Renal Replacement Therapy

CASE REPORT

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Nephrotic syndrome caused by recurrent podocytopathy after living donor renal transplantation with elevated anti-nephrin antibody levels: a case report and a review

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Abstract

Background Approximately 95% of patients with idiopathic nephrotic syndrome (INS) have a favorable prognosis, though 4–5% progress to end-stage renal disease. The recurrence rate of INS following kidney transplantation is approximately 30%. Treating nephrotic syndrome (NS) after kidney transplantation is challenging and often results in graft loss. In the present case, following transplantation, the patient experienced recurrent NS caused by podocytopathy in which elevated anti-nephrin antibody levels were closely associated with the degree of proteinuria. We present this case and discuss it in the context of the existing literature.

Case presentation The patient was a 59-year-old male who first developed INS in 1980 at the age of 15 and was diagnosed with minimal change disease (MCD) on the basis of a renal biopsy. He initially achieved complete remission with steroids, but gradually developed steroid resistance and started hemodialysis in 2006. In 2014, he received a living-donor kidney transplant from his younger brother, but in 2017 his NS recurred. A biopsy of the transplanted kidney revealed MCD. The biopsy results were MCD, but clinically, it was FSGS, and low-density lipoprotein cholesterol apheresis (LDL-A) was performed 12 times per course for a total of four courses. However, his proteinuria persisted and he continued to have NS. In December 2023, a blood test revealed elevated levels of anti-nephrin antibody. In January 2024, following steroid pulse therapy with methylprednisolone at 500 mg/day for 3 days combined with a single rituximab administration at 200 mg/body, the anti-nephrin antibodies became undetectable, and the proteinuria resolved. Subsequent super-resolution microscopic examination of a biopsy specimen collected before treatment revealed co-localization of immunoglobulin (Ig)G and nephrin.

Conclusions We report a case of recurrent NS caused by podocytopathy following renal transplantation in a patient who tested positive for anti-nephrin antibodies. Biopsy of the transplant kidney revealed co-localization of IgG and nephrin. Combined steroid pulse therapy and treatment with rituximab induced complete remission, with the anti-nephrin antibody titer correlating with the proteinuria volume.

Keywords Podocytopathy, Nephrotic syndrome, Post-transplant recurrence, Anti-nephrin antibodies

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Background

Most idiopathic nephrotic syndrome (INS) in childhood is due to minimal change disease (MCD) or focal segmental glomerulosclerosis (FSGS) caused by podocytopathy. INS is the most common form of nephrotic syndrome (NS) in childhood, and most cases are steroid-sensitive with a good prognosis. In some cases, however, the disease is steroid-resistant, and 4–5% of patients progress to end-stage renal disease (ESRD). In recent years, anti-nephrin antibodies have gained attention as a cause of NS related to podocytopathy. Here, we report a case of NS caused by podocytopathy after living-donor renal transplantation. In this case, a correlation was observed between anti-nephrin antibody levels and the degree of proteinuria.

Case presentation

The patient was a 59-year-old male who developed INS in 1980 and was diagnosed with MCD through renal biopsy. Although complete remission was initially achieved with steroid therapy, the disease recurred and his renal function gradually declined, leading to the initiation of hemodialysis in 2006. In 2014, he received a living-donor ABO-compatible kidney transplant from his younger brother. In early 2017, his NS recurred, prompting a biopsy of the transplanted kidney at the transplant center. The results indicated MCD, The biopsy results were MCD, but clinically it was FSGS, and low-density lipoprotein cholesterol apheresis (LDL-A) was performed 12 times per course for a total of four courses at the transplant hospital and nearby hospitals. However, the effect was limited. During this period, in November 2015, a single dose of rituximab (RTX) 500 mg without methylprednisolone pulse therapy was administered at a nearby hospital, but no reduction in proteinuria was observed. Because his treatment could not be continued at the nearby hospital, in October 2023 the patient was referred to our department by the transplant hospital for the purpose of continuing LDL-A. At our hospital, LDL-A performed once a week for 11 sessions did not reduce the proteinuria. The patient was then admitted in January 2024 for a repeat biopsy of the transplanted kidney and a reassessment of the treatment plan.

The patient's medical history includes undergoing a colectomy for colorectal cancer in 2010. In 2015, he underwent transurethral resection of a bladder tumor followed by intravesical chemotherapy for bladder cancer. On physical examination at the time of admission, the patient's height was 171.7 cm, weight was 67.7 kg, body temperature was 36.1 °C, and blood pressure was 113/71 mmHg. Moon face was observed. There was no evidence of anemia in the conjunctiva. In the lower abdomen, a midline surgical scar from the colorectal cancer surgery was noted, and a surgical scar from the kidney transplant was observed in the right lower quadrant. No edema was detected in the anterior tibial region. His oral medications were prednisolone 5 mg/day, tacrolimus 3 mg/day, mizoribine 200 mg/day, febuxostat 10 mg/day, telmisartan 20 mg/day, atorvastatin 5 mg/day, pemafibrate XR 0.4 mg/day, lafutidine 20 mg/day, and sulfamethoxazole 400 mg-trimethoprim 80 mg/day. The test results at the time of admission were as follows. Urinalysis showed proteinuria at 4(+), with a quantitative value of 7.98 g/day and was negative for glucose and occult blood. His leukocytes were 4800/μL; erythrocytes were 531×10^4/μL; hemoglobin was 16.1 g/dL; hematocrit was 47.6%; and platelets were 26.0×10^4/μL. Other laboratory findings included blood urea nitrogen (BUN) at 12.1 mg/dL; creatine at 1.31 mg/dL; estimated glomerular filtration rate (eGFR) at 44.8 mL/min./1.73 m^2; uric acid at 6.6 mg/dL; total protein at 4.9 g/dL; albumin at 2.9 g/dL; calcium at 8.9 mg/dL; phosphorus at 3.2 mg/dL; magnesium at 1.87 mg/dL; AST at 27 IU/l (normal value 8–38 IU/l); ALT at 24 IU/l (normal value 4–40 IU/l); γ-GTP at 126 IU/l (normal value <70 IU/l); total bilirubin at 0.43 mg/dl; and ALP at 71 IU/l (normal value 38–113 IU/l l). Immunological tests revealed immunoglobulin (Ig)G at 359 mg/dL, IgM at 43 mg/dL, and IgA at 86 mg/dL. Anti-nephrin antibody levels were elevated at 517 U/mL (cutoff value: 226 U/mL). In the biopsy specimen collected from the transplanted kidney at the time of admission, the cortex-to-medulla ratio was 7:3, and 21 glomeruli were identified. Three glomeruli showed collapse, but no segmental sclerosis was observed, which is consistent with the diagnosis of MCD. Conventional immunofluorescent staining revealed no IgG deposition. Electron microscopy (EM) showed diffuse foot process effacement (Fig. 1). Figure 2 presents the analysis using super-resolution microscopy. Green represents IgG, and red represents nephrin. Nephrin and IgG are co-localized in the glomerular capillary wall. These findings suggest binding of the anti-nephrin antibody to nephrin.

The clinical course is shown in Fig. 3. Prior to the present hospitalization, 11 sessions of LDL-A were performed, but proteinuria remained at approximately 3 g or more. After admission, because the trough level of tacrolimus was low, the dosage was increased from 3.0 to 4.5 mg/day. In addition, three administrations of methylprednisolone 500 mg pulse therapy were combined with one administration of RTX 200 mg. This treatment led to a dramatic reduction in proteinuria, which decreased to less than 0.1 g/gCr. The patient was discharged on the sixth day of hospitalization. On the fifth day after discharge, the cluster of differentiation (CD)19 lymphocyte count was 1.5/μL, indicating that B cells were nearly depleted. At the same time, serum Alb was normalized.

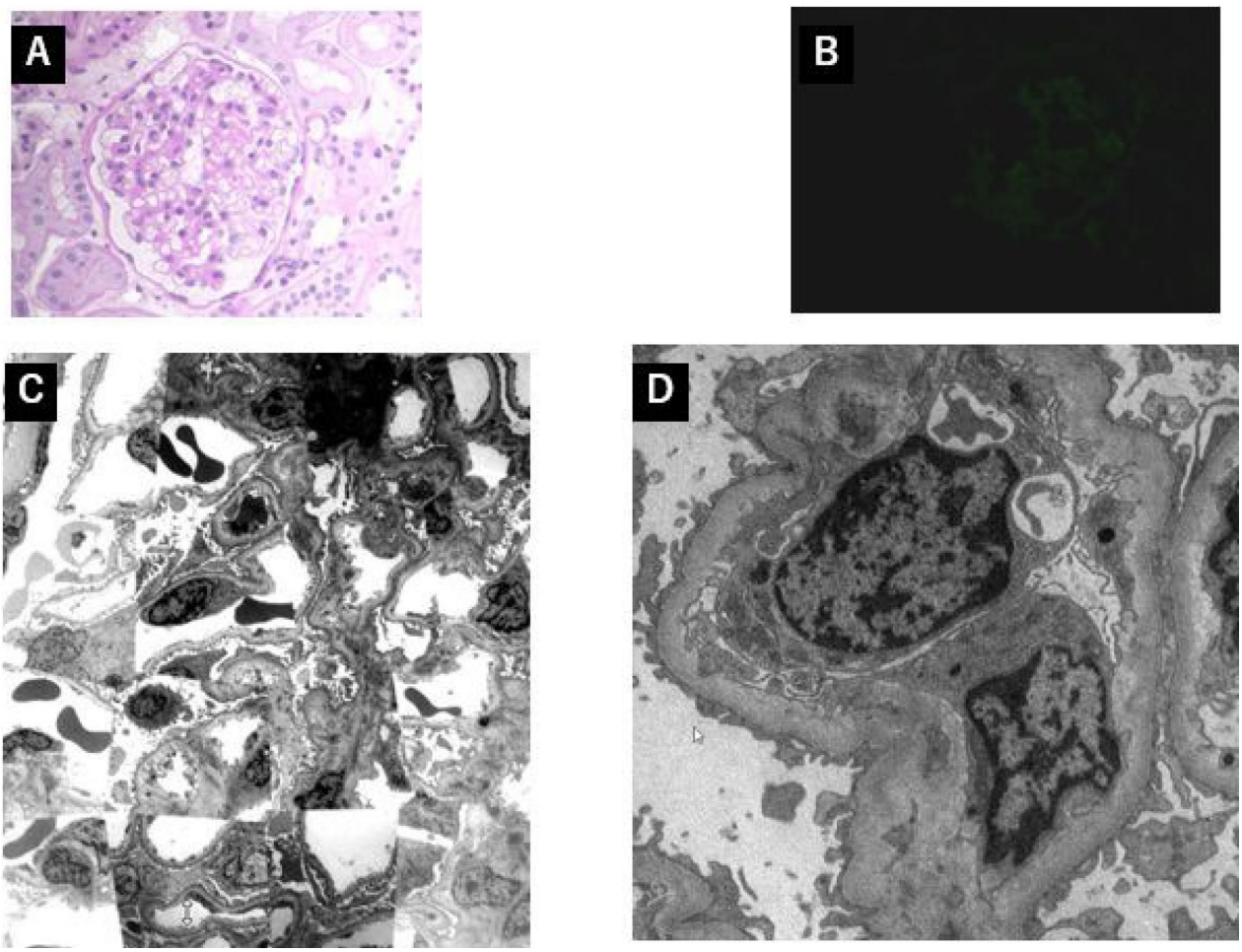

Fig. 1 Findings of the first biopsy of a transplanted kidney at our hospital: light microscopy using periodic-acid Schiff (PAS), conventional fluorescence microscopy (IgG), and electron microscopy (EM). Three glomeruli showed collapse, but no segmental sclerosis was observed in light microscopy (**A**), consistent with findings of minimal change disease. Conventional immunofluorescence staining revealed no IgG deposition (**B**). Electron microscopy (EM) showed diffuse foot process effacement (**C**; low magnification) and no dense depositions were seen anywhere (**D**; high magnification)

Although eGFRcr showed a slight decline, the change was not significant. Owing to a bladder cancer recurrence, the patient underwent a second transurethral tumor resection on the 122nd day after discharge. Consequently, proteinuria was observed at a level of 2+ on the 128th day after discharge. On the 141st day after discharge, the qualitative proteinuria was 2+, and the quantitative proteinuria reached 1.87 g/gCr. As there was also a suspicion of a recurrence of NS, his prednisolone dosage was increased from 15 to 20 mg/day. That increase promptly led to the disappearance of the proteinuria. During the course, the level of anti-nephrin antibodies and the degree of proteinuria were correlated. In July 2024, a second renal graft biopsy was performed at our hospital approximately 6 months after the initial biopsy. Unfortunately, the specimen collected consisted of only cortical tissue, which contained 45 glomeruli. Of those, 22 glomeruli showed collapse, but no segmental sclerosis was observed. These findings are consistent with MCD, and, as with the previous biopsy, no deposition of immunoglobulins (e.g., IgG) was detected. In addition, on EM, the degree of podocyte foot process effacement had declined to approximately 10% (Fig. 4), while immunostaining showed that nephrin clearly localized along the capillary loops, with only minimal nonspecific IgG staining. No anti-nephrin antibodies were detected in the tissue. These findings are consistent with the clinical remission of NS (Fig. 5). At the time of this renal biopsy, the CD19 lymphocyte count was 5.4/μL, indicating a slight recovery; however, given the instability of the patient's condition, a second dose of RTX 200 mg was administered after the biopsy.

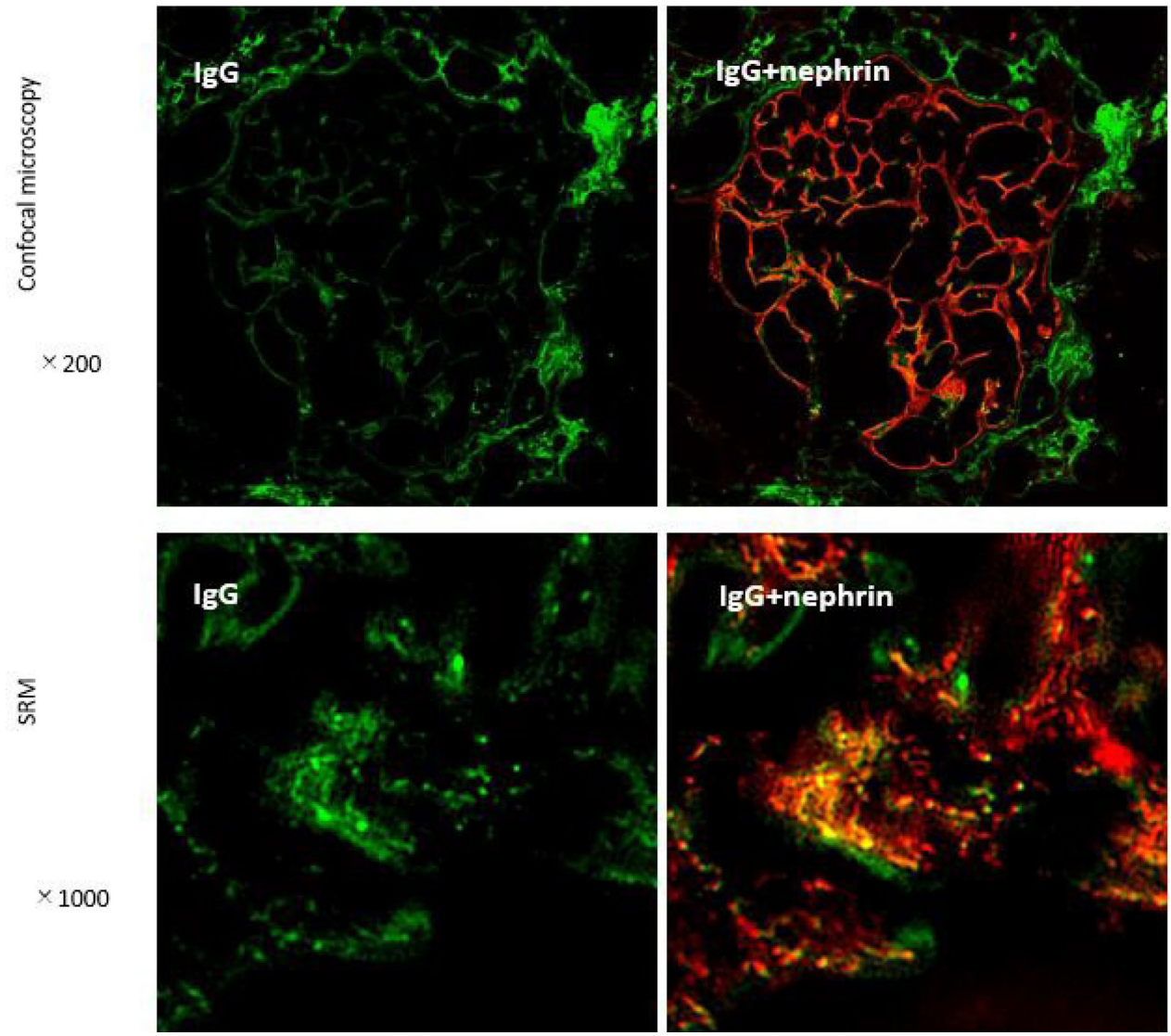

Fig. 2 Findings of dual immunofluorescence staining for IgG and nephrin using confocal microscopy and super-resolution microscopy (SRM) in graft biopsies of the first biopsy of a transplanted kidney at our hospital. Green represents IgG, and red represents nephrin. Owing to resolution limitations, the co-localization of nephrin and IgG in the glomerular capillary wall could not be determined in confocal microscopy. However, their co-localization was confirmed with SRM

Discussion

The most common form of NS in childhood is INS, which includes MCD and FSGS, both caused by podocytopathy. Kikunaga et al. reported the incidence of INS in Japan to be 6.49 cases per 100,000 children per year. This incidence rate was 3 to 4 times higher than in white populations. They found that 50% of pediatric patients diagnosed with frequently relapsing NS continued to experience recurrence or similar symptoms even 10 years after the initial treatment, despite being initially treated with cyclosporine. They also reported that steroid-resistant NS is a common cause of ESRD in these patients [1], while Tarshish et al. reported that 4–5% of patients with steroid-resistant NS progressed to ESRD [2].

Severe podocytopathies that commonly lead to NS include MCD, primary FSGS, and membranous nephropathy. Podocyte dysfunction is associated with a variety of factors, including genetic mutations, allergies, infections, lymphoid neoplasms, certain drugs, and autoimmune diseases [3]. In MCD and primary FSGS, diffuse foot process effacement (DFPE) can be observed under EM. However, in genetic FSGS, as well as secondary FSGS, such as obesity-related nephropathy, reflux nephropathy, and nephropathy associated with viral

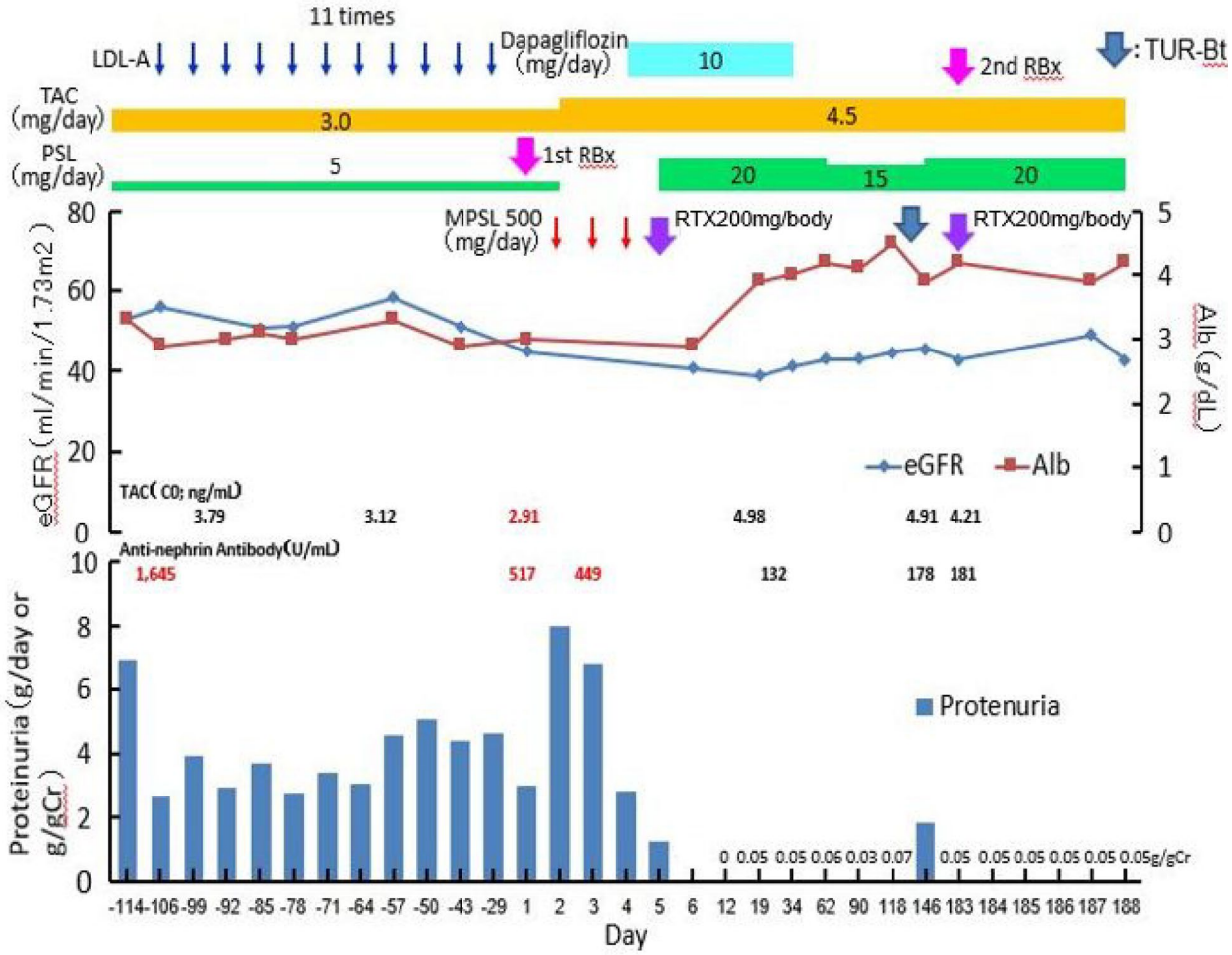

Fig. 3 Clinical course of the present case. Prior to the present hospitalization, 11 sessions of LDL-A were performed, but proteinuria remained at approximately 3 g or more. After admission, because the trough level of tacrolimus (TAC) was low, the dosage was increased from 3.0 to 4.5 mg/day. Thereafter, the patient receive three administrations of methylprednisolone (MPSL) 500 mg pulse therapy and one administration of RTX 200 mg. This treatment led to a dramatic reduction in proteinuria to less than 0.1 g/gCr, and the patient was discharged on the sixth day of hospitalization

infections or medication use, foot process effacement is reportedly segmental [4]. In our patient, the initial graft kidney biopsy, collected at our hospital when the patient was experiencing active NS, revealed DFPE in the glomeruli. However, the second biopsy, collected during NS remission, revealed that the DFPE had significantly diminished.

Pelletier et al. examined 158 INS patients ranging in age from infancy to 12 years who underwent kidney transplantation and reported the following results. NS recurrence was observed in 64 of those patients (41%). Among them, 78% of those with late steroid-resistant NS and 40% of those with primary steroid-resistant NS experienced recurrence after transplantation. Multivariable analysis showed that MCD histology (OR; 95% CI 5.6; 1.3–23.7) was more predictive of disease recurrence than FSGS in those patients.

INS recurrence after kidney transplantation has long been thought to involve some type of permeable factor. Ye et al. reviewed seven novel autoantibodies contributing to autoimmune podocytopathies [5]. In recent years, there have been numerous reports indicating that antibodies against nephrin, which is located in the slit diaphragm of the glomerular basement membrane, are deeply involved in the pathogenesis of INS (Table 1). Anti-nephrin antibodies have been detected in 38–91% of MCD cases and in 9–85.7% of primary FSGS cases [2, 6–11]. Moreover, it is known that the levels of anti-nephrin antibodies correlate with disease activity in NS (degree of proteinuria) [3, 6–8, 10]. Batal et al. demonstrated that pretransplant

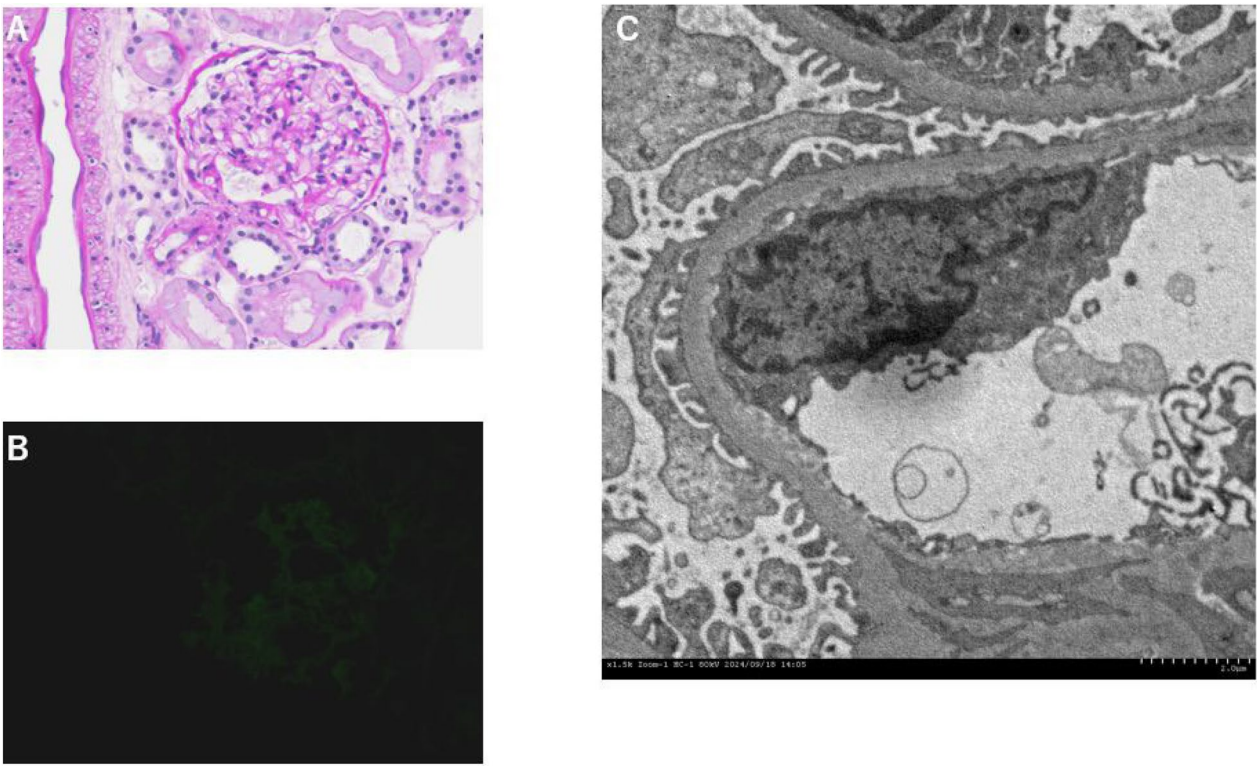

Fig. 4 Findings of the second biopsy of a transplanted kidney at our hospital: light microscopy using PAS (**A**), fluorescence microscopy for IgG (**B**), and EM (**C**). The glomeruli showed collapse, but no segmental sclerosis was observed. The findings were consistent with minimal change disease, and, as with the previous biopsy, no deposition of immunoglobulins such as IgG was detected. On EM of the transplant kidney, the degree of podocyte foot process effacement had improved to approximately 10%

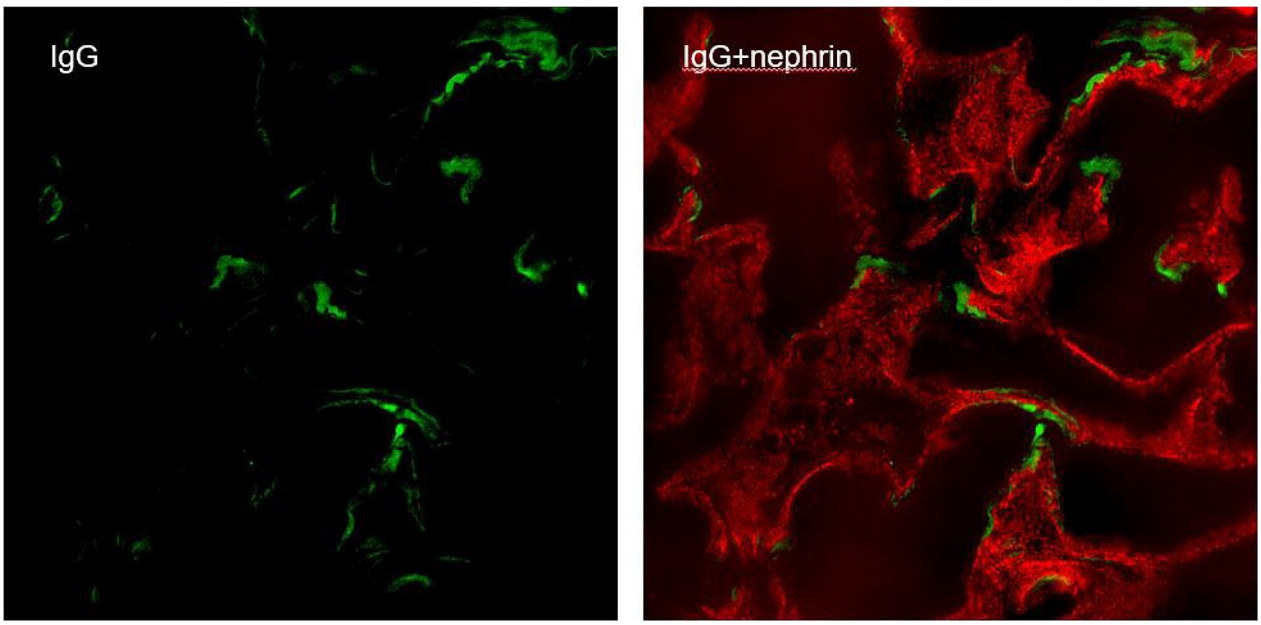

Fig. 5 Findings of dual immunofluorescence staining for IgG and nephrin in graft biopsies of the second biopsy of a transplanted kidney at our hospital; IgG and nephrin staining from the graft kidney biopsy. Nephrin was clearly localized along the capillary loops, and only minimal, nonspecific IgG staining was observed. No anti-nephrin antibodies were detected in the tissue

Table 1 Anti-nephrin autoantibodies in patients with podocytopathies (MCD and FSGS) [3, 6–10]

Study	No. of participant	Age	Female:Male	Positve rate of anti-nephrin autoantibodies
Hengel et al. [3]	MCD: 105	MCD: 47 (35–62)	MCD: 38:67	MCD: 44%
	pFSGS: 74	pFSGS: 52 (37–60)	pFSGS: 21:53	pFSGS: 9%
Watts et al. [6]	62	16 (5.5–37.5)	27:35	29%
Chebotareva et al. [7]	MCD: 11	MCD: 36.5 (25.8–47.8)	MCD: 7:4	MCD: 91%
	pFSGS: 32	pFSGS: 36 (27–56)	pFSGS: 21:20	pFSGS: 68.8%
Shirai et al. [8]	gFSGS: 8	gFSGS: 12.3 (9.2–15.5)	gFSGS: 4:4	gFSGS: 0%
	pFSGS: 14	pFSGS: 10.4 (6.9–12.8)	pFSGS: 4:10	pFSGS: 85.7%
	MCD: 13	MCD: N.A.	MCD: N.A.	MCD: 38.0%
Batal et al. [9]	rDP: 22	rDP: 38 (30–45)	rDP: 19:20	rDP: 38%
	nrDP; 17	nrDP: 29 (26–56)	nrDP: 12:5	nrDP: 0%
Raglianti et al. [10]	MCD: 50	MCD: 20.6 (1.8–72.6)	MCD: 22:28	MCD: 48.0%
	FSGS: 58	FSGS: 22.7 (0.25–78.5)	FSGS: 26:32	FSGS: 22.4%
	CG: 2	CG: 11.2 (10.25–12.16)	CG: 1:1	CG: 50.0%

gFSGS, genetic focal segmental glomerulosclerosis; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease; N.A., not available; nrDP, non recurrent diffuse podocytopathy; pFSGS, primary focal segmental glomerulosclerosis; rDP, recurrent diffuse podocytopathy, ssNS, steroid sensitive nephrotic syndrome

anti-nephrin antibody levels serve as a predictor of post-transplant recurrence of diffuse podocytopathy [9]. In addition, Cui et al. reported that anti-nephrin antibodies in INS are not merely markers but actively contribute to the pathogenesis of MCD and primary FSGS. They further stated that the discovery of anti-nephrin antibodies represents a paradigm shift in this field [11]. That insight not only provides a noninvasive diagnostic alternative to kidney biopsies but also suggests the potential for novel targeted therapies. Hengel et al. reported that administering nephrin to mice induced the production of anti-nephrin autoantibodies. In that mouse model, NS developed, and EM revealed widespread effacement of podocyte foot processes in the nephrin-immunized mice. Immunohistochemical examination using dual immunofluorescent staining revealed co-localization of nephrin deposits and IgG dots within active ISN lesions [6, 8–10]. In our present case, the initial biopsy from the transplanted kidney, collected during active NS, showed a punctate distribution of nephrin co-localized with IgG along the glomerular capillary walls. In the second biopsy collected during remission, nephrin was neatly localized along the capillary walls, with only a minimal presence of nonspecific IgG.

In treating recurrent INS caused by podocytopathy following kidney transplantation, Muso recognized the efficacy of LDL-A for promoting remission of NS. She hypothesized that adsorption of certain permeable factors contributes to the mechanism by which LDL-A alleviates INS [12]. In our case, the anti-nephrin antibody level was high (1645 IU/mL) at the start of LDL-A; however, it had decreased to 517 IU/mL prior to the intensified treatment during the patient's hospitalization. Sannomiya et al. reported that in five cases of kidney transplantation for FSGS, performing LDL-A 1–2 times prior to transplantation and simultaneously administering a low dose (100 mg) of RTX successfully prevented FSGS recurrence after transplantation [13]. Plonsky-Toder et al. reported that early plasma exchange and RTX administration were effective treatments for recurrent FSGS after transplantation [14]. We consider that, theoretically, a treatment strategy entailing removal of permeable factors, such as anti-nephrin antibodies, through plasma exchange and subsequent prevention of their re-expression could be beneficial. It is unclear why a single 200 mg dose of RTX was highly effective in our case, whereas a single 500 mg dose of RTX had been ineffective at the previous hospital. We believe that the interval between the LDL-A and RTX administration, as well as the presence or absence of methylprednisolone pulse therapy prior to RTX administration, may have played a role. The interval between LDL-A and RTX administration was 1 month at our hospital. However, at the previous hospital, the interval was thought to be somewhat longer, although the details are unknown. In addition, methylprednisolone pulse therapy was not administered before RTX administration at the previous hospital. Iijima et al. reported that in children aged 2 years and older with FRNS or steroid-dependent NS, the period until NS relapse was significantly longer in those receiving RTX (27 patients) than in a group receiving a placebo (25 patients). The RTX dosage at that time was 375 mg/m^2 per week, administered for four consecutive weeks [15]. There are also several reports suggesting that a

lower dose of RTX is effective for steroid-dependent NS [16–18]. Fujimoto et al. demonstrated that a low dose of RTX (200 mg/body) was effective for maintaining remission in steroid-dependent NS [16], while Zhang et al. found that in adults with FRNS, a low-dose RTX protocol (a single 200 mg dose per week for 4 weeks administered every 6 months) maintained remission in 90.9% of cases [17]. The efficacy of low-dose RTX was also demonstrated after ABO-incompatible kidney transplantation [18].

Rosenberg et al. reported that FSGS lesions are focal and, as a result, sampling errors may lead to a diagnosis of MCD [19]. The present case is clinically considered to be FSGS, though the results of all three renal transplant biopsies indicated MCD. In the first biopsy at our hospital, the corticomedullary junction was included, and 21 glomeruli were observed, leading to the conclusion that there was no sampling error. In recent years, it has become widely accepted that both MCD and FSGS are part of the same disease spectrum, presenting as NS caused by podocytopathy, and that the progression from MCD to FSGS occurs as podocyte damage becomes more severe [20, 21]. There is controversy regarding the relationship between the duration of B cell depletion and NS remission. Several reports suggest an association between the number of CD19-positive lymphocytes and INS recurrence [22, 23]. In contrast, several recent reports suggest that the number of CD19-positive cells is not associated with INS recurrence [16, 24, 25]. In the present case, transient proteinuria was observed during the course, but the CD19 lymphocyte count remained below 10/μL.

Conclusions

We report a case of NS caused by podocytopathy with high levels of anti-nephrin antibodies following living-donor kidney transplantation. Combined LDA-A, steroid pulse therapy and treatment with a single low dose administration of RTX resulted in complete remission of NS. The anti-nephrin antibody titers correlated with the degree of proteinuria, suggesting these antibodies play a significant role in the pathogenesis of the patient's condition.

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Author contributions
R.M., K.M., and T.M. took care of patients and participated in the decisions about treatment. R.M. prepared the manuscript. S.H., K.I., I.M., and Y.I. were responsible for the examination of renal biopsy specimens using light microscopy, fluorescence microscopy, and electron microscopy. Y.S., K.M., and M.H. investigated the measurement of anti-nephrin antibodies and the localization of IgG and nephrin using super-resolution microscopy. All authors have read and approved the final manuscript.

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Availability of data and materials
No datasets were generated or analyzed during the current study.

Declarations

Ethics approval and consent to participate
The study was conducted in compliance with the Declaration of Helsinki and approved by the ethics committee in the Fujita Memorial Hospital, Fukui, Japan (approval number: 67).

Consent for publication
Written informed consent was obtained from the present patient.

Competing interests
The authors declare no competing interests.

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References

1. Kikunaga K, Ishikura K, Terano C, Sato M, Komaki F, Hamasaki Y, et al. Japanese pediatric survey holding information of nephrotic syndrome (JP-SHINE) study of the Japanese study group of renal disease in children. High incidence of idiopathic nephrotic syndrome in East Asian children: a nationwide survey in Japan (JP-SHINE study). Clin Exp Nephrol. 2017;21(4):651–7.
2. Tarshish P, Tobin JN, Bernstein J, Edelmann CM Jr. Prognostic significance of the early course of minimal change nephrotic syndrome: report of the international study of kidney disease in children. J Am Soc Nephrol. 1997;8(5):769–76.
3. Hengel FE, Dehde S, Lassé M, Zahner G, Seifert L, Schnarre A, et al. International Society of Glomerular Disease. Autoantibodies targeting nephrin in podocytopathies. N Engl J Med. 2024;391(5):422–33.
4. Sethi S, Glassock RJ, Fervenza FC. Focal segmental glomerulosclerosis: towards a better understanding for the practicing nephrologist. Nephrol Dial Transplant. 2015;30(3):375–84.
5. Ye Q, Zhou C, Wang D, Fu H, Wang J, Mao J. Seven novel podocyte autoantibodies were identified to diagnosis a new disease subgroup-autoimmune podocytopathies. Clin Immunol. 2021;232:108869.
6. Watts AJB, Keller KH, Lerner G, Rosales I, Collins AB, Sekulic M, et al. Discovery of autoantibodies targeting nephrin in minimal change disease supports a novel autoimmune etiology. J Am Soc Nephrol. 2022;33(1):238–52.
7. Chebotareva N, Vinogradov A, Birukova Y, Alentov I, Sergeeva N, Chemodanova D, et al. A pilot study of anti-nephrin antibodies in podocytopathies among adults. Nephrology. 2024;29(2):86–92.
8. Shirai Y, Miura K, Ishizuka K, Ando T, Kanda S, Hashimoto J, et al. A multi-institutional study found a possible role of anti-nephrin antibodies in post-transplant focal segmental glomerulosclerosis recurrence. Kidney Int. 2024;105(3):608–17.
9. Batal I, Watts AJB, Gibier JB, Hamroun A, Top I, Provot F, et al. Pre-transplant anti-nephrin antibodies are specific predictors of recurrent diffuse podocytopathy in the kidney allograft. Kidney Int. 2024;106(4):749–52.
10. Raglianti V, Angelotti ML, Cirillo L, Ravaglia F, Landini S, Palazzo V, et al. Anti-slit diaphragm antibodies on kidney biopsy identify pediatric

patients with steroid-resistant nephrotic syndrome responsive to second-line immunosuppressants. Kidney Int. 2024;6:1124–34.
11. Cui Z, Zhao MH. Anti-nephrin autoantibodies: a paradigm shift in podocytopathies. Nat Rev Nephrol. 2024;20(10):639–40.
12. Muso E. Beneficial effect of LDL-apheresis in refractory nephrotic syndrome. Clin Exp Nephrol. 2014;18(2):286–90.
13. Sannomiya A, Murakami T, Koyama I, Nitta K, Nakajima I, Fuchinoue S. Preoperative low-density lipoprotein apheresis for preventing recurrence of focal segmental glomerulosclerosis after kidney transplantation. J Transplant. 2018;2018:8926786.
14. Plonsky-Toder M, Pollack S, Tibi R, Libinson-Zebegret I, Yaakobov R, Eisenstein I, et al. Management and long-term outcome of recurrent idiopathic FSGS in pediatric kidney transplant recipients. Sci Rep. 2024;14(1):25493.
15. Iijima K, Sako M, Nozu K, Mori R, Tuchida N, Kamei K, et al. Rituximab for childhood-onset refractory nephrotic syndrome (RCRNS) study group. Rituximab for childhood-onset, complicated, frequently relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2014;384(9950):1273–81.
16. Fujimoto K, Kagaya Y, Kumano S, Fujii A, Tsuruyama Y, Matsuura T, et al. Retrospective single-arm cohort study of steroid-dependent minimal change nephrotic syndrome treated with very low-dose rituximab. Clin Nephrol. 2021;95(1):29–36.
17. Zhang J, Zhao H, Li X, Qian R, Gao P, Lu S, et al. Efficacy of low-dose rituximab in minimal change disease and prevention of relapse. BMC Nephrol. 2023;24(1):112.
18. Lee HR, Kim K, Lee SW, Song JH, Lee JH, Hwang SD. Effect of rituximab dose on induction therapy in ABO-incompatible living kidney transplantation: a network meta-analysis. Medicine. 2021;100(10):e24853.
19. Rosenberg AZ, Kopp JB. Focal segmental glomerulosclerosis. Clin J Am Soc Nephrol. 2017;12(3):502–17.
20. Maas RJ, Deegens JK, Smeets B, Moeller MJ, Wetzels JF. Minimal change disease and idiopathic FSGS: manifestations of the same disease. Nat Rev Nephrol. 2016;12(12):768–76.
21. Sim JJ, Smoyer WE, Schachter AD. Minimal change disease and FSGS are a spectrum of a single disease within immune-mediated nephrotic syndrome. Kidney360. 2024;5(8):1197–9.
22. Ruggenenti P, Ruggiero B, Cravedi P, Vivarelli M, Massella L, Marasà M, et al. Rituximab in nephrotic syndrome of steroid-dependent or frequently relapsing minimal change disease or focal segmental glomerulosclerosis (NEMO) study group. Rituximab in steroid-dependent or frequently relapsing idiopathic nephrotic syndrome. J Am Soc Nephrol. 2014;25(4):850–63.
23. George J, Alex S, Thomas ETA, Gracious N, Vineetha NS, Kumar S. Clinical response and pattern of B cell suppression with single low dose rituximab in nephrology. Kidney360. 2020;1(5):359–67.
24. Colucci M, Carsetti R, Cascioli S, Casiraghi F, Perna A, Ravà L, et al. B cell reconstitution after rituximab treatment in idiopathic nephrotic syndrome. J Am Soc Nephrol. 2016;27(6):1811–22.
25. Del Vecchio L, Allinovi M, Rocco P, Brando B. Rituximab therapy for adults with nephrotic syndromes: standard schedules or B cell-targeted therapy? J Clin Med. 2021;10(24):5847.

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