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Telitacicept for lupus nephritis with BAFF and APRIL double positivity in children: a case report

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Abstract

We present a case of pediatric lupus nephritis (LN) with double positivity for BAFF and APRIL, highlighting the efficacy and safety of telitacicept in achieving complete remission. The patient, a 14-year-old Chinese male, presented with severe renal impairment and thrombotic microangiopathy (TMA). Conventional treatments were ineffective, and the patient experienced severe adverse reactions to rituximab. Subsequent treatment with telitacicept and sirolimus led to significant clinical improvement. After 6 months of follow-up, the patient achieved complete remission with an SLEDAI score of 0. This case underscores the potential of precision medicine in LN treatment. Individualized treatment based on pathological mechanisms is necessary, and telitacicept can improve the prognosis of lupus nephritis with good safety.

Keywords Telitacicept, Children, Lupus nephritis, Thrombotic microangiopathy, Precision medicine

Background

Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease characterized by inflammation and immune-mediated damage in multiple organ systems, including skin, blood, bones, muscles, and kidneys [1]. Lupus nephritis (LN) is one of the severe organ manifestations, and LN remains a major cause of morbidity and mortality of SLE, with 5–30% of LN patients develop end-stage renal disease within 10 years [2].When SLE occurs in childhood, the course of disease development is more unpredictable, and its mortality rate is higher [3].

The renal biopsy pathology guides the treatment plan for LN, and the conventional treatment plan includes corticosteroids, immunosuppressants, hydroxychloroquine, etc. For refractory LN or severe adverse reactions in standard therapy, additional biological agents are required. The pathogenesis of SLE is very complex, and numerous studies have shown that excessive activation and proliferation of B lymphocytes play a core role, with B-cell activation factor (BAFF) and a proliferation-inducing ligand (APRIL) being crucial [4]. With in-depth research into the pathogenesis, previous reports have indicated that targeted B-lymphocyte therapy may have similar or better efficacy compared to traditional treatment plans, which has fewer adverse reactions and faster onset [5]. In SLE treatment, common biological agents targeting B lymphocytes include rituximab, belimumab, and telitacicept. Telitacicept is a new biological agent that was launched in China in 2021, capable of simultaneously blocking the binding of BAFF and APRIL to transmembrane activator and calciummodulator and cyclophilin

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ligand interactor (TACI), thereby inhibiting the differentiation and survival of plasma cells and the antibody isotype switching of marginal zone B lymphocytes and follicular B lymphocytes to treat SLE [6]. Phase I and II trials of telitacicept have shown good efficacy and safety [7–9]. Among a lot of B lymphocyte biological agents, the literature reports differ. Although sirolimus is not a standard conventional treatment, it has also shown good tolerance and broad prospects in SLE treatment. This article reports a case of a child with lupus nephritis who was positive for BAFF and APRIL, and also for mTOR. The patient responded well to a combination of telitacicept and sirolimus, providing a reference for precision-targeted treatment of lupus nephritis based on pathogenic mechanisms. This case report originally described precision treatment in a child with lupus nephritis who is BAFF and APRIL double positive.

Case report

A 14-year-old Chinese male child was admitted to the pediatric ward due to facial edema for 2 weeks and gross hematuria for 1 week. After admission, the edema gradually worsened, accompanied by dyspnea and dark soy sauce-colored urine. Prior to admission, he had urinary protein 3+, occult blood 3+, hemoglobin 89 g/L, platelet count 57 × 10^9/L, serum creatinine 517 μmol/L, and albumin 24.9 g/L. He had no significant past medical history, personal history, or family history and was unmarried. On the day of admission, his respiratory rate was 22 breaths/min, blood pressure was 147/107 mmHg, and weight was 50 kg. After admission, urine examination: protein 3+, occult blood 3+, red blood cells 960/μl, casts 7/LPF, urine showed dysmorphic red blood cells (acanthocytes), 24-hour urinary protein quantification: 3307 mg/24 h (300 ml/24 h), serum creatinine 584μmol/L, white blood cells 2.91 × 10^9/L, neutrophils accounted for 65.8%, hemoglobin 87 g/L, platelet count 48 × 10^9/L, D-dimer 5.21 mg/L, fibrinogen degradation products 9 mg/L, lactate dehydrogenase (LDH) elevated to 500 IU/L. Antinuclear antibodies (ANA) were positive (ANA 1:320). Double-stranded DNA (ds-DNA), nucleosomes, and histones, complement C3 and C4 were decreased (Anti-C1q > 200 IU/mL, dsDNA 66 IU/Ml). Anti-cardiolipin antibodies were positive. ANCA, anti-GBM, anti-platelet antibodies, β2-GP1 antibodies, and Coomb's test were negative. Rheumatoid factor (RF) was normal. See Table 1 for all investigations. Bilateral renal color Doppler ultrasound showed good blood flow, slightly enhanced parenchymal echo, chest CT presented left lower lung inflammation, and a small amount of left pleural effusion. Based on the history, physical examination, and testing, the admission diagnosis was: (1) Systemic lupus erythematosus SLEDAI score of 12, lupus nephritis with lupus hematologic damage (2) Secondary thrombotic microangiopathy?

Table 1

Test	Result
Urinary protein	3+
Occult blood	3+
Hemoglobin	89 g/L
Platelet count	57 × 10^9/L
Serum creatinine	517 μmol/L
Albumin	24.9 g/L
Anti-cardiolipin antibodies	Positive
C3、C4	Decreased
Anti-C1q	> 200 IU/mL
Double-stranded DNA	66 IU/mL
ANA	1:320
ANCA, anti-GBM, anti-platelet antibodies, β2-GP1 antibodies, Coomb's test	Negative
Rheumatoid factor (RF)	Normal

*Arrows show intimal lax oedema and TMA-like changes in the arteries
mTOR(++) BAFF(+~++)

In terms of treatment, pediatricians firstly used methylprednisolone 20 mg three times a day, hydroxychloroquine 100 mg twice a day; a total of 1 week of treatment. Due to the decrease in urine volume (daily urine volume 0-300 ml), soy sauce-colored urine accompanied by general edema worsening, continuous blood purification, hemodialysis were used. After one week of treatment, the effect was not significant, and due to acute kidney injury, the patient was transferred to the Department of Nephrology for further treatment. Our treatment team suspected a combination of lupus nephritis (LN) and thrombotic microangiopathy (TMA). We conducted a peripheral blood smear test, which revealed that schistocyte accounted for 2.6% of the total. The ADAMTS 13 activity was measured at 72.91%, with no detectable ADAMTS 13 inhibitory antibodies. Additionally, anti-cardiolipin antibody IgG was positive.

Based on these findings, we adjusted the treatment plan. The patient was administered methylprednisolone at a dose of 250 mg on the first day, followed by 500 mg on the second and third days. After the shock phase resolved on the fourth day, the dose was reduced to 40 mg of methylprednisolone once daily. We also initiated plasma exchange (PE). However, the patient developed an allergic reaction following PE, characterized by widespread wheals and itching. As a result, we suspended the PE treatment and proceeded with a renal biopsy.

The renal biopsy results were as follows:

Light microscopy The biopsy specimen contained 22 glomeruli. We observed 1 segment with segmental sclerosis, 4 cellular crescents, and 3 fibrocellular crescents. Many capillary loops exhibited increased cellularity accompanied by inflammatory cell infiltration, leading to

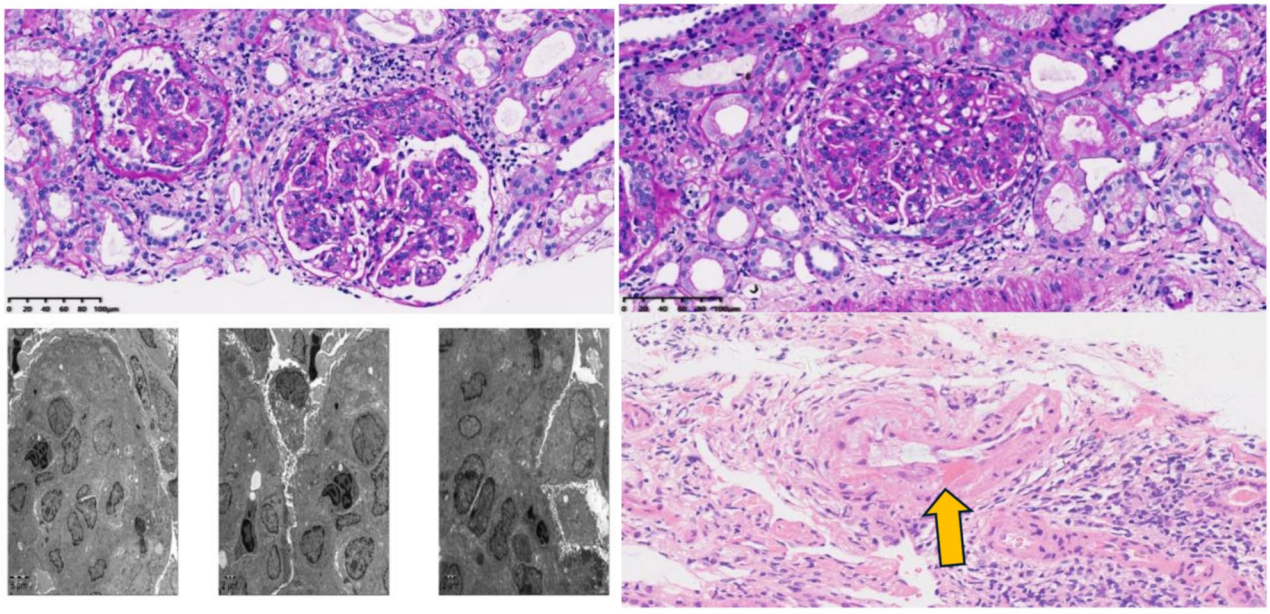

Fig. 1 Pathological light and electron microscopy. *Arrows show intimal lax oedema and TMA-like changes in the arteries

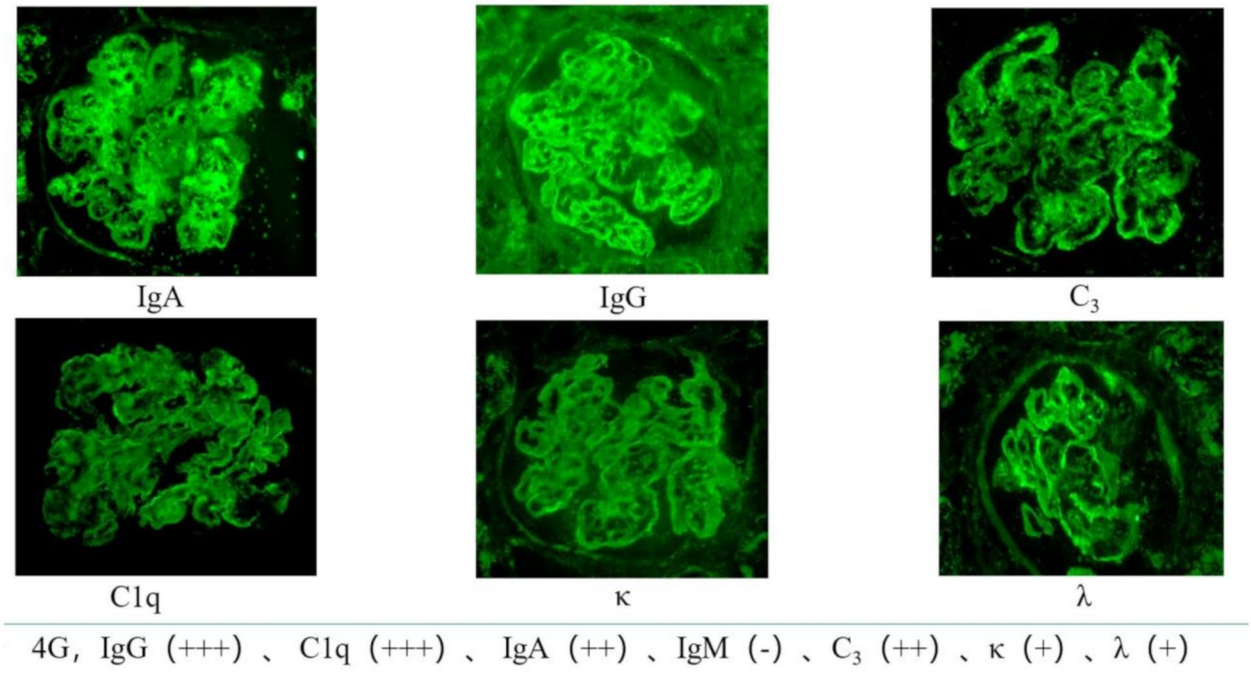

Fig. 2 Pathological IF

loop blockage. The remaining glomeruli showed mild to moderate mesangial cell and matrix proliferation, with segmental severe proliferation (Fig. 1).

Electron microscopy Examination of 3 glomeruli revealed capillary endothelial cell proliferation with obvious vacuolar degeneration. A few red blood cells were gathered in individual lumens, and a few lymphocytes, monocytes, and neutrophils were visible. Some capillary loops were compressed, and some lumens were narrowed. The renal capsule wall layer was thickened and stratified, and the wall layer cells were vacuolated (Fig. 1), immunofluorescence (IF) results are shown (Fig. 2); the pathological diagnosis was lupus nephritis (IV + V) with TMA; based on the pathology, we added rituximab, but the patient had severe chills during the infusion process.

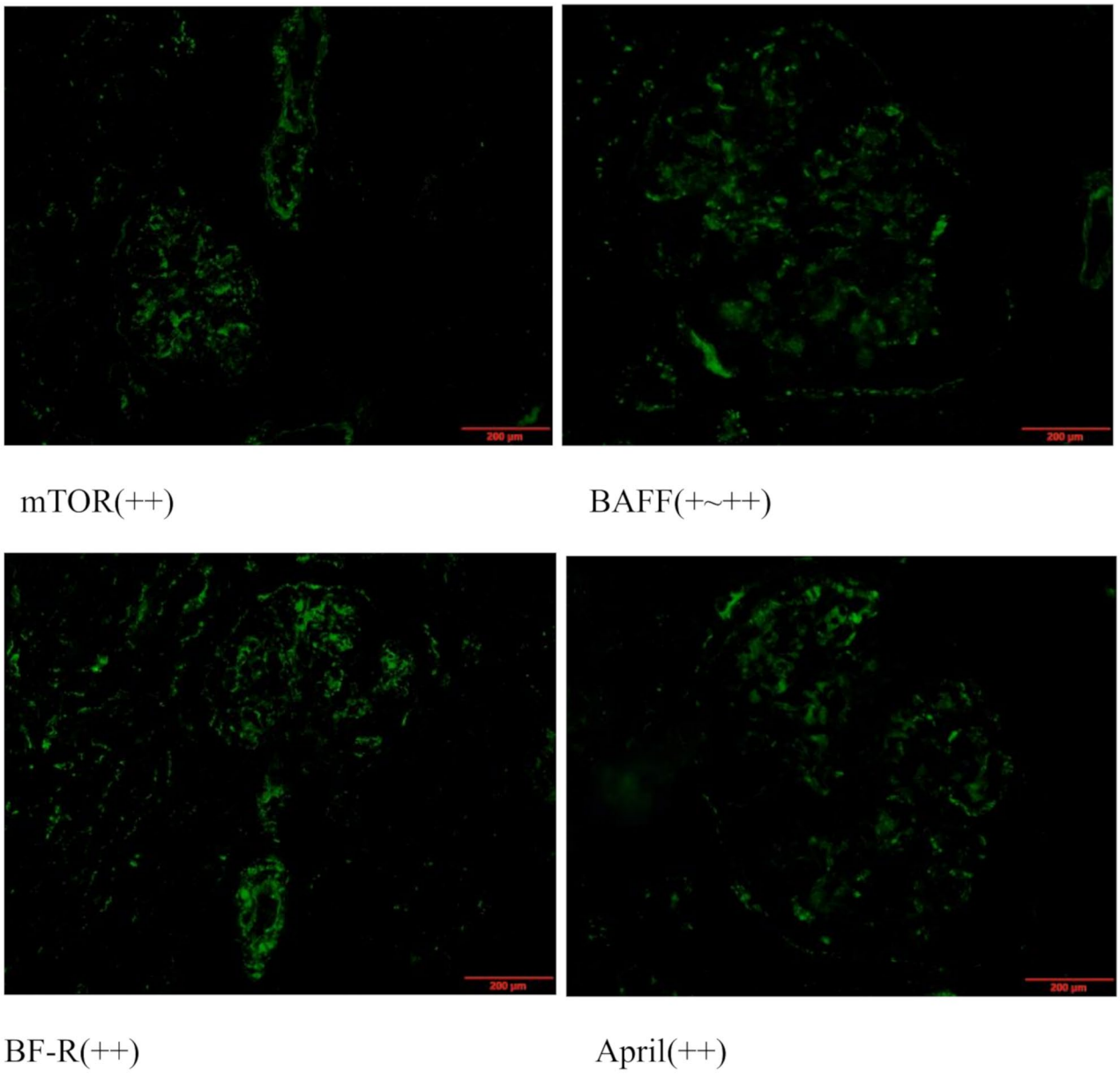

Fig. 3 Specific IF: mTOR(++),BAFF(+~++), BF-R(++), April(++)

After pausing the infusion for 1 h, the peak body temperature continued to rise, forcing us to discontinue rituximab. We maintained conventional treatment and intermittent hemodialysis and performed special IF on the patient's kidney tissue and found mTOR (++), BAFF (+~++), April (++) (Fig. 3). Further immunosuppressive therapy was adjusted to sirolimus 1 mg once a day (drug concentrations of sirolimus were maintained at 2–4 ng/ml), telitacicept 160 mg once a week, urine volume gradually recovered, serum creatinine decreased, hemodialysis was stopped, and the discharge treatment plan was: prednisone 40 mg once a day, sirolimus 1 mg once a day, hydroxychloroquine 0.1 g twice a day, telitacicept 160 mg once a week. After 2 weeks of induction therapy, patients began to show significant clinical improvement, as evidenced by a gradual return of urine output, a decrease in serum creatinine levels and a significant reduction in proteinuria. Telitacicept was used for a total of 27 weeks.

The patient had a good clinical outcome. After 6 months of follow-up, the SLEDAI score was 0. The 24-hour proteinuria quantification was 262 mg/24 h; serum creatinine, 73.8 μmol/L; albumin, 40.7 g/L; hemoglobin, 142 g/L; platelet count, 340 × 10^9/L; double-stranded DNA, 4.15 IU/mL; and complement C3, 1.18 g/L. These results indicated that the patient had achieved complete remission. The maintenance

treatment plan was: prednisone 5 mg once a day, sirolimus 1 mg once a day, hydroxychloroquine 0.1 g once a day. Serum drug concentrations of sirolimus were maintained at 2–4 ng/ml. After 6.5 months of treatment, the regimen was adjusted to: merti-mescaline 0.5 g twice daily, prednisone 5 mg once daily. The patient's condition is stable on continuous follow-up.

Discussion

The organ that the most commonly and first to be damaged by SLE is kidney, and its pathogenesis also complex. Renal biopsy helps to clarify the diagnosis, understand the pathogenesis, provide reference value for further treatment, and improve prognosis. The ultimate goal of treatment is to preserve kidney function and reduce the mortality associated with chronic kidney disease and kidney failure. Different LN pathological morphological manifestations can determine the best treatment plan. Glucocorticoids can quickly reduce inflammatory reactions and help control the disease, but they have many adverse reactions and complications after cumulative doses. Therefore, it is very important to add immunosuppressants and biological agents according to the LN pathological manifestations to help reduce the cumulative dose of glucocorticoids; Mammalian Target of Rapamycin (mTOR) plays a significant role in regulating cell proliferation, growth, and survival. There are already some papers reported that mTOR activation can lead to kidney diseases, such as lupus nephritis. Sirolimus is a specific mTOR inhibitor [10]. Preliminary confirmation in vitro and animal experiments has shown that sirolimus is a potential treatment plan for LN [10]. Telitacicept is one of the biological agents currently used for LN, which depends on its dual-channel mechanism of action of BAFF and APRIL in telitacicept. By blocking BAFF, it inhibits the further development and maturation of immature B cells, which helps control the development of future conditions. By blocking APRIL, it inhibits the differentiation of mature B cells into plasma cells and affects autoantibodies secreted by autoreactive plasma cells, better controlling disease activity [5], which showed its unique advantages in treating LN. The treatment plan for LN is comprehensive and diverse, but we believe that precision treatment based on the mechanism of action is more conducive to controlling the disease and improving the prognosis. This is a case report on precision treatment of LN in our center that has never been reported before.

In this case, we successfully used telitacicept and sirolimus to treat a pediatric LN patient with double-positive BAFF and APRIL and positive mTOR. The patient initially presented with severe renal impairment and TMA, suggesting a highly active disease. The ineffectiveness of conventional therapies (e.g., high-dose glucocorticoids and plasma exchange) and the patient's severe adverse reactions to rituximab underscored the need to find an alternative therapeutic strategy.

Because the immunohistochemical results showed high expression of BAFF and APRIL, the dual mechanism of action of telitacicept on BAFF and APRIL was particularly important in this case. By blocking BAFF, telitacicept inhibits further development and maturation of immature B cells, thereby controlling future disease progression. By blocking APRIL, it inhibited the differentiation of mature B cells to plasma cells, which in turn reduced autoantibody secretion by self-reactive plasma cells and better controlled disease activity. This mechanism showed a unique advantage in LN treatment, consistent with the significant reduction in proteinuria and normalisation of renal function that we observed in this case. In addition, we added sirolimus to further enhance the therapeutic effect. mTOR plays an important role in cell proliferation, growth and survival, and its activation is closely associated with the development of LN.

The efficacy and safety of telitacicept have been reported in a small number of cases. Hui-Zhi Jin and others published a multi-center study of using telitacicept to treat SLE. After 52 weeks of telitacicept treatment, the efficacy was good, and the median 24-hour proteinuria in LN patients decreased from 1323.5 mg to 224.0 mg. No serious adverse events were observed [11]. Ruilin Chen and other scholars used telitacicept to treat SLE for at least 4 weeks, with an 80% SLE index-4 (SRI-4) response rate, and the adverse reactions were all mild to moderate and controllable [12]. HONG ZHU and others also came to the same conclusion. Thirteen LN patients who received telitacicept were included in the study. After 12–48 weeks of treatment, 11 patients (84.6%) saw a reduction in symptoms, SLEDAI score decreased by more than 4 points, all patients' proteinuria levels decreased, and the dose of glucocorticoids and immunosuppressive drugs used were reduced [13]. The safety and efficacy of telitacicept in treating SLE and LN have been confirmed in the literature, consistent with the treatment outcome observed in this case. There are also relevant reports on the clinical research of sirolimus. Yap DYH and other scholars observed 16 LN patients who received sirolimus treatment, all of them accepted sirolimus because they were intolerant to other immunosuppressants or had a history of tumors, the ds-DNA and proteinuria in 5 cases who received induction treatment were all improved, the complement and their renal function in 11 cases who received maintenance treatment were improved and stable, and the safety of the drug was also good [14]. In a meta-analysis, systematic review study, it is also believed that sirolimus has a good prospect and safety in the treatment of SLE [15]. There is only one retrospective study of telitacicept in children for the treatment of systemic

lupus erythematosus, and Sun L and other scholars have verified the safety and efficacy of telitacicept through a pre- and post-treatment self-controlled trial [16]. Therefore, both sirolimus and telitacicept have been proven to be safe and effective in the treatment of SLE and LN.

We believe that different SLE and LN patients have different tolerances and responses to different drugs. Treating completely according to the existing diagnostic and guidelines may have different effects on different individuals, so individualized precision treatment is urgently needed.

There are still some research defects in this case report, such as the low level of evidence for this kind of study, which needs to be verified through cohort studies and randomized controlled trials. Our center has designed a clinical research plan for precision treatment of LN and has entered the stage of enrollment of participants. We also look forward to being able to verify the advantages and feasibility of precision treatment through studies at higher levels of evidence.

Conclusion

SLE and LN pose a huge disease burden to patients. Precision medicine is a rapidly developing medical model that can formulate treatment plans based on the different physiological and pathological characteristics of each patient. By special IF, the conventional treatment plus precision telitacicept and sirolimus treatment greatly improved the prognosis of the diseases, and no adverse reactions were observed.

Abbreviations

BAFF	B-cell Activation Factor
APRIL	A Proliferation Inducing Ligand
LN	Lupus nephritis
LDH	Lactate dehydrogenase
TMA	Thrombotic microangiopathy
SLE	Systemic lupus erythematosus
ds-DNA	Double-stranded DNA
TACI	Transmembrane activator and calciummodulator and cyclophilin ligand interactor
RF	Rheumatoid factor
ANA	Antinuclear antibodies
PE	Plasma exchange
IF	Immunofluorescence

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-025-05778-3.

Supplementary Material 1

Author contributions

Write a manuscript: Yang Meng, Meng YingCollect data: Meng YingStatistical analysis: Huang Li, Zhao HongwenRevise a manuscript: Tang Xiaopeng.

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Data availability

All data are included in this study.

Declarations

Ethical approval

Fast review by the Ethics Committee of the First Affiliated Hospital of the PLA Army Military Medical University.

Consent to participate

Informed consent of patient and guardian. In the case of a patient using a specific treatment, such as Taitacept, when we sign a consent form, the patient and legal guardian agree that the data may be used for medical research and will not affect the course of treatment.

Consent for publication

All the authors agreed to publish the manuscript. The patient's father signed a written informed consent for publication and uploaded supplementary materials.

Competing interests

The authors declare no competing interests.

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