

Title: - Rituximab Hypersensitivity in Rheumatic and Inflammatory Diseases: Role Of Skin Testing

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Background: -

Rituximab, a chimeric monoclonal antibody targeting the CD20 antigen on B lymphocytes, is used in many rheumatological conditions such as rheumatoid arthritis and ANCA associated vasculitides. Infusion related reactions have been reported with rituximab and may result in discontinuation of the medication and/or changing to a potentially less effective alternative agent. Rituximab skin testing in lymphoma patients may correlate with severity of hypersensitivity¹. To our knowledge, there is no data establishing the value of rituximab skin testing in patients with rheumatological conditions who have a hypersensitivity reaction. We present our observational analysis on skin testing results in rheumatology patients who previously developed hypersensitivity reactions to rituximab, and whether the skin testing results correlated to severity of clinical response.

Methods: -

We present the skin testing results from a retrospective review of 8 patients followed from January 2000 through September 2019 with systemic rheumatologic conditions who developed hypersensitivity reactions while receiving rituximab. Patients previously underwent epi-cutaneous prick testing using rituximab at a concentration of 10 mg/mL. If negative testing resulted at 10mg/ml concentration (defined as a wheal diameter measured less than 3mm), testing proceeded to intradermal injections of 1:1000, 1:100 and 1:10 dilutions of the full strength. Testing was discontinued and defined as a positive with a wheal 3mm or greater than the histamine control. We defined a “mild” IgE mediated reaction as that involving one organ system which did not require epinephrine. A “severe” IgE reaction has two or more organ system involvement which required epinephrine administration.

Results: -

Regardless of background immunosuppressive agents, all patients except one mounted an appropriate histamine response. Patients 1-5 and 7 developed “mild” hypersensitivity reactions and had negative skin testing. Patient 8 had a severe reaction requiring

¹ Rituximab Hypersensitivity: Evaluation, Desensitization, and Potential Mechanisms Wong, Johnson T. et al. The Journal of Allergy and Clinical Immunology: In Practice, Volume 5, Issue 6, 1564 – 1571

Abstract 77

epinephrine IM and subsequently mounted a positive intradermal test. A summary of patient characteristics and skin testing results are provided in Table 1.

Conclusion:

Rituximab skin testing has not been studied in patients with underlying rheumatic and inflammatory diseases. Our preliminary analysis demonstrates mild reactions can possibly predict a negative skin testing which may not be an IgE mediated process. Thus, a negative test may allow clinicians to have discussions with patients on the possibility of re-challenging the medication if no alternative medications are suitable. Additionally, our analysis demonstrates that patients are able to mount an adequate histamine response despite immunosuppression by their disease and current medications.

Further studies will be needed to evaluate the utility in evaluation of skin testing in rheumatic and inflammatory conditions.

Table 1 below

References:

- 1) Rituximab Hypersensitivity: Evaluation, Desensitization, and Potential Mechanisms Wong, Johnson T. et al. The Journal of Allergy and Clinical Immunology: In Practice, Volume 5, Issue 6, 1564 – 1571
- 2) Vultaggio A, Castells MC. Hypersensitivity reactions to biologic agents. Immunol Allergy Clin N Am. 2014;34(3):615–632

Abstract 77

#	Diagnosis	Immunosuppressant Medications use at the time of skin testing	Severity of reaction and manifestations	Medications used to suppress allergic reaction	Skin testing Results: Positive/Negative
1	Granulomatous polyangitis	Prednisone 3mg daily	Hives and Skin rash - Mild	IV decadron 10mg and Benadryl 25mg IV	Negative
2	Rheumatoid arthritis	None	Shortness of breath, tightness in throat and chest, and dizziness- Mild	IV Solumedrol and Benadryl 25mg IV	Negative
3	Rheumatoid arthritis	Arava 20mg daily	Tightness in chest and shortness of breath-Mild	IV Decadron 10mg and Benadryl 25mg	Negative
4	Neuromyelitis optica	Methotrexate	Diffuse Skin rash -Mild	IV Solumedrol and Benadryl 25mg IV	Negative
5	Pemphigus Vulgaris	Prednisone 20mg daily	Shortness of breath- Mild	IV Solumedrol and Benadryl 25mg IV	Negative
6	Rheumatoid arthritis	Certolizumab pegol	Rash on scalp, shortness of breath- Mild	IV Solumedrol and Benadryl 25mg IV	Could not complete testing due to poor histamine response (control)
7	Rheumatoid arthritis	Certolizumab pegol	Shortness of breath and mild rash-Severe	IV Solumedrol and Benadryl 25mg IV and Epinephrine Subcutaneous	Negative
8	Systemic Lupus Erythematosus	Prednisone 20mg daily	Shortness of breath, skin rash, throat tightness and abdominal pain- Severe	IV Solumedrol and Benadryl 25mg IV and Epinephrine Subcutaneous	Positive