

## Successful Rituximab Treatment of Severe Pemphigus Vulgaris Resistant to Multiple Immunosuppressants

Joerg Wenzel, Ralf Bauer, Thomas Bieber and Thomas Tüting

Department of Dermatology, University of Bonn, Sigmund-Freud-Strasse 25, DE-53105 Bonn, Germany.

E-mail: joerg.wenzel@ukb.uni-bonn.de

Accepted August 10, 2004.

Sir,

Pemphigus vulgaris (PV) is an autoimmune disease characterized by blisters and widespread erosions involving skin and mucous membranes. The disorder is mediated by antibodies, predominantly directed against the epidermal cell adhesion molecules desmoglein 1 and 3. Systemic corticosteroids are the established first-line treatment, but their use is limited due to the well known side effects, especially in long-term treatment. To reduce these side effects, several combinations with other immunosuppressive drugs have been tested in recent years, e.g. azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide, intravenous immunoglobulins, plasmapheresis and photopheresis. Unfortunately, multiresistant courses exist and present a complex therapeutic challenge.

We present here the case of a 55-year-old woman suffering from PV for 13 years. She needed continuous treatment with methylprednisolone doses around 20 mg/day to prevent widespread blistering. Treatment with azathioprine (2 mg/kg body weight/day for 1 year), cyclophosphamide (1.5 mg/kg body weight/day for 6 months), methotrexate (25 mg/week i.v. for 8 months), mycophenolate mofetil (3 g/day for 1 year) and intravenous immunoglobulins (three cycles of Intraglobin<sup>TM</sup>CP using 2 g/kg body weight per cycle) did not improve the clinical picture and was not able to prevent recurrences. Due to long-term steroid treatment, she had severe

Cushing's syndrome including osteoporosis leading to two vertebral fractures with a loss of about 9 cm of her body height. She suffered from steroid-induced diabetes mellitus, glaucoma and arterial hypertension, and experienced an episode of bacterial sepsis necessitating intensive care treatment.

When widespread new lesions developed (Fig. 1a) we decided to treat this patient with anti-CD20 monoclonal antibody rituximab (MabThera<sup>TM</sup>), as successful treatment of recalcitrant PV had recently been reported (1–4). We applied four weekly cycles of 600 mg rituximab (corresponding to 375 mg/m<sup>2</sup> body surface) within 5 weeks. Additional low-dose oral treatment with methylprednisolone was performed (8 mg/day).

Remarkably, her skin lesion cleared up between the second and sixth weeks after the last rituximab cycle (Fig. 1b). Simultaneously, the titre of anti-epithelial antibodies, detected by indirect immunofluorescence, declined from 1:160 to 1:40. Peripheral B cells, counted by flow cytometry, decreased from normal numbers to 2 cells/ $\mu$ l. Severe clinical side effects were not observed. During the clinical follow-up period (now 3 months) no new lesions have appeared. Methylprednisolone dosage could be reduced to 6 mg/day.

Our findings in this extremely recalcitrant patient support the clinical efficacy of rituximab for the treatment of severe PV. Further prospective controlled

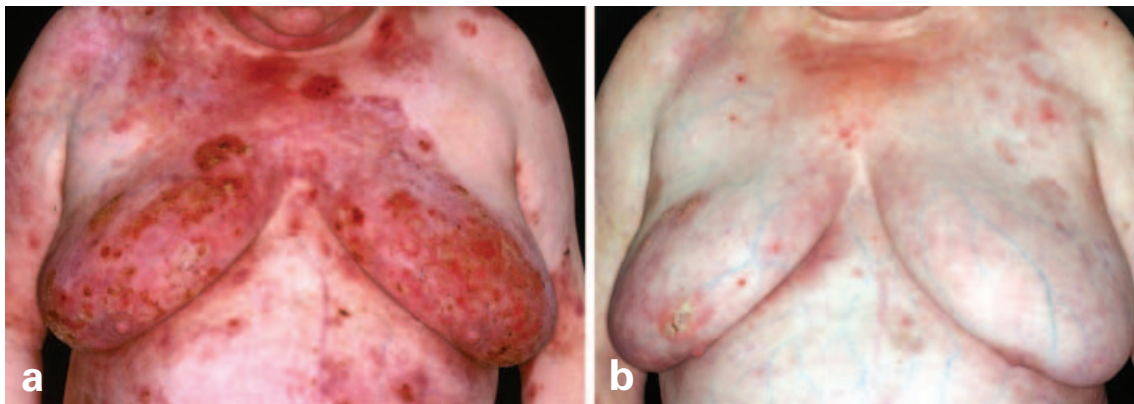


Fig. 1. The patient presented with blisters and widespread erosions involving her chest, back, axilla and inguinal areas (a). Her skin lesion cleared up remarkably between the second and eighth weeks after the last rituximab cycle (b).

studies will have to substantiate the effectiveness and to investigate side effects of rituximab in patients with PV.

#### REFERENCES

1. Virgolini L, Marzocchi V. Anti-CD20 monoclonal antibody (rituximab) in the treatment of autoimmune diseases. Successful result in refractory pemphigus vulgaris: report of a case. *Haematologica* 2003; 88: 24.
2. Cooper HL, Healy E, Theaker JM, Friedmann PS. Treatment of resistant pemphigus vulgaris with an anti-CD20 monoclonal antibody (Rituximab). *Clin Exp Dermatol* 2003; 28: 366–368.
3. Herrmann G, Hunzelmann N, Engert A. Treatment of pemphigus vulgaris with anti-CD20 monoclonal antibody (rituximab). *Br J Dermatol* 2003; 148: 602–603.
4. Dupuy A, Viguier M, Bedane C, Cordoliani F, Blaise S, Aucouturier F, et al. Treatment of refractory pemphigus vulgaris with rituximab (anti-CD20 monoclonal antibody). *Arch Dermatol* 2004; 140: 91–96.