Successful Treatment of New-Onset Pediatric Nephrotic Syndrome With Rituximab as a First-Line Therapy

To the Editor: Idiopathic nephrotic syndrome (INS) is the most common glomerular disease in children.[1] Steroids, as first-line therapy for INS, have been associated with many side effects. Limiting or preventing the side effects of steroid therapy and identifying other safe and effective treatments for INS are always priorities for nephrologists.

Rituximab has been shown to be an effective and safe response in patients with difficult-to-treat, frequently relapsing nephrotic syndrome and/or steroid-dependent nephrotic syndrome to reduce the relapse frequency and to maintain remission despite the cessation or tapering of steroids.[2–5] The successful use of rituximab as a first-line therapy in patients with membranous nephropathy or antineutrophil cytoplasmic antibody–associated vasculitis[S1] has raised the question of whether and when anti–B-cell therapy could be considered as first choice in INS. We describe 3 children with new-onset INS successfully treated with rituximab as a first-line therapy.

The 3 Chinese patients were aged 2.8 (boy), 3.1 (boy), and 6.6 (girl) years. They were admitted for unprovoked eyelid or lower extremity edema. The clinical characteristics of the patients at baseline are summarized in Supplementary Table S1. They were diagnosed with INS because of the presence of both nephrotic range proteinuria and hypoalbuminemia (defined in Supplementary Table S2). Secondary causes were carefully ruled out. None of them had a family history of kidney disease.

After informed consent was obtained, all patients were treated with 4 doses of 375 mg/m^2 rituximab at 1-week intervals. These 3 patients had decreased proteinuria on the 5th, 3rd, and 4th days and achieved complete remission on the 13th, 7th, and 8th days, respectively, after the first dose (Figure 1). Complete B-cell depletion was observed 1 to 2 weeks after the first injection of rituximab. During the 4-month follow-up period, no recurrence occurred. With regard to safety, no patient experienced serious infusion-related or hematologic reaction, or serious infection. Patient 1 had detectable B cells at 3 months after rituximab, without infection or relapse. Although a clear correlation between B-cell counts and relapse could not be identified, continued monitoring of B-cell counts may be helpful to offer clues about whether relapse is likely.

To our knowledge, this is the first report of children with new-onset INS treated with rituximab as a first-line therapy without steroids or immunosuppressive drugs who achieved rapid complete remission (8.5–11.5 days for mean time to remission on steroid therapy[S2]) without serious side effects. Although long-term outcomes remain unclear, our observations thus far are encouraging that rituximab may be effective and safe as a front-line therapy in new-onset pediatric INS.

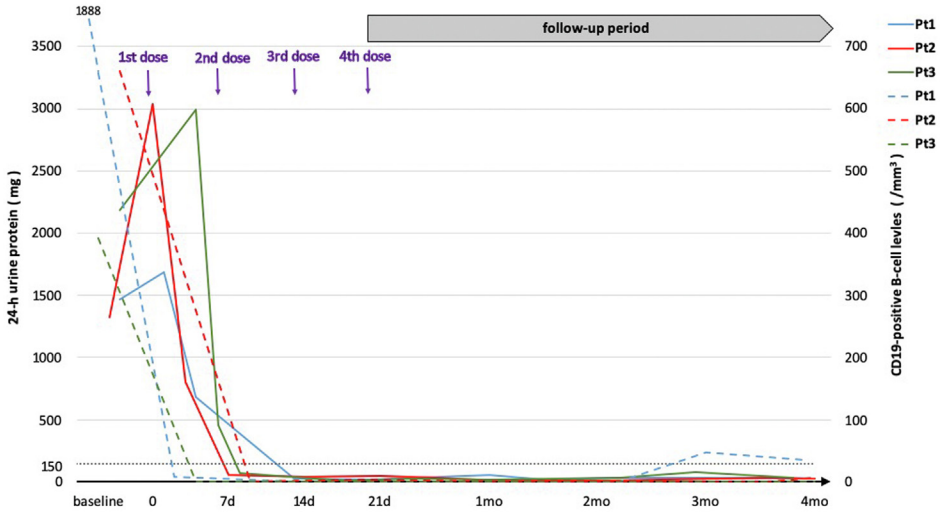

Figure 1. Evolution of proteinuria and trends of circulating CD19-positive B-cell levels. Solid line indicates evolution of proteinuria, and dashed line indicates trends of circulating CD19-positive B-cell levels. Pt, patient.

PATIENT CONSENT

The authors declare that they have obtained consent from the patients.

ACKNOWLEDGMENTS

Funding

This study was supported by the National Natural Foundation of China (U20A20351) and Key Research and Development Plan of Zhejiang Province (2021C03079).

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Demographic and clinical baseline characteristics of the patients.

Table S2. Definitions relating to nephrotic syndrome in children.

Supplementary References.

1. Downie ML, Gallibois C, Parekh RS, Noone DG. Nephrotic syndrome in infants and children: pathophysiology and management. *Paediatr Int Child Health*. 2017;37:248–258. https://doi.org/10.1080/20469047.2017.1374003
2. Sinha A, Bagga A. Rituximab therapy in nephrotic syndrome: implications for patients' management. *Nat Rev Nephrol*. 2013;9:154–169. https://doi.org/10.1038/nrneph.2012.289
3. Iijima K, Sako M, Nozu K, et al. Rituximab for childhood-onset, complicated, frequently relapsing nephrotic syndrome or steroid-dependent nephrotic syndrome: a multicentre, double-blind, randomised, placebo-controlled trial. *Lancet*. 2014;384:1273–1281. https://doi.org/10.1016/s0140-6736(14)60541-9
4. Ruggenenti P, Ruggiero B, Cravedi P, et al. Rituximab in steroid-dependent or frequently relapsing idiopathic nephrotic syndrome. *J Am Soc Nephrol*. 2014;25:850–863. https://doi.org/10.1681/ASN.2013030251
5. Chan EY, Yu ELM, Angeletti A, et al. Long-term efficacy and safety of repeated rituximab to maintain remission in idiopathic childhood nephrotic syndrome: an international study. *J Am Soc Nephrol*. 2022;33:1193–1207. https://doi.org/10.1681/ASN.2021111472

Xiaojing Zhang[1], Yanyan Jin[1], Qiuyu Li[1], Yi Xie[1], Fei Liu[1], Guoping Huang[1], Junyi Chen[1], Haidong Fu[1], Jingjing Wang[1], Huijun Shen[1] and Jianhua Mao[1]

[1]Department of Nephrology, The Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, China

Correspondence: Jianhua Mao, Department of Nephrology, The Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, No. 3333, Binsheng Road, Binjiang District, Hangzhou 310052, Zhejiang, China. E-mail: maojh88@zju.edu.cn

Received 21 August 2022; revised 13 October 2022; accepted 17 October 2022; published online 22 October 2022

Kidney Int Rep (2022) **7,** 2750–2751; https://doi.org/10.1016/j.ekir.2022.10.016