PSORIASIFORM DERMATITIS AFTER DOSE OPTIMIZATION OF TWO DIFFERENT BIOLOGICS IN A PATIENT WITH ULCERATIVE COLITIS: A CASE REPORT

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Summary

Adalimumab and Vedolizumab are two of the targeted treatments for ulcerative colitis, which may be used as the drugs of initial choice (if conventional therapy was inefficient or is not tolerated), and in the case of primary nonresponse or loss of efficacy of another targeted therapy. Although we are aware that biological agents can be associated with various dermatological side effects, the development of psoriasiform dermatitis induced by the separate administration of two types of biologics has been narrowly described and, to our knowledge, has never been reported before only after dose escalation of biologic drugs. We report a case of a drug reaction consisting of psoriasiform dermatitis in a female patient treated with biologics for ulcerative colitis, highlighting the aspect that these cutaneous manifestations appeared only after dose optimization of biological agents.

Keywords: *psoriasiform dermatitis, adalimumab, vedolizumab, dose optimization.*

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Introduction

Biological agents have made far-reaching changes in the management of immune-mediated inflammatory diseases, including inflammatory bowel disease such as ulcerative colitis (UC) and Crohn's disease (CD). However, it is widely known that biological agents can be associated with various dermatological side effects. These adverse effects consist of psoriasis and psoriasiform lesions, infusion reactions, eczema, lupus, alopecia areata, vitiligo, lichenoid reactions, granulomatous disorders, vasculitis, skin cancer, and cutaneous infections. [1]

Regarding biologic therapies used in the management of inflammatory bowel disease, TNF-α inhibitors have the highest rate adverse cutaneous reactions followed by ustekinumab (interleukin-12 and interleukin-23 inhibitor) and anti-integrin receptor blockers. [1]

It is essential to recognize these cutaneous manifestations as treatment-induced adverse effects and adjust the treatment in order to allow an optimal management of them. There are no specific therapeutic guidelines for proper management of these cases; part of these skin reactions can be treated topically while others requisite cessation or switch of the biological agent. The decision on drug stoppage or switching should be made based on the condition of underlying diseases and the severity of lesions. [1, 2]

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Case report

A 26 year old female patient was referred to our clinic due to a pruritic eruption with salmon-colored, confluent papules and plaques, accompanied by scaling and crusting, initially distributed in the ear region, later extended also on scalp, nasolabial-alar creases, central chest, upper back, umbilicus region, upper and lower limbs, and buttocks (Figure 1-2). Her past medical history revealed that she was diagnosed with ulcerative colitis (UC) in May 2018. She did not have any personal or familial history of skin diseases. The patient was treated with mesalazine, systemic glucocorticoid and adalimumab, the latter being introduced in February 2019 with good control of UC. In September 2019, she developed symptoms of UC flare, including bloody diarrhea and colonoscopy examination revealed features of active colitis. Subsequently, was decided to increase the frequency of adalimumab injections (weekly instead of every 2 weeks), achieving good disease control. About one month after the dose optimization of adalimumab, the patient developed the eruption. The patient initially presented in another dermatology unit and a clinical diagnosis of psoriasis was made. She received multiple topical treatments, without a clinical response. Systemic treatment with methotrexate was also associated but was inefficient. Considering that the eruption did not improve instead it worsened under recommended treatment, the patient was referred to our clinic and a skin biopsy was proposed. Histological findings were consistent with psoriasiform dermatitis with a differential diagnosis including psoriasis, seborrheic dermatitis and chronic dermatitis: superficial perivascular and perifollicular lymphohistiocytic inflammatory infiltrates, slight psoriasiform acanthosis, spongiosis, parakeratosis and small neutrophilic collections strictly confined at the edges of the follicular ostia (Figure 3). After discussing the case with the gastroenterologist, adalimumab therapy was discontinued and switched to vedolizumab, and her skin condition pro-

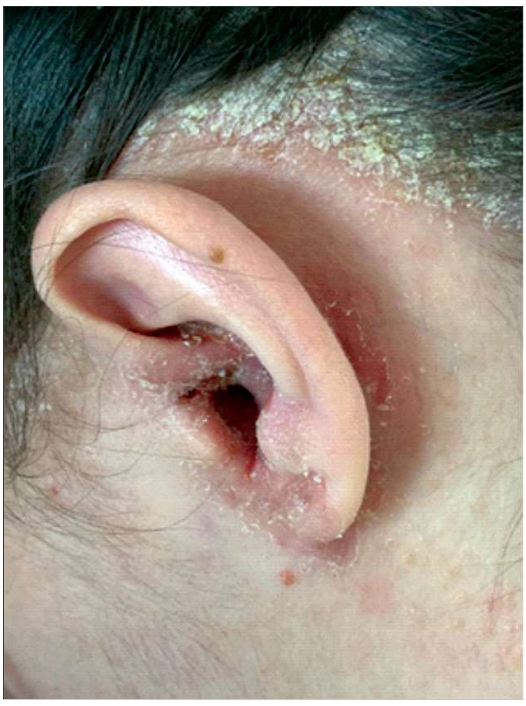

Figure 1 – Initial clinical presentation in our clinic (under adalimumab therapy). Salmon-colored plaques, accompanied by scaling and crusting, distributed on scalp and ear region.

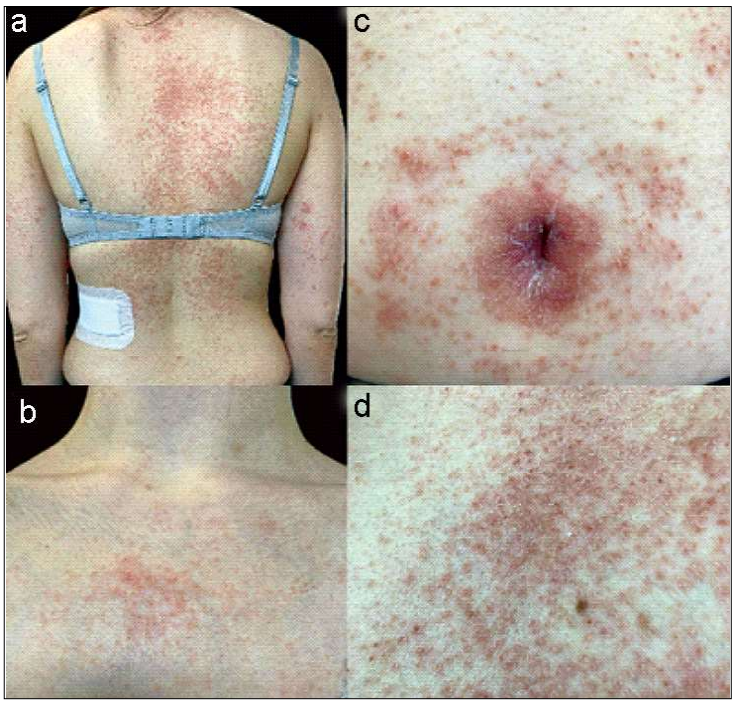

Figure 2 – Initial clinical presentation in our clinic (under adalimumab therapy). Salmon-colored, confluent papules and plaques, accompanied by scaling, distributed on: (a) - upper back, (b) - central chest and (c) - umbilicus region; (d) - close-up of the upper back lesions.

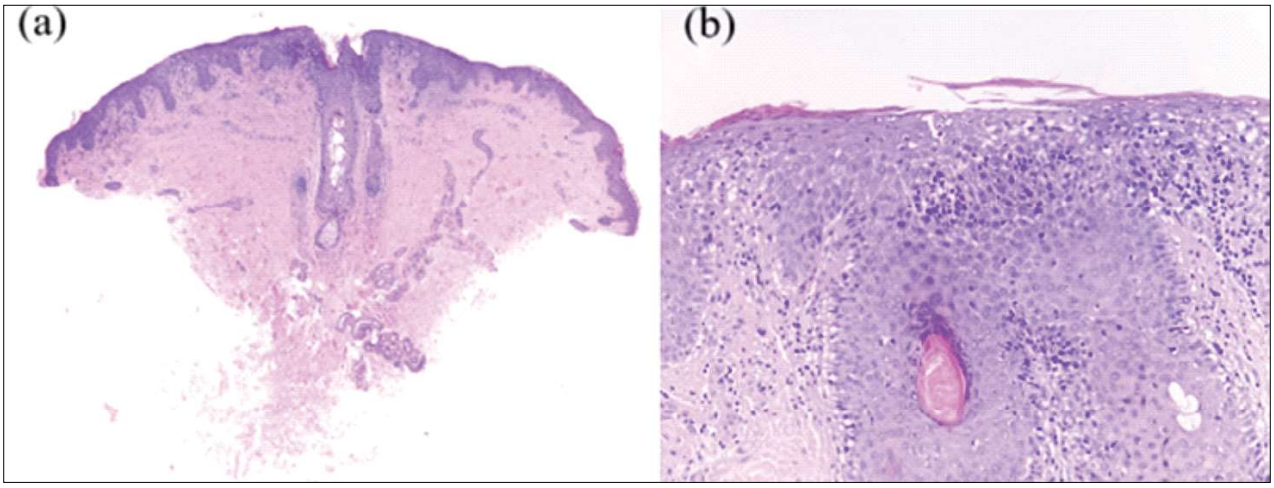

Figure 3 – Histological findings (hematoxylin and eosin stain): (a) – psoriasiform acanthosis (magnification 40x); (b) – foci of spongiosis, associated with exocytosis of lymphocytes and parakeratosis predominantly at the level of follicular ostia (magnification 400x).

gressively resolved. Taking into account the clinical and histopathological findings, the history of adalimumab therapy and the improvement of the eruption after stopping the adalimumab therapy, led to the diagnosis of a drug reaction pattern consisting of disseminated psoriasiform dermatitis. Three years after the introduction of vedolizumab, the patient was admitted to the gastroenterology ward due to UC flare and, considering the results of investigations, was agreed vedolizumab dose escalation. About 4 weeks later, she developed a similar eruption that she had in the past confined in the ear region (Figure 4). The patient's lesions

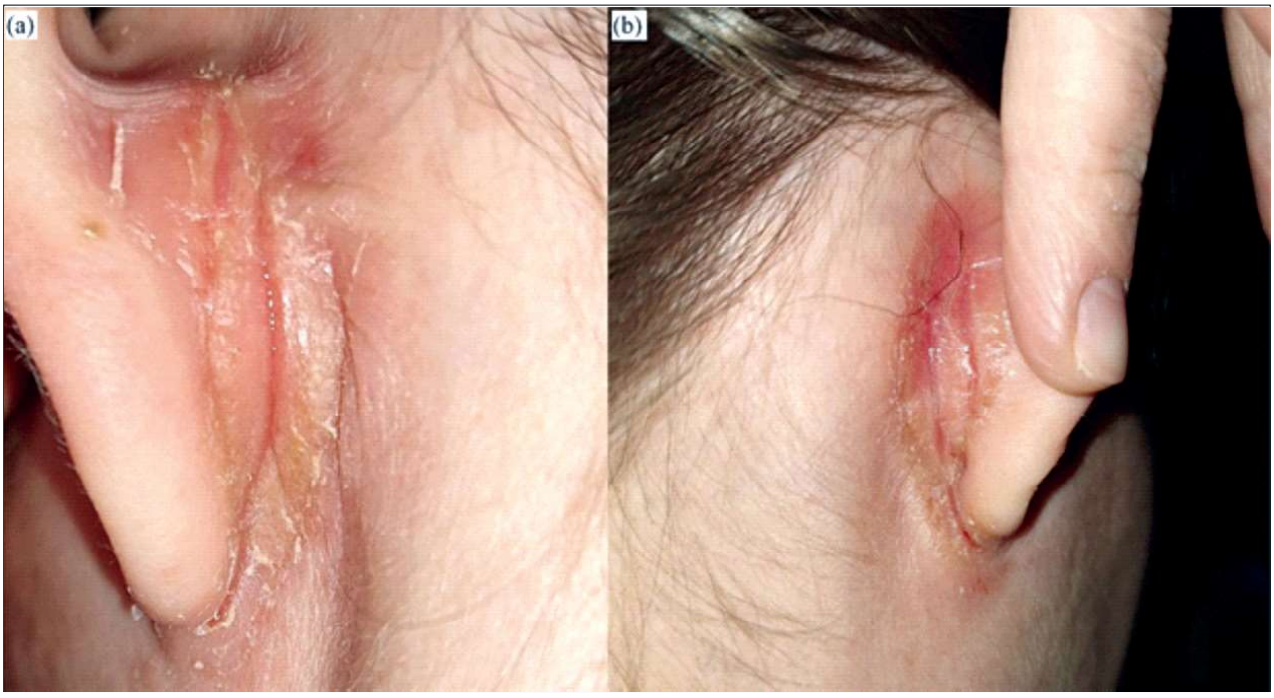

Figure 4 – Clinical presentation after dose escalation of vedolizumab. Salmon-colored plaques, accompanied by scaling and crusting distributed on ear region; (a) – left ear, (b) – right ear.

did not improve with initial topical therapy 2% ketoconazole cream, which was subsequently changed to a corticosteroid-antibiotic-antifungal combination (triamcinolone acetonide, neomycin sulfate, nystatin cream). Two weeks later, the patient showed improvement in skin lesions compared to the last visit. Considering non-resolution of gastroenterological symptoms and a colonoscopy confirming disease activity despite dose optimization together with the risk that continuing with the administration of vedolizumab after the cessation of topical dermatologic therapy could lead to exacerbation of skin lesions, was decided to stop vedolizumab therapy and replace it with tofacitinib, an oral non-selective JAK inhibitor.

Discussions

Targeted immune-modulating therapy with biological agents has become a very important therapeutic option in the management of immune-mediated inflammatory diseases, including inflammatory bowel disease. Despite their therapeutic potential, it is widely known that biological agents can be associated with various dermatological side effects and is essential to recognize these cutaneous manifestations as treatment-induced adverse effects and adjust the treatment in order to allow an optimal management of them. [1, 2]

Adalimumab and Vedolizumab are two of the targeted treatments for ulcerative colitis, which may be used as the drugs of initial choice (if conventional therapy was inefficient or is not tolerated), and in the case of primary non-response or loss of efficacy of another targeted therapy. [3]

Adalimumab is a human antibody of the IgG1 class, acting as an inhibitor of tumor necrosis factor-alpha (TNF-α). The recommended subcutaneous dosage of Adalimumab for adult patients with UC is 160 mg initially on Day 1, followed by 80 mg two weeks later (Day 15) and two weeks later (Day 29) continue with a dosage of 40 mg every other week during maintenance therapy. In cases of loss of response over time, Adalimumab can be optimized to either an injection of 40 mg every week or an injection of 80 mg every other week. [3, 4] Even though the association between anti-TNF-α and different dermatological side effects has been documented in the literature with the most frequent form of presentation being the overlap syndrome termed 'psoriasiform eczema' or 'psoriasiform dermatitis', it has never been reported before only after dose escalation of the biologic drug. The occurrence of psoriasiform dermatitis induced by anti-TNF-α still represents a significant clinical challenge that merits deeper investigation, being essential to recognize this disease as a separate entity that is different from psoriasis and eczema. In these patients, both symptoms typical of dermatitis (xerosis, pruritus, bacterial superinfection) and psoriasis (thick white scales, orange-red color, sharp borders of the lesion) are present. Likewise, histological examination shows aspects of both disorders. Bacterial superinfection, which is rarely seen in psoriasis, is frequent in anti-TNF-α-induced psoriasiform dermatitis. Regarding the management of this entity, no clear recommendations have been made. In most cases, the anti-TNF-α is stopped, although conservative treatment (e.g., topical steroids) can also be successful and considered as a first option. Switching to an interleukin-12 and interleukin-23 inhibitor or an anti-integrin receptor blocker can be necessary in refractory cases. In the case of superinfection, topical or systemic antibiotics can be considered. [1, 5]

Vedolizumab is a humanized anti-α4β7 integrin antibody used for the treatment of inflammatory bowel disease, that blocks the interaction between α4β7 integrin and MAdCAM-1(mucosal vascular addressin cell adhesion molecule-1), selectively inhibiting gastrointestinal inflammation. [6] Vedolizumab is administered first in induction therapy by intravenous infusion (300 mg in a 0–2–6 week regimen), and then in maintenance therapy by intravenous infusion (300 mg every 8 weeks). In case of loss of response over time, dose optimization can be done by administering 300 mg intravenously every 4 weeks. [3, 4] Despite vedolizumab was thought to have gut-specific action, there is new

evidence to suggest that the principal ligand of the α4β7 integrin, MAdCAM-1, is not only expressed on gut endothelial cells but also on fibroblasts and melanomas, which may explain the possibility of extraintestinal side effects of vedolizumab. [7,8] It usually is well tolerated, and only a few cases comprising dermatological adverse events (such as acne fulminans, acneiform eruption, psoriasis, purpuric dermatitis) have been reported in literature concerning vedolizumab. [8, 9, 10, 11, 12] Moreover, vedolizumab is regarded as an effective alternative in inflammatory bowel disease patients with anti-TNF-alpha therapy-induced cutaneous side effects. [1, 13]

Conclusions

In spite of the fact that psoriasiform dermatitis is a well-known adverse effect of biologic drugs, it was particular in two aspects in our patient. First, the patient experienced the same type of cutaneous adverse event caused by the separate administration of two different types of biologics, one of them (Vedolizumab) being regarded in the literature as an effective alternative in inflammatory bowel disease patients with anti-TNF-alpha therapy-induced cutaneous side effects. Second, we aim to highlight that these cutaneous manifestations appeared only after dose optimization of both biological agents used in our patient therapy.

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Conflict of interest

NONE DECLARED

DATA AVAILABILITY STATEMENT

Data are available upon request to the correspondence author.

ETHICS STATEMENT

All patients in this manuscript have given written informed consent for participation in the study and the use of their de-identified, anonymized, aggregated data and their case details (including photographs) for publication. Ethical approval: not applicable.

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