

## **Rituximab, a clinical update**

Over the last five years there has been growing interest in the effect of rituximab in the treatment of steroid resistant and steroid dependent forms of FSGS and minimal change disease (MCD) by both the scientific and lay communities. This has been evidenced by the number of case reports and studies that have been published and presented at nephrology conferences nationally and internationally this year alone.

Researchers have long suspected that T cells, a type of white blood cell important in immune response, plays a role in the development of nephrotic syndrome (NS) <sup>1</sup> and now, there is increasing evidence that B cells, another category of white blood cells, may play an important role in NS as well<sup>2</sup>. This potential role for B cells has been gaining acceptance with reports of successful use of rituximab as a rescue therapy in NS.

Rituximab is an antibody directed against an antigen (receptor) found on B cells. When administered, it results in reduction of the number of B cells. Treatment with rituximab has been successful in B cell lymphomas, resulting when B cells are mutated and become cancerous, as well as in patients with autoimmune diseases<sup>3</sup>. Recently, several case reports have suggested that rituximab may be effective in treating patients with MCD and FSGS.

Reports have documented the value of rituximab in steroid sensitive nephrotic syndrome (SSNS). Kemper and colleagues describe the effects of rituximab in 20 children with SSNS. The authors regarded the treatment as a success in 19 of the 20 patients, and in 13 patients immunosuppressive medications were able to be discontinued. However, an average of nine months following treatment, 11 patients had a relapse. This study documents that rituximab may be used as a therapeutic option in SSNS but while long term remission may take place, relapses may also occur<sup>3</sup>.

Relapses of NS and steroid dependency are therapeutic challenges to physicians. An abstract presented at the World Congress of Nephrology examines the use of rituximab in three female patients who are steroid dependent and experience multiple relapses of MCD. The patients each received two doses of rituximab.



Following therapy, remission was maintained at follow up 16, 9 and 6 months respectively suggesting that rituximab may be of clinical use in the management of steroid dependent multi-relapsing MCD<sup>5</sup>. The importance of this study lies in the fact that MCD accounts for 10 to 15 percent of cases of NS in adults, and is the most common cause of NS in children<sup>1</sup>. Fifty to 75% of adults who initially respond to steroid therapy will experience a relapse<sup>5</sup>.

A second study documenting the effects of rituximab in steroid dependent MCD included eight male patients all either in complete or partial remission with the use of calcineurin inhibitors (CIs). Dependence on the CIs was found when the attempt was made to lower the dose. The patients received four doses of rituximab. Six months following the last dose, CIs were withdrawn in all cases and all patients remained in partial remission. The authors noted that there were no significant changes in blood pressure, no patients had late relapses and no side effects were observed<sup>6</sup>.

A study by Bagga presented similar results when examining the effects of rituximab in steroid dependent NS. Seven patients, all of whom had been treated with a number of traditional immunosuppressive medications, were included and given two doses of rituximab. At an average follow up of five months, six of seven patients were sustained in remission, and one patient had multiple relapses at nine months<sup>7</sup>.

Within the same study, the authors also examined the use of rituximab in 11 patients with steroid resistant NS but the results did not prove as positive. All 11 patients had failed to respond to traditional therapy and were given four doses of rituximab. Only five patients showed partial or complete remission four weeks after therapy. In three of the 11 patients, no response was seen and the final three patients showed impaired filtration rate<sup>7</sup>.

It is well known that FSGS follows a less favorable course than MCD. Many FSGS patients fail to respond to steroids and may progress to kidney failure requiring dialysis or transplantation<sup>1</sup>. Recurrence of FSGS after a kidney transplant is frequently observed and may result in loss of the transplanted kidney<sup>8</sup>. Recently, anecdotal reports have described long-term resolution of FSGS after treatment with rituximab.



The effect of rituximab on FSGS was evaluated in a study by Fernandez-Fresnedo and colleagues. Rituximab was administered to seven adult patients following resistance to several immunosuppressive medications. Five of the seven patients continued to show massive proteinuria following treatment and two of these five patients had rapidly deteriorating kidney function. The remaining two patients showed a remarkable reduction in proteinuria. In summary, only a minority of patients (2/7), showed a positive influence on rituximab<sup>9</sup>.

To date, information is available from only a small number of patients and the positive results may be overestimated due to publication bias. Overall, the review of the literature suggests that while rituximab may provide physicians with another option as a rescue treatment for patients with MCD or FSGS, larger, controlled trials are needed to determine the true value and efficacy of rituximab. More information is needed in order to determine which patients are likely to benefit and what the risks of treatment may be.

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