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CASE REPORT

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Rituximab-induced psoriasis in a patient with pemphigus vulgaris: A case report and literature review

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Key Clinical Message

Rituximab which is established as a main treatment for pemphigus vulgaris can be a potential causative factor for development of psoriasis in some patients. It is preferred to avoid using rituximab in patients who had a history of psoriasis. Acquainting medical doctors about rituximab-related cutaneous complications will help them in detection and management.

Abstract

Rituximab is a human/murine monoclonal antibody targeting the CD20 antigen on B-lymphocytes surface. Although it is used as promising treatment for pemphigus, nowadays it is also a new therapy for other autoimmune diseases including systemic lupus erythematosus and rheumatoid arthritis, and others like non-Hodgkin's lymphoma. Although there is increasing evidence regarding the safety and effectiveness of rituximab in these diseases, many cutaneous adverse effects have been reported. Here, we describe a 48-years-old patient affected with pemphigus vulgaris who developed psoriatic lesions on her on scalp, trunk, and extremities, 4 months after the second course of rituximab.

KEYWORDS

pemphigus, psoriasis, rituximab-induced psoriasis

1 | INTRODUCTION

Psoriasis and pemphigus are two chronic inflammatory immune mediated cutaneous disorders. Rituximab (RTX) is a chimeric murine/human anti-CD20 monoclonal antibody known as a potential drug for the treatment of pemphigus vulgaris. It is administrated via intravenous infusion.[1] Here we present a case of a 48-year-old patient affected with pemphigus vulgaris and developed psoriatic plaques on her scalp, trunk, and extremities 4 months after the second course of RTX.

2 | CASE HISTORY/EXAMINATION

A 48-year-old female known case of pemphigus vulgaris, presented to our dermatology clinic with a 2 month history of pruritic lesions on the scalp, trunk, and extremities (Figure 1).

The patient had been diagnosed with mucocutaneous pemphigus vulgaris from 16 years earlier. She had received multiple courses of corticosteroid pulse therapy, followed by maintenance treatment with oral prednisolone. Four months before the current presentation,

the patient was admitted due to pemphigus recurrence (Figure 2) and treated with a course of RTX (two infusions of 1 g 2 weeks apart) in addition to 30 mg of oral prednisolone. One month later, she had complete resolution for her skin lesions, and prednisolone was tapered gradually to 10 mg/day.

Physical examination revealed multiple sharply demarcated, scaly, and erythematous plaques distributed over the scalp, retroauricular area, abdomen, presacral, and extensor surfaces of the extremities (PASI score 14.1). Examination of nails, mucosa, and joints was normal.

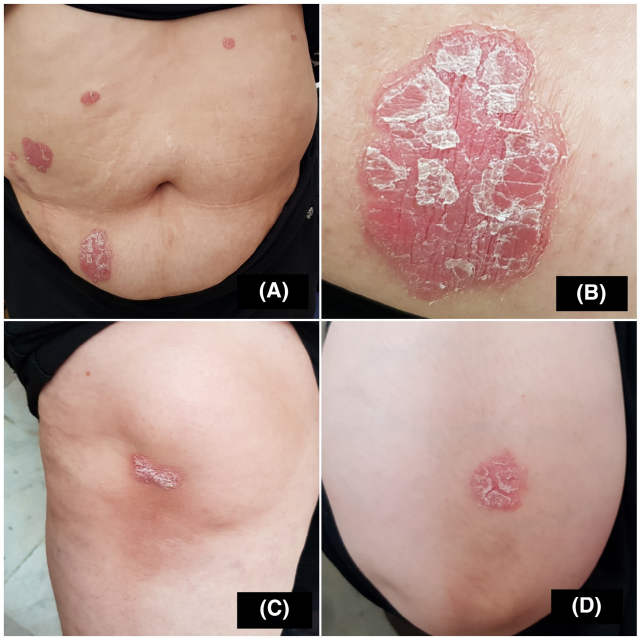

FIGURE 1 Multiple scaly erythematous plaques on the abdomen (A, B), extensor surfaces of the lower (C) and upper (D) extremities.

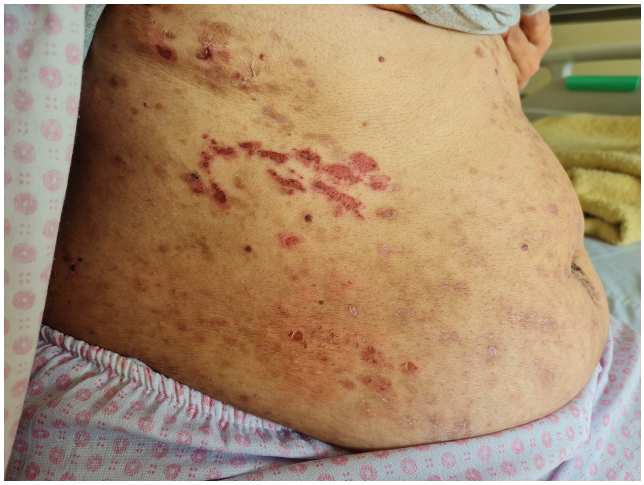

FIGURE 2 Photo of patient when she had pemphigus vulgaris; multiple erosions on trunk.

3 | DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT

Skin biopsy revealed psoriasiform acanthosis, munds of parakeratosis, and suprapapillary plate thinning. Papillary dermis showed vascular tortuosity and perivascular lymphocytic infiltration compatible with the diagnosis of psoriasis. Laboratory tests, including complete blood count, lipid profile, liver function tests, urea, creatinine, ESR, and CRP, were normal. We administered treatment for psoriasis included tablet methotrexate 7.5 mg/week and topical clobetasol.

4 | OUTCOMES AND FOLLOW UP

During 6 months' of follow-up, psoriatic plaques had partially improved (PASI score = 3.2), and no other sites were involved. The patient was maintained on oral methotrexate (10 mg/week), and prednisolone was also tapered to 2.5 mg/day.

5 | DISCUSSION

The exact underlying mechanism for the association between psoriasis and RTX is still unclear, but there are various hypotheses that could clarify this relationship to some extent.

First of all, RTX leads to B-cell depletion, resulting in the elimination of B-cell regulation on T-cell and therefore T-cell activation.[2,3] Since psoriasis has been regarded as a T-cell-driven disease, the T-cell dysregulation after RTX therapy might be responsible for the development of psoriasis.[3]

RTX, which is widely used for treatment of pemphigus vulgaris, can be a potential contributing factor for the development of psoriatic plaques in some patients. Several psoriasis cases have been reported following RTX administration in previous studies (Table 1).

According to the literature, in patients with RTX-induced psoriasis, nail changes, pustular and plantar psoriasis, and psoriatic arthritis, as well as all the plaque type psoriasis were detected in patients. Psoriasis onset varied between 10 days and 2 years after the first course of RTX. In our case, psoriatic lesions developed 4 months after the second course of RTX.

Among the blistering disorders, Bullous pemphigoid is the most common auto-immune bullous disease associated with psoriasis,[15] followed by pemphigus vulgaris, pemphigus foliaceous,[2,3,15–17] and herpetiform pemphigus.[16] On the other hand, less commonly, there are some

TABLE 1 Review of literature for rituximab-induced psoriasis for a variety of underlying disorders.

Author	Underlying disease	Age	Sex	Type of lesions	Time onset	Treatment
Dae-Woo Kim[4]	NHL	6	M	Psoriatic plaques on shoulder, chest, abdomen, back and scalp	3 month after starting RTX	Topical corticosteroid
Mielke[5]	NHL	66	F	Psoriatic arthritis onycholysis tenosynovitis of the Achilles tendon	6–8 weeks	Methotrexate 15 mg/week including initial prednisolone 20 mg/d
Venables[6]	NHL	53	F	Palmoplantar pustulosis psoriasis	About 2–3 weeks after each cycle	Self-limited Topical corticosteroid
Shouvik Dass[7]	RA	17	F	Scalp psoriasis onycholysis, pan-uveitis, and ruptures of the Achilles tendon	6 months	Not reported
Markatseli[2]	RA	55	F	Plaques on arms and thighs	6 month after first course and 10 days after second	Not reported
Shouvik Dass[7]	RA	52	F	Psoriatic plaques over both knees and on the extensor surfaces of thighs.	12 month	Topical corticosteroid
Alexandra Maria Giovanna Brunasso,[8]	RA	45	F	Plantar pustlosis	3 month	Topical clobetasol Intramuscular methotrexate at 15 mg/week
Guidelli[9]	RA	69	F	Psoriatic papuloplaques on her trunk and arms	3 months (14 weeks after first infusion) after the second course of rituximab	Topical fluticasone
Gulsen Ozen[10]	RA	50	F	Psoriatic patch-plaque on extremities	Five months after 3rd cycle, 25 months after 1st infusion	Not reported
Hardcastle[11]	RA	49	F	Plantar pustular psoriasis nail changes. Two months later itchy, scaly patches around the ankles and heels were seen, including some well-defined plaques	4 weeks	Topical corticosteroid, topical salicylic acid, and coal
Jayasekera[12]	RA	80	F	Plantar pustular psoriasis	2 years	Tocilizumab
Fiorillo[13]	ITP	16-month-old	M	Psoriatic plaques on the legs, arms, back, and over the scalp over	7 weeks	Course of 6 weeks Methotrexate
Dass[7]	SLE	26	F	Psoriatic plaques on elbows and the extensor surfaces of arms and thighs, trunk, onycholysis	4 month	Topical corticosteroid
Mok[14]	IMN	51	M	Psoriatic papulopustules over trunk and limbs	4 month	Topical corticosteroid
Alahmar[3]	GPA	38	F	Plaques over the abdomen, and extensor surface of the upper and lower extremities bilaterally	Three months after the third course of RTX (18 months from the first course)	Subcutaneous adalimumab 40 mg every 2 weeks along with a topical corticosteroid

Abbreviations: F, female; GPA, granulomatosis with polyangiitis; IMN, idiopathic membranous nephropathy; ITP, immune thrombocytopenic purpura; M, male; NHL, non-Hodgkin lymphoma; RA, rheumatoid arthritis; RTX, rituximab; SLE, systemic lupus erythematosus.

reports of pemphigus preceding psoriasis similar to our case.[18,19]

In a recent study recorded by Balighi et al., three patients with pemphigus vulgaris developed psoriasis; two of them did not receive RTX.[17] This may also highlight another contributing factor other than RTX. For instant, corticosteroids used for treatment of vesiculobullous diseases could be a trigger for psoriasis.[15] Furthermore, the role of spreading epitope may be a suggested etiology for this coincidence. According to this model, many proteins, which were not recognizable by immune system cells, become identifiable after the activation of a chronic autoimmune response that leads to a new autoimmune reaction (epitope phenomenon, 1998).[20]

In 1987, Yokoo et al. reported a case of pemphigus foliaceous coexistence with psoriasis in one patient, focusing on the fact that the activation of plasminogen is involved in acantholysis in pemphigus.[18] Also, increased concentrations of plasminogen activator have been detected in psoriasis lesions.[18]

Based on genome-wide association studies, psoriasis and pemphigus are both related to HLA DRB1 alleles.[19,21] As a result, genetic factors may also play a remarkable role in the association between these two auto-inflammatory skin diseases.

Some data mentioned that Th17 and neutrophils play an important role in the pathogenesis of psoriasis, which are stimulated by IL-6.[22] A study was recorded by Zhong et al. mentioned that there is an increased level for IL-6 and IL-17A after administration of RTX,[23] which mean that it may have played a main role in our patient.

Rituximab has rarely been used to treat psoriasis[24]; however, there are a few cases that have shown some improvement in psoriasis following RTX therapy.[25,26] According to our study and to previous recorded studies, it is better to avoid using RTX who had a history of psoriasis.

6 | CONCLUSION

Rituximab is a human/murine monoclonal antibody targeting the CD20 antigen on B-lymphocytes surface. Although it is used as a promising treatment for pemphigus, nowadays it is also a new therapy for other autoimmune diseases, including systemic lupus erythematous and rheumatoid arthritis, and others like non-Hodgkin's lymphoma. Although there is increasing evidence regarding the safety and effectiveness of RTX in these diseases, psoriasis rarely occurs after RTX.

Physicians should be aware of this complication, and may be it is better to avoid using RTX who had a history of psoriasis. More studies should be recorded.

AUTHOR CONTRIBUTIONS

Leila Ghadirzade Arani: Resources; writing – original draft. **Shima Moslemi Haghighi:** Formal analysis; writing – original draft. **Soheila Nasiri:** Validation; visualization; writing – review and editing. **Sahar Dadkhahfar:** Writing – review and editing.

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Not applicable.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data used to support the findings of this study are available from the corresponding author upon request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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