

ADVERSE EVENTS OF TREATMENT WITH RITUXIMAB IN PATIENTS WITH MYOSITIS

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Introduction

Rituximab and its biosimilars have been used to treat autoimmune rheumatic diseases for just over 20 years. It is of interest that these partially humanized monoclonal antibodies seem to induce biologic responses/side effects at different rates in different diseases. A classification utilizing a different approach to diagnosis and management of each reaction has been reported (1). Thus, in patients with rheumatoid arthritis, allergic responses were reported in about 22.6% of the patients (2). These were mild (three patients developed rash and itching, two other had mild laryngospasm, one had chest heaviness with non-specific ECG changes and the last one had a bronchospasm) and they appeared not to be related to the immunosuppressant drug given in addition to the biosimilar, the infusion rate and the total amount of drug administered. In contrast, in patients with systemic lupus erythematosus, we have reported that 17.6% of patients and 5.8% of total infusions (3).

We wondered where on this spectrum patients with myositis treated with rituximab were to be found.

We have carefully reviewed all the available records on patients with myositis under our care in the past 20 years to report the frequency of recorded allergic responses. In all, we have identified 139 patients with myositis, diagnosed by criteria of Bohan and Peter (4, 5).

Background

In 2005, Levine *et al.* showed the efficacy of the treatment with rituximab in six patients with dermatomyositis who had been previously treated with the standard therapy for this disorder (6).

Since then, rituximab has been widely used for the treatment of these disorders, especially in threatening-life situations or when the symptoms do not improve or even get worse despite standard immunosuppressive therapies.

In 2013, the RIM trial (Rituximab in the Treatment of Refractory Adult and Juvenile Dermatomyositis and Adult Polymyositis: A Randomized, Placebo-phase Trial) was published (7). Even though the primary endpoint (defined as a shorter time to achieve improvement in patients with rituximab than those with placebo) was not achieved, it reported that most patients (83%) did show some clinical improvement in their symptoms. No corticosteroids were administered at the time of study medication infusion. There were significantly more infusion reactions with rituximab (15.4%) than placebo (5.3%), $p < 0.01$, but no difference was seen between the first and second rituximab infusions. Most reactions (88%) were considered to be related to rituximab; four were deemed severe, 24 moderate, and 32 mild.

Methods

We reviewed a total of 154 patients diagnosed with myositis who have been followed-up in the University College Hospital London in the past 40 years.

We excluded 35 patients, including those who had died before 2005 and those lost to follow-up or with inadequate data available from the hospital notes/computer records system.

Of the remaining 119 individuals, 31 (15 with dermatomyositis and 16 with polymyositis – among 6 had antisynthetase syndrome–) have been treated with rituximab/biosimilar (invariably because of inadequate control of their disease by corticosteroids and concomitant immunosuppressants). [1gm IV x 2, two weeks apart accompanied by 250mg methylprednisolone IV].

Only two patients (6,45%) suffered an adverse reaction: one of them developed a lower back pain 90 minutes after the infusion began (it was actually the second infusion of the second cycle received); the infusion was stopped and the patient received hydrocortisone and additional codeine phosphate. Two hours later, the pain subsided and the patient was discharged home.

The other one started with chest pain and palpitations (during the second infusion), which was stopped for 15 minutes and then resumed at a slower rate; this patient subsequently received three more infusions with no side effects reported.

Conclusions

Among the 31 (20.12%) myositis patients under our care treated with rituximab, only two (6.45% – 1.29% of the total amount –) developed an adverse reaction. Furthermore, both reactions were mild and did not necessitate abandoning the use of B cell depletion for these patients. The lower rate we have observed compared to that reported in the RIM trial may be linked to our use of concomitant corticosteroids.

Although more studies with a bigger sample size are needed to confirm our data, they support the view that side effects due to rituximab/a biosimilar given to patients with inflammatory muscle disease may be a little less common and milder than have been reported in patients with RA and SLE and are minimised by the co-administration of corticosteroids

References

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