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RESEARCH ARTICLE

A Seventeen-year-old Boy Patient with Lupus Nephritis as a Complication of Systemic Lupus Erythematosus (SLE) at Sanglah General Hospital, Bali, Indonesia: a Case Report

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Abstract

Background: The systemic lupus erythematosus (SLE) is an autoimmune disease with various clinical manifestations. SLE indicated by the presence of autoantibodies to the nucleus components and immune complex deposits. Prevalence ratio of SLE is higher in women than in men, but male patients seem to have a higher frequency of symptoms and more aggressive disease. So, this case study aims to evaluate A seventeen-year-old boy patient with lupus nephritis as a complication of Systemic Lupus Erythematosus (SLE) based on laboratory evaluation. Case Description: A seventeen-year-old male patients referred to the emergency department in Sanglah General Hospital with swelling on both eyelids and legs for two weeks before admission. The patient has high blood pressure, discolouration of urine and significant weight gain about 14 kilograms in two weeks due to swelling. Several examinations performed and the results were indicating anaemia, proteinuria, hematuria, hypoalbuminemia, high BUN and creatinine level, hyperkalemia, hyperphosphatemia and high titer of ANA-IF and anti-ds-DNA level. The patient diagnosed with lupus nephritis and treated with antihypertension and diuretic. Conclusion. The most common complication of SLE is lupus nephritis, and its prevalence varies significantly by region, race and tribe. Although overall improvements in the treatment of SLE patients have increased in kidney survival rates, the prognosis remains unsatisfactory. Early detection and diagnosis should be done so that the patient's condition worsens not occur because the late diagnosis of LN can increase the risk of End-Stage Renal Disease.

Keywords: *Autoimmune Disease, Lupus Nephritis, Systemic Lupus Erythematosus*.

Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with an estimated prevalence per 144 black women (>18 years) compared with 1 per 492 white women (>18 years), according to the increased risk of black African-American descent this is more common in women [1].The ratio of women to men in adults is around 9: 1. Based on age, the proportion of women: men are 3:1 before puberty, reaching a peak of 10 -15: 1 during the fertile period with a slight decrease after menopause which 1s 8:1.The peak age for diagnosis of SLE is between 15 and 44 years [1]. SLE has several clinical manifestations; one of them is Lupus Nephritis (LN).Lupus nephritis is the most common manifestation of SLE [2].

It can be defined as clinical and laboratory manifestations according to the criteria of the American College of Rheumatology (ACR). The criteria included a discovery of persistent proteinuria 0.5 g/days or more than 3+ by dipstick urine examination, and/or the presence of erythrocytes cylinders, haemoglobin, granular, tubular, or mixed [3].

It is well known that the incidence of SLE is 6-10 times higher in women than in men. But male patients seem to have a higher frequency of constitutional symptoms, neurological, haematological and also renal manifestations, including lupus nephritis [4, 5].Although overall improvements in the treatment of SLE patients have increased in

kidney survival rates, the prognosis remains unsatisfactory. Several studies also suggest that male SLE patients also have a more aggressive disease such as a higher incidence of hypertension, glomerulonephritis and renal failure [2, 4].Based on those mentioned above, this case report will explain about lupus nephritis in a seventeen-year-old male patient as a complication of SLE at Sanglah General Hospital, Bali, Indonesia.

Case Description

Seventeen years old male referred from Bali Jimbaran Hospital to Sanglah General Hospital with chief complaint swollen in the eyelids and legs for two weeks before entering the hospital. Initially, swelling seen on the eyelids in the morning, then swelling also in both legs and abdomen. There are no pain and redness in the swollen body parts. Chest pain, shortness of breath and palpitations were denied. The previous history of trauma was also denied. The colour of the urine initially was murky yellow, but from one day before the urine was reddish, bubbling but with average volume. Pain during urination is denied.

The patient also complains having sore throat one month ago without fever. Previously, the patient was treated in Bali Jimbaran Hospital and advised to do follow up due to his hypertension. Because the patient's body was getting more prominent due to swelling (patient gained 14 kilograms in two weeks) the patient then referred to Sanglah General Hospital. History of diabetes, heart disease, low back pain and urinary tract infections were denied in the patient. History of hypertension and heart disease is dismissed in the patient's family. Still, the patient's sibling reported died due to a history of vomiting of blood due to Systemic Lupus Erythematosus (SLE). The patient was in a stable condition with moderate pain, high blood pressure 180/110 mmHg, pulse 84 bpm, respiratory rate 20 times per minute, temperature 36,6oC, oxygen saturation 97%.

From the physical examination, we found palpebral oedema on both eyes with conjunctival anaemic but no jaundice. There are no enlarged lymph nodes. Chest movement was symmetric, without abnormal breathing sound. From abdomen examination liver and spleen are impalpable. Four extremities are warm, and there are pitting oedema on both legs. Several laboratory examinations were performed. As seen in Table 1, serial complete blood counts were performed and found red blood cell (RBC) and haemoglobin (HGB) level below the normal range.

This result was indicating anaemic condition in the patient with normochromic normocyte anaemia. Besides, the WBC level, it's increasing and above the normal range in the third examination (Table 1). Moreover, the hematocrit level and platelet level also found below the normal range in the two of three tests, indicating thrombocytopenia condition (Table 1).

Table 1: Complete Blood Count Result

Parameter	1/8/19	6/8/19	4/9/19	Reference range
WBC	5.15	2.36	22.90	4.1 - 11.0 x 10^3/µL
Neutrophil	61.01	36.77	90.41	47.00 - 80.00 %
Lymphocytes	26.36	49.89	4.32	13.00 - 40.00 %
Monocyte	10.72	8.12	4.83	2.0 - 11.0 %
Eosinophil	0.69	4.15	0.01	0.0 - 5.0 %
Basophil	1.22	1.07	0.44	0.0 - 2.0 %
RBC	3.03	3.29	3.03	4.5 - 5.9 x 10^6/µL
HGB	7.98	8.60	8.43	13.5 - 17.5 g/dL
HCT	25.63	25.74	25.25	41.0 - 53.0 %
MCV	84.48	78.35	83.99	80.0 - 100.0 fL
MCH	26.30	26.18	27.99	26.0 - 34.0 pg
MCHC	31.13	33.46	30.99 4	31 - 36 g/dL
RDW	11.55	11.61	12.04	11.6 - 14.8 %
PLT MPV	145 5.90	215.30 5.34	43.89 6.31	150 - 440 10^3/µL 6.80-10.00 fl
%Reticulocyte	1.5			0 .61-2.24%

From urine analysis, the patient has hematuria and proteinuria with a very high level of erythrocytes at the first examination (>2 LPB) and positive protein evaluation. Urine colour found orange at the first examination but then went normal at the second and third examination with cloudy clarity (Table 2). Urine sediment showed

positive leukocytes, erythrocytes, squamous cell, cylinder cell with granule, and bacteria also found positive (Table 2).

Table 2: Urine analysis result

Parameter	1/8/19	22/8/19	6/9/2019	Reference range
Specific gravity	1.011	1.009	1.007	1.003-1.035
Clarity	Cloudy (+)	Cloudy (+)	Cloudy (+)	Clear
pH	7.00	6.50	6.00	4.5-8
Leukocytes	Negative	(2+) 75	Negative	Negative
Nitrite	Negative	Negative	Negative	Negative
Protein	(4+) OVER	(3+) 300	(3+) 600	Negative
Glucose	Negative	Negative	Negative	Negative
Ketone	Negative	Negative	Negative	Negative
Blood	(3+)	(3+)	(2+)	Negative
Urobilinogen	Normal	Normal	Normal	Normal
Bilirubin	Negative	Negative	Negative	Negative
Colour	Orange	Yellow	Light yellow	Light yellow-Yellow
Urine sediment: Leukocytes	33	41	12	≤ 2 LPB
Erythrocytes	503	213	58	≤ 2 LPB
Epithelial cell sediment:				≤ 1 LPB
Squamous	0	1	4	LPB
Cylinder	Granule+	Granule +	Granule+	LPB
Lain-lain	Bacteria+	Bacteria+	Bacteria+	LPB

From clinical chemistry examination, BUN (29.30 and 74.30 mg/dL) and creatinine level were found above the normal range (3.15 and 1.78 mg/dL). Also, the albumin level was found below the normal range (2.40 and 2.80 g/dL) indicating hypoalbuminemia condition (Table 3).

Table 3: Clinical Chemistry Analysis

Parameter	1/8/2019	4/9/2019	Reference range
BUN	29.30	74.30	8.00-23.00 mg/dL
Creatinine	3.15	1.78	0.70-1.20 mg/dL
AST	32	13.9	11.00-34.00 U/L
ALT	32.60	18.40	11.00-34.00 U/L
Albumin	2.40	2.80	3.50-4.80 g/dL

From electrolyte examination, several examinations were found above the normal range. The potassium level was found higher in every examination (4.13; 6.65; 6.47; and 6.77 mmol/L) indicating for hyperkalemia. Besides, the phosphate concentration also higher than the reference range on the 1st-day examination (4.61 mg/dL) suggest for hyperphosphatemia (Table 4). However, the immuno-serology analysis also showed positive ANA-IF with homogenous nuclear pattern with titer 1:1000 and positive anti-ds-DNA with level 317.6 IU/ml (Table 5).

Table 4: Electrolyte Analysis

Parameter	1/8/2019	4/9/2019	7/9/2019	9/9/2019	Reference range
Potassium	4.13	6.65	6.47	6.77	3.50-5.10 mmol/L
Sodium	141	139	134	137	136-145 mmol/L
Chloride	107.6	106.4	106.2	107.4	96 – 108 mmol/L
Calcium	8.3	8.3	8.9	8.1	8.4-9.70 mg/dL
Phosphate	4.61				2.5-4.5 mg/dL

Table 5: Immuno-serology Result

Parameter	1/8/2019	13/8/2019	Reference range
ASTO	Negative		Negative
ANA IF		Pattern: Nuclear Homogenous Titer 1: 1000	< 1:100
Anti- ds-DNA		317.6	< 100 IU/mL

Discussion

Systemic Lupus Erythematosus (SLE) is an autoimmune disease with various clinical manifestations as indicated by the presence of autoantibodies to the nucleus components and immune complex deposits [6].Systemic Lupus Erythematosus is characterized by chronic inflammation that can decrease the function of various organs, but the kidney is the organ that suffers the most frequent injury. This disease is more common in women in all groups and populations, the

ratio of women: men of productive age is 8: 1 to 15: 1 and has a close relationship with genetic factors [1].Prevalence ratio of SLE is higher in women than in men, but male patients seem to have a higher frequency of symptoms and more aggressive disease.

One of the most common complications of SLE is Lupus nephritis (LN). The prevalence of Lupus Nephritis (LN) in SLE varies significantly by region, race and tribe. LN is a significant risk factor that affects morbidity and mortality in SLE [2]. Although overall improvements in the treatment of SLE patients have increased in kidney survival rates (5 and 10 years of LN).

The prognosis remains unsatisfactory, a new strategy that is more sensitive and specific is needed to enable earlier action for management plans. Late diagnosis of LN can increase End-Stage Renal Disease (ESRD) [4, 7].Lupus Nephritis defined as clinical and laboratory manifestations according to the criteria of the American College of Rheumatology (ACR), an example the discovery of persistent proteinuria 0.5 g days or more than 3+ by dipstick urine examination, and or the presence of erythrocytes cylinders, haemoglobin, granular, tubular, or mixed [3].

Pathogenesis of SLE due to complex interactions between genetic and environmental factors that cause the loss of immune tolerance resulting in chronic autoimmune. Under normal conditions, immune tolerance takes place well, but the process of apoptosis which functions to clear dead cells and damaged genetic material experiences a decrease in function in SLE showing the occurrence of self-antigen exposure to the immune system. Some genetic disorders also result in decreased self-antigen clearance [8].

Kidney involvement in SLE originates from the deposition of circulating immune complexes (CIC) in kidney tissue or due to the formation of immune complexes (IC) in situ. IC deposits in kidney tissue activate the classic complement pathways, macrophages, and neutrophils through bonds between immunoglobulin complexes and receptors on the surface of phagocytic cells. Activation of the classic complement pathway forms the complement protein system (C3a and C5a), which also induces neutrophil recruitment.

Neutrophil activation will trigger the release of Reactive Oxygen Species (ROS), the production of proinflammatory cytokines, and the amplification of immune and inflammatory responses in kidney tissue [9]. Proinflammatory and profibrotic cytokines include Interleukin-4 (IL-4), transforming growth factor-beta (TGF – beta), and tumour necrosis factor (TNF). The interferon-gamma (IFN-gamma) induces podocyte injury, mesangial proliferation, endothelial and parietal epithelial cells, increasing the synthesis and deposit of extracellular matrix thereby causing kidney damage [9].

Symptoms of kidney disease in SLE vary widely, starting without symptoms (detected by kidney biopsy or called silent lupus nephritis), proteinuria trace, or active urine sediment (microscopic hematuria, pyuria or cellular cylinder). In the worst case, it can also relate to severe proteinuria (nephrotic syndrome) and acute nephritic syndrome with rapid progression to Acute Renal Failure. Some patients also came with chronic kidney failure, renal insufficiency, and hypertension as manifestations beginning [10, 11]. Initial immunosuppression therapy for class III and IV lupus nephritis usually using glucocorticoids and mycophenolate mofetil or, cyclophosphamide [6].

Nephrotic syndrome is a glomerular disease that often encountered, characterised by high levels of proteinuria, hypoalbuminemia, hyperlipidemia, (hypercholesterolemia and hyper-triglycerides) and edema [12].This is a cause of serious complication including infection, hypertension and hypercoagulability. Percentage of lupus nephritis found with symptoms nephrotic syndrome as much as 30% -70%. Nephrotic syndrome is important in prognosis lupus nephritis, which often occurs in class II-V LN. On the biopsy, it was found the relationship between the destruction of podocytes with protein.

For example, the higher levels of protein were associated with the more podocytes destroyed. The antibody complex deposits in subendothelial glomerulus or sub epithelium thought to trigger podocytes [7]. In this patient, we found hypertension, hypoalbuminemia, proteinuria, and oedema that support the diagnosis of nephrotic syndrome.

Polymorphonuclear or neutrophil cells are important mediators in the innate immune system.

Neutrophils will respond quickly if present pathogens in damaged tissue. Neutrophil accumulation will occur. Consistently and often found in early kidney damage [13].This explains the increase in leukocyte levels, especially neutrophils in this patient. Anaemia is a haematological disorder that usually occurs in SLE, defined as haemoglobin levels < 12 g/dL for women and < 13.5 g/dL for men.

Anaemia that occurs in SLE categorised as anaemic disease chronic (most common, 60-80%) iron deficiency anaemia, hemolytic anaemia, autoimmune and anaemia due to chronic renal insufficiency. Mechanism thrombocytopenia in SLE is likely due to an increasing destruction of peripheral platelets and the presence of anti-platelet antibodies [14]. Ischemia, hypertension, or failure to regenerate will result in the occurrence of renal tubular epithelial cell atrophy.

The condition of the injured tubule causes immune cell infiltration fibrosis. The latest study indicates that injured kidney tubule cells have internal weakness oxidizes fatty acids that cause mitochondrial dysfunction, and will cause cell death [5]. In the patient, found visible tubular damage in the presence of hematuria and granular cylinders in urine analysis.

In SLE, there is the production anti-dsDNA and complex antibodies immune deposits in the kidneys will result in the infiltration of immune cells and proteinuria in mice. Anti-dsDNA antibodies have also isolated from glomerular LN patients with the disease, and various histopathological patterns observed in lupus patients is the result of deposition of immune cells in the location different in the glomerulus. Nephritogenic anti-dsDNA antibodies have shown to regulate gene and protein expression in inflammatory and fibrotic mediators in kidney cells, resulting in kidney inflammation and fibrosis directly [15].

In this patient, we found increased levels of anti-dsDNA antibodies that are compatible with the diagnosis of SLE. Hyperkalemia occurs due to excessive potassium intake, disorders potassium excretion or due to transcellular shift. Decreased function kidney, drug use and hyperglycemia are several factors which are often the aetiology of hyperkalemia potassium intake. Increased will be accompanied by increased potassium excretion in healthy people, so this condition rarely results in hyperkalemia. Kidney dysfunction is the most common cause of hyperkalemia [16].

In this patient seen hyperkalemia condition, which is likely very closely related to decreased kidney function characterised by increased levels of urea and creatine. Hyperphosphatemia defined as an increase in serum phosphate levels which can be caused by hypoparathyroidism, pseudo hyperphosphatemia, excessive phosphate intake, excessive cells injury, (rhabdomyolysis and tumour lysis syndrome), intracellular shift, (metabolic or respiratory acidosis).And vitamin D toxicity [17]. However, the most common cause of hyperphosphatemia is decreased phosphate excretion due to interference kidney function [18]. In this patient, we found levels of phosphate increased, possibly due to impaired renal function due to LN.

Conclusion

The most common complication is lupus nephritis, and its prevalence varies significantly by region, race and tribe. Although overall improvements in the treatment of SLE patients have increased in kidney survival rates, the prognosis remains unsatisfactory. Early detection and diagnosis should be done so that the patient's condition worsens not occur.

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Author Contribution

All of authors are equally contributed to the study from selecting case, laboratory evaluation, until interpreting the results of case study.

References

1. Askanase A, Shum K, Mitnick H (2012) Systemic lupus erythematosus: an overview. Soc Work Health Care, 51(7): 576-586.
2. Almaani S, Meara A, Rovin BH (2017) Update on Lupus Nephritis. Clin J. Am Soc. Nephrol., 12(5):825-835.
3. Hahn BH, McMahon MA, Wilkinson A, et al (2012) American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. Arthritis Care Res, (Hoboken). 64(6):797-808.
4. Resende AL, Titan SM, Barros RT, Woronik V (2011) Worse renal outcome of lupus nephritis in male patients: a case-control study. Lupus, 20(6):561-567.
5. Davidson A (2016) What is damaging the kidney in lupus nephritis?. Nat. Rev. Rheumatol., 12(3):143-153.
6. Kado R (2018) Systemic Lupus Erythematosus for Primary Care. Prim Care, 45(2):257-270.
7. Gomez Mendez LM, Cascino MD, Katsumoto TR, et al (2019) Outcome of participants with nephrotic syndrome in combined clinical trials of lupus nephritis. Lupus Sci. Med., 6(1):e000308.
8. Anders HJ, Rovin B (2016) A pathophysiology-based approach to the diagnosis and treatment of lupus nephritis. Kidney Int., 90(3):493-501.
9. Pinheiro SVB, Dias RF, Fabiano RCG, Araujo SA, Silva ACSE (2019) Pediatric lupus nephritis. J. Bras. Nefrol., 41(2):252-265.
10. Mok CC (2012) Understanding lupus nephritis: diagnosis, management, and treatment options. Int. J. Women's Health., 4: 213-222.
11. Markowitz GS, D'Agati VD (2007) The ISN/RPS 2003 classification of lupus nephritis: an assessment at 3 years. Kidney Int., 71(6):491-495.
12. Macé C, Chugh SS (2014) Nephrotic syndrome: components, connections, and angiopoietin-like 4-related therapeutics. J. Am Soc. Nephrol., 25(11):2393-2398.
13. Kinsey GR, Okusa MD (2012) Role of leukocytes in the pathogenesis of acute kidney injury. Crit. Care, 16(2):214.
14. Bashal F (2013) Hematological disorders in patients with systemic lupus erythematosus. Open Rheumatol. J., 7: 87-95.
15. Yung S, Chan TM (2015) Mechanisms of Kidney Injury in Lupus Nephritis - the Role of Anti-dsDNA Antibodies. Front Immunol., 6: 475.
16. Viera AJ, Wouk N (2015) Potassium Disorders: Hypokalemia and Hyperkalemia. Am Fam Physician, 92(6):487-495.
17. Shaman AM, Kowalski SR (2016) Hyperphosphatemia Management in Patients with Chronic Kidney Disease. Saudi Pharm J., 24(4):494-505.
18. Savica V, Calò LA, Granata A, et al (2007) A new approach to the evaluation of hyperphosphatemia in chronic kidney disease. Clin Nephrol., 68(4):216-221.

