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Ocrelizumab-induced Psoriasis in A Patient with Relapsing-Remitting Multiple Sclerosis

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ABSTRACT

Background: **Ocrelizumab is widely used as a Disease Modifying Drug (DMD) in Multiple sclerosis. The complete side effects are yet not known.**

Materials and Methods: **We describe a 34-year-old female with longstanding relapsing-remitting Multiple Sclerosis for whom Ocrelizumab was started as an escalation therapy. She reported severe itchy and patchy lesions two months after the first full dose of Ocrelizumab. Pathohistological findings revealed the diagnosis of guttate psoriasis. Psoriasis continued to flare against treatment with topical steroids, and UV therapy and progressed to developed arthritis psoriasis.**

Results: **Treatment escalated to an IL-17 antagonist (Secukinumab), with a favorable outcome. Ocrelizumab was discontinued. After one year of follow-up, the patient remained stable from an MS standpoint.**

Conclusion: **This is the third report showing the possible cutaneous side effect of Ocrelizumab.**

Keywords: Multiple sclerosis, Ocrelizumab, psoriasis, side effect.

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I. Introduction

Psoriasis is a T-cell-mediated, systemic inflammatory disease that affects the skin and joints. In the US population, it occurs about 2–4%, with similar estimations in Europe. Plaque psoriasis is the most common variant of psoriasis [1]. It is stated that some medications induce or exacerbate psoriatic. The link between Multiple Sclerosis (MS) and Psoriasis is controversial [2]. However, regarding MS treatment, there are published reports that some Disease Modifying Drugs (DMDs) such as interferon-β and natalizumab induce or exacerbate psoriasis in patients with Multiple Sclerosis (MS) may induce or exacerbate psoriasis in MS patients [3]. A new humanized monoclonal antibody targeting CD20+ B-cells, Ocrelizumab (OCR), has been approved by the U.S. FDA for the treatment of relapsing-remitting (RRMS) and primary progressive multiple sclerosis (PPMS), however cutaneous side effects of Ocrelizumab (OCR) are no well documented, and its association with psoriasis is unidentified. [4]. We describe a woman who developed drug-induced guttate psoriasis dermatitis following the administration of Ocrelizumab. Ocrelizumab was discontinued, and Psoriasis was improved by systemic treatment of interleukin (IL) 17 antagonist with a favorable impact on the baseline disease.

II. Case Presentation

The patient was a 34-year-old female with longstanding RRMS. She had no significant medical or dermatological history and was not taking any medications. Family history was negative for any autoimmune diseases. Her first attack started in 2008 with bilateral leg numbness. The treatment started with interferon beta-1a. She tolerated it well but had severe episodes of flare ups/exacerbation presented with lower extremities numbness and weakness, gait and balance impairment Dimethyl fumarate was started. MS symptoms continue to worsen so decision was made to escalate her treatment to Ocrelizumab. After the first full dose she experienced itchy patches of thick, raised skin with scale covering the lesions. Lesions initially started on her scalp and spread elsewhere on the body skin after two months. She was treated with steroids, antifungals, and antibiotics with no resolution. Physical exam showed well-defined adherently scaling erythematous plaques on the trunk, extremities, and vagina along with erythematous papules scattered on the face. At that time two skin biopsies were measured. One reveal diffuse parakeratosis, hyper granulosis, marked regular epidermal hyperplasia, papillary dermal edema, and superficial perivascular lymphocytic infiltrate characteristic of early plaque psoriasis. Another specimen reveals multiple foci of parakeratosis with neutrophils admixed with basket weave stratum corneum, a collection of neutrophils within the granular layer, mild spongiosis, and mild irregular acanthosis. The pathohistological findings revealed early or guttate psoriasis parakeratosis. Based on her symptoms and pathohistological findings, the diagnosis of guttate psoriasis was made. Treatment with topical steroids and UV therapy failed and psoriasis worsened and continued to flare, and after 10 months, she developed arthritis psoriasis. Finally, she was treated with Secukinumab which is a human IgG1κ monoclonal antibody binds to the protein IL-17A with a favorable improvement of psoriasis. At the time of diagnosis,

it was decided not to proceed with additional Ocrelizumab. The treatment was switched to Siponimod (Sphingosine 1-phosphate receptor modulator) which was stopped after start of due to concern for additive immunosuppressant side effects. There are also data to show IL-17 antagonist such as Secukinumab might help with treatment of MS. The disease remained stable so far in terms of clinical symptoms and serial MRI imaging.

III. Discussion

In this report, we described a case of RRMS who was diagnosed with Guttate Psoriasis following Ocrelizumab infusion. The timeline of new-onset skin disease and improvement of skin changes after cessation of therapy in this patient indicate that psoriasis might be a possible side effect of ocrelizumab. It should be noted that studies are controversial in the sense that if Multiple Sclerosis is associated with Psoriasis and if these two entities are related. [2]

To date, rare similar reports in relapsing-remitting multiple sclerosis have been reported-one with an exacerbation of previously present psoriasis after Ocrelizumab in a 45-year-old male after the first cycle of OCR [5], and another in a 68-year-old female after 3.5 months after initiating ocrelizumab, both with relapsing MS.

In addition, in a report [6], two cases with long-lasting PPMS were presented who were diagnosed with psoriasis/psoriasiform dermatitis after being treated with Ocrelizumab. The first case was A 40-year-old female, who was diagnosed with pustulosis psoriasis after 1 month after the second cycle of Ocrelizumab. The other one was a 66-year-old female who experienced psoriasis/psoriasiform dermatitis after being treated with Ocrelizumab for a half year. In either case, it was decided not to proceed with further ocrelizumab treatment. Skin lesions partially or moderately regressed with oral and topical therapy [6].

So far, other anti-CD20 therapies, such as rituximab, have been reported to cause psoriasis as a side effect with disease onset at ten days to six months following the second dose. However, the exact pathophysiology behind the Anti-CD-20 treatment-induced psoriasis remains obscure. Lymphocyte regulatory homeostasis and/or increased vulnerability to bacterial/viral infections as psoriasis triggers are hypothesized as the pathophysiology of CD20 antibody-psoriasis [7].

In this patient, OCR was decided to be discontinued along with the psoriasis dermatological treatments. There is no robust evidence to answer whether to titrate, continue or stop the therapy. Moreover, regarding MS control after OCR was stopped, Siponimod started briefly but again in a shared decision-making process, it was decided to discontinue the drug after the anti IL17 antibody was started. Anti-IL17 antibody (Secukinumab) is approved for use in psoriasis (PsO) which manifests itself on the skin, as well as psoriatic arthritis (PsA). Although further research is warranted, there is some evidence showing that the anti-IL17 antibody (Secukinumab) has been applied successfully in RRMS patients with a reduction in MRI lesion activity in MS. It appears to be safe in patients with MS. patients as well [2], [8]-[10]. So far, during follow-ups, our patient has remained stable with no evidence of relapses, disability progression, or MRI activity.

IV. Conclusion

In conclusion, drug-induced psoriasiform dermatitis might be an adverse event of Ocrelizumab. Future research should clarify the mechanism by which ocrelizumab leads to psoriasiform dermatitis. Clinicians should be alert to this possible side effect. The decision on whether to titrate or continue or stop the therapy is yet obscure. In the abovementioned cases, discontinuation of Ocrelizumab was chosen. In this case, the systemic treatment led to the improvement of the lesions.

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Conflict of Interest

Authors declare that they do not have any conflict of interest.

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