

REVIEW ARTICLE

Patients with specific skin disorders who are affected by COVID-19: What do experiences say about management strategies? A systematic review

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Abstract

In patients with specific dermatologic disorders who are affected by new corona virus, we know little about disease course (underlying disease and new onset infection), and the most proper management strategies include both issues that are what this systematic review targets. Databases of PubMed, Scopus, Google Scholar, Medscape, and Centre of Evidence-Based Dermatology, coronavirus dermatology resource of Nottingham University searched completely up to May 15, 2020, and initial 237 articles were selected to further review and finally 9 articles (including 12 patients) entered to this study. From 12 patients with chronic underlying dermatologic disease treated with systemic therapies, only 1 patient required Intensive Care Unit admission, the others have been treated for mild-moderate symptoms with conventional therapies. The biologic or immunosuppressive/immunomodulator agents have been ceased during the course of disease. The course of coronavirus diseases 2019 (COVID-19) and its management was as similar as normal populations. Their underlying dermatologic disease were exacerbating from mild to moderate. Their treatment has been continued as before, after the symptoms improved. Exacerbation of patients underlying dermatologic disease was mild to moderate. Discontinuing the treatment in the acute period of COVID and the restart after recovery may prevent severe recurrence and disturbing cytokine storms in these patients.

KEYWORDS

biologic, concomitant, concurrent, corona virus, COVID-19, cutaneous, immunobullous, immunomodulator, immunosuppressive, manifestation, novel human coronavirus (SARS-CoV-2), pemphigoid, pemphigus, psoriasis, psoriatic arthritis, simultaneous, skin, specific skin disease, systematic review, systemic drug

1 | INTRODUCTION

Considering new coronavirus pandemic, medical approaches affect significantly by many aspects including new encountered virus-associated

primary or secondary outcomes like various clinical conditions and their related managements,¹⁻¹¹ so that dermatology is not an exception. Recently, there are many published coronavirus diseases 2019 (COVID-19) and related dermatology articles, so that many data resources centers like coronavirus dermatology resource of Nottingham University (Centre of Evidence-Based Dermatology [CEBD]) categorize articles into some main domains as skin manifestations of coronavirus, Implications of coronavirus for use of biologics and other immune-modulating

Abbreviations: BMI, body mass index; CEBD, Centre of Evidence-Based Dermatology; COVID-19, coronavirus diseases 2019; CsA, cyclosporine; IL-23, interleukin-23; IVIg, intravenous immunoglobulins; MPM, mycophenolate mofetil; MTX, methotrexate; RTX, rituximab; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

therapies, Occupational skin disease, including effects of gloves, personal protective equipment and handwashing on the skin, coronavirus and specific patient groups, dermatology service delivery during the coronavirus epidemic, teledermatology, hydroxychloroquine, chloroquine, antibiotics and antivirals, coronavirus etiology, severity and transmission, dermatologic guidelines on coronavirus or relevant for coronavirus.

It is documented that there are specific skin and mucosal primary presentations of COVID-19 that could proceed or concomitantly accompany other clinical signs of disorder with diagnostic or prognostic values in approaching the patients.¹⁻¹⁰ Exanthematous (morbilliform) or maculopapular eruptions,¹²⁻¹⁶ generalized urticaria^{17,18} and "COVID toes" (an acral vasculopathic rash also known as pseudo-chilblain or Pernio-like lesions),¹⁹⁻²² acral and digital ischemia,²³⁻²⁶ petechial²⁷⁻²⁹ and vesicular chicken-pox like lesions,^{30,31} levidoreticularis,³² and conjunctivitis¹ are among the most reported virus-related dermatologic manifestations. There are growing reports of dermatologic manifestation among children like morbilliform or urticarial rash and conjunctivitis^{33,34} or nonspecific exanthematous, urticarial rashes, and facial ulceration in affected infants may born from infected mothers.^{33,35} Hydroxychloroquine-induced rashes solely or in combination with other therapies, are responsible for the main cutaneous drug reactions especially generalized pustular eruptions.³⁶⁻³⁸

There are some secondary COVID-19-related dermatoses like incidence of an acute new dermatologic entity for a limited time period that could be stress related (eg, herpes simplex, herpes zoster, alopecia areata, ...) or physical-environmental related (eg, contact dermatitis, acute urticaria, ...) or presence of a new dermatoses which have tendency to become chronic, like telogen-effluvium, various types of dermatitis, neurocutaneous, or psychocutaneous disorders. In the pandemic, some preexisting chronic dermatoses may become poorly controlled or aggravated by the stress, irregular visits, treatment interruptions, delayed therapies, physical and environmental situations like wearing masks and latex gloves, frequent washing and disinfectants, excessive sweating, and so on.¹¹ Dermatologic visits and cosmetic or elective surgical procedure have been affected largely by a decreasing manner during pandemic.³⁹ Adherence to personal and social hygiene strategies, social isolation, and distance are the rules of pandemic for better controlling any situations and the role of teledermatology is really important in this area regarding educational and therapeutic issues.⁴⁰

In dermatology, one of the most important concerns in the pandemic setting is the manner of disease management especially in the case of patients under treatment with immunosuppressive immunomodulators. Noninfected non-at-risk patients do not need to any change in their therapeutic protocols but at-risk patients or who suspected to being infected (like having suggestive symptoms) need altering drug regimen as dose reduction, increase dose interval or transient stop of drug usage for at least 2 weeks. It is not any doubt that, every patient with an active corona virus infection should discontinue systemic biologic or nonbiologic immunosuppressive for at least 1 month or completely being symptom free. A more severe COVID-19 course is usually predictable in the setting of dermatologic diseases which are treating by systemic immunomodulators. Presence

of any comorbidities related to underlying dermatologic disorder (like older age, metabolic syndrome and vital organ dysfunctions especially respiratory and cardiovascular involvements that may be seen in psoriatic or atopic patients or who with hidradenitis suppurativa, immunobullous, or collagen vascular disorders) is associated with poorer outcomes in the case of being infected by COVID-19. Some studies suggested that more severe skin conditions are at risk for higher rate of pneumonia and symptomatic respiratory involvement. In future, vaccination of these groups of patients is one of priority issues. It seems that in patients with any severe and serious dermatologic disorders, under treatment with systemic agents, if there is not any suspicion about concurrent infection or any high risk exposures, not only it is not recommend to cessation therapy but only emphasize that these drugs could prevent disease flare-up and control cytokine storm that both in a negative direction, affect the COVID-19 course.⁴¹⁻⁴⁸

One of the most important perspectives in the field of dermatology is approaching to patients with any documented skin or mucosal disorders especially who are using immunomodulators and now are affected by COVID-19. For consensus and more exact expert recommendations in this group of patients, we need data gathering about people who were in this situation and know more about what experiences say about dermatologic disease course, COVID-19 course and the manner of managing both conditions in the best possible way? So in this systematic review we focused on specific patient groups with a dermatologic disorder (usually under therapy) that concomitantly have been infected by the new corona virus and summed up their data in all aspects of underlying dermatologic and infectious disease courses and managements.

2 | METHOD

2.1 | Protocol and registration

This study is implemented according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

2.2 | Eligibility criteria

Inclusion criteria comprised all studies about patients with any documented skin or mucosal disorders especially who were using immunomodulators and now were affected by COVID-19. The exclusion criteria consisted of all publications not meeting the above contents and non-English literature.

2.3 | Information sources and search strategy

We searched Databases of PubMed, Scopus, Google Scholar, Medscape, and CEED coronavirus dermatology resource of Nottingham University (<https://www.nottingham.ac.uk/>). Our key words were "COVID-19" OR

TABLE 1 Patients with specific dermatological disorder who were affected by coronavirus diseases 2019 (COVID-19)

First author	Title	Type of study	Case characteristic	Patients underlying dermatologic disease	Patients comorbidity	Drug history	COVID-19 sign and symptoms	COVID-19 courses	Managements of disease
A. Conti	Evolution of COVID-19 infection in 4 psoriatic patients treated with biological drugs	Case report	Case 1: A 62-y-old man	Psoriasis	Hypertension, diabetes, chronic renal failure, and overweight (BMI: 29)	Guselkumab	ARDS	1 mo of hospitalization with 2 wk Intensive Care Unit admission	Almost complete resolution of respiratory symptoms; despite discontinuation of guselkumab, psoriasis remained in complete remission
			Case 2: A 66-y-old man	Psoriasis	Hypertension, dyslipidemia, and previous myocardial infarction	Ustekinumab	Asthenia, anosmia, and ageusia	He achieved complete remission of symptoms without any medications after a month	Maintenance of the remission of psoriasis
			Case 3: A 67-y-old woman	Psoriasis	Hypertension and metabolic syndrome	Adalimumab	She had several contacts with three of her family members suffering from a mild SARS-CoV-2 and she was therefore subjected to quarantine for 15 days, without developing any symptoms of the disease and without stopping psoriasis therapy.		
			Case 4: A 66-y-old man	Psoriasis	Hypertension, diabetes, metabolic syndrome, and obesity (BMI: 32)	Secukinumab	He had a continuous contact with his wife affected by a mild SARS-CoV-2 infection; he was therefore quarantined for 15 days, without developing any symptoms of the disease and without stopping psoriasis therapy		
R. Balestri	Occurrence of SARS-CoV-2 during mycophenolate mofetil (MPM) treatment for pemphigus	Case report	A 65-y-old female	Pemphigus	Not reported	MPM	Severe nausea, fever, anorexia, and asthenia	She had her symptoms for 12 days and the treatment was only symptomatic with paracetamol.	The patient did not experience any pemphigus recurrence, but reported only some posterior tongue "discomfort." Moreover, she never developed cough, dyspnea, anosmia, ageusia, myalgia or other symptoms of the infection
M. Daneshpazhooh	Mucous membrane pemphigoid and COVID-19 treated with high-dose intravenous immunoglobulins: a case-report	Case report	A 43-y-old man	Mucous membrane pemphigoid (MMP)	Diabetes, hypertension and benign prostatic hypertrophy	Prednisolone Rituximab (RTX) MPM/high-dose intravenous immunoglobulins (IVIg)	Fever, chills, malaise, dry cough and mild dyspnea	Upon admission, MPM was discontinued, prednisolone was tapered, and IVIg was started.	The patient was discharged on day 7 with significant improvement. His lymphopenia also recovered completely. He was followed for 2 wk

(Continues)

TABLE 1 (Continued)

First author	Title	Type of study	Case characteristic	Patients underlying dermatologic disease	Patients comorbidity	Drug history	COVID-19 sign and symptoms	COVID-19 courses	Managements of disease
C. Mugheddu	COVID-19 pulmonary infection in erythroidemic psoriatic patient with oligodendroglioma: safety and compatibility of apremilast with critical intensive care management	Case report	A 45-y-old man	Psoriasis/brain oligodendroglioma	Obesity, recent chemotherapy, persistence of brain oligodendroglioma	Chemotherapy with temozolomide/prednisone/apremilast	Severe cough with high fever	Lopinavir/ritonavir, ceftriaxone	The infection recovered rapidly and the patient was discharged 6 d after the onset of symptoms. Apremilast had never been stopped during the COVID-19 hospitalization, with acceptable control of the psoriasis, limited to mild scaling and erythema, especially on the trunk
S. Nasiri	A challenging case of psoriasis flare-up after COVID-19 infection	Case report	A 73-y-old male	Psoriasis	Not reported	Methotrexate cyclosporine (CsA)	Fever, malaise, dry cough	CsA and MTX were ceased. The patient was treated with hydroxychloroquine, lopinavir/ritonavir	His symptoms resolved in 2 wk but he returned with flare-up of his underlying psoriasis manifesting as diffuse erythematous scaly plaques progressing to erythroderma. Two weeks after the improvement of COVID-19 symptoms, psoriasis treatment with CsA 100 mg daily was restarted
V. Di Lerni	COVID-19 in an elderly patient treated with secukinumab	Case report	A 73-y-old woman	Psoriasis/psoriatic arthritis	Not reported	Secukinumab	Fever, sore throat, mild dry cough	Hydroxychloroquine	The symptoms were relieved after about a week. The injection of secukinumab was continued during disease
Ö. Kurtlu	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	Case report	A 71-y-old woman	Psoriasis	Not reported	Not reported	Not reported	The patient has been managed by oseltamivir and hydroxychloroquine	Not reported

TABLE 1 (Continued)

First author	Title	Type of study	Case characteristic	Patients underlying dermatologic disease	Patients comorbidity	Drug history	COVID-19 sign and symptoms	COVID-19 courses	Managements of disease
F. Benhadou	Improvement of SARS-CoV-2 symptoms following guselkumab injection in a psoriatic patient	Case report	A 40-y-old woman	Psoriasis	Not reported	Guselkumab	Severe cough, myalgia, fatigue, fever, shortness of breath	She had received only symptomatic treatment such as paracetamol	She had still continued her injection and surprisingly, the day after the injection, she reported a major improvement of her respiratory condition, a normalization of her body temperature and a progressive relief of myalgia and fatigue symptoms
F. Messin	SARS-CoV-2 infection in a psoriatic patient treated with IL-23 inhibitor	Case report	A 32-y-old woman	Psoriasis/psoriatic arthritis	Not reported	Guselkumab/methotrexate	Mild rhinorrhea and fever	She had received only symptomatic treatment	She had discontinued the methotrexate and the next guselkumab injection. Her symptoms relieved in 2 wk

“Severe Acute Respiratory Syndrome Coronavirus 2” AND “Skin” OR “Skin Diseases” OR “Skin Manifestations” OR “Dermatology” OR “Skin and Connective Tissue Diseases” OR “Eczematous” OR “Eczema” OR “Eczematous Dermatitis” OR “Eczematous Eruption” OR “Eczematous Skin” OR “Dermatitis, Atopic” OR “Papulosquamous” OR “Psoriasis” OR “Hidradenitis, Suppurativa” OR “Alopecia” OR “Pemphigus” OR “Pemphigoid” OR “Immunobullous” OR “Skin Cancer” OR “Dermatologic Agents” OR “Immunomodulator” OR “ Systemic Drugs” OR “Biologics” OR “Immunomodulator” OR “Immunospress” OR “Immunospressive.” In the search of CEBD coronavirus dermatology resource of Nottingham University we focused on the link of skin manifestations of coronavirus and coronavirus and specific patient groups. We finally complete our search up to May 15, 2020.

2.4 | Study selection

In the first screening 237 articles assigned to the inclusion and exclusion groups and then the titles and abstracts of articles were reviewed by 2 expert dermatologists and acceptable articles²³ searched to find their full text and finally 9 articles (including 12 patients) selected to data entry for this systematic review.^{37,49-56}

3 | RESULTS

After researching, we have found nine related articles and the information of these articles are prepared as a table. Of the 12 patients reviewed in these articles, 10 had psoriasis/psoriatic arthritis and 2 had immunobullous disease included pemphigus and mucous membrane pemphigoid. Their underlying disease was treated with the following drugs:

- From patients with psoriasis/psoriatic arthritis, eight patients were treated with biologic agents (guselkumab: three patients, secukinumab: two patients, apremilast: one patient, adalimumab: one patient, ustekinumab: one patient); two patients were on other immunosuppressive/immunomodulators agents include cyclosporine (CsA) and methotrexate.
- One patient with mucous membrane pemphigoid was treated with prednisolone, rituximab (RTX), mycophenolate mofetil (MPM), and high-dose intravenous immunoglobulins (IVIg).
- One patient with pemphigus was treated with MPM.

In Table 1, we summerized all data about concomitant presence of dermatologic diseases and COVID-19.

4 | DISCUSSION

At the time of the pandemic, many patients were diagnosed with various dermatoses treated with biological agents or immunosuppressive/immunomodulators.⁵⁷ Although, there is still no strong evidence

of a higher risk of infection with COVID-19 in these patients, and clinicians emphasize that the symptoms and management of disease in these patients are similar to those in the general population.²⁶ In addition, for many dermatoses like other medical problems, any mental or physical stress, such as anxiety or infection, may exacerbate the disease course. This study has evaluated nine case reports of patients with chronic dermatologic diseases treated with systemic agents. Of the 12 patients reported, the two patients did not show any symptoms despite close contact with people with confirmed cases of COVID-19; at the time of quarantine, these patients showed no signs of the disease and their treatment continued as before. Of the remaining 10 patients, only one required hospitalization in the intensive care unit. Five patients were treated with conventional therapies such as hydroxychloroquine, oseltamivir, lopinavir/ritonavir, antibiotics. Other patients were treated with supportive/symptomatic therapies. At the time of the COVID-19, the biologic agents were discontinued except for one case (which was treated with guselkumab) but the patients did not report any severe exacerbation of their underlying dermatologic disease despite treatment discontinuation. There was only one case of severe relapse of psoriasis after COVID-19, in which the patient was previously treated with CsA and methotrexate.

Investigation of these articles showed that the severity of COVID-19 in patients with underlying dermatologic disease treated with biological agents was not more than in the general population. The management of these patients was in the form of discontinuation of the biological agents or immunosuppressive/immunomodulators and the use of routine and conventional treatments. After the symptoms have improved, treatment of the underlying dermatologic disease can be recommenced as before.

5 | CONCLUSIONS

Our knowledge about managing patients with dermatologic disorders (especially chronic disorders under treatment with systemic immunomodulators) who are affected by COVID-19 in the pandemic is really scarce given this issue for better controlling and managing both underlying dermatoses and concurrent corona virus infections, we need to sum up current relevant data that we did in this systematic review so far. We found that the severity of the disease or the need for hospitalization in these patients was not greater than in normal population. The treatment of the disease in confirmed cases with COVID-19 were similar to that of affected normal population, with the difference that it is better to stop the patient's previous medications until the symptoms improve. In patients who have already been treated with biological drugs, recurrence or exacerbation of underlying dermatologic disease was mild. After the symptoms of the disease have improved, the patient's treatment could be continued as before.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

The authors contribute equally to all stages of this study. The team has reviewed the manuscript and the data, and all contributors were in full agreement.

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