Research letters

Clinical response to rituximab and improvement in quality of life in patients with bullous pemphigoid and mucous membrane pemphigoid

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Dear Editor, Pemphigoid is a heterogeneous group of rare and chronic autoimmune subepidermal bullous diseases, characterized by circulating autoantibodies against structural proteins in the hemidesmosomes. Long-term therapy with systemic oral prednisone and immunosuppressants is often required and has been associated with severe adverse reactions.[1,2] Rituximab, an anti-CD20 monoclonal antibody, is increasingly used in pemphigoid, mainly in patients who failed conventional immunosuppressive therapies. Our study aimed to evaluate the clinical outcomes and the patient-reported outcome measures (PROMs) of patients with bullous pemphigoid (BP) and mucous membrane pemphigoid (MMP) who were treated with rituximab. We performed a single-centre retrospective observational study of patients with BP and MMP who were treated with rituximab between November 2016 and January 2020, and who have previously failed conventional immunosuppressive therapies. A single course of two infusions of 1000 mg of rituximab was administered within an interval of 2 weeks (M0 and M0·5), followed by 500 mg at month 6 (M6) and month 12 (M12). Clinical outcomes according to definitions of an international consensus conference were applied.[3,4] Reported adverse events and PROMs including Dermatology Life Quality Index (DLQI), Treatment of Autoimmune Bullous Disease Quality of Life (TABQOL) and Hospital Anxiety Scale (HADS) were collected. A lower score indicates a better outcome. $P < 0{\cdot}05$ was considered significant.

In total, seven patients with BP and 16 patients with MMP were included; eight were male (35%) and 15 were female (65%) with a median age of 64 years [interquartile range (IQR) 58–70]. The median BP Disease Area Index score at M0 (n = 18) was 4·0 (IQR 1·8–7·0), owing to concomitant use of immunosuppression or immunomodulators. Mucosal involvement in MMP included ocular (n = 8, 50%), nasal (n = 6, 38%), oral (n = 12, 75%), laryngeal (n = 3, 19%), pharyngeal (n = 8, 50%) and genital involvement (n = 5, 31%).

Disease control was achieved in 19 patients (83%), six of whom had BP (86%) and 13 of whom had MMP (81%). Remission (partial or complete) was achieved in 17 patients (74%), five of whom had BP (71%) and 12 of whom had MMP (75%). Complete remission off therapy was achieved by two patients (29%) with BP and five patients (31%) with MMP (Table 1). At M0, 21 patients (91%) received adjuvant immunosuppression or immunomodulators (Table 1). This decreased to 17 patients (74%) at M6 and nine patients (39%) at M12. In particular, the number of patients receiving prednisone decreased from 18 patients (78%) at M0 to 13 patients (57%) at M6. Only six patients (26%) were treated with prednisone at M12. B cells were rapidly depleted in the peripheral blood at M0·5 in all patients. During treatment, the DLQI score showed a decrease of 50% between M0 and M6 ($n = 19$, $P = 0{\cdot}012$). The TABQOL score showed a decrease of 41% between M0 and M12 ($n = 14$, $P = 0{\cdot}001$). Finally, the HADS score decreased by 50% between both M0 and M6 ($n = 18$; $P = 0{\cdot}01$) and M0 and M12 ($n = 14$; $P = 0{\cdot}044$).

The reappearance of B cells was observed in five patients (22%) at M6 and in 13 patients at M12 (57%). Overall, eight patients (35%) relapsed after a median time of 56 weeks [two patients with BP (29%) and six patients with MMP (38%)] (Table 1). Overall, 22 patients (96%) reported adverse events, the majority of which were infections (n = 21, 95%). Hypogammaglobulinaemia was reported in 12 patients (55%), reduced CD3 and CD4 T cells were reported in eight patients (36%) and reduced CD8 T cells were reported in nine patients (41%) (Table 1). The majority of these patients were treated for bacterial or viral infections. None of these infections were severe or life-threatening. The 1-year mortality was 0%. These results support the beneficial effects of rituximab therapy on the clinical response in patients with pemphigoid, in line with previous studies.[5–7] Concomitant immunosuppression or immunomodulators were reduced during rituximab treatment, in particular the percentage of patients using prednisone decreased from 78% to 26% between M0 and M12. A major concern with rituximab treatment is the increased risk of infection. In this study, the majority of patients reported infections, but none were severe. In our cohort, the 1-year mortality was 0%, but this result may be biased owing to the small sample size. Previous studies have observed a lower 1-year mortality rate in patients receiving rituximab compared with those receiving conventional therapy.[6,8]

Importantly, we observed a positive effect of rituximab therapy on quality of life and treatment burden in patients with pemphigoid, which was reflected by a significant

Table 1 Highest clinical outcome reached and reported adverse events (AEs) after rituximab treatment in patients with pemphigoid

	Total (n = 23)	BP (n = 7)	MMP (n = 16)
Clinical outcome			
DC	19 (83)	6 (86)	13 (81)
Median TTDC, weeks (IQR)	14·0 (4·0–23·0)	13·0 (5·0–21·5)	14·0 (5·0–21·5)
Remission, PR/CR	17 (74)	5 (71)	12 (75)
PR on therapy	2 (9)	0 (0)	2 (13)
Median TTPR, weeks (n)	28·0	–	28·0
PR off therapy	6 (26)	1 (14)	5 (31)
Median TTPR off therapy, weeks (IQR)	59·0 (20·3–69·8)	52	66·0 (18·5–72·5)
CR on therapy	2 (9)	2 (29)	0 (0)
Median TTCR, weeks	56·5	56·5	–
CR off therapy	7 (30)	2 (29)	5 (31)
Median TTCR off therapy, weeks (IQR)	62·0 (52·0–68·0)	57·5	62·0 (46·0–87·5)
Relapse	8 (35)	2 (29)	6 (38)
Median time to relapse, weeks (IQR)	56·0 (12·8–81·5)	32·5	61·5 (24·3–95·8)
Adjuvant systemic therapy			
M0 (%)	21 (91)	7 (100)	14 (88)
Prednisone	18 (78)	6 (86)	12 (75)
Dapsone	4 (17)	2 (29)	2 (13)
Methotrexate	1 (4)	1 (14)	0 (0)
Cyclophosphamide	3 (13)	0 (0)	3 (19)
Azathioprine	1 (4)	0 (0)	1 (6)
M6 (%)	17 (74)	6 (86)	11 (69)
Prednisone	13 (57)	5 (71)	8 (50)
Dapsone	4 (17)	2 (29)	2 (13)
Methotrexate	0 (0)	0 (0)	0 (0)
Cyclophosphamide	1 (4)	0 (0)	1 (6)
Azathioprine	1 (4)	0 (0)	1 (6)
M12 (%)	9 (39)	5 (71)	4 (25)
Prednisone	6 (26)	4 (57)	2 (13)
Dapsone	3 (13)	2 (29)	1 (6)
Methotrexate	0 (0)	0 (0)	0 (0)
Cyclophosphamide	1 (4)	0 (0)	1 (6)
Azathioprine	1 (4)	0 (0)	1 (6)
AEs			
Number of patients with AEs (%)	22 (96)		
Malaise	19 (86)		
Pain	9 (41)		
Dyspnoea	8 (36)		
Headache	3 (14)		
Rash	2 (9)		
Lymphopenia	11 (50)		
Anaemia	8 (36)		
Tromboctyopenia	1 (5)		
Leucocytosis	1 (5)		
Late-onset neutropenia	1 (5)		
Hypogammaglobulinaemia	12 (55)		
Reduced number of CD8 T cells	9 (41)		
Reduced number of CD3 T cells	8 (36)		
Reduced number of CD4 T cells	8 (36)		
Infections, bacterial or viral	21 (95)		
Candida	4 (18)		

BP, bullous pemphigoid; CR, complete remission; DC, disease control; IQR, interquartile range; MMP, mucous membrane pemphigoid; M0, first infusion of 1000 mg of rituximab; M6, third infusion of 500 mg of rituximab at month 6; M12, fourth infusion of rituximab at month 12; PR, partial remission; TTCR, time to CR; TTDC, time to DC; TTPR, time to PR. Data are presented as n (%) unless otherwise stated.

decrease in the DLQI and TABQOL score and a decline in anxiety scores during rituximab treatment. Limitations of this study include its retrospective nature and the small sample size. In conclusion, our study demonstrated a 74% remission rate in patients with pemphigoid who received rituximab treatment, which had a steroid-sparing benefit, and

importantly, we also observed a significant improvement in quality of life and a decrease in treatment burden.

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H. Rashid, J.M. Meijer, M.C. Bolling and B. Horváth

Department of Dermatology, Center of Blistering Diseases, European Reference Network-Skin Member, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
Email: h.rashid@umcg.nl

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Use of thermal imaging and a dedicated wound-imaging smartphone app as an adjunct to staging hidradenitis suppurativa

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Dear Editor, Hidradenitis suppurativa (HS) presents with painful nodules, draining tunnels, abscesses, ulcers and fistula formation.[1] Grading systems [e.g. Hurley Staging System, International Hidradenitis Suppurativa Severity Score System (IHS4), Severity Assessment of Hidradenitis Suppurativa Score (HS-Physician's Global Assessment), and Hidradenitis Suppurativa Area and Severity Index (HASI)] assess disease severity in terms of lesion count, extension and morphology. Major limitations of these systems include their inability to capture disease progression and treatment responsiveness,[2] in addition to their low interrater agreement, limiting reliability and highlighting the need for improvements in objectively quantifying disease severity.[3] Infrared thermography (IRT) captures the heat of the skin through reproducible temperature quantification,[4] detecting inflammation and assisting surgical intervention.[5] We aimed to assess IRT patterns in patients with HS and determine their correlation with clinical severity.

A prospective cross-sectional study was conducted in a consecutive sample of patients receiving care in an HS clinic in Toronto, Canada. The protocol was approved by the clinic's Research and Ethics Committee. Inclusion criteria were any adult patients with a prior diagnosis of HS and exclusion criteria were the coexistence of any other inflammatory skin or vascular disease. Clinical assessment and scoring of HS severity were performed by an HS specialist (A.A.) using the aforementioned staging systems. Photographs were obtained using the Skin and Wound app (Swift Medical, Toronto, ON, Canada Canada),[6] and IRT images were acquired using a mobile FLIR ONE Pro camera (FLIR Systems, Wilsonville, OR, USA). Blinded image analysis was performed using the Swift Medical Dashboard, superimposing the HS-affected area and IRT images. Mean temperatures (°C) were recorded for the affected area and a 25-cm^2 patch of adjacent healthy skin. The temperature difference between these areas [thermal asymmetry (TA)] was also recorded. A consecutive sample of axillae, abdomen and thighs from six healthy individuals were used as negative controls. TA differences between controls and patients with different HS severity scores, in addition to the size of the affected area and main lesion type, were assessed using linear models followed by Tukey post hoc tests. Correlation between clinical scores and TA in patients with HS was calculated using Spearman's correlation coefficient.

Among the 38 patients enrolled in the study, the median area of HS-affected skin measured was 6·6 cm^2 (interquartile