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

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Introduction

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

Case presentation

A 48-year-old female known and previously treated case of pemphigus vulgaris, presented with a two month history with a pruritic scaly plaques scattered on scalp, trunk and extremities.

She was complaining from mucocutaneous pemphigus vulgaris from 16 years before the current presentation. She had received multiple courses of corticosteroid pulse therapy followed by maintenance treatment with oral prednisolone. In august 2021, the patient was admitted due to pemphigus recurrence and treated with a course of Rituximab (two infusions of 1 gr 2 weeks apart) in addition to 30 mg of oral prednisolone. One month later, she had complete resolution for her skin lesions. Later prednisolone was tapered gradually.

Her physical examination showed a sharply demarcated, scaly and erythematous plaques distributed over the scalp, retro auricular skin, abdomen, presacral area and extensor surface of the upper and lower extremities. Examination of nails, mucosa, and joints were normal. 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 lab test including complete blood count, lipid profile, liver function tests, urea, creatinine, ESR and CRP were normal. Treatment for psoriasis included methotrexate 7.5 mg/week and topical clobetasol. Oral prednisolone was tapered over six months to 2.5 mg/day. During six months' of follow up, the psoriatic plaques had partially improved (PASI score =3.2), erythema and induration had significantly decreased, and no other sites were involved. Currently, she is still on methotrexate (10 mg /week) and low-dose systemic corticosteroid therapy (prednisolone 2.5 mg daily).

Discussion

The exact underlying mechanism for the association of psoriasis and pemphigus vulgaris is still unclear, but there are various hypotheses which could clarify the relationship to some extent. For example, Rituximab which is widely used for treatment of pemphigus vulgaris can be a potential contributing factor for development of psoriatic plaques in some patients.

In addition to rituximab-induced psoriasis in pemphigus vulgaris, several psoriasis cases has been also reported in patients with rheumatoid arthritis, non-Hodgkin's lymphoma, systemic lupus erythematosus, granulomatosis with polyangiitis, idiopathic membranous glomerulopathy and chronic idiopathic demyelinating polyneuropathy disorder after receiving rituximab for controlling the underlying disorder.

Rituximab may induce psoriasis via a variety of mechanisms. First, rituximab leads to B-cell depletion resulting in elimination of B-cells regulation on T-cells and therefore T-cells activation (2, 3). Rituximab also has been shown to impair the response to infection leading to the psoriasis development (2). Since psoriasis has been regarded as a T-cell-driven disease, the T cell dysregulation after rituximab therapy might be responsible for development of psoriasis (3).

According to the literature, in patients with rituximab-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 to 2 years after the first dose. In our case, psoriatic lesions developed 4 months after the second course of rituximab.

Several studies have shown a link between bullous disease and psoriasis. Bullous pemphigoid is known as the most common auto-immune bullous disease associated with

psoriasis (2), followed by pemphigus vulgaris, pemphigus foliaceous (2-6), and

herpetiform pemphigus (7). On the other hand, less commonly, there are some reports of development psoriasis in pemphigus vulgaris patients similar to our case (8, 9).

In a recent study recorded by Balighi et al, three patients with pemphigus vulgaris developed psoriasis, two of them did not receive rituximab. This may also highlight another contributing factor other than rituximab. For instant, 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 activation of chronic autoimmune response that leads to a new autoimmune reaction (epitope phenomenon 1998)

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

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

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)	non-Hodgkin lymphoma	6	male	Psoriatic plaques on shoulder, chest, abdomen, back and scalp	3 month after starting rtx	topical corticosteroid
F Mielke(5)	non-Hodgkin lymphoma	66	female	psoriatic arthritis onycholysis tenosynovitis of the Achilles tendon	6-8 weeks	methotrexate 15 mg/week including initial prednisolone 20 mg/d

author	Underlying disease	age	sex	Type of lesions	Time onset	treatment
Z C Venables (6)	non-Hodgkin lymphoma	53	female	Palmoplantar pustulosis psoriasis	About 2–3 weeks after each cycle	Self-limited topical corticosteroid
Shouvik Dass (7)	rheumatoid arthritis	17	female	scalp psoriasis onycholysis, pan-uveitis, and ruptures of the Achilles tendon	6 months	Not reported
Markatseli TE(8)	rheumatoid arthritis	55	female	Plaques on arms and thighs	6 month after first course and 10 days after second	Not reported
Shouvik Dass (7)	rheumatoid arthritis	52	female	Psoriatic plaques over both knees and on the extensor surfaces of thighs.	12 month	topical corticosteroid
Alexandra Maria Giovanna Brunasso,(9)	rheumatoid arthritis	45	female	Plantar pustlosis	3 month	Topical clobetasol Intramuscular methotrexate at 15mg/wk
G M Guidelli(10)	rheumatoid arthritis	69	female	Psoriatic papulo-plaques on her trunk and arms	three months(14 weeks after first infusion) after the second course of rituximab	Topical fluticasone
Gulsen Ozen(11)	rheumatoid arthritis	50	female	psoriatic patch-plaque on extremities	Five months after 3rd cycle, 25 months after 1st infusion	Not reported

author	Underlying disease	age	sex	Type of lesions	Time onset	treatment
Sarah A Hardcastle(12)	rheumatoid arthritis	49	female	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
P Jayasekera(13)	rheumatoid arthritis	80	female	plantar pustular psoriasis	2 years	tocilizumab
Loretta Fiorillo (14)	ITP	16-month-old	male	Psoriatic plaques on the legs , arms, back, and over the scalp over	7 weeks	course of 6 weeks Methotrexate
Shouvik Dass (7)	Systemic lupus erythematosus	26	female	Psoriatic plaques on elbows and the extensor surfaces of arms and thighs, trunk, onycholysis	4 month	topical corticosteroid
Maggie Ming Yee Mok (15)	IDIOPATHIC MEMBRA-NOUS NEPHROPATHY	51	male	Psoriatic papulopus-tules over trunk and limbs,	4 month	topical corticosteroid
Hana S. Alahmar(16)	Granulomatosis with Polyangitis	38	female	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 two weeks along with a topical corticosteroid

author	Underlying disease	age	sex	Type of lesions	Time onset	treatment
Filomena Russo (17)	Chronic idiopathic demyelinating polyneuropathy disorder					

Key Clinical Message:

Acquainting medical doctors about rituximab-related cutaneous complications like psoriasis will help them in detection and management.

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Patient consent for publication Written informed consent was obtained from the patient's family for publication of this case report and any accompanying images

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Figure legend:

Figure 1:

Multiple scaly erythematous plaques on abdomen