

Rituximab treatment for dermatitis herpetiformis in the setting of type 1 diabetes mellitus, celiac disease, vitiligo, autoimmune hemolytic anemia, and autoimmune thrombocytopenia



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INTRODUCTION

Few case studies have indicated that rituximab may be helpful in achieving clinical and serologic remission of dermatitis herpetiformis. We present a case of a 47-year-old man with celiac disease refractory to standard treatments who achieved clinical resolution of dermatitis herpetiformis with rituximab.

CASE REPORT

A 47-year-old man with a history of celiac disease, vitiligo, type 1 diabetes mellitus, warm autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (also known as Evans syndrome) presented after splenectomy with pruritic rash and worsening hemolytic anemia and thrombocytopenia. Despite attempts at strict adherence to a gluten-free diet, his rash, composed of erythematous plaques scattered on bilateral extensor surfaces, buttocks, head, neck, abdomen, and groin, was worsening.

Before presentation, the patient had intermittent flares of pruritic papules and vesicles on the extensor surfaces of the upper and lower extremities and buttocks after ingesting gluten, coinciding with dyspepsia, diarrhea, bloating, and nausea. Two days before presentation, he went to an outside urgent care clinic for worsening rash and yellowing skin, at which time his temperature was 37.8°C and he had elevated unconjugated hyperbilirubinemia at 3.7 mg/dL, which was concerning for active

Abbreviation used:

AIHA: autoimmune hemolytic anemia

hemolysis. He was treated with intravenous diphenhydramine and intravenous ondansetron and was instructed to take oral hydroxyzine and loratadine for pruritus and apply topical triamcinolone 0.1% ointment twice daily as needed. His symptoms of rash and pruritus were not alleviated and continued to progress.

Upon admission, a dermatology specialist was consulted, and 2 4-mm punch biopsy specimens were taken from the right flank for hematoxylin-eosin staining and direct immunofluorescence. Histopathologic analysis showed papillary dermal edema with neutrophilic inflammation, and direct immunofluorescence showed 2+ granular IgA deposition within the papillary dermis, consistent with dermatitis herpetiformis. Laboratory test results were significant for hematocrit of 35.5% (hemoglobin, 12.8 g/dL), platelet count of 437 000/ μ L, and total bilirubin of 4 mg/dL (direct bilirubin, 0.3 mg/dL), as well as prior positive warm and cold autoantibodies (Coombs positive, with 3+ C3 and 1+ IgG), which was concerning for ongoing hemolysis. The patient's hemoglobin A1c was 8.2%.

Throughout the hospitalization, the patient had difficulty sleeping because of significant pruritus and further dissemination of his dermatitis herpetiformis

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lesions. Treatment with dapsone was considered but was not feasible due to continued hemolysis. The patient was started on high-dose prednisone at 80 mg (1 mg/kg) daily. His prednisone dose was increased to 120 mg (1.5 mg/kg) daily on his second day of hospitalization because of further progression. In the setting of high-dose steroids, the patient's blood glucose levels were extremely labile, despite up-titration of basal and sliding-scale insulin ranging between 90 and 400 mg/dL.

The decision was made to start rituximab and taper prednisone. The patient was started on rituximab at 375 mg/m² per week for 4 weeks according to the lymphoma protocol. He was discharged home after his first dose. He was readmitted after his second rituximab dose the following week because of worsening anemia, with hematocrit of 23.1% (hemoglobin, 7.8 g/dL), platelets at 437 000 K/ μ L, and resurfacing of his dermatitis herpetiformis due to likely unintentional gluten exposure. He was given dexamethasone 40 mg daily and started mycophenolate mofetil 500 mg twice daily as a steroid-sparing agent because of labile blood glucose.

Upon discharge, the patient's autoimmune hemolytic anemia had resolved and dermatitis herpetiformis was quiescent, so dexamethasone was stopped after 4 days and mycophenolate mofetil after 5 days. He continued to be stable and clear while receiving his third and fourth doses of rituximab. He experienced complete clinical remission of his autoimmune hemolytic anemia and significant improvement in his celiac and dermatitis herpetiformis while adhering to a gluten-free diet. His follow-up hematocrit level almost 4 months after treatment was 43.6% (hemoglobin, 14.9 g/dL), with a total bilirubin level of 1.4 mg/dL and platelets at 455 000/ μ L.

DISCUSSION

Gluten avoidance is the criterion standard in treatment for dermatitis herpetiformis and the intestinal gluten-sensitive enteropathy of the usually associated celiac disease. Cases refractory to gluten-free diet often require dapsone or sulfapyridine therapy. Despite significant pruritus and widespread dermatitis significantly affecting our patient's quality of life, dapsone therapy was not feasible in

our patient in the setting of hyperbilirubinemia and active hemolytic anemia. Case report studies suggest that rituximab for celiac disease may be successful.^{1,2} Similarly, Go et al³ showed that refractory cases of AIHA may be treated with rituximab with varying degrees of success.

Furthermore, Albers et al⁴ reported an 80-year-old man successfully treated to achieve clinical and serologic resolution of dermatitis herpetiformis (test results for transglutaminase 2 and 3 were negative after 13 months of therapy) with rituximab after failure of high-dose prednisone and azathioprine. Our patient's situation was complicated by Evans syndrome and steroid-induced hyperglycemia, which made standard treatment even more difficult.

After treatment with rituximab, our patient experienced improvement in both his dermatitis herpetiformis in the setting of celiac disease as well as in his AIHA. He also has a theoretical lowered risk of mucosa-associated lymphoid tissue lymphoma, because there is no longer a mechanism of inflammation with the targeted loss of CD20⁺ cells and memory B cells from treatment.⁵

In our patient's case, rituximab proved to be effective therapy, as reported during follow-up. Although he reports occasional minor flares of dermatitis herpetiformis, he denies any widespread involvement, and his hemoglobin and platelet counts remain stable. This suggests that rituximab for dermatitis herpetiformis in the setting of autoimmune disease may be an effective treatment option.

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