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Use of B-lymphocyte (CD19+) Count as a Guide to Adjust the Doses of Rituximab Infusion in Paediatric Patients

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Introduction: Rituximab is a chimeric murine /human monoclonal antibody which has emerged as a novel therapy for various glomerular diseases in Children. The optimal doses remain uncertain. We presented our experience by monitoring the B-lymphocyte (CD19+) subset count as a guide to adjust the dose of rituximab infusion. This indicator helps to avoid over-immunosuppression and to optimize the duration of B-lymphocyte (CD19+) depletion.

Case Summaries: Patient 1: A 10-year-old boy had been diagnosed with steroid-dependent nephrotic syndrome since 2 years of age and was resistant to cyclophosphamide therapy. His nephrotic syndrome remitted with cyclosporin A but with frequent relapses. Renal biopsy confirmed focal segmental glomerulosclerosis. He had serious complications of steroid and became tacrolimus dependent. Two doses of rituximab infusion (375 mg/m²) were given weekly. Depletion of B-lymphocyte (CD19+) was achieved after the 2nd dose of rituximab. His proteinuria improved and his steroid was weaned off 5 months after rituximab (Figure 1). Patient 2: A 16-year-old girl was diagnosed with systemic lupus erythematosus at 6 years of age. She had class III lupus nephritis diagnosed at 11 years old and was given a course of oral cyclophosphamide, followed by maintenance azathioprine and prednisolone. Mycophenolate mofetil and tacrolimus were added for recurrent relapses and uncontrolled disease. Two doses of rituximab infusion 500 mg (375 mg/m²) were given weekly. She achieved better disease control with B-lymphocyte (CD19+) depletion which lasted for 4 months. Prednisolone was tapered to 7 mg daily. She experienced another relapse with nephrotic range proteinuria 9 months later. Another two doses of rituximab were given with good response. B-lymphocyte (CD19+) depletion lasted for another 10 weeks (Figure 2) and her prednisolone was reduced to 5 mg daily.

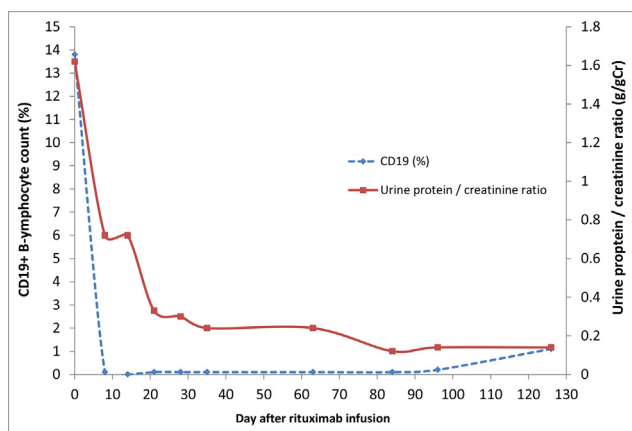


Figure 1. CD19+ count and urine protein / creatinine ratio after rituximab infusion of patient 1.

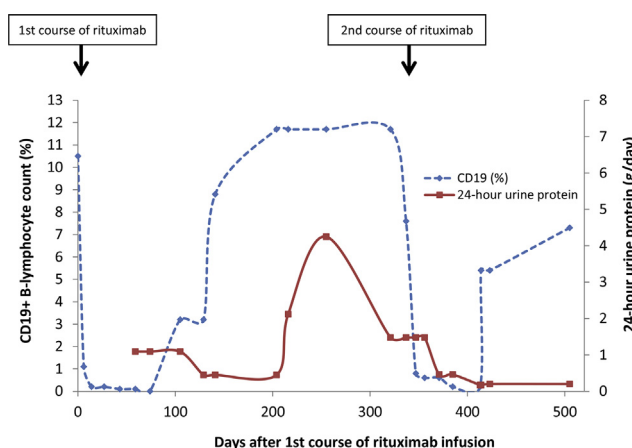


Figure 2. CD19+ count and urine protein / creatinine ratio after rituximab infusion of patient 2.

Conclusion: Two doses of rituximab can successfully deplete B-lymphocyte (CD19+). Monitoring of B-lymphocyte (CD19+) counts helps to adjust the dose of rituximab so as to prolong the duration of lymphocyte subset depletion.

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"Late" is the Most Prominent Feature and Risk Factor for Patients with Late-onset Lupus Nephritis

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Objective: To distinguish the clinical and pathological characteristic of late-onset lupus nephritis (LN) patients and their prognosis.

Methods: This is a retrospective cohort study. Patients who were diagnosed as LN with age ≥ 14 from January 1st 1996 to December 31st 2011 were enrolled. Baseline clinical characteristics and pathological information were compared between late-onset group (LG) (onset age of LN ≥ 50) and the control group (CG) (onset age of LN < 50), while the patient survival and renal outcome (defined as serum creatinine doubled or ESRD) were followed-up.

Results: Totally, 1264 patients were enrolled, with 102 cases in LG and 1162 cases in CG. (1) The male to female ratio of LG was 2:5, doubling to the CG ($P = 0.001$). Patients in LG had more complications, higher systolic blood pressure and worse renal function (median eGFR: 59.59 vs 104.9 ml/min, $P < 0.001$). Patients with late-onset LN had a higher incidence of AKI (27.5% vs 16.5%, $P = 0.005$). No difference was shown on activity index of SLE between the two groups. The renal pathological comparisons indicated that chronic lesions of the LG were much more conspicuous than the CG, while the activity lesions of LN in two groups were similar. (2) During the follow-up time of 55 (1, 207) months, 291 patients reached the end-point, including 114 (13.1%) deaths, 107 (12.2%) creatinine doubled, and 80 (9.1%) ESRD. Kaplan-Meier curves showed that 5-year and 10-year survival rates of LG were 68.5% and 49.1%, respectively, much lower than that of the CG ($P < 0.001$). Patients in the LG had a worse renal survival compared to CG (log rank = 0.849, $P = 0.008$). The older onset-age was an independent risk factor for LN patients survival after adjusted for confounders (HR = 3.034, $P = 0.005$). Increased Scr at baseline was independently associated with renal survival while 1.1 mg/dL-increment of Scr would lead to the hazard ratio of renal dysfunction increasing by 45% ($P < 0.001$).

Conclusion: The worse renal outcome of late-onset LN patients was more likely to be associated with the decline renal function with aging than the activity of SLE itself.

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Clinicopathological Characteristics and Outcomes in Male Patients with Lupus Nephritis

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Objective: Long-term outcome of lupus nephritis (LN) in male patients is a controversial issue. The objective is to evaluate clinicopathological characteristics as well as renal and patient survival in male patients with lupus nephritis.

Methods: All patients who fulfilled American College of Rheumatology lupus Criteria were enrolled in the study. Clinicopathological data of lupus nephritis patients with different gender were retrospectively analyzed and compared. Kaplan-Meier analysis and the Cox proportional hazards models were used to evaluate the risk factors associated with renal and patient survival in male lupus nephritis patients.

Results: A total of 1272 lupus nephritis patients were enrolled, with a mean age of 31.3 ± 13.4 years. Among them, 215 were male and 1057 were female. Clinical presentation was similar except that males had a significantly lower proportion of alopecia, arthralgia and leucocytopenia,