



Correspondence

Rituximab desensitization protocol in a child with secondary lymphoproliferative disease



We read with interest the article by Yang and Castells¹ about rituximab hypersensitivity and desensitization. Their discussion underlines that hypersensitivity and desensitization occur despite the management of rituximab infusion-related reactions. Several strategies have been used to deal with the different reactions caused by this monoclonal antibody.

Lymphoproliferative disease after solid organ transplantation (posttransplant lymphoproliferative disease [PTLD]) is one of the most prevalent forms of lymphatic proliferation in childhood. Approximately 90% of pediatric PTLDs originate from CD20-positive B cells and are associated with Epstein-Barr virus (EBV).² One of the recommendations for the treatment of PTLD is the combination of chemotherapeutic agents and rituximab.

Therefore, rituximab was prescribed for a 9-year-old girl with monomorphic lymphoproliferative disease whose EBV test results were positive after cardiac transplantation. During the first infusion, 1 hour after its onset, the patient presented with pruritus and sneezing, motivating the interruption of rituximab treatment. In the second attempt, she developed hives, chills, and fever after 40 minutes of infusion, even though she had been previously medicated with antihistamines and a decreased infusion rate and did not receive the medication at full dose. During the third attempt, she presented with anaphylaxis (dyspnea and urticaria) 3 minutes after infusion onset and was treated with intramuscular epinephrine.

Faced with the possibility of a classic IgE-mediated reaction, the patient underwent rituximab skin tests,³ with positive results. On the basis of risk stratification that classified this reaction as severe, a 4-bag, 16-step protocol for desensitization was recommended.³ The patient was previously treated with antihistamines and leukotriene modifiers. No adverse reactions occurred during infusions, and the 4 doses of rituximab required for treatment were administered. Next, the viral load for EBV constituted a negative result. Currently, the patient is well without further treatment.

Monoclonal antibody therapy has modified the results of treatment of several diseases, mainly oncologic and immunologic ones. For the drugs that are considered as the only therapeutic option, without equivalents with the same efficacy, desensitization protocols are being developed for the patient who presented with immediate hypersensitivity reactions. These protocols are based on an induction process of the state of temporary tolerance in the

sensitized patient by sequential exposure to increasing doses of the drug.³

Another important consideration to be discussed is the possible formation of the IgG isotype against the monoclonal antibodies, which would lead to their therapeutic failure. Serum IgG anti-offending drug may aid in the early diagnosis and development of immunomodulatory methods to control this adverse situation. This is a new field that deserves attention in the treatment of patients who are using biological agents.^{4,5}

Desensitization protocols are extremely important and represent a revolutionary milestone in the treatment of allergic patients. To our knowledge, this is the first pediatric case in which a child underwent desensitization to rituximab after presenting with an anaphylactic reaction. Continuity of first-line therapy should be performed, and desensitization may contribute to achieving this goal, especially in children.

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References

1. Yang BC, Castells MC. Rituximab hypersensitivity and desensitization: a personalized approach to treat cancer and connective tissue diseases. *Ann Allergy Asthma Immunol*. 2019;123(1):11–15.
2. Montanari F, Radeski D, Seshan V, Alobeid B, Bhagat G, O'Connor OA. Recursive partitioning analysis of prognostic factors in post-transplant lymphoproliferative disorders (PTLD): a 120 case single institution series. *Br J Haematol*. 2015; 171(4):491–500.
3. Sloane D, Govindarajulu U, Harrow-Mortelliti J, et al. Safety, costs, and efficacy of rapid drug desensitizations to chemotherapy and monoclonal antibodies. *J Allergy Clin Immunol Pract*. 2016;4(3):497–504.
4. Krishna M, Nadler SG. Immunogenicity to biotherapeutics: the role of anti-drug immune complexes. *Front Immunol*. 2016;7:21.
5. Stenger EO, Kazi Z, Lisi E, Gambello MJ, Kishnani P. Immune tolerance strategies in siblings with infantile Pompe disease: advantages for a preemptive approach to high-sustained antibody titers. *Mol Genet Metab Rep*. 2015;4:30–34.

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