



Case Report

Successful Dialysis Weaning in Refractory Membranous Nephropathy Through Long-Term Multi-Disciplinary Management: A Case Report

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Abstract

Membranous nephropathy (MN) is a leading cause of nephrotic syndrome (NS). The remission rate of MN remains limited, and effective strategies for refractory MN are not established. We present the case of a 49-year-old Japanese woman with severe NS caused by MN. Kidney biopsy revealed glomerular basement membrane thickening with granular deposition of immunoglobulin G (IgG) and complement component 3. IgG subclass analysis showed predominant IgG1 deposition, with weak IgG2 and IgG3 deposition. Phospholipase A2 receptor (PLA2R) deposition was equivocal in the first kidney biopsy and negative in the second. Serum anti-PLA2R antibody was not detected. Electron microscopy revealed subepithelial, subendothelial, and mesangial electron-dense deposits. Detailed screening revealed no significant abnormalities other than appendiceal findings, suggesting secondary MN associated with appendiceal infection. Although combined therapy with prednisolone, cyclosporine, rituximab, and low-density lipoprotein apheresis was administered during the first 6 months, remission of MN was not achieved. During dialysis, initiated because of kidney failure, long-term multidisciplinary management, including control of appendiceal infection and inflammation and initiation of angiotensin II receptor blocker therapy, ultimately led to remission of MN and discontinuation of dialysis. Overall, even refractory MN requiring dialysis may have a reversible clinical course with careful conservative management and long-term follow-up.

Keywords: nephrotic syndrome; membranous nephropathy; dialysis

Academic Editor: Jan Malík

Received: 21 May 2026

Revised: 29 June 2026

Accepted: 2 July 2026

Published: 3 July 2026

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1. Introduction

Membranous nephropathy (MN), a leading cause of nephrotic syndrome (NS) in adults, is characterized by immune complex deposition along the glomerular basement membrane [1]. MN is broadly classified into primary and secondary forms, based on the presence or absence of identifiable underlying conditions [2]. Primary MN accounts for approximately 70% of all MN cases, and MN may occur secondary to well-defined causes [3]. Secondary MN is associated with autoimmune diseases, chronic infections, malignancies, and certain medications [3].

As treatment strategies differ substantially between primary and secondary MN, distinguishing between these two forms is of critical clinical importance. Immunosuppressive therapy is often indicated for primary MN, whereas management of secondary MN is primarily directed toward treating the underlying cause [4,5]. Nevertheless, patients with severe NS and/or acute kidney injury (AKI) may require intensive therapeutic interventions, including corticosteroids, calcineurin inhibitors, cyclophosphamide, rituximab, and adjunctive therapies such as low-density lipoprotein apheresis (LDL-A), irrespective of the underlying etiology [6,7]. In Japan, LDL-A, a blood purification therapy that selectively removes circulating LDL cholesterol, has been used for steroid-resistant NS. Several studies in patients with refractory NS caused by focal segmental glomerulosclerosis (FSGS) have demonstrated its efficacy in reducing proteinuria and improving kidney dysfunction [8,9]. The therapeutic effects of LDL-A are thought to involve not only the removal of LDL-cholesterol but also the reduction in nephrotoxic and proinflammatory mediators. Recently, accumulating evidence has suggested that LDL-A may be effective for FSGS as well as other kidney diseases, such as MN, as an initial induction therapy [10].

However, effective strategies for refractory MN have not been established. Herein, we report a case of secondary MN possibly associated with recurrent appendicitis in which severe refractory NS persisted despite combined treatment with corticosteroids, multiple immunosuppressive agents, and LDL-A. Temporary hemodialysis was required because of advanced kidney injury, and volume management remained challenging throughout the clinical course. However, after approximately 2 years of multidisciplinary treatment, the patient ultimately achieved clinical remission and was successfully withdrawn from dialysis.

2. Case Presentation

2.1. Clinical History and Laboratory Data

A 49-year-old Japanese woman was referred to our hospital with a 1-week history of generalized edema. At referral to our department, her urinary protein-to-creatinine (Cr) ratio was 18.0 g/gCr and serum albumin level was 1.1 g/dL. Based on these findings, NS was diagnosed. On admission, physical examination revealed a height of 154 cm and body weight of 52.5 kg, which had increased by 3 kg over the preceding week. Blood pressure was 124/92 mmHg, and pulse rate was 88 beats/min with a regular rhythm. She had no history of abnormal urinalysis and had not taken any supplements or over-the-counter medications. She had received a second dose of the coronavirus disease 2019 (COVID-19) vaccine approximately 2 months before admission.

Laboratory findings are shown in Table 1. Her 24-h urinary protein excretion was 10.9 g with a total urine volume of 430 mL. High-grade microscopic hematuria was also observed. Her serum Cr level was 1.06 mg/dL (normal range: 0.46–0.79 mg/dL), corresponding to an estimated glomerular filtration rate (eGFR) of 44.3 mL/min/1.73 m², calculated using the Japanese equation. Her serum albumin level was markedly decreased to 0.9 g/dL (normal range: 4.1–5.1 g/dL). No clinical or laboratory signs of infection, vasculitis, or collagen vascular disease were observed. Serum phospholipase A2 receptor (PLA2R) antibody test results were negative. Computed tomography revealed a concomitant appendiceal abscess. The patient was diagnosed with NS complicated by AKI and appendiceal infection.

Table 1. Laboratory data on admission.

Urinalysis	On Admission	Reference Range
pH	6.0	5.0–8.5
Specific gravity	1.02	1.005–1.030
Protein	(4+)	(–)
Occult blood	(2+)	(–)
Glucose	(–)	(–)
White blood cell (/HPF)	1–4	1–4
Red blood cell (/HPF)	>100	1–4
U-TP (g/day)	10.9	<0.15
U-μAlb/Cr (mg/gCr)	9659	<30
U-TP/Cr (g/gCr)	17.94	<0.15
U-β2MG (μg/mL)	1.27	≤0.22
U-NAG/Cr (U/gCr)	56	0.1–8.0
Bence Jones protein	(–)	(–)
Selectivity Index	0.04	
Peripheral blood		
White blood cell (/μL)	6820	3300–8600
Red blood cell (×10 ⁴ /μL)	499	386–492
Hemoglobin (g/dL)	11.8	11.6–14.8
Platelet (×10 ³ /μL)	244	158–348
Chemistry		
Total protein (g/dL)	4.1	6.6–8.1
Albumin (g/dL)	0.9	4.1–5.1
Lactate dehydrogenase (U/L)	268	124–222
Triglyceride (mg/dL)	323	30–149
Total cholesterol (mg/dL)	438	142–219
LDL-C (mg/dL)	345	65.0–139.0
Total bilirubin (mg/dL)	0.3	0.4–1.5
AST (U/L)	30	13–30
ALT (U/L)	16	7–23
γ-GTP (U/L)	49	9–32
ALP(IF) (U/L)	85	25–51
Blood urea nitrogen (mg/dL)	16.2	8.0–20.0
Creatinine (mg/dL)	1.06	0.46–0.79
eGFR (mL/min/1.73 m ²)	44.3	60<
Uric acid (mg/dL)	8.9	2.6–7.0
Sodium (mEq/L)	135	138–145
Potassium (mEq/L)	3.5	2.7–4.6
Chloride (mEq/L)	104	101–108
C-reactive protein (mg/dL)	0.37	≤0.14
Glucose (mg/dL)	114	73–109
Hemoglobin A1c (%)	6.1	4.9–6.0
Serology		
Immunoglobulin G (mg/dL)	514	861–1747
Immunoglobulin A (mg/dL)	320	93–393
Immunoglobulin M (mg/dL)	169	50–269
C3 (mg/dL)	79	73–138
C4 (mg/dL)	27	11–31
CH50 (CH50U/mL)	35	30–45
Antinuclear antibody	×40	<×40
Anti-dsDNA antibody (IU/mL)	1.8	<10.0

Anti-SS-A antibody (U/mL)	<0.4	<7.0
Anti-SS-B antibody (U/mL)	<0.4	<7.0
MPO-ANCA (IU/mL)	<2.0	<3.5
PR3-ANCA (IU/mL)	<3.5	<2.0
Antistreptolysin O (IU/mL)	39.2	<50
sIL-2R (U/mL)	653	122–496
Serum IFE	(–)	(–)
Tumor markers		
CA19-9 (U/mL)	16	<37
CEA (ng/mL)	1	<5.0
Infection markers		
HBs Ag (IU/mL)	<0.01	<0.05
HBs Ab (mIU/mL)	<2.5	<10.0
HBc Ab (S/CO)	0.07	<1.00
HCV Ab (S/CO)	0.03	<1.00
T-SPOT	(–)	(–)
TP-Ab (U/mL)	<5.0	<10.0
Rapid plasma reagin	(–)	(–)

HPF, high-power field; U-TP, urinary total protein; U-μAlb/Cr, urinary microalbumin-to-creatinine ratio; U-TP/Cr, urinary total protein-to-creatinine ratio; U-β2MG, urinary β2-microglobulin; U-NAG/Cr, urinary N-acetyl-β-D-glucosaminidase-to-creatinine ratio; LDL-C, low-density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; eGFR, estimated glomerular filtration rate; C3, complement component 3; C4, complement component 4; CH50, 50% hemolytic complement activity; Anti-dsDNA antibody, anti-double-stranded DNA antibody; Anti-SS-A antibody, anti-Sjögren's syndrome-related antigen A antibody; Anti-SS-B antibody, anti-Sjögren's syndrome-related antigen B antibody; MPO-ANCA, myeloperoxidase-antineutrophil cytoplasmic antibody; PR3-ANCA, proteinase 3-antineutrophil cytoplasmic antibody; IFE, immunofixation electrophoresis; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; HBs Ag, hepatitis B surface antigen; HBs Ab, hepatitis B surface antibody; HBc Ab, hepatitis B core antibody; HCV Ab, hepatitis C virus antibody; T-SPOT, T-SPOT tuberculosis test; TP-Ab, Treponema pallidum antibody.

In this case, two kidney biopsies were performed: an initial biopsy to determine the cause of NS with AKI and a second biopsy during follow-up to assess the treatment response.

2.2. Kidney Biopsy Findings

The first renal biopsy was performed on day 61. The light microscopy specimen contained 20 glomeruli, none of which showed global sclerosis, crescent formation, endocapillary proliferation, fibrinoid necrosis, or thrombosis of the glomerular capillaries. Periodic acid–methenamine silver staining demonstrated diffuse thickening of the glomerular basement membrane, with spike and bubble formations (Figure 1). Immunofluorescence staining revealed diffuse granular deposits of IgG and C3 along the glomerular capillary walls. IgG subclass staining demonstrated predominant deposition of IgG1 without detectable IgG4. PLA2R staining results were equivocal. Electron microscopy revealed subepithelial, subendothelial, and mesangial electron-dense deposits (EDD), supporting the diagnosis of secondary MN.

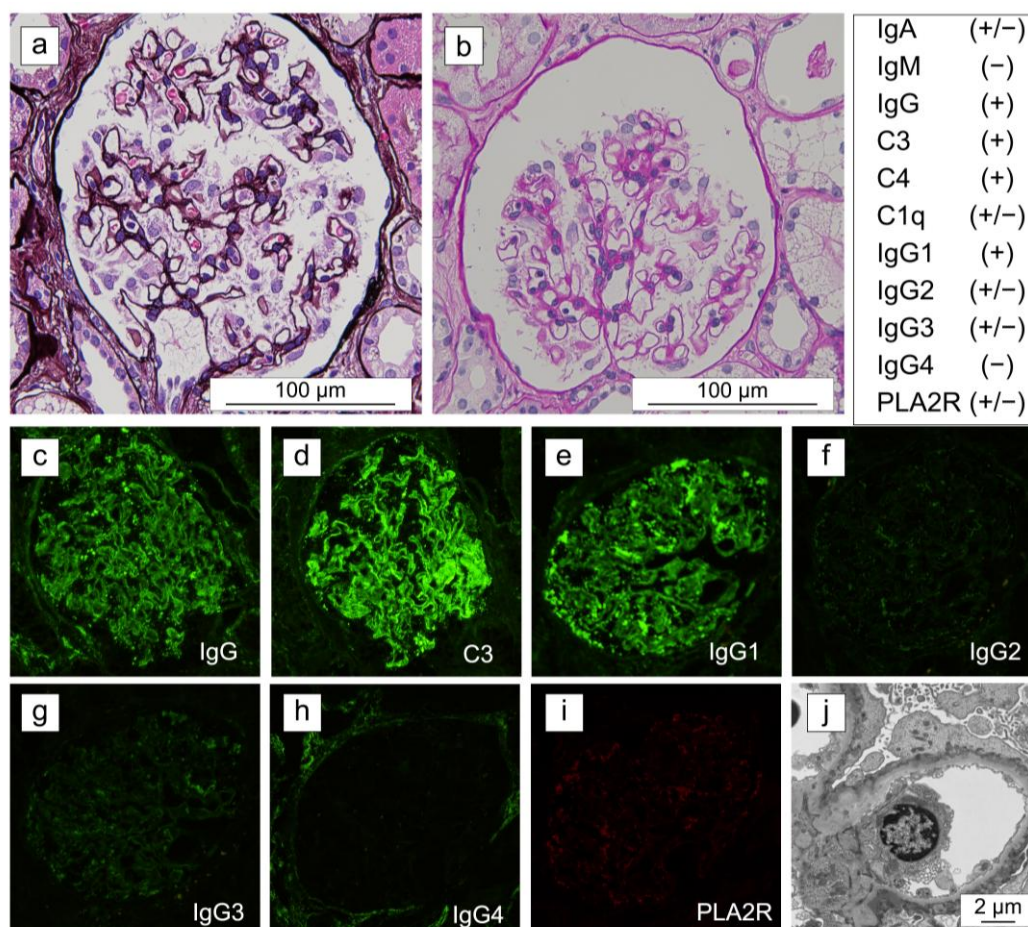


Figure 1. Initial kidney biopsy performed on day 61. (a) The glomerular basement membrane is mildly thickened, with spike formation and a bubble appearance (periodic acid-methenamine silver staining, $\times 400$). (b) Light micrograph reveals 20 glomeruli without global sclerosis (periodic acid-Schiff staining, $\times 400$). No segmental sclerotic lesions or crescent formation can be observed. No mesangial cell proliferation or increase in mesangial matrix is noted. (c–i) Immunofluorescence staining ($\times 400$) reveals deposition of IgG (c), C3 (d), IgG1 (e), IgG2 (f), IgG3 (g), IgG4 (h), and PLA2R (i). (j) Transmission electron microscopy shows variably sized subepithelial deposits. Ig, immunoglobulin; C3, complement component 3; PLA2R, phospholipase A2 receptor.

A second kidney biopsy was performed on day 813 to assess the response to treatment. It revealed one globally sclerotic glomerulus among 48 glomeruli. Periodic acid-methenamine silver staining demonstrated diffuse thickening of the glomerular basement membrane with persistent spike formation. Mild monocyte infiltration, moderate to severe tubular atrophy, and interstitial fibrosis were observed in the tubulointerstitium. Immunofluorescence demonstrated persistent IgG and C3 positivity with predominant IgG1 subclass staining and negative PLA2R staining. Electron microscopy revealed EDDs located in the subepithelial and intramembranous regions, as well as within the mesangial area, supporting the diagnosis of secondary MN (Figure 2).

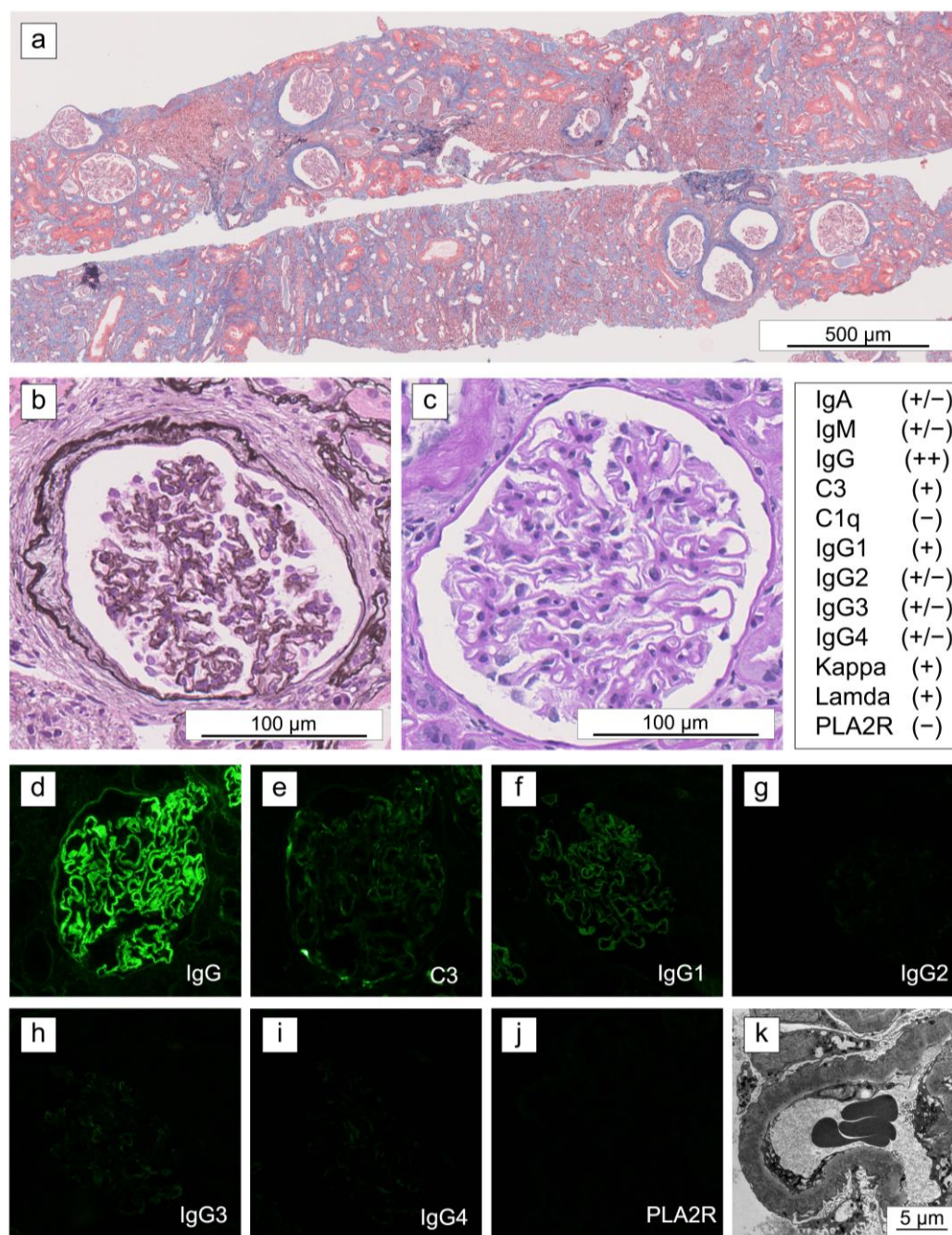


Figure 2. Second kidney biopsy performed on day 813. (a) Masson's trichrome staining shows tubular atrophy in approximately 40–50% of the cortex, along with mild to moderate laminar intimal thickening of small arteries. (b) Periodic acid-methenamine silver staining shows 48 glomeruli, including one globally sclerotic glomerulus, with no segmental sclerosis and crescent formation. Diffuse thickening of the glomerular capillary walls with spike formation is observed (×400). (c) Periodic acid-Schiff staining shows glomerular hyalinosis, tuft adhesion, and collapse, with fibrous thickening of Bowman's capsule. (d–j). Immunofluorescence staining (×400) reveals deposition of IgG (d), C3 (e), IgG1 (f), IgG2 (g), IgG3 (h), IgG4 (i), and PLA2R (j). (k) Transmission electron microscopy shows a thickened glomerular basement membrane with electron-dense deposits (EDDs) extending from the subepithelial area into the basement membrane. Focal EDDs are also observed in the mesangial region. Ig, immunoglobulin; C3, complement component 3; PLA2R, phospholipase A2 receptor.

2.3. Diagnosis and Treatment

Based on the laboratory and biopsy findings, the patient was diagnosed with secondary MN concomitant with asymptomatic appendiceal abscesses, and corticosteroid therapy was initiated. The clinical time course is shown in Figure 3. Prednisolone (PSL) was started at 50 mg/day (1 mg/kg body weight) and tapered by 5–10 mg every 2–4 weeks in accordance with Japanese clinical practice guidelines for NS. During the first month of steroid therapy, the patient's eGFR progressively declined and proteinuria markedly increased. An albumin infusion was regularly administered to manage the hemodynamic instability caused by severe hypoalbuminemia. Appendicitis developed on day 38 of steroid therapy; however, the patient's abdominal symptoms were managed conservatively and improved with antibiotic treatment alone. Additionally, screening tests, including upper and lower gastrointestinal endoscopy, were performed to evaluate other possible secondary causes of MN; however, no abnormalities were identified. Given the insufficient steroid response after 1 month of high-dose steroid therapy and the concerns about worsening infection, further intensification of immunosuppression was considered inappropriate; hence, LDL-A was initiated on day 32 twice weekly, with a planned total of 12 sessions. For LDL-A, polyethylene fibers (Plasmaflo® OP-08D; Asahi Kasei Medical Co., Ltd., Tokyo, Japan) were used as the plasma separator, and a dextran sulfate cellulose column (Liposorber® LA-40 system; Kaneka, Osaka, Japan) was used as the LDL absorber.

As the nephrotic-range proteinuria remained unchanged despite the completion of LDL-A under steroid treatment, administration of oral cyclosporine at a dose of 100 mg/day was initiated on day 67; further, the patient received intravenous rituximab on day 80, four times over 2 months, at a dose of 500 mg per infusion. The cyclosporine dose was adjusted to maintain a C2 level within a 600–1000 ng/mL range. However, no improvement in NS was observed. During this period, she experienced two additional episodes of appendicitis, both of which were managed conservatively. Surgical consultation was obtained during each episode; however, urgent appendectomy was deferred because of concerns regarding infection risk and impaired wound healing associated with high-dose PSL. As the immunosuppressive treatment remained ineffective and volume control became increasingly difficult, the immunological medications were gradually tapered and discontinued. Repeated albumin infusions were also required. On day 317, her serum creatinine increased to a peak level of 3.42 mg/dL (eGFR 12.2 mL/min/1.73 m²) and urine output could not be adequately maintained and remained below 300 mL/day, accompanied by progressive pleural effusion, ascites, and generalized edema. Hence, maintenance hemodialysis was initiated on day 317. She received maintenance hemodialysis three times weekly, with extracorporeal ultrafiltration and albumin infusions as needed for volume control. During maintenance hemodialysis, urine output was persistently <300 mL/day, with intradialytic weight gain of 1–2 kg.

Angiotensin II receptor blockers (ARBs) could not initially be started because of symptomatic hypotension; however, candesartan was carefully introduced during dialysis on day 582. With multidisciplinary treatment, including hemodialysis, initiation and continuation of ARB therapy, and infection control, the patient's serum albumin level gradually increased, and the urinary protein-to-Cr ratio (UPCR) decreased. As urine output had increased to >1 L/day, with no interdialytic weight gain, improvement in serum albumin to >3.0 g/dL, and attenuation of disease activity, she was successfully withdrawn from hemodialysis on day 812.

Additionally, she was readmitted and underwent a second kidney biopsy on day 813 for re-evaluation of disease activity. After her kidney function had stabilized and complete NS remission was achieved, an elective appendectomy was performed to prevent further episodes of appendicitis on day 892. At 2 years after hemodialysis discontinuation, she has remained in clinical remission, with a UPCR of approximately 0.5 g/gCr and an

eGFR of approximately 20–25 mL/min/1.73 m², without progression to end-stage kidney disease.

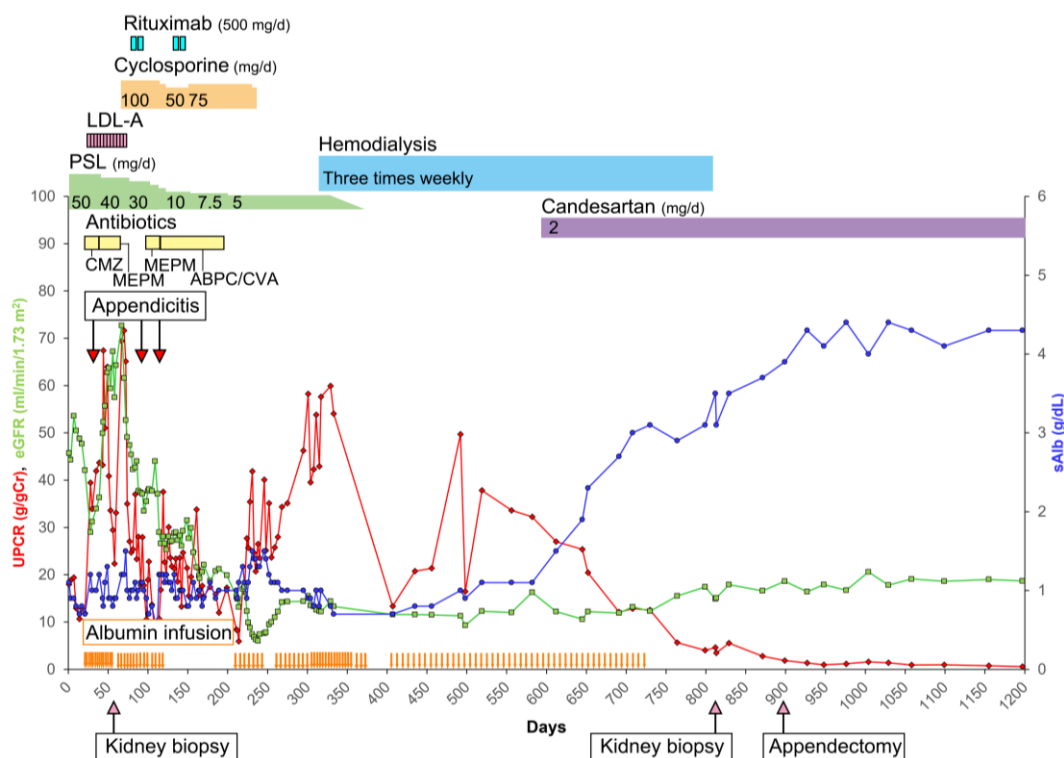


Figure 3. Clinical time course. Day 0 represents the day of admission. UPCR, urine protein-to-creatinine (Cr) ratio; eGFR, estimated glomerular filtration rate; PSL, prednisolone; sAlb, serum albumin; LDL-A, low-density lipoprotein apheresis.

3. Discussion

This study describes a case of severe and refractory NS caused by MN, concomitant with recurrent appendicitis. The patient required careful balancing between control of severe nephrotic disease activity and management of appendiceal infection. Corticosteroid-based therapy was introduced and tapered under antibiotic treatment; however, appendicitis developed early after treatment initiation, making additional immunosuppression difficult. Although LDL-A was added as an adjunctive therapy to reduce proteinuria and suppress inflammation, severe NS persisted; therefore, multiple immunosuppressive agents were required under careful infection control. However, severe NS persisted, leading to progressive kidney impairment and difficult volume management that required hemodialysis. At this stage, these agents were tapered and discontinued because of limited efficacy. During the prolonged dialysis-dependent course, hemodynamic stabilization, initiation of ARB therapy, and control of infection and inflammation may have collectively contributed to gradual remission and successful withdrawal from dialysis.

In this case, the histopathological findings, including PLA2R assessment, strongly suggested secondary MN; however, no systemic disease that represented an underlying condition, such as infection, collagen vascular disease, vasculitis, or malignancy, could be identified. Particularly, typical systemic lupus erythematosus-associated lupus nephritis was not supported by the absence of systemic manifestations, negative anti-dsDNA antibody, preserved complement levels, and the lack of a full-house pattern on kidney immunofluorescence. However, the diverse immune deposits, including subendothelial and mesangial EDDs, raised the possibility of lupus-like immune-complex glomerulonephritis. Nevertheless, given the absence of a full-house immunofluorescence pattern, lupus-like

immune-complex glomerulonephritis could not be definitively identified. In infection-associated MN, pathogen-derived antigens may serve as targets of the host immune response, leading to the formation of antigen–antibody immune complexes that are subsequently deposited along the glomerular basement membrane [3]. In the present case, chronic appendicitis was considered a potential source of persistent inflammation and immune activation, which may have contributed to immune complex formation and subsequent deposition along the glomerular basement membrane, potentially promoting the development of MN. However, evidence directly linking appendiceal abnormalities to MN is lacking, and the mechanism derived from the appendiceal lesion that may induce immune complex formation has not been established. Hence, although appendiceal disease was suspected to be involved in the pathogenesis of MN, a definitive causal relationship could not be demonstrated.

Furthermore, according to a nationwide survey conducted by the Japanese Society of Nephrology, approximately 55.6% of new-onset NS cases following COVID-19 vaccination occurred after the second dose, with minimal change disease being the most common pathology (44.4%), although MN was observed in 14.8% of cases [11]. Reports of NS developing nearly 90 days after vaccination have been published, which is similar to the interval observed in this case. However, similar to appendicitis, the association between COVID-19 vaccination and the development of MN remained presumptive, and a definitive causal association could not be established in this case.

Several factors may have contributed to disease control and the eventual achievement of clinical remission. First, antibiotic treatment for recurrent appendicitis and withdrawal of immunosuppressive agents may have reduced the systemic inflammatory burden and susceptibility to infection, thereby attenuating the immune activation associated with secondary MN. As kidney function improved and dialysis was successfully discontinued before appendectomy, the clinical recovery in this case cannot be attributed to the surgical removal of the appendiceal lesion itself. Nevertheless, an unidentified pathogenic factor originating from chronic appendicitis may have contributed to NS persistence. Computed tomography findings obtained at admission and on day 811 after discontinuation of dialysis (Supplemental Figure S1) demonstrated a marked improvement in appendiceal enlargement and surrounding tissue inflammation, suggesting that these changes may have been associated with the improvement in NS.

Second, the initiation of ARB therapy may have contributed to the partial remission of disease activity. According to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines [5], patients with MN and persistent proteinuria should receive conservative treatment, including ARBs, to reduce proteinuria and NS-related symptoms. Renin–angiotensin system inhibition may facilitate remission by lowering the intraglomerular pressure, reducing podocyte stress, and stabilizing the glomerular filtration barrier [12]. Polanco et al. [13] reported that patients with idiopathic MN and proteinuria of <8 g/day who were treated with ARB showed significantly higher rates of spontaneous remission. In the present case, ARB therapy was initiated at an early stage; however, symptomatic hypotension caused by severe hypoalbuminemia due to NS made initiation and maintenance difficult. After hemodynamic stabilization with dialysis support was achieved, candesartan was administered at a later stage. Following ARB initiation, proteinuria improved without worsening kidney function, suggesting that ARB therapy may be beneficial for maintaining remission.

Third, as shown in Figure 3, dialysis treatment itself contributed to the favorable clinical outcomes by serving as supportive therapy. Although dialysis cannot directly remove autoantibodies or immune complexes central to MN, it may have improved volume control and stabilized the patient's hemodynamic status. This supportive effect may have provided a safer clinical environment for the initiation and continuation of ARB therapy.

Overall, these interventions may have collectively reduced proteinuria and allowed the patient's condition to gradually improve toward remission over a prolonged clinical course.

Furthermore, LDL-A is generally considered an adjunctive therapy for refractory NS with persistently severe proteinuria despite corticosteroids and other immunosuppressive agents. In Japan, LDL-A has long been covered by the National Health Insurance for drug-resistant FSGS, and its indication was recently expanded to include refractory NS caused by MN and minimal change disease (MCD) [9,10]. Under the current Japanese criteria, LDL-A can be performed in patients with FSGS, MN, or MCD who remain nephrotic despite conventional drug therapy and whose serum cholesterol level cannot be reduced to ≤ 250 mg/dL, with a maximum of 12 sessions within 3 months. Although LDL-A is usually considered in steroid-resistant cases, a previous study has suggested that early adjunctive use in combination with corticosteroids may enhance proteinuria reduction and remission induction in selected patients [8]. The therapeutic effects of LDL-A are thought to involve not only the removal of LDL-cholesterol but also the reduction in nephrotoxic and proinflammatory mediators. In the present case, LDL-A was introduced relatively early based on these considerations; however, it did not lead to a sufficient clinical response, possibly because persistent secondary inflammatory stimuli continued to drive disease activity.

This case highlights the fact that even severe refractory secondary MN requiring temporary dialysis may achieve clinical remission through long-term multidisciplinary management. Although the definitive etiology remains unclear, sustained control of infection and inflammation, discontinuation of immunosuppressive therapy, temporary dialysis support, and ARB treatment may synergistically reduce disease activity and support gradual kidney recovery.

4. Conclusions

We describe a case of severe refractory NS caused by secondary MN. Although temporary hemodialysis was required because of severe kidney injury and hypotension due to hypoalbuminemia, long-term multidisciplinary management, including control of appendiceal infection and inflammation, hemodynamic stabilization with dialysis support, and ARB therapy, ultimately led to NS remission and discontinuation of dialysis. This case suggests that even refractory NS requiring dialysis may have a reversible clinical course with careful conservative management and long-term follow-up.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/kidneydial6030046/s1>, Figure S1: Changes in appendiceal infection on abdominal computed tomography.

Author Contributions: R.S.-I. and H.S. wrote the original draft of the paper; R.S.-I. and H.S. conceived the study; R.S.-I., M.M. (Megumi Matsumoto), H.S., M.M. (Motoki Matsuki), M.Y., Y.O., and N.N. reviewed the literature; R.S.-I., H.S. and N.N. planned the research; R.S.-I. collected the data; and R.S.-I., M.M. (Megumi Matsumoto), and H.S. prepared the published work. Each author has made substantial contributions to the conception of the work, acquisition of data, and revision of the paper; each author has approved the submitted version, agreed to be personally accountable for the author's own contributions, and ensured that questions related to the accuracy or integrity of any part of the work, even those in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature. All authors have read and agreed to the published version of the manuscript.

Funding: This study received no external funding.

Institutional Review Board Statement: Ethical review and approval were waived for this study, as case reports do not require mandatory review under the policies of the Asahikawa Medical University Research Ethics Committee.

Informed Consent Statement: Informed consent was obtained from the patient for the publication of this paper.

Data Availability Statement: The original contributions presented in this study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Acknowledgments: The authors acknowledge the assistance of the medical staff of Asahikawa Medical University Hospital and the dialysis care clinic.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MN	Membranous nephropathy
NS	Nephrotic syndrome
Ig	Immunoglobulin
PLA2R	Phospholipase A2 receptor
AKI	Acute kidney injury
LDL-A	Low-density lipoprotein apheresis
FSGS	Focal segmental glomerulosclerosis
Cr	Creatinine
eGFR	Estimated glomerular filtration rate
EDD	Electron-dense deposits
PSL	Prednisolone
ARBs	Angiotensin II receptor blockers
UPCR	Urinary protein-to-Cr ratio
MCD	Minimal change disease

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