CLINICAL CHARACTERISTICS AND LABORATORY PARAMETERS OF LUPUS NEPHRITIS WITH IGA NEPHROPATHY: A CASE SERIES AND LITERATURE REVIEW OF ATYPICAL LUPUS NEPHRITIS REMISSION

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ABSTRAK

Secara global, insidensi LN terjadi pada 20–65% kasus SLE. Meskipun LN merupakan komplikasi utama SLE, glomerulopati yang disebabkan oleh etiologi lain pada pasien SLE merupakan temuan yang jarang terjadi. Studi tentang koeksistensi sindrom nefritik seperti nefropati IgA (IgAN) dengan LN sebagai sindrom nefrotik saat ini masih jarang. Dalam studi ini, penulis menyajikan penilaian, terapi, dan evaluasi gejala dari tiga kasus LN dengan hasil histopatologi biopsi ginjal yang didominasi oleh endapan IgA. Studi ini ditulis menurut kriteria pelaporan Case Report Guidelines (CARE). Pengumpulan data meliputi informasi demografi, gejala klinis, tes laboratorium darah, urinalisis, analisis histologis biopsi ginjal, ultrasonografi ginjal (USG), dan terapi. Tanda-tanda klinis dan pengujian laboratorium dilakukan sebelum biopsi serta pada bulan pertama dan ketiga setelah memulai pengobatan. Ketiga kasus tersebut memenuhi kriteria diagnostik untuk SLE yang ditetapkan dalam pedoman European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) tahun 2019. Studi ini melaporkan tiga kasus nefropati IgA pada pasien nefritis lupus. Evaluasi dalam waktu tiga bulan setelah pengobatan menunjukkan prognosis yang baik. Kombinasi metilprednisolon, asam mikofenolat, dan ACEI terbukti berhasil menginduksi remisi gejala dan perbaikan hasil laboratorium. Saat ini, belum ada rekomendasi yang ditetapkan untuk penanganan IgAN dan LN yang terjadi bersamaan. Investigasi lebih lanjut terhadap kasus histopatologi serupa dan studi yang lebih luas tentang pengobatan IgAN dalam konteks SLE mungkin diperlukan.

Kata kunci : karakteristik, laboratorium, parameter nefritis lupus

ABSTRACT

Globally, incidence of LN occurs in 20–65% of SLE cases. Although LN is a major complication of SLE, glomerulopathy caused by other etiologies in SLE patients is an uncommon finding. Studies on the co-existence of nephritic syndromes such as IgA nephropathy (IgAN) with LN as a nephrotic syndrome are currently scarce. In this study, the authors present the assessment, therapy, and symptoms evaluation of three LN cases with histopathological results of renal biopsies dominated by IgA deposits. This study was written according to the Case Report Guidelines (CARE) reporting criteria. Data collection comprised of demographic information, clinical symptoms, blood laboratory tests, urinalysis, histological analysis of renal biopsies, renal ultrasonography (USG), and therapy. Clinical signs and laboratory testing were taken before biopsy as well as in the first and third month after starting medication. All three cases met the diagnostic criteria for SLE defined in the 2019 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) guidelines. This study reports on three cases of IgA nephropathy in lupus nephritis patients. Evaluation within three months of treatment showed a favorable prognosis. The combination of methylprednisolone, mycophenolic acid, and ACEI was proven to successfully induce symptom remissions and improvement of laboratory results. At present, there are no established recommendations for the management of co-existing IgAN and LN. Further investigation into similar histopathological cases and broader studies on IgAN treatment in the context of SLE may be required.

Keywords *: characteristics, laboratory, parameters of lupus nephritis*

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune illness that affects several organ systems, including the kidneys, where it causes persistent inflammation known as lupus nephritis (LN). Globally, incidence of LN occurs in 20–65% of SLE cases. Although LN is a major complication of SLE, glomerulopathy caused by other etiologies in SLE patients is an uncommon finding. Studies on the co-existence of nephritic syndromes such as IgA nephropathy (IgAN) with LN as a nephrotic syndrome are currently scarce. In this study, the authors present the assessment, therapy, and symptoms evaluation of three LN cases with histopathological results of renal biopsies dominated by IgA deposits. This study was written according to the Case Report Guidelines (CARE) reporting criteria.

CASE ILLUSTRATION

Three cases of LN with IgA dominant deposits were taken from K.R.M.T Wongsonegoro Regional Hospital Semarang. Data collection comprised of demographic information, clinical symptoms, blood laboratory tests, urinalysis, histological analysis of renal biopsies, renal ultrasonography (USG), and therapy. Clinical signs and laboratory testing were taken before biopsy as well as in the first and third month after starting medication. All three cases met the diagnostic criteria for SLE defined in the 2019 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) guidelines. LN were categorized according to the recommendations of The World Health Organization (WHO) and the International Society of Nephrology/Renal Pathology Society.

Case 1

A 21-year-old man came with complaints of swelling in both eyes, hands, and feet since one-week prior admission to the hospital. Swelling appeared starting from the eyes and gradually progressed to the hands and feet, and did not improve with rest. The patient also complained of foamy urine for one month before coming to the hospital. Examination of vital signs were normal. General system examination revealed peripheral and periorbital edema. Laboratory results showed hemoglobin 14.9 g/dL, hematocrit 44.4%, platelets 419/□L, leukocytes 20.4/□L, urea 28.7 mg/dL, creatinine

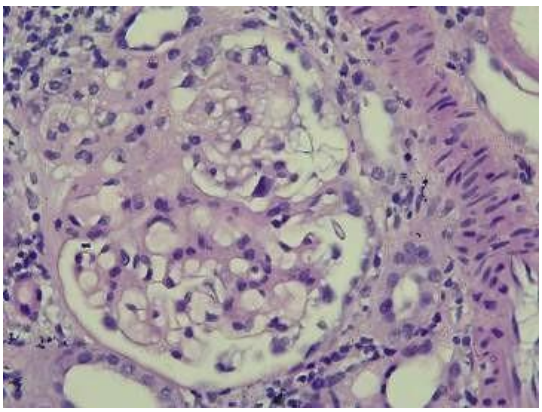

Figure 1. Light microscopic histological findings from renal biopsy showed mesangial expansion

0.8 mg/dL, albumin 1.5 mg/dL, total cholesterol 441 mg/dL, triglycerides 423 mg/dL, and uric acid 5.6 mg/dL. Urinalysis showed positive protein (+3); erythrocytes 0- 1/HPF; negative ketones; negative nitrite; negative urobilinogen; leukocytes 1-2/HPF. The results of the USG showed an increase in echogenicity in the renal parenchyma that indicates a chronic activity.

Histopathological analysis from renal biopsy showed focal segmental mesangial proliferation, mesangial expansion, leukocyte infiltration, with mainly IgA deposits (Figure 1). The diagnosis of atypical LN class II with the majority of IgA deposit images was confirmed.

The patient received immunosuppressive therapy of mycophenolic acid 2x360 mg, methylprednisolone 2x16 mg, lisinopril 1x5 mg, gemfibrozil 1x300 mg, and simvastatin 1x20 mg. After one month of therapy, the patient still experienced swelling in the face, but the swelling in the upper and lower extremities had diminished. The patient denied complaints of foamy urine. In the third month of therapy, the patient denied experiencing swelling or foamy urine. An improvement of laboratory parameters can be seen in both evaluation periods (Table 1). Examination of the patient's vital signs were within normal ranges during both evaluations.

Case 2

A 20-year-old woman was referred to our hospital with complaints of swelling all over her body since three days prior coming to the hospital. The patient brought a laboratory test that showed a positive Antinuclear antibody (ANA) test. Evaluation of the patient's vital signs were within normal limits. On examination, anasarca edema was found. Laboratory examination showed hemoglobin 9.3 g/dL, hematocrit 28.5%, platelets 202/□L, leukocytes 8.8/□L, albumin 2.4 g/dL, urea 41.7 mg/dL, creatinine 0.9 mg/dL, total cholesterol 222 mg/dL, triglycerides 102 mg/dL, uric acid 5.2 mg/dL. While urinalysis showed positive protein (+3), erythrocytes 50-60/HPF, negative ketones, negative nitrite, negative urobilinogen, leukocytes 10-15/HPF. The results of the USG examination did not show any increase in echogenicity in the renal parenchyma. The renal biopsy revealed focal segmental mesangial proliferation, vascular wall thickening, and interstitial inflammation accompanied by IgA deposits (Figure 2). The diagnosis of atypical LN class II with a majority of IgA deposit was confirmed.

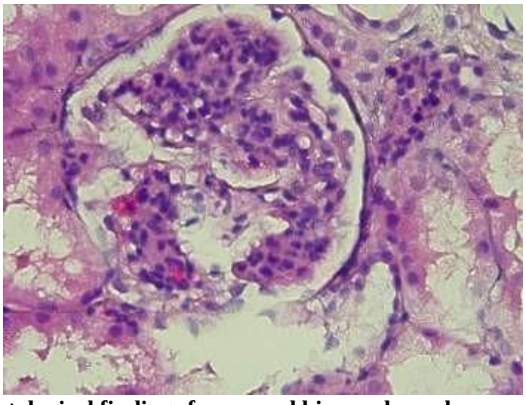

Figure 2. Light microscopic histological findings from renal biopsy showed mesangial hypercellularity

The patient was treated with mycophenolic acid 2x360 mg, methylprednisolone 2x32 mg, ramipril 1x5 mg, fenofibrate 1x300 mg, furosemide 1x40 mg, ranitidine 2x150 mg, simvastatin 1x20 mg, and ondansetron 2x8 mg. The results of the evaluation in the first month showed improvement in symptoms. Swelling only appeared in the eyes. In the third month, the patient no longer had any complaint. The laboratory results from both evaluation period showed an improvement (Table 1). The patient's vital signs in both evaluation periods were within normal limits.

Case 3

A 28-year-old woman presented with complaints of swelling in both legs for one month and was worsening. Examination of vital signs were normal, while examination of the system showed peripheral edema. Laboratory examination showed hemoglobin 11.9 g/dL, hematocrit 36%, platelets 239/□L, leukocytes 5.9/□L, albumin 1.8 g/dL, urea 19.6 mg/dL, creatinine

0.6 mg/dL, total cholesterol 248 mg/dL, triglycerides 87 mg/dL, uric acid 4.5 mg/dL. While urinalysis showed positive protein (+3), erythrocytes 0- 1/HPF, negative ketones, negative nitrite, negative urobilinogen, and leukocytes 1- 2/HPF. ANA test was positive for SLE. The results of USG examination showed no increase in echogenicity in the renal parenchyma. Histopathological analysis of the renal biopsy showed focal sclerosis, fibrinoid necrosis, and interstitial inflammation with IgA deposits. The diagnosis of atypical LN class IV with the majority of IgA deposit was confirmed.

Mycophenolic acid 2x360 mg was given as an immunosuppressant. The patient also received methylprednisolone 2x16 mg, ramipril 1x2.5 mg, folic acid 1x1 mg, simvastatin 1x20 mg. In the first month of evaluation, the patient reported that the swelling of both legs had decreased. The patient did not experience any complaints in the third month evaluation. The evaluation results in the first and third month after therapy can be seen in Table 1. During both evaluations, both laboratory markers showed an improvement and the patient's vital signs were normal.

Table 1. Laboratory Findings One-Month and Three-Month Following Therapy

No	Diagnosis	Therapy	Parameters	Pre-	First Month Post Therapy	Third Month Post Therapy
	Lupus Nephritis IgA	Mycophenolic Acid ACE-I	Ureum	28,7	73,2	18,7
			Creatinine	0,8	2	0,7
			Albumin	1,5	2,3	3,8
			cholesterol (mg/dL)	441	270	184
			Proteinuria	POS (3+)	POS (2+)	POS (2+)
	Lupus Nephritis IgA	Mycophenolic Acid ACE-I	Ureum	41,7	20,9	28,9
			Creatinine	0,9	0,6	0,7
			Albumin	2,4	3,4	3,9
			cholesterol (mg/dL)	222	165	198
			Proteinuria	POS (3+)	POS (1+)	POS (1+)
	Nephritis IgA Nefropathy	Mycophenolic Acid	Ureum	19,6	21,6	16,4
			Creatinine	0,6	0,5	0,6
			Albumin	1,8	2,7	3,7
			Total cholesterol	248	249	167
			Proteinuria	POS (3+)	POS (2+)	POS (1+)

DISCUSSION

In this study, two cases were classified as LN class II and one as LN class IV. All cases showed atypical LN features with dominant IgA deposits. Initial symptoms in all patients included edema that prompted patients to seek treatment. Signs of infection, such as fever or pain during urination—potentially associated with IgA nephropathy were not observed. Laboratory tests revealed hypoalbuminemia, hypercholesterolemia, hypertriglyceridemia, and positive proteinuria (+3) on urinalysis. Most lupus nephritis (LN) cases are classified as nephrotic syndrome, characterized by severe proteinuria, hypoalbuminemia, hyperlipidemia, and edema. Genetic and immunological factors are key in damaging the filtration barrier in nephrotic syndrome. Conversely, environmental factors also play a significant role in triggering glomerular inflammation in IgA nephropathy (IgAN). Nephritic syndrome, characterized by hematuria, hypertension, and edema, differs from nephrotic syndrome. Since both disease has distinct clinical findings and pathogenesis, careful differentiation between LN and IgAN is crucial for effective treatment and prognosis.

The primary goal in managing IgAN is to control proteinuria and hypertension. First-line treatment involves conservative measures with angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs) to manage blood pressure and lifestyle changes. In contrast, lupus nephritis (LN) is managed with immunosuppressants and anti-inflammatory therapies. In accordance with the KDIGO 2024 guidelines for LN, all three cases in this study were treated with methylprednisolone and mycophenolic acid as immunosuppressants, alongside ACE inhibitors to control proteinuria. ACE inhibitors reduce proteinuria by inhibiting the renin-angiotensin system (RAS), lowering intraglomerular pressure, and minimizing hyperfiltration. No side effects such as constipation, diarrhea, or painful urination were observed in these patients.

In both evaluation periods, all three patients showed symptom and laboratory improvements and reduced proteinuria. This suggests that glucocorticoids and mycophenolic acid effectively treat atypical LN with IgA deposits. Prior published cases support these findings, and a summary of ten cases detailing IgAN findings in SLE is listed in Appendix 1. From ten previous cases, two LN cases with IgAN were treated with glucocorticoids; four with a combination of glucocorticoids and immunosuppressants; three with glucocorticoid and ACE inhibitors; and one with both ACE inhibitors and ARBs. Eight cases showed symptom remission, and Horino et al. suggested that IgAN might develop following SLE remission. In their case, symptom remission occurred after treatment with ACE inhibitors and ARBs. Jiang Z.'s study reported a case of LN with IgAN and crescentic glomerulonephritis, where no improvement was seen after three months of glucocorticoids, immunosuppressants, and hemodialysis. This lack of improvement may be due to the presence of crescents, which suggest a more severe and progressive glomerulopathy.

There is currently no consensus on the relationship between IgAN and LN. The presence of IgAN in SLE patients may be an independent condition or a subtype of nephropathy related to SLE. Conversely, some studies suggest that IgAN may be a complication of SLE when both conditions occur simultaneously. Although LN and IgAN share some pathological features, they lead to distinct clinical symptoms, diagnostic findings, and treatment approaches. Accurate differentiation is crucial, especially in severe glomerulopathy cases, to guide appropriate therapy.

CONCLUSION

This study reports on three cases of IgA nephropathy in lupus nephritis patients. Evaluation within three months of treatment showed a favorable prognosis. The combination

of methylprednisolone, mycophenolic acid, and ACEI was proven to successfully induce symptom remissions and improvement of laboratory results. At present, there are no established recommendations for the management of co-existing IgAN and LN. Further investigation into similar histopathological cases and broader studies on IgAN treatment in the context of SLE may be required.

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