient has not taken his medication [23]. Results from patient 's ANA profile 1 year ago show results of strongly positive anti-Sm where it possibly correlate to resulting worse condition of lupus nephritis caused by anti-SM involvement in formation immune complex so that causing massive damage of kidney in a way [23].

Diagnose of LN on this patient based on criteria, namely: (i) active founding of urine sediments with or without increased proteinuria; (ii) improvement of serum creatinine concentration by ≥ 25%; and (iii) persistent increase in proteinuria > 0.5–1.0 g/day. Based on results of anamnesis, examination physical, laboratory, and imaging, patient diagnosed SLE, lupus nephritis, chronic kidney disease, normocytic normochromic anemia, and community-acquired pneumonia [24].

Objective treatment of LN patients are resolution of active inflammation symptom in clinical and full remission of kidney [25]. Immunosuppressive therapy used for proliferative form of LN like classes III, IV, and V. SLE patients with organ involvement will given glucocorticoids to suppress inflammation so that there aren't more inflamation that damaging organ, GC work in a way genomics with translocation to nucleus and bonded on DNA binding place so it can suppresses inflammatory processes. This therapy also need to given without waiting patient

to do kidney biopsy, because high risk of progressivity in LN [26]. During maintenance phase, this patient given MP 3 x 125 mg intravenously, for LN treatment aside with glucocorticoids patient also given immunosuppressant agent in the form of MMF 500 mg tablets consumed 2 tablets 2 times a day, in morning and night, MMF can become drug of choice on younger patient because lower risk to disturbance testicular function and ovaries if compared with other immunosuppressants such as cyclophosphamide (CYC) [1].

Besides given immunosuppressants and glucocorticoids, KDIGO 2021 recommend drugs that blocks renin-angiotensin system as antihypertensive therapy and antiproteinuria on patients that experiencing nephrotic symptomps [27]. In this case the patient received candesartan 8 mg administered orally per day [28]. Despite receiving immunosuppressive treatment, 10%-30% of LN patients can develop to become end staged renal disease (ESRD) in ±15 years after the diagnosis was made, various kinds of infections can also occur in patients with active LN disease whose are undergoing immunosuppressive treatment, the condition of LN with ESRD still needs to dialysis as replacement therapy for disturbed kidney function as well as lowering activity of clinical and serological of LN [29]. SLE patients with LN have higher risk to morbidity and mortality, so that LN treatment that not respond to standard medication can used other therapies such as calcineurin inhibitor (CNI) or drugs that targeting B cells show positive results so that can be considered to use, with possibility in the future can significantly impactful to treat LN [30].

4.CONCLUSION

An 18-year-old male patient was anamnesis and examined, physical examination, laboratory and imaging were carried out result in diagnosis of systemic lupus erythematosus, lupus nephritis, chronic kidney disease, normochromic normocytic anemia and community-acquired pneumonia. Patients are given immunosuppressant therapy, glucocorticoids, ARBs, antibiotics, as well as therapy for accompanying symptoms. Apart from being given medication, this patient also underwent hemodialysis as kidney replacement therapy, and later a kidney biopsy will be carried out.

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