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SHORT PAPER

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Treatment concerns for bullous pemphigoid in the COVID-19 pandemic era

Seyyede Zeinab Azimi[1] | Alireza Firooz[1] | Dedee F. Murrell[2] | Maryam Daneshpazhooh[3]

[1]Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Tehran, Iran

[2]Department of Dermatology, University of New South Wales, Sydney, New South Wales, Australia

[3]Department of Dermatology, Autoimmune Bullous Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran

Correspondence
Seyyede Zeinab Azimi, Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, 415 Taleghani Avenue, Tehran, 1416613675, Iran.
Email: sz.azimi@yahoo.com

Abstract

Bullous pemphigoid (BP) is the most common autoimmune blistering disease with subepidermal involvement, typically affecting the elderly. It has spontaneous remissions and exacerbations with significant morbidity. A novel coronavirus called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for the new universal coronavirus disease 2019 (COVID-19) pandemic. The pandemic made concerns, especially about immunosuppressive therapy. In this article, we reviewed the management of BP in the COVID-19 pandemic era. The data about the best management of autoimmune bullous diseases like BP, during the outbreak of COVID-19, are evolving and updated every day.

KEYWORDS

autoimmune bullous disease, COVID-19, Dermatologic Therapy

The novel coronavirus disease 2019 (COVID-19), also named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has caused a serious pneumonia pandemic. Advanced age, male gender, and comorbidities such as immunosuppression are the main mortality risk factors. Mostly, individuals between 30 and 80 years old are involved. A low mortality rate has been reported in healthy individuals while COVID-19 can be life-threatening due to sepsis, multiorgan failure, and acute respiratory distress syndrome.[1]

Generally, patients with autoimmune bullous disorders (AIBDs), such as BP patients who are under immunosuppressive treatment, are at increased risk of developing opportunistic infections, including viral infections and microbial pathogens that may potentially trigger the bullous diseases. Of note, the risk of death in patients with BP is increased especially due to pneumonia.[2,3]

A higher risk of infection with corticosteroids during COVID-19 restricts its administration.[4] AIBD patients on immunomodulatory treatment, especially old aged patients with comorbidities, may be at higher risk of poor outcomes of COVID-19.[5] However, their suppressive effects on inflammation and the presence of pulmonary inflammation and overactivation of the immune system induced by COVID-19 attracted the physicians during the COVID-19 outbreak.[1,6] Data about the administration of steroid-sparing immunosuppressive drugs during COVID-19 are scarce and inconclusive.[4]

Patients should consult with their dermatologist before discontinuing any medications. Current guidlines for handling immunosuppression in autoimmune disease patients include advice for outpatients with known contact, those who are under quarantine and for certain patients who are experiencing symptoms of COVID-19 and are under investigation for the disease; in these cases it may be prudent to hold maintenance immunosuppression for 2 weeks following contact or travel. However, patients with autoimmune diseases without obvious evidence of exposure should continue their treatment.[7-9]

Some authors recommend that, during COVID-19 pandemic, AIBD patients treated with immunomodulating therapy should continue the treatment as needed because unjustified withdrawal might lead to uncontrolled activity of AIBD which results in high morbidity and mortality.[2,3,9]

Others suggest that the basic principle of treatment, including corticosteroids and immunosuppressants, such as azathioprine and mycophenolate mofetil, should be reduced to the lowest effective dose.[10]

For BP patients infected with COIVID-19 on immunomodulating therapy, it is recommended that confirmed cases of COVID-19 should undergo risk evaluation at first and these drugs are only discontinued in

proven cases of active COVID-19 after an individual risk-benefit analysis.[3,8,9]

The immunomodulating medications that are considered to impose the highest risks in patients with COVID-19 are azathioprine, mycophenolate mofetil/sodium, cyclophosphamide, and methotrexate, while topical corticosteroids, prednisolone ≤10 mg/d, dapsone/sulfapyridine, doxycycline/tetracycline, colchicine, and Intravenous immunoglobulin (IVIG) can be continued.[5,9] The antimalarial drugs such as hydroxychloroquine, which had been suggested for COVID-19, do not seem to be effective in BP.[11]

Prednisone >10 mg/d may be reduced depending on the activity/severity of the BP, age, comorbidities, and severity of COVID-19. It is generally not safe to cease chronic corticosteroids abruptly because of adrenal suppression. Until now, there is little information specifically concerning COVID-19 and BP, despite these patients usually being very elderly and often in care homes.

Since IVIG is safe for long-term use in all age groups,[12] it has been suggested as a potential option for COVID-19.[13] In BP patients with COVID-19 who are unresponsive to low-dose corticosteroids and/or antimicrobials and dapsone, this therapeutic option can be considered. Potential side effects, particularly thromboembolism, should be considered.[4] Since IVIG is helpful as adjuvant treatment in both BP and COVID-19 and supports immunity, it is likely to be valuable in this situation.[10]

General precautions for the protection of the elderly and immunosuppressed should be strictly adhered to in BP patients, including social distancing, avoiding gatherings, application of teledermatology, and screening the patients for symptoms of COVID-19, as well as evaluating the psychological tolerance of patients during quarantine, especially in those with high doses of corticosteroids; these should be considered as supportive strategies.[14]

While evidence of plasmapheresis effectiveness is generally anecdotal in BP and COVID-19, it could also be considered.[10]

Interestingly, here in Iran, most of the patients with BP continued their treatment with no complication. Most of them had been on topical clobetasol due to their old age and accompanied comorbidities. In new cases and in a few cases of relapse, clobetasol was added/increased, and/or doxycycline was added, and as a last resort oral corticosteroids up to 0.5 mg/kg were prescribed. We discontinued/tapered methotrexate if patients were taking it.

In conclusion, low doses of oral corticosteroids and potent topical corticosteroids are effective in the acute and maintenance phases in most cases of BP. Topical corticosteroid therapy is much safer than oral corticosteroid therapy for extensive disease.[15] It is better not to use high-dose corticosteroids and limit them to the lowest effective doses. In unavoidable cases, minimally effective doses of immunosuppressive drugs or IVIG might be used.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Seyyede Zeinab Azimi https://orcid.org/0000-0001-8213-6056
Alireza Firooz https://orcid.org/0000-0001-7274-4840
Dedee F. Murrell https://orcid.org/0000-0003-2971-0199
Maryam Daneshpazhooh https://orcid.org/0000-0003-1020-8895

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