OBSERVATIONS

Successful Use of Omalizumab in an Inadequately Controlled Type 2 Diabetic Patient With Severe Insulin Allergy

A 62-year-old male patient with type 2 diabetes for 16 years developed a severe anaphylactic shock upon administration of intravenous, short-acting regular insulin. The patient's medical history comprised allergic reactions to an unknown agent as a child as well as injection site reactions, urticaria, and dyspnea to subcutaneous NPH-insulin injections. The diagnostic work-up revealed a type 1 IgE-mediated insulin allergy by positive skin prick tests and elevated specific IgE levels against insulins of human, porcine, and bovine origin by ImmunoCAP-Assay. The insulins used were free of proinsulin. Skin prick tests with all solvents and additives of the insulin solutions were negative. Genetic sequencing of the patient's insulin molecule revealed a normal insulin gene. Because of unsatisfactory glycemic control, specific desensitization (1) and maintenance therapy with insulin detemir was performed, but improvement of urticaria and dyspnea was only transient.

Because insulin therapy seemed to be indispensable to control glycemia, treatment with intramuscular injections of 300 mg of omalizumab, a monoclonal antibody against IgE, every 4 weeks was initiated. A second desensitization therapy with insulin was successfully performed 6 months later. Insulin detemir was started again, and doses were gradually increased without reappearance of allergic symptoms. Subsequently, glycemia improved. After another 6 months, omalizumab was tapered until urticaria reappeared; currently, a dose of 300 mg every 9 weeks suffices for full control of allergic symptoms and adequate glycemia (HbA_{1c} 7.1%).

Insulin allergy is a very rare adverse reaction to insulin (1)—in the present case to all types of insulins tested. Because sufficient blood glucose control is not always achieved under oral antidiabetic medication alone in patients with insulin allergy, desensitization therapy is proposed to treat patients with disabling allergic symptoms. Omalizumab, an anti-IgE antibody, has been approved for severe persistent allergic asthma patients (2). The rationale to use omalizumab in our patient is supported by different studies showing favorable effects of omalizumab as treatment before desensitization therapy in IgE-mediated diseases (3). With respect to IgE-mediated insulin allergy, the use of omalizumab has been described in two case reports so far. One patient received rituximab, a B-cell–depleting monoclonal antibody, prior to omalizumab 375 mg fortnightly in order to reduce high levels of IgE (4). In another type 1 diabetic patient, omalizumab was also given as pretreatment before a second desensitization therapy (5). Our report describes for the first time successful omalizumab therapy in a type 2 diabetic patient severely allergic to insulin where omalizumab was applied in long-term use. The follow-up of 36 months shows that such a therapy is not only highly effective in the short term, but can lead to sustained immune tolerance, which allows tapering of omalizumab according to allergy symptoms. In the present case, omalizumab could be reduced to an interval of 9 weeks between injections. If intervals were increased to 10 weeks, urticarial skin lesions restarted at injection sites as in the beginning, whereas otherwise no such allergic symptoms were seen.

In summary, our report describes long-term use of omalizumab in a type 2 diabetic patient with severe insulin allergy, thus enabling the use of exogenous insulin.

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DOI: 10.2337/dc12-0115

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Acknowledgments—This work was supported by the Swiss National Science Foundation, which had no involvement in the design, data collection, analysis, writing, and publication of the study.

No potential conflicts of interest relevant to this article were reported.

C.C.-W., B.M., C.K., A.B.-B., A.B.-L., M.Y.D., and P.S.-G. took care of the patient and were involved in the diagnosis and treatment of the patient. C.C.-W., M.Y.D., and P.S.-G. wrote the manuscript. B.M., C.K., A.B.-B., and A.B.-L. contributed to discussion and reviewed and edited the manuscript. M.Y.D. and P.S.-G. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

References

1. Heinzerling L, Raile K, Rochlitz H, Zuberbier T, Worm M. Insulin allergy: clinical manifestations and management strategies. Allergy 2008;63:148–155
2. Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. Allergy 2005;60:309–316
3. Massanari M, Nelson H, Casale T, et al. Effect of pretreatment with omalizumab on the tolerability of specific immunotherapy in allergic asthma. J Allergy Clin Immunol 2010;125:383–389
4. Yong PFK, Malik R, Arif S, et al. Rituximab and omalizumab in severe, refractory insulin allergy. N Engl J Med 2009;360:1045–1047
5. Matheu V, Franco A, Perez E, Hernández M, Barrios Y. Omalizumab for drug allergy. J Allergy Clin Immunol 2007;120:1471–1472