GA101 (a Novel Anti-CD20 Monoclonal Antibody)-Induced Lichenoid Eruption

Waseem Bakkour · Ian H. Coulson

To view enhanced content go to www.dermtherapy-open.com
Received: November 14, 2011 / Published online: March 30, 2012
© The Author(s) 2012. This article is published with open access at Springerlink.com

ABSTRACT

Introduction: Obinutuzumab (GA101) is a novel anti-CD20 monoclonal antibody that has been shown to be effective for the treatment of non-Hodgkin's lymphoma, and is currently being evaluated in phase 3 clinical trials. The side-effect profile of the drug is not yet well established.

Case report: The authors report a case of a 62-year-old patient who developed widespread lichenoid eruption as a result of GA101 treatment for his follicular non-Hodgkin's lymphoma.

Conclusion: This is the first case report of cutaneous side effects of GA101.

Keywords: Anti-CD20 monoclonal antibody; GA101; Lichenoid drug eruption; Rituximab

INTRODUCTION

Obinutuzumab (GA101) is a new anti-CD20 monoclonal antibody that is currently being evaluated in phase 3 clinical trials for the treatment of non-Hodgkin's lymphoma. The initial results are promising and the drug is likely to be in wide use soon. However, the side-effect profile is not yet well known. The authors report a case of a lichenoid eruption that developed in a patient with follicular non-Hodgkin's lymphoma as a result of treatment with GA101.

CASE REPORT

A 62-year-old man presented to our Dermatology Department with a 4-month history of widespread pruritic rash. He had follicular non-Hodgkin's lymphoma, which had been diagnosed 3 years ago and initially treated with eight cycles of rituximab, cyclophosphamide, vincristine, and prednisolone, with good response. A year later he relapsed, requiring six cycles of retuximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone to gain control of the disease. No cutaneous side effects were recorded

W. Bakkour (✉) · I. H. Coulson
Department of Dermatology, Burnley General
Hospital, Burnley, UK
e-mail: Waseem.Bakkour@srft.nhs.uk

Enhanced content for this article is
available on the journal web site:
www.dermtherapy-open.com

during this period. He deteriorated again 2 years later and was started on a phase 2 clinical trial with GA101 combined with fludarabine and cyclophosphamide, and received five cycles at monthly intervals. During the third cycle he started to develop a rash that worsened during the next two cycles before stabilizing after the treatment had finished. On physical examination he had a widespread violaceous lichenoid maculopapular eruption on his trunk, back, arms and legs (Fig. 1). The rash on his lower back and thighs had a psoriasiform appearance. The patient also had ulcers and erosions inside his mouth. Biopsies were taken from the violaceous and the psoriasiform rash and both areas showed mild degree of hyperkeratosis and parakeratosis. The subjacent prickle cell layer showed focal infiltration by polymorphs and a mild degree of spongiosis. There was also basal layer degeneration and papillary dermis edema with patchy infiltration by a mixture of lymphocytes, eosinophils and histiocytes some of which were pigment laden. Civatte bodies were recognized in areas. These findings favored a diagnosis of lichenoid drug eruption. Direct immunofluorescence from normal perilesional

skin (taken to exclude paraneoplastic pemphigus) was negative. The patient was treated with topical clobetasol propionate 0.05 % ointment and had no further cycles of GA101. This resulted in clearance of the rash in 3 weeks with no recurrence (Fig. 2).

DISCUSSION

The authors feel that GA101 is the most likely culprit here. A latency period of few months is not uncommon with lichenoid drug eruptions and the patient developed the rash 2 months after starting GA101. The only other new drug given at the same time was fludarabine, which has been used for a long time in hematology and to the author's knowledge has not been reported to cause lichenoid eruptions.

Cutaneous side effects of anti-CD20 monoclonal antibodies have been reported with rituximab, which is a type I monoclonal anti-CD20 antibody that has been approved for the treatment of non-Hodgkin's lymphoma since 1997. These range from mild effects, such as sweating, pruritus, and urticaria, to more serious ones such as vasculitis,

Fig. 1 Lichenoid eruption secondary to treatment with GA101

Fig. 2 Improvement following treatment with clobetasol propionate 0.05 % ointment

Stevens-Johnson syndrome, toxic epidermal necrolysis, paraneoplastic pemphigus, and lichenoid dermatitis [1]. The onset of the reaction in the reported cases has varied from 1 to 13 weeks following rituximab exposure [1]. Serum sickness has also been reported with rituximab [2, 3].

GA101 is a novel type 2, glycoengineered, humanized anti-CD20 monoclonal antibody designed to bind with high affinity to the CD20 type II epitope, resulting in the induction of cytotoxicity that is fivefold to 100-fold greater than observed upon treatment with type I anti-CD20 antibodies such as rituximab [4]. Obinutuzumab demonstrated promising efficacy in difficult-to-treat patients with non-Hodgkin's lymphoma in phase 2 clinical trials and it is currently being evaluated in phase 3 trials [5].

Currently, all the cutaneous side effects of anti-CD20 monoclonal antibodies reported in the literature are related to rituximab, while there are no reports of GA101 cutaneous side effects. Although lichenoid eruptions have been reported with rituximab, the lichenoid reaction our patient developed was unlikely to be due to a class effect. Had this been the case we would have expected him to have developed the reaction when he was treated with rituximab. This might suggest that the GA101 cutaneous side-effect profile is different to that of rituximab, although it is difficult to be sure at this stage.

CONCLUSION

In summary, GA101 is a promising new treatment for refractory non-Hodgkin's lymphoma that is likely to be in wide use soon. This makes it important to identify its side effects, including cutaneous ones. This is the first case report of a cutaneous side effect of GA101.

Conflict of interest. The authors declare that they have no conflicts of interest.

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

REFERENCES

1. Scheinfeld N. A review of rituximab in cutaneous medicine. *Dermatol Online J.* 2006;12:3.
2. Hellerstedt B, Ahmed A. Delayed-type hypersensitivity reaction or serum sickness after rituximab treatment. *Ann Oncol.* 2003;14:1792.
3. Herishanu Y. Rituximab-induced serum sickness. *Am J Hematol.* 2002;70:329.
4. Robak T. GA-101, a third-generation, humanized and glyco-engineered anti-CD20 mAb for the treatment of B-cell lymphoid malignancies. *Curr Opin Investig Drugs.* 2009;10:588–96.
5. Sehn LH, Goy A, Offner FC, et al. Randomized phase II trial comparing GA101 (obinutuzumab) with rituximab in patients with relapsed CD20+ indolent B-cell non Hodgkin lymphoma: preliminary analysis of the GAUSS study. Paper presented at: 53rd ASH annual meeting and exposition, December 10–13, 2011, San Diego, CA, USA.