

can be used to monitor research activities in dermatology.

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Low prevalence of late-onset neutropenia after rituximab treatment in patients with pemphigus



To the Editor: The autoimmune blistering disease pemphigus is caused by IgG autoantibodies binding to desmosomal autoantigens, most commonly desmoglein (Dsg) 1 and 3, leading to the loss of cellular adhesion¹ and resulting in the formation of blisters and erosions on the skin or oral mucosa, or both. Rituximab (anti-CD20 antibody) is a first-line treatment option,² but its use across a range of nondermatologic conditions has been associated with development of late-onset neutropenia (LON), occurring 4 to 48 weeks after treatment, with a prevalence between 1.3% and 29.9%.^{3,4} Despite cases of rituximab-associated LON reported in other autoimmune blistering diseases,⁵ a systemic evaluation of rituximab-associated LON in pemphigus is lacking.

Thus, we retrospectively identified all patients with pemphigus treated in our department between 2008 and 2019. We identified 161 patients with pemphigus, of which 132 could be included, consisting of 102 with pemphigus vulgaris and 30 with pemphigus foliaceus. Follow-up data were insufficient for 29 patients. Most patients (n = 117) received rituximab treatment (Table I). A total of 209 cycles of rituximab were administered. LON was defined as neutropenia (absolute neutrophil count $<1.5 \times 10^9/L$) 4 to 48 weeks after the last dose of rituximab.

LON was identified in 5 of 117 rituximab-treated patients and in 0 of 15 patients treated without rituximab. Indeed, LON was observed after 6 of 209 rituximab cycles. In more detail: LON developed in a 76-year-old woman (pemphigus foliaceus) after 95 days (lowest point [nadir] of absolute neutrophil count: $0.73 \times 10^9/L$), which lasted 6 days. Co-medications included mycophenolate mofetil, citalopram, and mirtazapine.

LON developed in the second patient, a 37-year-old woman (pemphigus vulgaris), 290 days after rituximab, prompting the substitution of azathioprine with mycophenolate. LON developed in the third patient, a 61-year-old woman (IgA pemphigus), 123 days after rituximab (nadir $1.42 \times 10^9/L$). Co-medications included dapsone, acitretin, intravenous immunoglobulin, torsemide, and simvastatin.

LON developed in patient 4, a 57-year-old man (pemphigus vulgaris), 127 days after rituximab (nadir $1.43 \times 10^9/L$), which lasted 1 day. LON developed after subsequent rituximab therapy; 114 days after the last administration of rituximab (nadir $0.83 \times 10^9/L$, duration 21 days). The interval between the rituximab cycles was 6 months. The extent to which rituximab-associated LON may predispose to LON in subsequent treatment cycles, potentially with increased severity, is unclear, but retreatment warrants increased laboratory and clinical surveillance. Patient 4 was also receiving entecavir for hepatitis B and mirtazapine for fibromyalgia. However, the temporal relationship between the rituximab treatment and the neutropenia suggested rituximab as the causal agent.

The final case of LON was observed in a 68-year-old woman (pemphigus foliaceus), which developed after 193 days. Again, azathioprine treatment was substituted with mycophenolate mofetil due to the neutropenia.

LON occurring after rituximab in our cohort did not require specific therapy (antibiotics, granulocyte-colony stimulating factor) or hospitalization, and LON

Table I. Patient characteristics

Variable	RTX treatment PV		RTX treatment, PF		No RTX treatment, PV (n = 10) and PF (n = 5)
	No LON (n = 89)	LON (n = 3)	No LON (n = 23)	LON (n = 2)	
Age, mean (range), y	56 (21-87)	57 (37-59)	62 (23-77)	72 (68-75)	67 (37-87)
Sex, No.					
Female	48	2	10	2	9
Male	41	1	13	0	6
Rituximab, No.					
1 cycle	51	1	12	1	...
2 cycles	19	...	8
≥3 cycles	19	2	3	1	...
Concurrent immunosuppression, No.	75	2	22	2	15
Azathioprine	30	1	9	1	8
Mycophenolate mofetil	34	...	12	1	5
Mycophenole sodium	7	2
Other	5	1	4
None	14	1	1

LON, Late-onset neutropenia; PF, pemphigus foliaceus; PV, pemphigus vulgaris; RTX, rituximab.

was short-lived. Given the limited data available, it is also difficult to determine whether LON in patients with pemphigus treated with rituximab is more common when additional immunosuppressive agents are used, and if so, by which agents in particular; nevertheless, occurring in only 6 of 209 rituximab cycles (2.8%). Rituximab-associated LON in pemphigus seems to be relatively rare.

Limitations of this analysis are the retrospective and single-center design. Collectively, our analysis reassuringly points toward a low prevalence of LON in patients with pemphigus treated with rituximab.

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Factors impacting patient ratings of Mohs micrographic surgeons: Lessons gleaned from analysis of 17,527 online reviews



To the Editor: Although patient satisfaction with Mohs micrographic surgery is high,¹ insufficient data exist regarding factors affecting patient satisfaction.^{2,3} We analyzed online reviews of 195 attending Mohs micrographic surgeons at all of the 72 American College of Mohs Surgery fellowship programs in the United States and Canada to determine the most discussed elements of care.