Sequential rituximab therapy sustains remission of nephrotic syndrome but carries high risk of adverse effects

Aditi Sinha, Georgie Mathew, Arushi Arushi, Srinivasavaradan Govindarajan, Kshetrimayum Ghanapriya, Neetu Grewal, Khushboo Rai, Megha Brijwal, Sree Laya Kalluru, Prachi Tewari, Angeli Misra, Priyanka Khandelwal, Pankaj Hari, Arvind Bagga

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ABSTRACT

Background

Sequential rituximab (RTX) administration has emerged as an important strategy to sustain remission of disease in patients with difficult-to-treat nephrotic syndrome.

Methods

We report the efficacy and safety of sequential therapy with two or more courses of intravenous RTX in 250 patients with difficult-to-treat steroid dependence (*n* = 127) and calcineurin inhibitor (CNI)-dependent or CNI-refractory steroid resistance (*n* = 123) managed at one center during 2015–2021. Subsets of patients were cross-sectionally tested for hypogammaglobulinemia, seroprotection against and hyporesponsiveness to vaccines for hepatitis B and tetanus, BK/JC viruria and human antichimeric antibodies (HACAs).

Results

Sequential RTX therapy, initiated at a median of 10 years [interquartile range (IQR) 7.3–14.4], was administered for 1.8 courses/person-year [95% confidence interval (CI) 1.7–2.0] over 2.0 years (95% CI 1.2–3.0). Therapy was associated with postponement of relapses by a median of 3 years in patients with steroid-sensitive disease and 2 years in those with steroid resistance. Relapses were reduced by a mean of 2.0 relapses/person-year (95% CI 1.8–2.2), enabling a reduction in prednisolone dose to 0.04 mg/kg/day (95% CI 0.01–0.11) and withdrawal of additional immunosuppression in 154 (62%) patients. RTX-associated adverse events, occurring at 0.20 events/person-year (95% CI 0.17–0.23), were chiefly comprised of infusion reactions (*n* = 108) and infections (*n* = 46); serious adverse events were observed in 10.8% patients, at 0.03 events/person-year (95% CI 0.02–0.05). Hypogammaglobulinemia was observed in 35% of 177 patients and was moderate to severe in 8.5% of cases. Rates of seroprotection at baseline and response following vaccination were lower for hepatitis B [1.9% and 29.4% (*n* = 52)] than tetanus [65.5% and 34.5%

(n = 58)]. BK/JC viruria, without viremia, was observed in 7.3% of 109 cases. A total of 19 of 107 patients (17.8%) had HACAs, which were associated with B cell nondepletion and serum sickness. Age at therapy of <9–10 years was associated with a risk of early relapse, treatment failure and hypogammaglobulinemia following RTX therapy.

Conclusions

Sequential therapy with RTX effectively reduces relapses in patients with difficult-to-treat steroid- and/or CNI-dependent or CNI-refractory nephrotic syndrome. Therapy is associated with high rates of hypogammaglobulinemia and infusion reactions.

Graphical Abstract