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Secondary Glomerulonephritis With Peripheral Arterial Disease Due To Systemic Lupus Erythematosus

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ABSTRACT
Glomerulonephritis (GN) is a heterogeneous disorder characterized by glomerular compartment damage of the nephron mediated by autoimmunity. Secondary GN can occur for the patients with systemic autoimmune disease and has higher prevalence of peripheral artery disease. Symptoms and signs of GN are characterized by periorbital oedema accompanied by leg oedema, massive proteinuria, decreased renal function, hypertension, hematuria and erythrocyte casts. We reported a 40 years old female patient found with anasarca oedema, pain in the right foot, and proteinuria who had a history of systemic lupus erythematosus for 7 years. On physical examination, we found hypertensive urgency, anasarca oedem and blackish ulcus on the dorsal pedis extremity dextra. Laboratory data showed hypoalbuminemia, hypernatremia, creatinine clearance 19.38 ml/min, and albumin creatinine ratio 18.949 mg albumin/gr cr, ANA profile arthritis + 4.2. Urynalysis showed massive proteinuria, erythrocytes and casts were present. CT angiography showed the impression of peripheral artery disease.

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INTRODUCTION

Glomerulonephritis (GN) is a heterogeneous disorder characterized by damage to the glomerular compartment of the nephron in the kidney mediated by autoimmunity with clinical oedema, proteinuria, hematuria and erythrocyte cylinders, decreased renal function, and hypertension (Anders et al., 2023). The relationship between autoimmunity and GN is closely related to anti-nucleus autoantibodies. One of the research evidence in Australia shows GN cases associated with autoimmune reactivation over 7-years period obtained as many as 22 patients consisting of 12 patients (54%) GN, who have positive autoimmune serology and 10 people (46%) have negative autoimmune disease (Choung & Grewal, 2022).

Vascular involvement often occurs in Systemic Lupus Erythematosus (SLE) patients, one of which is vasculitis. Vasculitis is related to complex interactions between vascular endothelium, inflammatory cells, cytokines, autoantibodies and immune complexes resulting in inflammation (Leone et al., 2021). Sherif et al's study, a total of 565 SLE patients (42 men, 523 women) with an age range of 13 years to 63 years, there were 191 patients proven to have SLE with vasculitis (Gamal et al., 2021).

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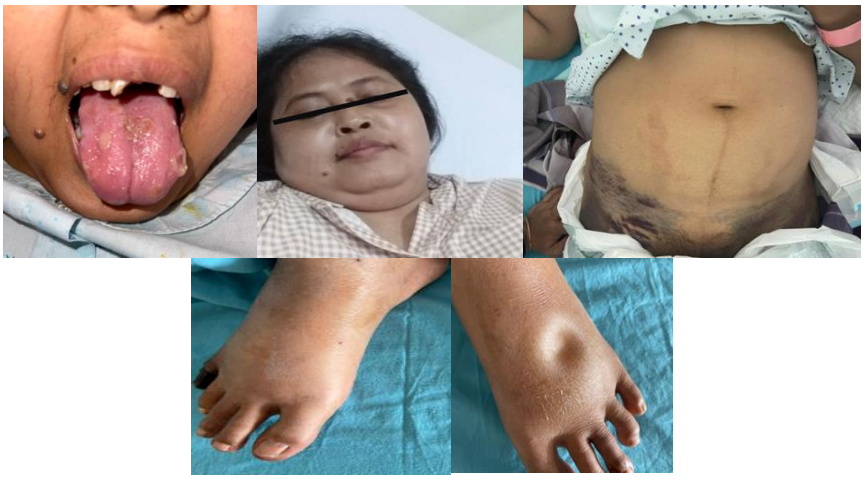
Peripheral Artery Disease (PAD) is also a vascular complication of SLE because immune complexes can trigger inflammation until ischemia occurs. Patients with GN have a higher incidence and prevalence of PAD. PAD often occurs in patients with decreased renal function associated with inflammation in the kidneys characterized by albuminuria. Jay et al's research in America found that the prevalence of GN with PAD was found in 4.3% of the adult population over 40 years of age (Shah et al., 2022). Chau and Hui's research in Australia found that patients with mild to moderate Chronic Kidney Disease (CKD) also increased the risk of developing PAD by 1.5 to 4 times (Chau L B Ho, Hui J Chih, Pranav S Garimella, Kunihiro Matsushita, Shirley Jansen, Christopher M ReidChau L B Ho, Hui J Chih, Pranav S Garimella, Kunihiro Matsushita, Shirley Jansen, 2021). Management of GN with SLE (often referred to as lupus nephritis) consists of specific treatment directed against SLE in the form of corticosteroids and immunosuppressants and non-specific treatment to inhibit the disease progression of glomerulonephritis (Foster & Ord, 2019).

CASE

Mrs. RA, 40 years old, complained of swelling of the whole body accompanied by foamy and cloudy urine since 2 months before admission to the hospital on June 03, 2022. The complaint was accompanied by pain and numbness in the right toe. Initially, the little toe of the right foot turned red, blue, and then going to black. Hair loss and recurrent mouth ulcers did not heal were also found in the patient. The patient has a history of hypertension and SLE since 2015. Before being referred to Arifin Achmad General Hospital Pekanbaru, the patient had undergone hemodialysis 4 times at Indrasari Hospital in Rengat. The patient's child has a history of nephrotic syndrome and the patient's parents have a history of hypertension.

On physical examination, it was found that the general condition appeared to be moderately ill, composmentis consciousness, 55 kg BW, 155 cm HB, with the calculation of dry weight (actual weight-corrected oedema) which was 33 kg with a body mass index was 13.7, the interpretation was underweight. Blood pressure 180/108 mmHg, pulse frequency 70 bpm, temperature 36.9 °C, and anasarka oedema. There were shallow ulcers on the tongue, convex abdomen, shifting dullness (+). On the dorsal extremity of digiti V pedis dextra there is a blackish ulcer.



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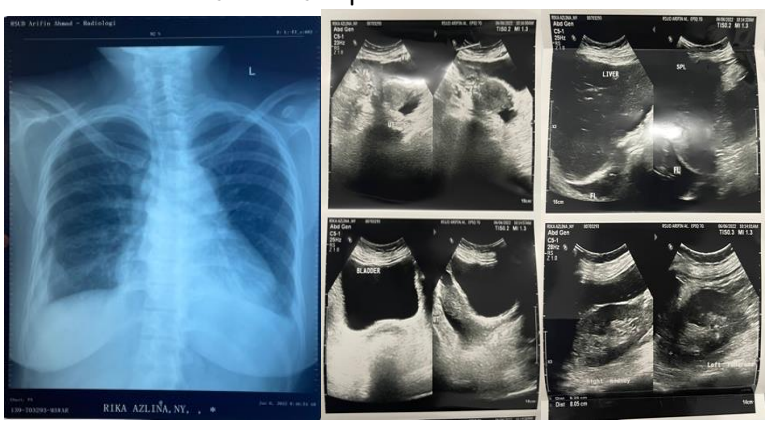
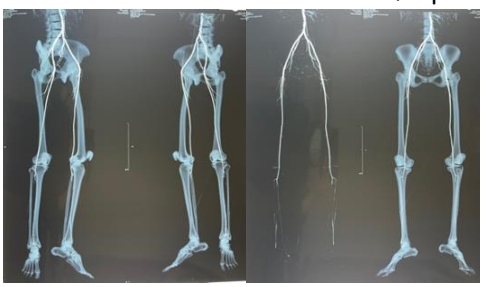
Calculation of ABI Score, the result was 0.83 with the interpretation of Mild to Moderate Peripheral Artery Disease. Laboratory examination showed hemoglobin 10.7 gr/dl, leukocytes 4,000/µL, platelets 18,000/µL, hematocrit 34.4%, albumin 2.4 gr/dl, sodium 152 mmol/l, ureum 137 mg/dl, and creatinine 2.01 mg/dl, ANA profile arthritis +4.2, creatinine-clearance with Cockcroft-Gault formula obtained 19.38 ml/min, the interpretation including category of "stage 4 severe for CKD". Albumin creatinine ratio was found to be 18.949 mg albumin/gr creatinine with interpretation including the category of "severely increased for CKD". Urine examination was found protein +3 and blood +2, urine sediment was found erythrocytes 15-20 /hpf and cylinders was positive. Chest photo was found cardiomegaly with a CTR of 54% and bilateral minimal pleural effusion and abdominal ultrasound examination obtained fluid collection in the pelvis.



CT-Angiography examination of the inferior extremities revealed PAD with stenosis of bilateral distal anterior tibial arteries and bilateral middle 1/3 peroneal arteries.



From the anamnesis data, physical examination and laboratory, the diagnosis of this patient is secondary glomerulonephritis with peripheral arterial disease due to SLE with Stage II Hypertension, Bisitopenia, Hypoalbuminemia, Hypernatremia.

The management given to this patient includes daily protein intake around 26.4 grams / day, a low sodium diet, and fluid retriction of less than 1 liter/day. For 3 days, the patient was given corticosteroid; pulse methylprednisolone 125 mg IV/day followed by methylprednisolone tablets 16 mg 3x1, immunosuppressants such as cyclosporine tablets 50 mg 2x1, spironolactone tablets 100 mg 1x1, candesartan tablets 8 mg 1x1, and amlodipine tablets 10 mg 1x1. For PAD, it has been consulted with a vascular surgeon but there is no action plan yet.

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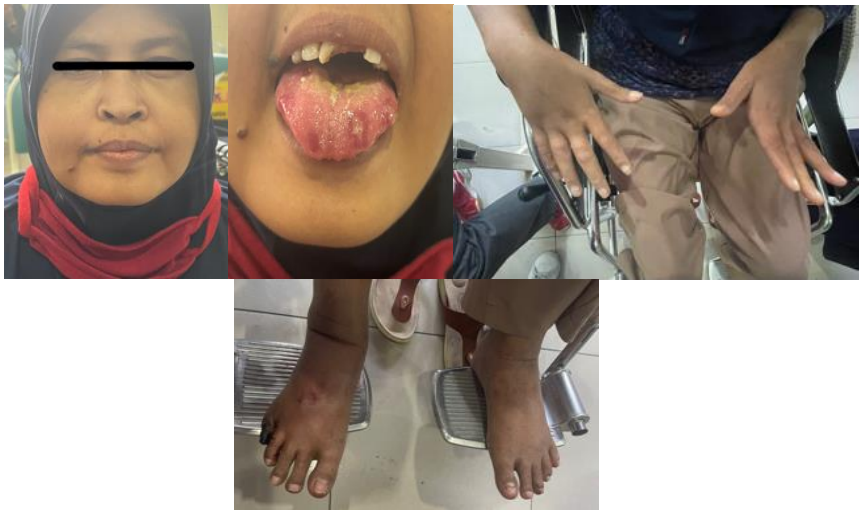
The last day of the patient's treatment, laboratory tests were showed hemoglobin 12.4 g/dl, leukocytes 9,420/µL, platelets 137,000/µL, hematocrit 36%, sodium 136 mmol/l, ureum 42 mg/dl and creatinine 0.64 mg/dl. Creatinine clearance calculations showing improvement (60.8 ml/min) including the category “stage 2 mild interpretation for CKD”. The patient was improved and discharged with medications were methylprednisolone tablets 8 mg 3x1, cyclosporine tablets 50 mg 2x1, candesartan tablets 8 mg 1x1, amlodipine tablets 10 mg 1x1, aspilet tablets 80 mg 1x1, and clopidogrel tablets 75 mg 1x1.



Two weeks after being discharged, the patient visited the internal medicine clinic with clinical improvement. There was no oedema on the body, no nausea and vomiting, ulcers on the tongue and feet were reduced. This patient did not undergo routine hemodialysis due to acute on CKD improvement.

Discussion

Female, 40 years old found elevated blood pressure, hypoalbuminemia, proteinuria, and found erythrocyte cylinders in the urine. Protein loss in GN is due to increased filtration of macromolecules through the glomerular capillary wall resulting in cloudy urine (Kim et al., 2024). Dysmorphic erythrocytes or erythrocyte cylinders in the urine, indicating glomerular hematuria. The thick part of the ascending henle arch secretes a mucoprotein called uromodulin, and this mucoprotein will turn into a gel substance and all the protein cells in the filtrate will be trapped during cylinder formation and form erythrocyte cylinders (Anders et al., 2023)(Kim et al., 2024).

The creatinine clearance calculation at the time of admission was 19.38 ml/min. Based on KDIGO, this patient is already at stage 4 severe for CKD (*KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease 2023*, 2023). The last day of patient care, the results of creatinine clearance was 60 ml/min with the interpretation of stage 2 mild for CKD, so it is concluded that the patient has Acute on CKD improvement. Acute Kidney Impairment (AKI) is a condition where there is an increase in serum creatinine and a decrease in glomerular filtration rate. In the state of AKI, serum creatinine is not stable. In the unstable state, there is a pause before the rise in serum levels because it takes time for the retention of endogenous filtration markers. Acute on CKD is a AKI patient who had previous

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Chronic Kidney Disease (CKD) in which there is a change in autoregulation of glomerular blood flow, hence the need for repeated creatinine tests for evaluation (Gilbert, 2018). Research by Darwin et al in the Intensive Care Unit (ICU) over the past 5 years, out of 401 CKD, there were 210 patients experiencing acute on CKD improvement by evaluating creatinine (Tejera et al., 2017).

The patient has a history of SLE which is a prototypical systemic autoimmune disease in which almost 100% of patients will experience renal manifestations (Casuscelli et al., 2023). The occurrence of inflammation in the kidneys is related to autoimmunity in patients. The autoimmune response in the kidneys is most often initiated by immune cell infiltration. Infiltrating cells including neutrophils, T cells, macrophages and platelets secrete soluble mediators and interact with cells in the kidney, causing abnormalities (Vaglio et al., 2023).

Research Augusto et al, that 50% of patients who have proteinuria can progress to end-stage renal disease (Vaglio et al., 2023). Research Jiaping Qi et al in China, for 10 years obtained 19.5% of 154 lupus nephritis patients occurred end-stage chronic kidney disease (Qi et al., 2024). From the research of Yuqiang et al in China, that SLE patients have a 10-fold greater risk of developing End Stage Renal Disease (ESRD) compared to non-SLE patients (Chen et al., 2022).

Patients with CKD have a higher incidence and prevalence of PAD due to atherosclerosis aggregation factors. In Northern Nigeria, the prevalence of GN with PAD in the adult population over 40 years old was 44.4%. The risk of PAD increases with a decrease in glomerular filtration rate (GFR) which is a marker of metabolic conditions, associated with progressive vascular dysfunction. In addition to GFR, albuminuria is also a marker of endothelial dysfunction which is associated with medial artery calcification leading to increased ABI (Ovwasa et al., 2023).

To complete the supporting diagnosis of glomerulonephritis, one of them is a kidney biopsy. Renal biopsy can determine the exact etiology of glomerulonephritis that occurs (Gilbert, 2018). From the case of this patient, it is suspected as a case of lupus nephritis. Due to the limited facilities for histopathological biopsy examination, this examination cannot be carried out.

Specific treatment for patient was given for 3 days pulse methylprednisolone IV 125 mg / day and cyclosporine 2x50 mg which can be given as a combination of steroids at a dose of 2-3 mg / kg / day, followed by methylprednisolone at a dose of 3x16 mg, because this patient has an autoimmune disease aimed at achieving a state of remission of disease activity characterized by resolution of hematuria, cellular crystals, and serum creatinine concentrations (Anders et al., 2023)(*Buku Ajar Ilmu Penyakit Dalam, Edisi VI*, n.d.).

A combination of CCB-dihydroperidine (amlodipine) and ARB (candesartan) was given as renal anti-hypertension which can reduce intra-glomerular pressure and can also reduce protein levels in the urine (Selly Septi Fandinata, Rizky Darmawan, Primanitha Ria Utami, 2022)(*KDIGO Clinical Practice Guideline for the Management of Glomerular Disease 2021*, 2021). On the last day of treatment, there was clinical improvement with laboratory results and creatinine clearance calculations showing improvement. In patients with CKD, blood

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creatinine levels can improve after treatment of the underlying disease and can reduce the potential for kidney damage to achieve a degree of recovery (Efros et al., 2023).

CONCLUSION

A female case was reported, diagnosed with glomerulonephritis secondary with peripheral arterial disease due to *SLE*. The patient had clinical improvement and the last laboratory result of the treatment showed normal results. Calculation of creatinine clearance was initially 19.38 ml/min, after therapy change to 60.8 ml/min, the patient going to acute on CKD improvement. The patient can be discharged and was given methylprednisolone tablets 8 mg 3x1, cyclosporine tablets 50 mg 2x1, candesartan tablets 8 mg 1x1, amlodipine tablets 10 mg 1x1, aspilet tablets 80 mg 1x1, and clopidogrel tablets 75 mg 1x1. At post-treatment control, the patient's clinical condition improved so that routine hemodialysis was not performed and only conservative therapy was given.

REFERENCE

Anders, H. J., Kitching, A. R., Leung, N., & Romagnani, P. (2023). Glomerulonephritis: immunopathogenesis and immunotherapy. In *Nature Reviews Immunology* (Vol. 23, Issue 7). https://doi.org/10.1038/s41577-022-00816-y

Buku ajar ilmu penyakit dalam, edisi VI. (n.d.).

Casuscelli, C., Longhitano, E., Maressa, V., Di Carlo, S., Peritore, L., Di Lorenzo, S., Calabrese, V., Cernaro, V., & Santoro, D. (2023). Autoimmunity and Infection in Glomerular Disease. In *Microorganisms* (Vol. 11, Issue 9). https://doi.org/10.3390/microorganisms11092227

Chau L B Ho, Hui J Chih, Pranav S Garimella, Kunihiro Matsushita, Shirley Jansen, Christopher M ReidChau L B Ho, Hui J Chih, Pranav S Garimella, Kunihiro Matsushita, Shirley Jansen, C. M. R. (2021). Prevalence and risk factors of peripheral artery disease in a population with chronic kidney disease in Australia: A systematic review and meta-analysis. *Nephrology (Carlton)*, *26*(10), 798–808. https://doi.org/10.1111/nep.13914

Chen, Y., Zhang, L., Xue, Q., & Wang, N. (2022). Infection profile and risk factors for mortality in patients with end-stage renal disease attributable to systemic lupus erythematosus: a two-center integrated study. *Journal of International Medical Research*, *50*(8). https://doi.org/10.1177/03000605221118702

Choung, H. Y. G., & Grewal, R. (2022). Autoimmunity in Infection-Related Glomerulonephritis. *Glomerular Diseases*, *3*(1). https://doi.org/10.1159/000528712

Efros, O., Beckerman, P., Basson, A. A., Cohen, R., Klang, E., Frenkel Nir, Y., Soffer, S., Barda, N., & Grossman, E. (2023). Fluctuations in Serum Creatinine Levels during Hospitalization and Long-Term End-Stage Kidney Disease and Mortality. *JAMA Network Open*, *6*(8). https://doi.org/10.1001/jamanetworkopen.2023.26996

Foster, M. H., & Ord, J. R. (2019). Emerging immunotherapies for autoimmune kidney disease. In *Human Vaccines and Immunotherapeutics* (Vol. 15, Issue 4). https://doi.org/10.1080/21645515.2018.1555569

Gamal, S. M., Mohamed, S. S., Tantawy, M., Siam, I., Soliman, A., & Niazy, M. H. (2021). Lupus-

related vasculitis in a cohort of systemic lupus erythematosus patients. *Archives of Rheumatology*, *36*(4). https://doi.org/10.46497/ARCHRHEUMATOL.2021.8804

Gilbert, S. J. & D. E. W. (2018). *National Kidney Foundation' s Primer on Kidney Diseases* (6th ed.). https://doi.org/https://doi.org/10.1016/C2015-0-05403-X

KDIGO Clinical practice guideline for the evaluation and management of chronic kidney disease 2023. (2023).

KDIGO Clinical Practice Guideline for the Management of Glomerular Disease 2021. (2021).

Kim, H., Hyun, Y. Y., Joo, Y. S., Yun, H. R., Kim, Y., Jung, J. Y., Jeong, J. C., Kim, J., Park, J. T., Yoo, T. H., Kang, S. W., Oh, K. H., & Han, S. H. (2024). Proteinuria, measured or estimated albuminuria for risk prediction in patients with chronic kidney disease? *Nephrology, Dialysis, Transplantation : Official Publication of the European Dialysis and Transplant Association - European Renal Association*, *39*(3). https://doi.org/10.1093/ndt/gfad195

Leone, P., Prete, M., Malerba, E., Bray, A., Susca, N., Ingravallo, G., & Racanelli, V. (2021). Lupus vasculitis: An overview. In *Biomedicines* (Vol. 9, Issue 11). https://doi.org/10.3390/biomedicines9111626

Ovwasa, H., Aiwuyo, H. O., Okoye CA, Ogochukwu, Umuerri, E. M., Obasohan, A., Unuigbe, E., & Rajora, N. (2023). Prevalence and Predictors of Peripheral Vascular Disease Amongst Predialysis Hypertensive Chronic Kidney Disease Patients in Southern Nigeria. *Cureus*. https://doi.org/10.7759/cureus.36752

Qi, J., Wu, T., Wang, J., Zhang, J., Chen, L., Jiang, Z., Li, Y., Jiang, H., Sun, Q., Gu, Q., & Ying, Z. (2024). Research trends and frontiers in lupus nephritis: a bibliometric analysis from 2012 to 2022. *International Urology and Nephrology*, *56*(2). https://doi.org/10.1007/s11255-023-03715-w

Selly Septi Fandinata, Rizky Darmawan, Primanitha Ria Utami, N. M. U. (2022). Monitoring Kidney Function Through the Use of Candesartan, Telmisartan or Valsartan Antihypertensive Therapy towards Patients CKD. *Media Kesehatan Masyarakat Indonesia*, *18*(1).

Shah, J., Luthra, K., Ghumman, G. M., Al-Dabbas, M., Ahsan, M., Avula, S., Ali, S. S., Kabour, A., & Singh, H. (2022). Impact of systemic lupus erythematosus on in-hospital outcomes of peripheral artery disease—insight from the National Inpatient Sample database. In *Baylor University Medical Center Proceedings* (Vol. 35, Issue 6). https://doi.org/10.1080/08998280.2022.2096361

Tejera, D., Varela, F., Acosta, D., Figueroa, S., Benencio, S., Verdaguer, C., Bertullo, M., Verga, F., & Cancela, M. (2017). Epidemiology of acute kidney injury and chronic kidney disease in the intensive care unit. *Revista Brasileira de Terapia Intensiva*, *29*(4). https://doi.org/10.5935/0103-507X.20170061

Vaglio, A., Gattorno, M., McAdoo, S., Obici, L. P., & Ghiggeri, G. M. (2023). Editorial: The kidney in auto-immune and auto-inflammatory processes: Definitions, mechanisms, and biomarkers. In *Frontiers in Medicine* (Vol. 9). https://doi.org/10.3389/fmed.2022.1129021