

Unmasking pustular psoriasis subsequent to COVID-19

Ronak Miladi, Alireza Janbakhsh, Arefeh Babazadeh*, Zeinab Aryanian**, Soheil Ebrahimpour*, Zeinab Mohseni Afshar

Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran.

* Infectious Diseases and Tropical Medicine Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R. Iran.

** Autoimmune Bullous Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Various cutaneous manifestations have recently appeared within context of 2019 novel coronavirus diseases (COVID-19). Currently, outbreaks of psoriasis were reported during COVID-19. We reported a case of a 32-year-old woman with COVID-19 who presented with pustular psoriasis. She was treated with oral prednisolone, hydroxyzine and topical clobetasol. The two-week follow-up revealed that her lesions were desquamating and that she was in a favorable situation. The current report will highlight specific skin manifestations of COVID-19, allowing clinicians to further confirm our suspicions.

Key words

Pustular psoriasis, COVID-19, azithromycin, hydroxychloroquine.

Introduction

2019 novel coronavirus disease (COVID-19) is an emerging disease caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that poses new challenges in various medical fields. The various cutaneous manifestations have recently appeared in the context of COVID-19 as a result of adverse drug reactions or immune response.¹ Recently, psoriasis flare-ups were reported during COVID-19.² Here, we present a case of pustular psoriasis in a patient suffering from COVID-19.

Case report

A 32-year-old woman with a positive family

history of psoriasis was admitted to the hospital with progressive annular skin lesions with small sterile pustules overlying painful, erythematous skin and urticarial eruptions, myalgia, and arthralgia for 10 days prior to admission. The lesions affected most parts of her body including the face, trunk, upper and lower limbs, forearm, and also palms and soles (**Figure 1,2**). She reported no fever, no dyspnea, and no cough.

Azithromycin and hydroxychloroquine (HCQ) had been given 40 days before. Again at the onset of her cutaneous eruptions, she started taking another course of azithromycin without a prescription. The examination of skin revealed diffuse, tender, erythematous plaques with diffuse pustules, scale and crust formation over 75% of her body. Pustules were found on the edges of expanding erythematous plaques or on erythematous skin. Pitting in some finger nails was obvious. No lymphadenopathy or organomegaly was detected. Initial laboratory tests were not significant except for a lymphopenia (white blood cell (WBC) count,

Address for correspondence

Zeinab Mohseni Afshar,
Clinical Research Development Center,
Imam Reza Hospital, Kermanshah University of
Medical Sciences, Kermanshah, Iran.
Ph: +989111156511
Email: baboldr2019@gmail.com



Figure 1.



Figure 2.

16.80×10⁹/L with 7% lymphocytes), and elevated inflammatory markers (lactate dehydrogenase (LDH) of 815 U/L; C-reactive protein (CRP) of 89 mg/L and erythrocyte sedimentation rate (ESR) of 50 mm/h). A nasopharyngeal swab tested for SARS-CoV-2 RNA amplification was positive. A lung computed tomography (CT) scan was normal. Although drug eruption especially acute generalized exanthematous pustulosis (AGEP) was the most probable diagnosis, due to constitutional symptoms and elevated inflammatory markers, rheumatologic and immunologic disorders were also suspected considering her age. Therefore, comprehensive diagnostic workup including antinuclear antibodies (ANA) titer, anti-double stranded DNA antibody (anti-dsDNA), anti-Smith antibodies (anti-Sm), anti-ribonuclear protein antibody, anti-Ro/La antibodies, anti-histone antibodies (AHAs), and HLA-B27 was conducted with negative results. Acute retroviral syndrome and serum sickness were also among the differential diagnoses, which were ruled out by negative test results of hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). According to the consulting dermatologist, prednisolone oral

50 mg/ day, cyclosporine 200 mg daily, hydroxyzine 75 mg daily in divided doses, and topical clobetasol was started for her and skin biopsy was suggested. Histological examination showed intermittent parakeratosis and exaggerated spongiform pustules of Kogoj and subcorneal microabscesses of Munro, mild acanthosis and neutrophilic exocytosis. Upper dermis had perivascular lymphocytes and neutrophils without eosinophils which were compatible with pustular psoriasis. The patient left the hospital without consent. However, the patient follow-up in two weeks revealed that her lesions were desquamating and that she was in a relatively favorable condition.

Discussion

Psoriasis is a cutaneous disorder which is triggered by a variety of factors such as medications and infections. Antimalarial agents with common adverse reactions are one of the medications used to treat COVID-19. The cutaneous side effects of antimalarials such as HCQ include xerosis, generalized pustulosis, hives, and most importantly, exacerbation of psoriasis.³ The exacerbation of psoriasis with chloroquine (CQ) occurs more frequently than HCQ.

Other factors responsible for this complication include drug dosage and duration of medications as well as underlying conditions of photosensitivity. Sometimes, cutaneous involvements are not typical for psoriasis and therefore may be mentioned as psoriasiformes. The difference is decrease in erythema and scale of psoriasiform lesions and sparing of knees and elbows compared to true psoriasis.⁴

HCQ is a well-known triggering factor in psoriasis flare-ups. The underlying mechanism contributing to this condition is the inhibitory effect of HCQ on the trans-glutaminase

epidermis, which leads to collection of the epidermal cells, in addition to its promoting effects on the production of IL-17, which results in the proliferation of keratinocytes.^{5,6}

Given the patient's medical history, these eruptions could be attributed to azithromycin and HCQ. Azithromycin has been shown to cause some cutaneous features such as acne, diffuse red or purple skin eruptions, blistering, rosacea, drug rash with eosinophilia, systemic symptoms (DRESS) syndrome, and psoriasis-like patches.³

However, our patient developed the eruptions at least one month after drug use, which would make azithromycin unlikely to be responsible for this event. On the other hand, HCQ might be responsible for different kinds of skin involvements. The most common cutaneous side effects of this agent are medication rash or skin rash, skin discoloration and pruritus, while the most critical ones include Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN).⁷ Psoriasis exacerbations and exfoliating dermatitis are the latest cutaneous lesions, perhaps due to the widespread use of HCQ and COVID-19 epidemics.

Pre-existing psoriasis flare up appears to occur most often, but there have been cases such as the current patient who has presented with an unmasking new skin disease. According to some studies, the median period between newly consumed HCQ and the first appearance of an eruption is 1 to 2.⁸ Appearance of rashes at least one month after the cessation of HCQ in the present case is a rare and also amazing phenomenon.

Other causes of new skin eruptions in a young female should have been definitively ruled out, such as connective tissue disorders, paraneoplastic syndromes and some sexually

transmitted disorders. The diagnostic challenge was present in this patient because of her age, and related symptoms such as myalgia and arthralgia. In a woman in her fourth decade of life, rheumatologic disorders such as systemic lupus erythematosus (SLE) should be primary differential diagnosis. It is important to note, because of the suspected psoriasis, its type should be considered such as: a drug-induced pustular type, Von Zumbusch type of generalized pustular psoriasis (GPP), the idiopathic annular type, and HCQ-induced type.

The important issue is that usually a pustular drug rash resolves at its own or responds to corticosteroids. Our patient partially responded to this first-line therapy, but eruptions reappeared immediately after stopping the treatment.

Because of the relatively long period spaced between drug use and appearance of skin eruptions, pustular psoriasis induced by HCQ seems unlikely. The von Zumbusch type of generalized pustular psoriasis appears as extended pustules on erythematous skin, leading to diffuse scaling after rupture.⁹ It is usually accompanied by fever and burning feel and if septicemia occurs, leads to death. Therefore, the von Zumbusch type of generalized pustular psoriasis or the idiopathic annular type may have occurred. Besides, in any psoriasis-like lesion, sub-acute cutaneous lupus erythematosus (SCLE) is still a significant impression. The main diagnostic markers for this disorder are Anti-Ro/ SSA antibodies, which were both negative in our patient.

First-line treatment options for pustular psoriasis in adults include systemic retinoids (acitretin), cyclosporine and methotrexate. Although retinoids are the most effective among the first-line treatment options, they pose a high risk of severe teratogenic effects lasting up to 3 years.¹⁰

They are therefore not good options for women of reproductive age, except in life threatening situations. Cyclosporine is a very effective treatment for the serious manifestations of psoriasis with a relatively quick onset of action with improvement seen within 2 weeks of treatment.¹¹ As there were some earlier evidences available in the literature about the effect of cyclosporine on coronaviruses replication in vitro, we assume the patient can benefit from its antiviral effects. Also, she will probably be less exposed to the serious symptoms associated with COVID-19. Methotrexate has a slower onset of activity and a risk of hepatotoxicity and haematologic toxicity.¹² We therefore recommended cyclosporine with prednisolone but the patient did not continue the therapy in the hospital.

The last important issue is that some infectious agents are documented to be responsible for psoriasis exacerbations such as HCV, rhinovirus and coronavirus. However, other viruses such as Epstein Barr Virus (EBV) have been precipitating factors for other skin disorders like pustular DRESS Syndrome.¹³ The fact is that any infection can induce psoriasis, particularly the significant role of COVID-19 in giving rise to the pustular form should not be neglected. This could be due to the release of inflammatory cytokine, which is the main factor in the pathogenesis of this dermatological condition and also the immunological reactions induced by SARS-CoV2. The current report will highlight several cutaneous presentations of COVID-19, allowing clinicians and researchers to better confirm this problem.

References

1. Wollina U, Karadağ AS, Rowland-Payne C, Chiriac A, Lotti T. Cutaneous Signs in COVID-19 Patients: A Review. *Dermatol Ther.*2020:e13549.

2. Nasiri S, Araghi F, Tabary M, Gheisari M, Mahboubi-Fooladi Z, Dadkhahfar S. A challenging case of psoriasis flare-up after COVID-19 infection. *J Dermatol Treat.*2020:1-6.
3. Türsen Ü, Türsen B, Lotti T. Cutaneous side-effects of the potential COVID-19 drugs. *Dermatol Ther.*2020:e13476-e76.
4. Gencler OS, Gencler B, Altunel CT, Arslan N. Levetiracetam induced psoriasiform drug eruption: a rare case report. *Saudi Pharm J.* 2015;**23**:720-22.
5. McCoy S, Nagaraja V, Paviol S, Gudjonsson J, Kahlenberg J. Exacerbation of Psoriasis due to Hydroxychloroquine. *Arch Med.* 2015;**7**:1-3.
6. Kutlu Ö, Metin A. A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: Will cases of psoriasis increase after COVID-19 pandemic? *Dermatol Ther.* 2020;**e13383**.
7. Davoodi L, Jafarpour H, Kazeminejad A, Soleymani E, Akbari Z, Razavi A. Hydroxychloroquine-Induced Stevens-Johnson Syndrome in COVID-19: A rare Case Report. *Oxf Med Case Reports.*2020;**2020**:omaa042.
8. Holman AJ. The value of rheumatologists to patients with fibromyalgia: comment on the presidential address by Weinblatt. *Arthritis Rheumatism.*2002;**46**:3390.
9. Naik HB, Cowen EW. Autoinflammatory pustular neutrophilic diseases. *Dermatol Clin.*2013;**31**:405-25.
10. Gooderham MJ, Van Voorhees AS, Lebwohl MG. An update on generalized pustular psoriasis. *Expert Rev Clin Immunol.*2019;**15**:907-19.
11. Rudnicka L, Goldust M, Glowacka P, Sikora M, Sar-Pomian M, Rakowska A, et al. Cyclosporine therapy during the COVID-19 pandemic is not a reason for concern. *J Am Acad Dermatol.*2020;**83**:e151-e2.
12. Boehner A, Navarini AA, Eyerich K. Generalized pustular psoriasis—a model disease for specific targeted immunotherapy, systematic review. *Experiment Dermatol.*2018;**27**:1067-77.
13. Choudhary S, McLeod M, Torchia D, Romanelli P. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome. *J Clin Aesthet Dermatol.*2013;**6**:31-7.