

Journal of Nephropathology

Nephrotic syndrome; is rituximab the light at the end of the tunnel in the treatment of adult steroid-dependent minimal change disease and focal segmental glomerulosclerosis?

Andreas Kronbichler^{1*}, Gert Mayer¹

¹Medical University Innsbruck, Department of Internal Medicine IV, Nephrology and Hypertension, Innsbruck, Austria

ARTICLE INFO

Article type:
Editorial

Article history:
Received: 10 January 2013
Accepted: 7 May 2013
Published online: 1 January 2014
DOI: 10.12860/jnp.2014.01

Keywords:
Nephrotic syndrome
Minimal change disease
Rituximab

Implication for health policy/practice/research/medical education:

Reports on patients with steroid-dependent nephrotic syndrome and underlying minimal change disease or focal segmental glomerulosclerosis have shown promising results. There is a strong need for more trials conducted in a prospective, controlled manner to clearly recommend rituximab therapy in this indication on a regular basis.

Please cite this paper as: Kronbichler A, Mayer G. Nephrotic Syndrome: is rituximab the light at the end of the tunnel in the treatment of adult steroid-dependent minimal change disease and focal segmental glomerulosclerosis? J Nephropathol. 2014; 3(1): 1-3. DOI: 10.12860/jnp.2014.01

Minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) are common causes of nephrotic syndrome in children and adults. Steroid dependence, steroid resistance and a relapsing disease course contribute to therapeutic difficulties since long-term glucocorticoid use leads to co-morbidities such as hypertension, impaired glucose tolerance, hypercholesterolemia or a reduced bone mineral density (1). However, the aim to spare steroids frequently necessitates the use of additional used immunosuppressants, such as calcineurin inhibitors, mycophenolate mofetil, azathioprine, cyclophosphamide or levamisole. These agents themselves, used as

second- or third-line treatment, exhibit a broad spectrum of adverse events limiting their long-term prescription.

B-cell depleting therapy with rituximab (RTX) has emerged as a valuable option in the treatment of refractory childhood nephrotic syndrome (2,3). A high proportion of reported patients were able to reduce and finally discontinue immunosuppressive treatment. RTX, a chimeric antibody targeting CD20-bearing cells, was first approved for the treatment of non-Hodgkin lymphoma and rheumatoid arthritis. Efficacy in diverse autoimmune disorders led to a broad use of RTX and to an increased off-label use (4). Several mechanisms are suggested to elucidate

*Corresponding author: Dr. Andreas Kronbichler, Medical University Innsbruck, Department of Internal Medicine IV, Nephrology and Hypertension, Innsbruck, Austria, Anichstraße 35.6020 Innsbruck, Email: andreas.kronbichler@i-med.ac.at

the efficacy of RTX: antibody-dependent cell-mediated cytotoxicity, elimination by phagocytosis or cytokine-mediated cytotoxicity (5).

Recently, reports on the use of this agent in adult patients with steroid-dependent nephrotic syndrome with underlying MCD or FSGS are accumulating. Long-term as well as excellent short-term remission rates have been reported, especially in patients with steroid-dependent nephrotic syndrome due to MCD (6,7). In both papers a reduction of relapses was reported and glucocorticoid use was lowered in the latter. In addition, a large proportion of patients included in these studies had extensive pre-treatment strategies. These findings indicate that RTX is highly effective in patients with a severe disease course and a failure of previously used immunosuppressive regimens. But there are some unanswered questions still dampening enthusiasm. We do not know the long-term effects of B-cell depleting therapy with RTX. The application mode varies very strong in the published reports and there is a need of a standardized administration. Moreover, most reports are case series and are conducted in a retrospective manner.

We have also shown our experience with RTX in the treatment of five consecutive patients in our center (8). Two patients with a sustained remission reported in this cohort relapsed after the publication date. Nonetheless it might turn out that regular re-application of RTX in this population at a fixed interval without concomitant glucocorticoid use might turn out to be favorable. Circulating B-cells as measured in the peripheral blood are an insufficient marker of response and relapse risk in these patients since patients with a complete re-population of B-cells do not necessarily relapse (9). Taken together, reports on patients with steroid-dependent nephrotic

syndrome and underlying MCD or FSGS have shown promising results. There is a strong need for more trials conducted in a prospective, controlled manner to clearly recommend RTX therapy in this indication on a regular basis.

Authors' contributions

AK wrote the manuscript. GM made substantial contributions to conception and design of the manuscript.

Conflict of interests

The authors declare no conflict of interests.

Funding/Support

None declared.

References

1. Moghadam-Kia S, Werth VP. Prevention and treatment of systemic glucocorticoid side effects. *Int J dermatol* 2010;49(3):239-48.
2. Prytula A, Iijima K, Kamei K, Geary D, Gottlich E, Majeed A, et al. Rituximab in refractory nephrotic syndrome. *Pediatr Nephrol* 2010;25(3):461-8.
3. Ito S, Kamei K, Ogura M, Udagawa T, Fujinaga S, Saito M, et al. Survey of rituximab treatment for childhood-onset refractory nephrotic syndrome. *Pediatr Nephrol* 2013;28(2):257-64.
4. Kronbichler A, Mayer G. Renal involvement in autoimmune connective tissue diseases. *BMC Med* 2013;11:95.
5. Datta SK. Anti-CD20 antibody is an efficient therapeutic tool for the selective removal of autoreactive T cells. *Nat Clin Pract Rheumatol* 2009;5(2):80-2.
6. Munyentwali H, Bouachi K, Audard V, Remy P, Lang P, Mojaat R, et al. Rituximab is an efficient and safe treatment in adults with steroid-dependent minimal change disease. *Kidney Int* 2013;83(3):511-6.
7. Takei T, Itabashi M, Moriyama T, Kojima C, Shiohira S, Shimizu A, et al. Effect of single-dose rituximab on steroid-dependent minimal-change nephrotic syndrome in adults. *Nephrol Dial Transplant* 2013;28(5):1225-32.

8. Kronbichler A, König P, Busch M, Wolf G, Mayer G, Rudnicki M. Rituximab in adult patients with multi-relapsing/steroid-dependent minimal change disease and focal segmental glomerulosclerosis: a report of 5 cases. *Wien Klin Wochenschr* 2013;125(11-12):328-33.
9. Sellier-Leclerc AL, Baudouin V, Kwon T, Macher MA, Guerin V, Lapillonne H, et al. Rituximab in steroid-dependent idiopathic nephrotic syndrome in childhood--follow-up after CD19 recovery. *Nephrol Dial Transplant* 2012;27(3):1083-9.