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Case Report

Comparative Study Between Two Protocols of Rituximab in Pemphigus: About 63 Cases

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Abstract

Background: Pemphigus is a rare autoimmune mucocutaneous bullous disease. It includes pemphigus vulgaris and pemphigus superficial. Rituximab is an antibody that targets CD-20 molecules on B-cells and has been approved as a first-line treatment for moderate to severe pemphigus vulgaris. The aim of our study is to evaluate the efficacy and safety of Rituximab in the treatment of pemphigus patients.

Materials and methods: It is a prospective study extending over a period of 6 years from December 2016 to July 2022, including all patients with severe or treatment-resistant pemphigus who received treatment with RITUXIMAB at a dose of 375 mg/m² /week for 4 weeks (lymphoma protocol) or 2 infusions of 1 g at 15-day intervals (rheumatoid arthritis protocol (PR protocol)), combined with oral corticosteroid therapy at a dose of 0.5 to 1 mg/kg/day (depending on severity) with a 6-month taper. Maintenance treatment depends on the IFI level. In the case of high levels, an infusion of 1 g after 6 months is given and in the case of low levels, an infusion of 500 mg after 1 year is given. Consent and authorization from the local ethics committee were required. The data were entered into an Excel program and analyzed via Epi info version 7 software. Patients receiving CNSS health insurance were excluded.

Results: 63 patients with pemphigus were using Rituximab (PR protocol: 44 lymphoma protocol: 19), 3 of which are currently being followed up (< 6 months). 44 cases of pemphigus vulgaris of which 15 received the lymphoma protocol and 29 received the PR protocol, 14 cases of superficial pemphigus of which 4 cases received the lymphoma protocol, and 10 cases of PR protocol and 5 cases of vegetative pemphigus received the PR protocol.

Keywords: Rituximab; Pemphigus Vulgaris; Mucocutaneous Bullous Disease; Antibody

Introduction

Pemphigus is a rare autoimmune mucocutaneous bullous disease with autoantibodies against epidermal adhesion proteins known as desmogleins. It includes pemphigus vulgaris and pemphigus superficial. Rituximab is a chimeric monoclonal antibody that targets CD-20 molecules on B-cells and recent consensus recommendations developed by the International Bullous Diseases Consensus Group have approved it as a first-line treatment for moderate to severe pemphigus vulgaris [1]. The aim of our study is to evaluate the efficacy and safety of Rituximab in the treatment of pemphigus patients.

Materials and Methods

It is a prospective study extending over a period of 6 years from December 2016 to July 2022, including all patients with severe or treatment-resistant pemphigus who received treatment with RITUXIMAB at a dose of 375 mg/m² /week for 4 weeks (lymphoma protocol) or 2 infusions of 1 g at 15-day intervals (PR protocol), combined with oral corticosteroid therapy at a dose of 0.5 to 1 mg/kg/day (depending on severity) with a 6-month taper. Maintenance treatment depends on the IFI level. In the case of high levels, an infusion of 1 g after 6 months is given and in the case of low levels, an infusion of 500 mg after 1 year is given. Consent and authorization from the local ethics committee were required. The data were entered into an Excel program and

analyzed via Epi info version 7 software. Patients receiving CNSS health insurance were excluded.

Case Report

Among 200 patients with pemphigus, there were 63 patients with pemphigus using Rituximab (PR protocol: 44 lymphoma protocol: 19), of which 3 are currently being followed up (< 6 months). 44 cases of pemphigus vulgaris of which 15 received the lymphoma protocol and 29 received the PR protocol, 14 cases of superficial pemphigus of which 4 cases received the lymphoma protocol, and 10 cases of PR protocol and 5 cases of vegetative pemphigus received the PR protocol (Table 1).

	Lymphoma Protocol (Number of patients)	**PR Protocol (Number of patients)**
Pemphigus vulgaris	15	29
Superficial pemphigus	4	10
Vegetative pemphigus	0	4

Table 1: Summary of cases using different protocols of Rituximab in pemphigus.

The average age of our patients was 56.3 years with extremes ranging from 33 to 77 years. There was a clear female predominance with a sex ratio of 3:1. Thirty-eight patients had severe disease and were treated with RITUXIMAB as first-line therapy and 25 patients were treated with second-line therapy after cortico-resistance, cortico-dependence, or failure of other immunosuppressive treatments. Among them, 47 (74.6%) patients achieved complete remission, including 16 (84.2%) under the lymphoma protocol and 31 (70.45%) under the RA protocol. The average time to complete remission was 2 months. Partial remission was noted in 13 patients, including 3 (15.78%) in the lymphoma protocol and 10 (22.7%) in the RA protocol, all of whom were put on maintenance therapy after 6 months. Relapse requiring a new cycle of Rituximab occurred in 13 (20.6%) patients, including 3 (15.78%) on the lymphoma protocol and 10 (22.72%) on the RA protocol, all of whom achieved remission after additional cycles. The main causes of this relapse were poor compliance and infections (Fig. 1).

Side effects of RITUXIMAB were dominated by herpetic superinfection with a higher rate in patients on the lymphoma protocol compared to the RA protocol (42.1% vs. 22.72%). There were no cases of hepatitis B reactivation or tuberculosis. The use of RITUXIMAB was associated with a significant reduction in the cumulative dose of corticosteroids and a significant decrease in the levels of antibodies against intercellular substances after 6 months (Fig. 2).

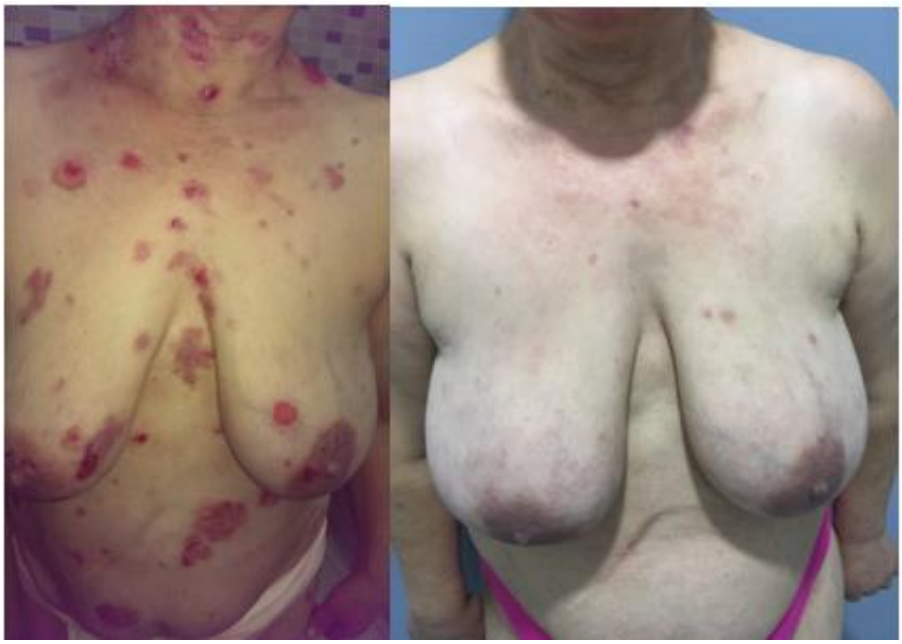

Figure 1: Image showing a patient with vulgaris pemphigus before and after 2 month of lymphoma protocol of Rituximab.

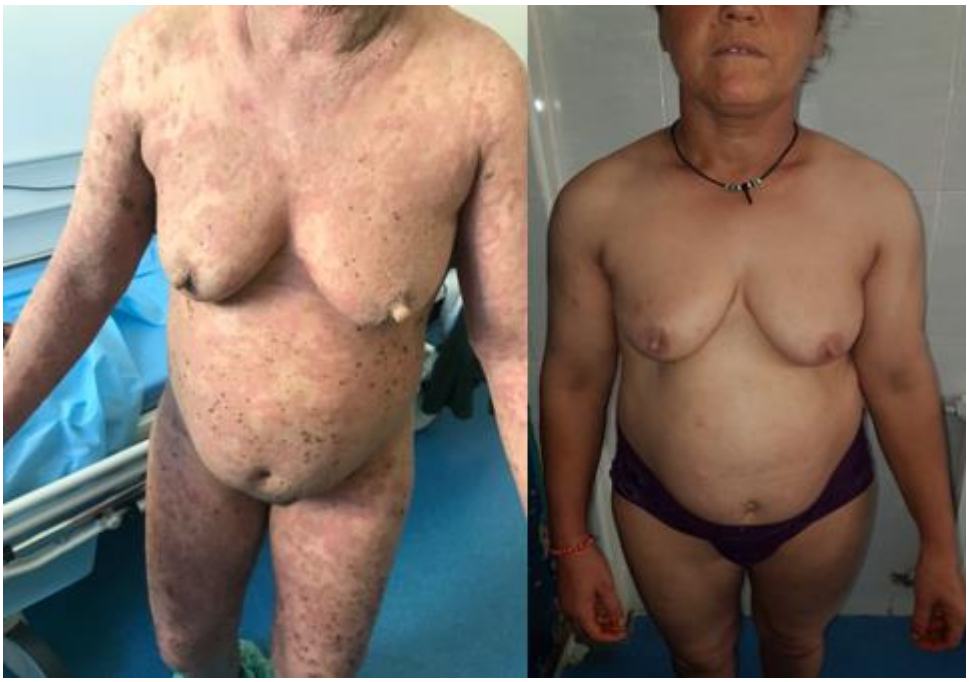

Figure 2: Image showing a patient with superficial pemphigus before and after 2 month of PR protocol of Rituximab.

Discussion

Rituximab has been found effective in the treatment of severe pemphigus and recalcitrant ones. The two protocols described for Rituximab are the lymphoma and rheumatoid arthritis protocols. The lymphoma protocol is based on four weekly infusions of Rituximab at a dose of 375 mg/m^2 whereas the rheumatoid arthritis protocol is based on two infusions of 1000 mg of Rituximab at two weeks intervals [2-7].

In our experience, Rituximab is a treatment with similar efficacy and tolerance for both protocols in the treatment of severe pemphigus with side effects dominated mainly by herpetic superinfection. In a review of 42 publications on 272 patients of pemphigus treated with rituximab, Zakka, et al., compared the efficacy and adverse effects of different protocols. According to the authors, complete remission was higher in patients under the PR protocol than in the lymphoma protocol (75% vs 66.6%) [8,9]. However, in our study, the complete remission rate was almost similar (74.6% vs 70.45%). According to Zakka, et al., the relapse rate was lower in patients under the lymphoma protocol compared to the PR protocol (22.8% vs 35.8%), which is almost similar to our study (15.78% vs 22.72%) (Table 2) [10,11].

Leshem, et al., used the rheumatoid arthritis protocol of rituximab infusion in 47 pemphigus patients. The relapse rate was 22%, which is similar to our study's (22.78%) [12]. According to Zakka, et al., the rate of infections was lower in the lymphoma protocol compared to the PR protocol [13,14]. This is contradictory to our study, where herpetic superinfection was more frequent in patients under the lymphoma protocol compared to the PR protocol (42.1% vs 22.72%) (Table 3).

	Lymphoma Protocol (%)	PR Protocol (%)
Zakka, et al.,	66.6%	75%
Notre étude	70.45%	74.6%

Table 2: Summary of the remission cases using different protocols of Rituximab in pemphigus.

	Lymphoma Protocol	PR Protocol
Zakka, et al.,	22.8%	35.8%
Leshem, et al.,	-	22%
Notre étude	15.78%	22,72%

Table 3: Summary of the relapse cases using different protocols of Rituximab in pemphigus.

Conclusion

In light of our results, preventive anti-herpetic treatment is recommended during the course of Rituximab treatment due to the frequency of herpetic infections which can be explained by the maximum lymphocyte depletion during the first 15 days of RITUXIMAB treatment.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

Conflict of Interest

The authors have no conflict of interest to declare.

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