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Case report

A pregnancy with nephrotic syndrome: A rare case

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ABSTRACT

Introduction: Systemic lupus erythematosus (SLE) found during pregnancy is often flared SLE.
Case presentation: This study reported a 23-year-old woman diagnosed with nephrotic syndrome with an 18/19-week pregnancy. The cause of nephrotic syndrome must be established by ruling out all possible secondary causes, especially in pregnancy with preeclampsia which can also occur with proteinuria. In lupus nephritis, renal biopsy as the standard gold examination plays a role in determining further management and the prognosis of the patient's future renal function. A kidney biopsy is recommended if the urinary protein excretion exceeds 500 mg/24 h with the aim of early detection and treatment to prevent long-term complications to the kidneys.
Discussion: Management of nephrotic syndrome in pregnancy used corticosteroid and immunosuppressive.
Conclusion: Pregnancy prognosis in women with active SLE is generally poor, with a high risk of miscarriage.

1. Introduction

Nephrotic syndrome is a collection of clinical symptoms consisting of peripheral edema, severe proteinuria, hypoalbuminemia, and often accompanied by hyperlipidemia. Patients usually present with peripheral edema and fatigue without any history of heart failure or severe liver disease [1,2]. Nephrotic syndrome in pregnancy is most precipitated by preeclampsia, type 2 diabetes mellitus, and/or systemic lupus erythematosus (SLE). The incidence of nephrotic syndrome in pregnancy is around 0.012–0.025 % of all pregnancy cases [3,4]. Based on this description, this study aimed to report nephrotic syndrome in Indonesian female pregnancy. The report is based on SCARE 2020 guidelines [5].

2. Case presentation

An Indonesian female, 18/19-week pregnant, 23 years old, complained of dyspnea and swellings on both feet and hands. The swellings initially started on both feet, followed by both hands. The patient had no swelling on her face. However, she felt heaviness in both of her eyes every morning. The medical history showed she was diagnosed 2 years ago. The patient received methylprednisolone with varying doses, Furosemide, hypertension drugs, and albumin capsules. However, the drugs were not routinely consumed. The patient had no complaints and stopped taking the medication for one year.

On physical examination, the patient showed a general condition of weakness and respiratory rate (RR) of 24×/min with a rapid breathing pattern. The examination of the extremities revealed pitting edema on both feet and hands, warm and dry acral, and no palmar erythema nor petechiae. Obstetric examination showed the patient's uterine fundal height was 13 cm, and the fetal heart rate was 148×/min with breech presentation and no contraction. The examination concluded: that $G_{II}P1001$ is a single live intrauterine fetus at 18/19 weeks of gestation. The laboratory results were as follows: Hb of 7.5 g/dL, hematocrit of 21 %, leukocytes of 18,530/mm^3 (neutrophils of 89.0 % and lymphocytes of 8.8 %), platelets of 256,000/mm^3, erythrocyte sedimentation rate (ESR) of 18 mm/h, creatinine of 2.79 mg/dL, blood urea nitrogen (BUN) of 96 mg/dL, albumin of 1.85 g/dL, and normal electrolyte value. HBsAg and HIV rapid tests were non-reactive. The urinalysis results were as follows: the urine specific gravity was 1.015, pH 5, leukocytes +1, protein +4, yellow in color, clear clarity, +5 erythrocytes, erythrocytes (microscopic) >100/field of view, leukocytes (microscopic) 2–5/field of view, little epithelium/field of view. The blood gas analysis showed pH of 7.36, pCO2 of 23.0 mm Hg, pO2 of 149.0 mm Hg, HCO3 of 13.0 mmol/L, TCO2 of 13.7 mmol/L, BE of −12.4 mmol/L, SO2 of 99 %, and temperature of 37.0 °C.

The patient's diagnosis was a nephrotic syndrome with acute kidney injury and $G_{II}P_{1001}$ at 18/19 weeks of gestation. The therapy included oxygen therapy, a high-calorie diet with adequate protein (0.8 g/kg/day) and low salt, 20 % albumin transfusion of 100 mL/4 h, folic acid of

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400 μg/day, and Furosemide 20 mg/12 h. The monitoring plan included complaints, vital signs, urine production, complete blood count, and post-correction albumin.

On the third day, the patient said the dyspnea had improved, but the swellings on both feet and hands remained. The laboratory examination showed increased serum creatinine of 3.91 mg/dL, BUN of 76.0 mg/dL, albumin of 1.9 g/dL, total cholesterol of 222 mg/dL, HDL of 18 mg/dL, triglycerides of 447 mg/dL, LDL of 118 mg/dL, ANA test of 129.3, C3 of 63.1, and C4 of 32.9. Protein excretion was examined using the Esbach test with 6.75 g/24 h. The patient was observed for renal function for 3 days. If there was no improvement, then the pregnancy should be terminated. The patient received another albumin transfusion and continued other therapies. On the seventh day, the results of blood and urine cultures were sterile. The patient underwent a urological ultrasound examination, showing bilateral parenchymal kidney disease with an unclear cortex echo limit in both kidneys (Fig. 1). The patient received an additional aspilets of 80 mg/day and a 20 % albumin transfusion of 100 mL/4 h. The patient had a pregnancy termination and underwent a spontaneous abortion.

On the thirteenth day, the patient complained of weakness and both legs were still swollen, but the dyspnea had disappeared. The vital sign showed stability, such as blood pressure (BP) of 130/80 mm Hg, pulse rate of 98×/min, RR of 18×/min, and temperature of 36.5 °C. Urine production of 3000 mL/day and SpO2 of 98 % without oxygen therapy. The laboratory results were included Hb of 11.5 g/dL, leukocytes of 14,570/mm^3, platelets of 200,000/mm^3, hematocrit of 34.8 %, serum creatinine of 3.18 mg/dL, BUN of 53.0 mg/dL, and albumin of 2.3 g/dL. Esbach's test showed 12 g of protein excretion per 24 h. The patient received a 20 % albumin of 100 mL/4 h, methylprednisolone 500 mg/day for 3 days, omeprazole of 40 mg/12 h, and lisinopril of 5 mg. The patient had received an explanation regarding the treatment with cyclophosphamide. However, the patient and her family refused after being aware of the side effects that could affect female fertility.

On the eighteenth day, there were minimal swellings of both legs. The laboratory results (after receiving the pulse dose of methylprednisolone) showed improvement in serum creatinine of 1.65 mg/dL, BUN of 25.0 mg/dL, and albumin of 2.5 g/dL. The ANA profile examination showed SS-A native +++ antigen, Ro-52 recombinant +, and Ribosomal Protein +. The methylprednisolone dose was tapered off to 62.5 mg for 2 days. The patient was discharged with a prescription of methylprednisolone of 16 mg/day, irbesartan of 150 mg, spironolactone of 25 mg, furosemide of 40 mg, and simvastatin of 20 mg every 24 h. The dose of methylprednisolone would be tapered off, and a kidney biopsy at the nephrology clinic was planned. A kidney biopsy was performed. The patient complained of swellings on both legs (sometimes exacerbated by tiredness) and foamy urine. The urinalysis results still showed +4 proteinuria. The biopsy showed a microscopic image of the tubules within normal limits at the interstitial it appeared as an inflammatory cell. The immunofluorescence of IgG, IgM, IgA, C3, and C1q showed an image of immune deposits on the vascular wall and mesangial (Fig. 2). The patient's diagnosis was class II Lupus Nephritis. The patient then continued the treatment at the nephrology clinic with a prescription of methylprednisolone 4 mg/day, spironolactone of 25 mg, Furosemide of 40 mg, simvastatin of 20 mg, as well as an increase in the irbesartan to 300 mg, and mycophenolate mofetil 500 mg/12 h.

3. Discussion

In pregnancy, there would be a significant physiological shift in hemodynamics and the immune system. The immediate hemodynamic changes in pregnancy include increased blood volume, decreased systemic vascular resistance, and increased cardiac output. This causes intravascular underfilling and triggers volume retention mechanisms, including changes in antidiuretic hormone secretion and activation of the renin-angiotensin-aldosterone system [6,7]. Pregnancy-related acute kidney injury (AKI) in young women worldwide is one factor that exacerbates the morbidity and mortality rates of mothers and neonates. AKI is defined as a sudden decrease in renal function, with the serum creatinine value or the amount of urine production as diagnostic parameters, which can be due to pre-renal, renal, and post-renal factors. Some causes of pre-renal AKI are insufficient intravascular volume, hypotension, sepsis, shock, over diuresis, heart failure, or drugs such as NSAIDs, diuretics, and others. To date, there are no definite criteria for AKI in pregnant patients. Based on KDIGO, AKI is defined as an increase in serum creatinine ≥0.3 mg/dL within 48 h or an increase in serum creatinine ≥1.5 times the expected value within the last 7 days, or the amount of urine production <0,5 cm^3/kg/h within 6 h [8,9].

Abnormalities in the innate and adaptive immune systems contribute to the pathogenesis of lupus nephritis. Circulating immune complexes can settle in the glomerulus or may form in-situ if autoantibodies target intrinsic glomerular antigens (such as annexin 2) or antigens released during apoptosis and/or appear when debris from the apoptotic process (including chromatin) is not entirely cleared. The intraglomerular immune complex can activate complement and attach to the leukocyte Fc receptors, causing inflammation and intrarenal injury [7,10].

Management of minimal change disease includes initial and follow-

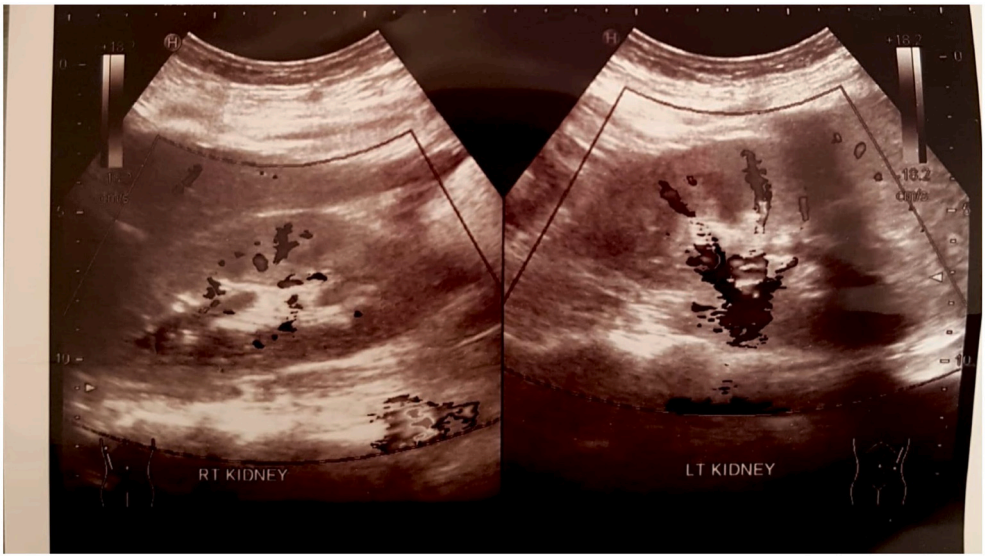

Fig. 1. Renal ultrasound result.

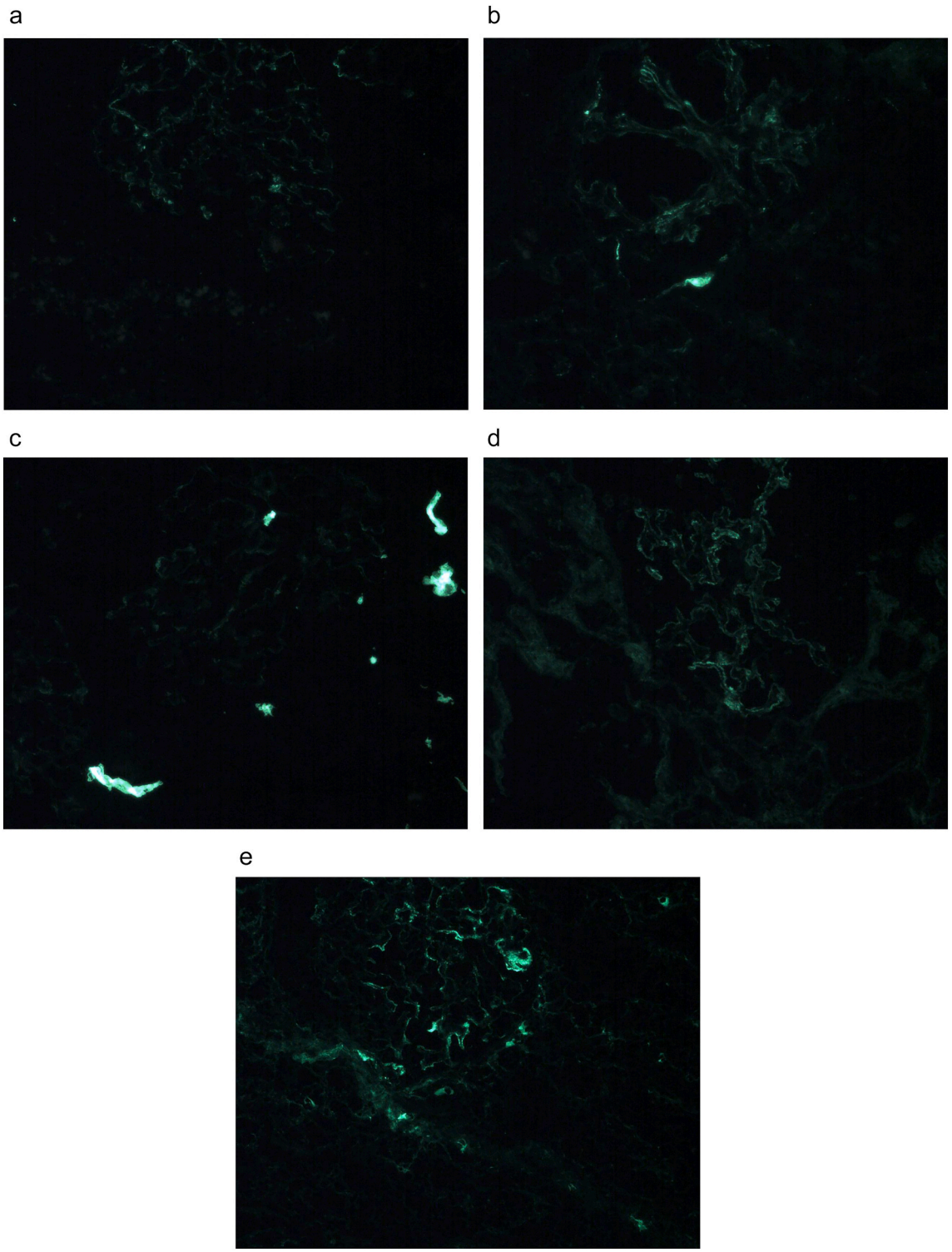

Fig. 2. Results of patient's immunohistochemistry.

up therapy for frequent relapsing and steroid-dependent conditions. As initial therapy, high doses of corticosteroids are given. In more advanced conditions that do not achieve remission, the choice of drugs given is cyclophosphamide, tacrolimus, or mycophenolate mofetil in patients who are intolerant of steroids cyclophosphamide and/or calcineurin inhibitors [8]. Corticosteroids have short- and long-term benefits for membranous nephropathy in adults with nephrotic syndrome. However, their use should be monitored and tapered off. The dose that can be used is 0.25-1 g of methylprednisolone/day for 1–3 days, followed by tapering until it reaches a minimum dose that can suppress disease activity [7]. Immunosuppressive therapy for nephrotic syndrome secondary to SLE is very effective and has been supported by many studies. Immunosuppressive is used in conjunction with corticosteroids which are slowly reduced. Some recommended immunosuppressants are oral cyclophosphamide, mycophenolate mofetil, mycophenolate sodium, and azathioprine [1,4,11].

Complications of nephrotic syndrome include hyperlipidemia, hypercoagulability, increased risk of infection, and end-stage renal failure.

Therefore, immunosuppressive alone is not sufficient to maintain kidney function. Treatment of other comorbid symptoms requires adequate therapy. Some experts recommend limiting sodium intake to <3 g and fluids <1500 mL/day as dietary management. Administration of anti-proteinuric therapy blocks the renin-angiotensin-aldosterone system with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, strict BP control, and improving other metabolic conditions have been shown to play roles in preventing further deterioration of kidney function. Reduced serum protein in nephrotic syndrome limits the effectiveness of loop diuretics. Therefore, patients may require higher than normal doses. Furosemide 40 mg twice daily is the recommended starting dose with a maximum dose of 600 mg/day. If the clinical response is inadequate, the patient can be given intravenous diuretics, thiazide, or 20 % albumin intravenous bolus beforehand [1,7].

4. Conclusion

SLE flares in women often occur when they are pregnant. Adherence to treatment plays an essential role because pregnancy prognosis in women with active SLE is generally poor, with a high risk of miscarriage.

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Consent

Written informed consent was obtained from the patient/guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Declaration of competing interest

Andi Ratna Kartika Maharani and Nunuk Mardiana declare that they have no conflict of interest.

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