

Case of class II lupus nephritis with nephrotic features in the context of belimumab: Intersecting clinical challenge with academic initiative to emphasize social barriers in care

SAGE Open Medical Case Reports
Volume 13: 1–5
© The Author(s) 2025
DOI: 10.1177/2050313X251336061
journals.sagepub.com/home/sco



Ahyeon Cho¹ , Joshua Shoemaker¹ , Ahmad Matarneh²,
Sundus Sardar³, Pankhuri Mohan^{3,4}, Erik Washburn⁵,
Amanda Karasinski², Gurwant Kaur² and Nasrollah Ghahramani²

Abstract

Lupus nephritis is a severe complication of systemic lupus erythematosus that can cause significant kidney damage, leading to symptoms such as proteinuria, hematuria, and renal failure. If not managed promptly, it can progress to chronic kidney disease or even end-stage renal disease. Early diagnosis and treatment are vital to prevent such outcomes. While traditional treatments focus on immunosuppressive therapies, the introduction of belimumab offers a new treatment approach. Kidney biopsies play a crucial role in diagnosing and classifying lupus nephritis, helping guide appropriate treatment. Class II lupus nephritis typically requires supportive care, but more severe cases demand aggressive therapy. Noncompliance with treatment can worsen the condition, highlighting the need to address social challenges that impact patient care and adherence. We hereby report a 19-year-old female with systemic lupus erythematosus and nephrotic-range proteinuria, diagnosed with Class II lupus nephritis shortly after initiating belimumab, highlighting the social challenges impacting her care and follow-up. We hereby report a 19-year-old female known with systemic lupus erythematosus with nephrotic-range proteinuria and Class II lupus nephritis. Diagnosed shortly after belimumab, and highlighting the social challenges in her care and follow-up.

Keywords

lupus nephritis, class II, belimumab, nephrotic syndrome

Received: 10 November 2024; accepted: 27 March 2025

Introduction

Lupus nephritis (LN) affects ~40% of individuals with systemic lupus erythematosus (SLE).¹ This condition involves the deposition of immune complexes in the glomerulus, leading to inflammation and potential damage. These immune deposits disrupt the normal function of the kidneys, resulting in symptoms such as proteinuria and hematuria. If not managed properly, the condition can lead to more severe kidney issues, including chronic kidney disease or end-stage renal disease.²

The revised International Society of Nephrology/Renal Pathology Society classifies LN into six distinct classes based on kidney biopsy results.^{3,4} Class II LN, also known as mesangial proliferative LN, is characterized by immune deposits primarily in the mesangial areas of the kidneys, with minimal involvement elsewhere. This classification

helps guide treatment decisions, with Class II LN typically requiring less aggressive treatment compared to other classes.⁵

¹Pennsylvania State University College of Medicine, Hershey, PA, USA

²Division of Nephrology, Department of Medicine, Penn State Milton S. Hershey Medical Center, PA, USA

³Department of Medicine, Penn State Health Milton S. Hershey Medical Center, PA, USA

⁴Department of Pediatrics, Penn State Health Milton S. Hershey Medical Center, PA, USA

⁵Division of Pathology, Penn State Health Milton S. Hershey Medical Center, PA, USA

Corresponding Author:

Ahyeon Cho, Penn State Health College of Medicine, Milton S. Hershey Medical Center, 700 HMC Cres Rd, Hershey, PA 17033, USA.
Email: acho1@pennstatehealth.psu.edu



Creative Commons CC BY: This article is distributed under the terms of the Creative Commons Attribution 4.0 License (<https://creativecommons.org/licenses/by/4.0/>) which permits any use, reproduction and distribution of

the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

In this case, a 19-year-old woman with a history of SLE was diagnosed with Class II LN shortly after starting belimumab for her underlying lupus. Her degree of proteinuria was severe and more than the degree that would be expected in Class II LN. This change suggests that belimumab might have altered the progression of her disease, resulting in kidney biopsy findings consistent with Class II LN rather than a more advanced classification, leading to a more severe presentation. In addition, this case highlights significant social challenges that impacted her ability to manage her condition effectively. Social challenges have significantly impacted the patient's care. This highlights the need for comprehensive care approaches addressing both medical and social needs as it would result in improved outcomes.

Case presentation

A 19-year-old female with a history of SLE presented to the emergency department with severe swelling throughout her body. Diagnosed with SLE at age 15, she had a complex medical history marked by positive autoimmune markers and fluctuating complement levels. Over the years, she had been treated with various immunosuppressive drugs, most recently transitioning to azathioprine 75 mg once daily. By early 2024, she struggled with medication adherence, leading to increased levels of dsDNA antibodies and decreased complement levels. Her difficulties included transportation issues, communication barriers, and missed appointments.

In March 2024, she began taking belimumab 600 mg IV while continuing on a daily dose of prednisone 5 mg. By April 2024, she was admitted to the hospital with nephrotic syndrome and leukopenia. Despite a kidney biopsy confirming Class II LN, the high level of proteinuria suggested that the disease might be more severe. The biopsy showed segmental sclerosis, mesangial expansion, and mild thickening of the basement membrane, with electron microscopy revealing extensive podocyte damage consistent with Class II LN (Figures 1 and 2). Table 1 shows laboratory findings on presentation.

Even with treatment, including steroids and mycophenolate mofetil, she continued to miss follow-up appointments and struggled with medication adherence. By June 2024, her condition worsened, and she returned to the emergency department with severe edema, fatigue, and vomiting. She had stopped all medications a few days before this visit due to feeling unwell and had received three doses of belimumab. Her physical examination revealed significant swelling and lab tests showed very low albumin levels and severe proteinuria. Imaging identified fluid accumulation in her chest and abdomen. She was treated with high-dose intravenous methylprednisolone, furosemide, and albumin. Upon discharge, her treatment plan was adjusted to include a higher dose of prednisone and a plan to increase mycophenolate mofetil, with close monitoring.

The patient was followed up in the outpatient setting within a week of discharge. She reported significant lower extremity edema. However, she was consuming a diet high in sodium, which contributed to urinary retention despite adherence to furosemide and prednisone as recommended. The patient did not increase her mycophenolate mofetil dose as advised, which further contributed to the complexity of her care.

Repeat laboratory tests showed normal renal function with a creatinine of 0.7 mg/dl and an estimated glomerular filtration rate of over 90 ml/min/1.73 m², with no electrolyte abnormalities. However, she continued to experience an active flare, marked by hypoalbuminemia and proteinuria. We collaborated closely with her pediatric rheumatologist and maintained regular contact through phone calls and portal messages, monitoring her labs every 2 weeks.

Discussion

Class II LN typically presents with mesangial expansion and mild proteinuria, not the severe nephrotic syndrome observed in this patient. Nephrotic syndrome, characterized by significant proteinuria, is more commonly associated with Class V LN, which involves more diffuse damage to the glomerular capillary walls and subepithelial deposits.⁶ The unusual presentation in this case, with extensive podocyte damage and severe proteinuria despite the biopsy showing Class II LN, suggests a complex interaction that may involve the new treatment regimen.⁷

Belimumab, a monoclonal antibody targeting B-cell activating factor, represents a newer approach to treating LN by reducing the survival of autoreactive B-cells and decreasing autoantibody production. Its introduction has provided an additional tool for managing LN, especially for patients with refractory disease.⁸ However, the unexpected findings, in this case, raise questions about how belimumab might influence the progression of LN or alter its classification.⁹

The possibility that belimumab might downplay the biopsy in nephrotic syndrome is intriguing. Belimumab's effects on the immune system could impact immune complex deposition and podocyte function, potentially leading to atypical presentations.¹⁰ The extensive podocyte damage observed in this patient is rare for Class II LN and might suggest that belimumab's impact on immune regulation could have contributed to findings a less severe biopsy finding that was encountered in this patient or could have contributed to the more severe presentation of Class II LN.¹¹

Another consideration is the potential for belimumab to interact with other treatments or underlying disease mechanisms in ways not fully understood. In this case, despite adding belimumab to her treatment regimen, the patient's ongoing medication noncompliance and social challenges may have further complicated her disease management. This highlights the importance of considering both

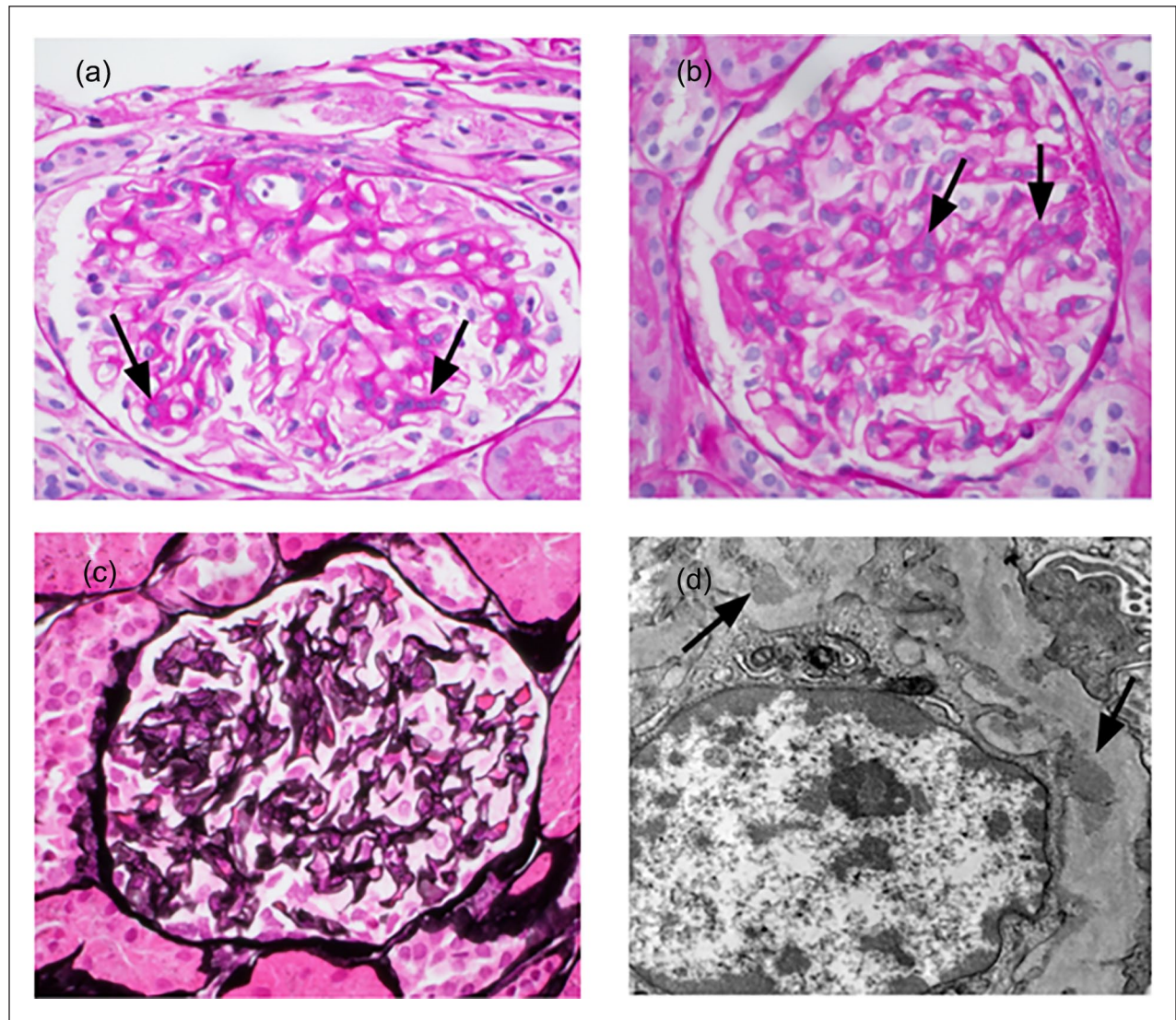


Figure 1. (a, b) The glomeruli show mesangial hypercellularity and matrix expansion (arrows) with no endocapillary hypercellularity, hyaline deposits, neutrophils/karyorrhexis, or cellular/fibrocellular crescents (PAS, 600 \times). (c) The silver stain shows mild basement membrane Glomerular basement membrane (GBM) thickening with no epimembranous spikes or GBM duplications. (Jones silver stain; 600 \times). (d) Electron microscopy images reveal mesangial deposits (shown; arrows) as well as subepithelial and subendothelial electron-dense deposits (not shown).

pharmacologic effects and real-world factors when assessing patient outcomes.¹²

Social determinants of health, such as socioeconomic status, access to healthcare, and social support, play a crucial role in the management of LN and SLE.¹³ This patient faced significant barriers, including difficulties with transportation, communication issues, and missed appointments, which impacted her ability to adhere to treatment and follow-up care. These social challenges not only hindered her treatment adherence but also likely contributed to her disease progression and worsening symptoms.

Addressing these social determinants requires a multifaceted approach. Providing practical support such as transportation assistance and financial aid, coupled with enhanced

patient education and engagement, is essential for improving adherence and health outcomes.¹⁴ Tailoring support systems to individual patient needs can help bridge gaps in care and address barriers to effective management.¹⁵

Moreover, this case underscores the importance of a collaborative approach in managing complex conditions such as LN. Effective communication and coordination among healthcare providers, including primary care physicians, rheumatologists, nephrologists, and social workers, are crucial. An interdisciplinary team can address both the medical and social aspects of patient care, ensuring a comprehensive and supportive treatment plan. By integrating clinical management with support for social challenges and ongoing research, healthcare providers can enhance the management

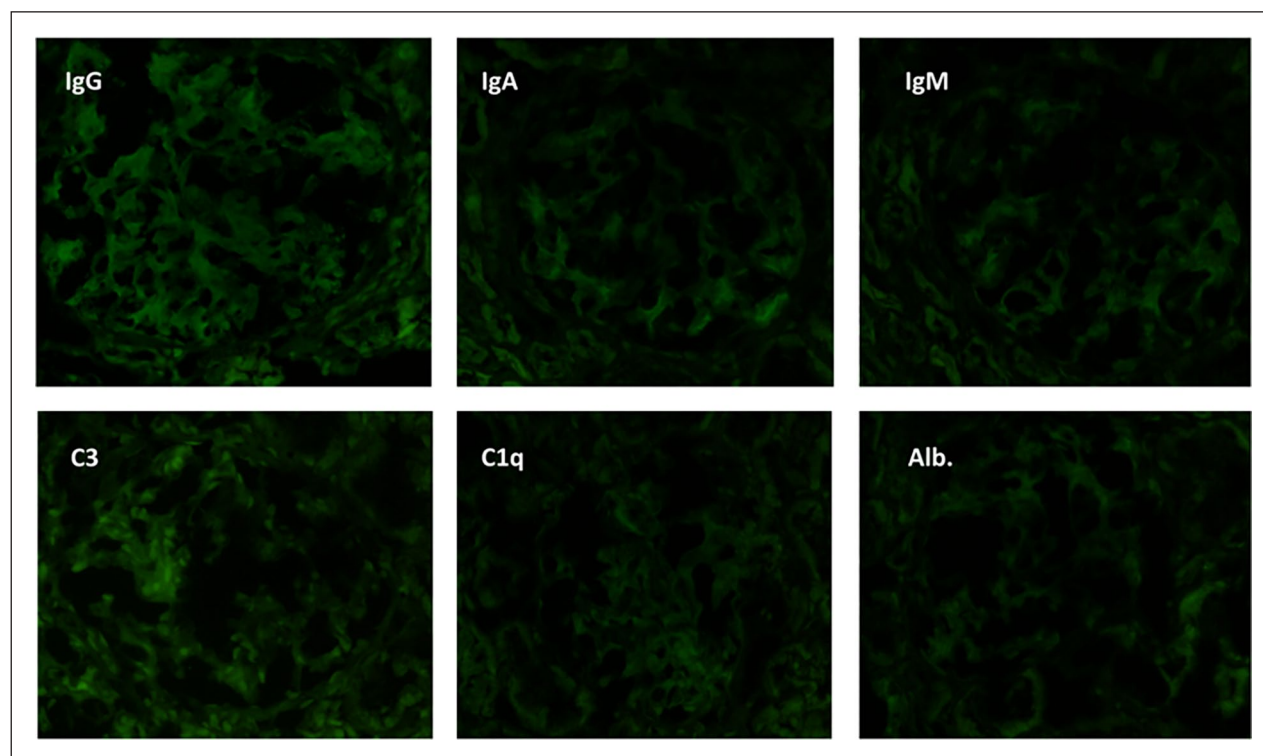


Figure 2. Immunofluorescence reveals a “full house” pattern with glomerular staining for IgG (4⁺), IgA (3⁺), IgM (3⁺), C3 (4⁺), and C1q (1+) mainly in the capillary wall and less in the mesangial area. There is negative staining for albumin.

Table 1. Laboratory findings on presentation.

Laboratory value	Reference range	On presentation
Hemoglobin	13–17 g/dl	9.3
White blood cells	4–10 k/ μ l	310.67
Platelets	150–300 k/ μ l	469
Creatinine	0.7–1.3 mg/dl	0.68
BUN	6–23 mg/dl	7
ALT	0–33 μ /l	9
AST	0–32 U/l	13
Albumin	3.5–5.2 g/dl	2
Urine PCR	<150 mg/g	20.3 g/g

ALT: alanine transaminase; AST: aspartate aminotransferase; BUN: Blood Urea Nitrogen.

of LN and improve the quality of life for patients facing this complex condition.

Conclusion

This case illustrates the complexities and challenges of managing LN, especially with the advent of new treatments such as belimumab. The unexpected biopsy findings and severe nephrotic syndrome highlight the need for detailed monitoring and personalized treatment plans. In addition, addressing social determinants of health is crucial for improving disease management and patient adherence. By combining clinical


care with support for social challenges, healthcare providers can significantly enhance patient management and well-being. A comprehensive approach that integrates both medical and social support is essential for achieving the best outcomes in patients with LN.

Acknowledgments

We thank the Division of Nephrology at Penn State Health for giving us the opportunity and support to conduct this work.

ORCID iDs

Ahyeon Cho  <https://orcid.org/0000-0001-8581-7586>

Joshua Shoemaker  <https://orcid.org/0009-0006-4528-3958>

Ethical considerations

Penn State ethical committee does not require ethical approval for reporting individual cases.

Consent for publication

Written informed consent was obtained from the patient for her anonymized information to be published in this article.

Author contributions

Ahyeon Cho, Joshua Shoemaker, Ahmad Matarnah, and Gurwant Kaur were involved with manuscript writing, literature review, and clinical care. Sundus Sardar, Pankhuri Mohan, and Amanda

Karasinski focused on manuscript writing and literature review. Erik Washburn clinical pathologist. Nasrollah Ghahramani has contributed to manuscript writing, literature review, and mentorship for this study. All authors read and agreed with the final manuscript.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The funding process is solely done from the writing authors.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

References

1. Cameron JS. Lupus nephritis. *J Am Soc Nephrol* 1999; 10(2): 413–424.
2. Anders HJ, Saxena R, Zhao MH, et al. Lupus nephritis. *Nat Rev Dis Primers* 2020; 6(1): 7.
3. Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. *Kidney Int* 2018; 93(4): 789–796.
4. Markowitz GS and D'Agati VD. The ISN/RPS 2003 classification of lupus nephritis: an assessment at 3 years. *Kidney Int* 2007; 71(6): 491–495.
5. Kiremitci S and Ensari A. Classifying lupus nephritis: an ongoing story. *Sci World J* 2014; 2014(1): 580620.
6. Yu F, Haas M, Glasscock R, et al. Redefining lupus nephritis: clinical implications of pathophysiologic subtypes. *Nat Rev Nephrol* 2017; 13(8): 483–495.
7. Yu X, Chen N, Xue J, et al. Efficacy and safety of belimumab in patients with lupus nephritis: subgroup analyses of a phase 3 randomized trial in the East Asian population. *Am J Kidney Dis* 2023; 81(3): 294–306.
8. Levy RA, Gonzalez-Rivera T, Khamashta M, et al. 10 Years of belimumab experience: what have we learnt?. *Lupus* 2021; 30(11): 1705–1721.
9. Wabl M. The 9th International Congress on SLE 2010 June 24–27, Vancouver, Canada. *Lupus* 2010; 19 (suppl 1): 1–185.
10. Sanz I, Yasothan U and Kirkpatrick P. Belimumab. *Nat Rev Drug Discov* 2011; 10(5): 335–337.
11. Furie R, Rovin BH, Houssiau F, et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med* 2020; 383(12): 1117–1128.
12. Williams JN, Drenkard C and Lim SS. The impact of social determinants of health on the presentation, management and outcomes of systemic lupus erythematosus. *Rheumatology* 2023; 62(suppl 1): i10–i14.
13. Braveman P, Egerter S and Williams DR. The social determinants of health: coming of age. *Annu Rev Public Health* 2011; 32(1): 381–398.
14. Hunter BD, Neiger B and West J. The importance of addressing social determinants of health at the local level: the case for social capital. *Health Soc Care Community* 2011; 19(5): 522–530.
15. Fosse E, Helgesen MK, Hagen S, et al. Addressing the social determinants of health at the local level: opportunities and challenges. *Scand J Public Health* 2018; 46(suppl 20): 47–52.