

CORRESPONDENCE



Ofatumumab for TTP in a Patient with Anaphylaxis Associated with Rituximab

TO THE EDITOR: We noted anaphylaxis in a patient with thrombotic thrombocytopenic purpura (TTP), which was associated with human antichimeric antibodies (HACA) to rituximab. Because of the high risk of relapse of TTP, further elective therapy was preferred. Treatment with ofatumumab, a human monoclonal anti-CD20 antibody, was successfully completed, with no reactions and with normalization of ADAMTS13 activity.

A 46-year-old black woman presented with acute TTP in 2006. She was initially treated with daily plasma exchange for 31 days and also received glucocorticoids and four infusions of rituximab (at a dose of 375 mg per square meter of body-surface area). Treatment with mycophenolate mofetil was initiated because the platelet count fell when plasma exchange was initially withdrawn; five further plasma exchanges were administered. Mycophenolate mofetil was tapered over a period of 1 year. ADAMTS13 activity peaked at 19% but fell to less than 5% in 2013 (there was no hemolysis or thrombocytopenia). Prophylactic weekly rituximab (at a dose of 100 mg

per square meter) was given. The initial two infusions were uncomplicated. At 90 minutes into the third infusion, however, chest pain and dyspnea developed. The patient had hypoxemia and bradycardia and became unresponsive. The infusion was stopped. Recovery followed fluid resuscitation. HACA testing was positive (low titer [283 allergy units per milliliter]; Promonitor anti-Rituximab, Grifols). ADAMTS13 activity had increased to 44%, so an approach of watchful waiting was adopted. In 2015, the ADAMTS13 activity fell to less than 5%, and the level of ADAMTS13 inhibitor increased to 25.7 U per milliliter. Mycophenolate mofetil was restarted, but ADAMTS13 activity remained below 5% and the inhibitor persisted. Three weekly doses of ofatumumab (of 300 mg, 1 g, and 1 g, in that order) were administered without a recurrence of reactions or anaphylaxis. At the time of this writing, the patient was well, with an ADAMTS13 activity of 64%.

Acquired TTP is a life-threatening condition, mediated by antibodies against ADAMTS13, that leads to ADAMTS13 deficiency with a resultant failure to cleave ultralarge von Willebrand multimers and widespread microthrombi. Inhibitor eradication is the key to treatment. Rituximab, a chimeric monoclonal antibody against CD20, has been shown to increase the remission rate and reduce the rate of relapse of TTP.^{1,2} A patient is more likely to have a clinical relapse of TTP (microangiopathic hemolytic anemia, thrombocytopenia, or microvascular thrombosis) if they have a severe ADAMTS13 deficiency (activity <10%). HACA has been described in patients with autoimmune disease who were previously treated with rituximab.³ Antibodies can lead to

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allergic-type or anaphylactic reactions to further treatment. Ofatumumab has been shown to be safe and efficacious in patients with autoimmune conditions, including those with allergic reactions to rituximab.^{4,5} We observed the successful use of ofatumumab in a patient with TTP.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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Weight and Metabolic Outcomes 12 Years after Gastric Bypass

TO THE EDITOR: The study by Adams et al. (Sept. 21 issue)¹ provides further evidence regarding the durable effects of bariatric surgery on both weight loss and type 2 diabetes. It also supports data from randomized, controlled trials indicating that bariatric surgery is the most effective current therapy for the management of both conditions. However, we note that the authors chose to define diabetes outcomes using criteria that differ from those used in other recent similar studies. Indeed, a number of differing diabetes outcome definitions have been used in the published literature, which raises concern regarding the comparability of these data.

To illustrate this, we report diabetes outcomes in 84 of our patients who had undergone Roux-en-Y gastric bypass at least 5 years earlier, according to definitions that have been used in other widely cited studies of bariatric surgery (Table 1). These data illustrate the substantial differences in reported diabetes outcomes depending on the definition used. We think that consistency in definitions of diabetes status after bariatric surgery would allow improved comparison among studies and procedures and would better inform patients of the expected outcomes of surgery.

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TO THE EDITOR: Adams et al. report impressive results of sustained weight loss and reductions in the incidence of diabetes, hypertension, and hyperlipidemia 12 years after Roux-en-Y gastric bypass. As a nephrologist, my exposure to patients who have undergone bariatric surgery is biased, since I am asked to see only patients who have kidney stones, chronic kidney disease, or both. Oxaluria and kidney stone disease after bariatric