Linear IgA/IgG bullous dermatosis successfully treated with omalizumab: A Case report

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September 25, 2021

Abstract

Linear IgA/IgG bullous dermatosis (LAGBD) is a rare, autoimmune blistering skin disease. We report a case of LAGBD in a 70-year-old woman. All common treatments were discontinued due to side effects or lack of treatment response. The patient was successfully treated with omalizumab which cleared her lesions after three months.

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Key clinical message

Treatment of bullous diseases such as LAGBD can be difficult due to lack of treatment response. Omalizumab is a biologic drug that has not been previously reported effective in the treatment of LAGBD. Omalizumab could be a future treatment for LAGBD.

Introduction

Linear IgA bullous dermatosis (LABD) is an autoimmune, blistering disease characterized by linear deposits of IgA along the basement membrane. In cases of concurrent deposits of IgG, the disease is considered a distinct subtype of LABD called linear IgA/IgG bullous dermatosis (LAGBD).[1] This disease has various clinical presentations including generalized vesiculobullous lesions with mucosal involvement.[2] Omalizumab (OMZ) is a humanized monoclonal antibody against IgE and has proved effective as an off-label treatment for other bullous diseases, notably bullous pemphigoid (BP). OMZ has not previously been reported as an effective treatment for LAGBD.[3,4]

Case report

A 61-year-old woman presented to the Department of Dermatology and Allergy in 2012 with general malaise and a 3-week history of vesicular ulcerations with itching and stinging located to the inner genital labia, upper extremities and oral mucosa. Her medications included carbamazepine, which she had received for 30 years, metoprolol and thiazide. She had recurring oral herpes simplex but had never needed oral antiviral treatment. She had no lymphadenopathy on examination, and laboratory testing showed normal leukocytes and mild eosinophilia (0.55 x 10^9 /L). Liver function, renal function, thyroid hormones and antinuclear antibodies were all within normal ranges and indirect immunofluorescence (IF) test for circulating autoantibodies was negative. The patient was initially treated with valaciclovir on suspicion of generalized herpes simplex infection and cutaneous punch biopsies for both histopathology and direct IF were performed. Two weeks after the first visit, histology showed epidermal spongiosis, subepidermal bullae with necrosis and infiltration of eosinophil granulocytes, while the dermis had perivascular infiltrates containing lymphocytes

and histiocytic cells. Direct IF showed IgG deposits along the basement membrane and absence of IgA and C3. On this basis the patient was diagnosed with BP and treated with azathioprine in increasing doses up to 2 mg/kg daily, prednisolone up to 37.5 mg daily and topical corticosteroid. The patient responded appropriately with minimal disease during the first six years of treatment while maintaining azathioprine combined with prednisolone 5mg daily. In 2019 she had secondary loss of response and worsening of active disease with vesicles, pustules and erosions clustered in rosette-like patterns, and there was involvement of the trunk and thighs. Renewed cutaneous punch biopsy for histopathology showed subepidermal bullae containing eosinophil granulocytes and sparse perivascular inflammation of eosinophil granulocytes in the dermis resembling BP (Figure 1A). Direct IF from the trunk showed linear IgA and faint linear IgG depositions along the basement membrane and absence of C3, which was consistent with LAGBD (Figure 1B). Renewed IF for circulating IgG antibodies was negative. Laboratory testing showed eosinophilia (0.75 x 10^9 /L) while analyses for coeliac disease were negative.

Treatment with dapsone 50 mg daily and increased doses of prednisolone was initiated, but the patient experienced adverse effects in the form of neuropathies and hemolysis. Both treatments were stopped, and she was then treated with sulfapyridine up to 3 grams daily divided into three doses. Her condition only slightly improved the following seven months and treatment with oral methotrexate up to 10 mg weekly was added. Subsequently, the patient developed anemia after two months while showing no signs of further improvement (Figure 2A and B). Methotrexate was stopped and the patient started subcutaneous OMZ 300 mg every four weeks in addition to sulfapyridine, which was slowly decreased to 500 mg twice daily. One month after the first injection with OMZ, the patient showed noticeable improvement, and she had almost complete remission after another month. She has currently received treatment with OMZ and sulfapyridine for 11 months with no side effects or signs of relapse (Figure 2C and D).

Discussion

We describe a case of treatment refractory LAGBD with onset eight years earlier, which was initially diagnosed as BP. In 2019 when the disease worsened, the vesicles had annular and herpetiform arrangements with mucosal involvement, which is a typical find in LABD but rarely reported in BP.[5] The first biopsy in 2012 showed histopathological features of BP though immunoglobulin deposits were absent. According to the few available case reports that describe its clinical features in detail, LAGBD can resemble both LABD and BP.[2,6] We are convinced that the patient in our case had LAGBD throughout the course of disease, even though the histological diagnosis was not confirmed until after eight years.

The same treatment strategies are described for both LABD and LAGBD, and there are reports of successful treatments of LAGBD with prednisolone, dapsone, azathioprine and sulfapyridine.[2,7] In our case, these treatments either proved ineffective or were discontinued due to side effects. Azathioprine in combination with prednisolone was the only treatment providing temporary disease control for four years until there was secondary loss of response. We refrained from initiating treatment with rituximab due to the recent pandemic with severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) infection.[8] Instead, we initiated treatment with OMZ in combination with sulfapyridine after which the patient's skin lesions almost cleared after two months. We are convinced that OMZ was decisive for the patient's sudden treatment response since sulfapyridine treatment alone previously only had a slight effect.

OMZ is a monoclonal IgE antibody approved for inflammatory diseases including chronic spontaneous urticaria and asthma. OMZ binds free circulating IgE and thereby prevents it from inducing allergic reactions. Its usefulness as a novel off-label treatment alternative for BP has previously been reported in multiple cases, while one case reports its efficacy in the treatment of LABD.[3,4,9]Although specific IgE directed against the autoantigen BP180 has been shown in BP, the exact mechanism of OMZ in BP, LABD and LAGBD is not fully understood.[10] Our case report supports the limited amount of evidence of OMZ and its usefulness in the treatment of LABD and LABGD.

Acknowledgements

We thank the patient for allowing us to present her case. Written informed consent to share and publish the

case details and photographs in this paper was granted by the patient.

Author contributions

Morten Bahrt Haulrig, Wrote the manuscript

Signe Ledou Nielsen, Data analysis and interpretation, final approval of the version to be published

Jesper Elberling, Critical revision of the article, final approval of the version to be published

Lone Skov, Critical revision of the article, final approval of the version to be published

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