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ACUTE PSORIATIC FLARE DURING COVID-19 INFECTION AND RESPONSE TO MOLNUPIRAVIR: A CASE REPORT

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Abstract

COVID-19 is a global health problem caused by SARS-CoV-2 that manifests as influenza-like symptoms. This has posed concerns to the population, especially to people with long-standing comorbidities. Among these comorbidities is psoriasis, a chronic inflammatory condition manifesting as generalized, well-circumscribed erythematous lesions with silvery plaques. Psoriatic flares are triggered by factors such as stress and infections. The treatment prior to the advent of the COVID-19 pandemic was the conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) such as methotrexate or the biologic DMARDs. There have only been a handful of case reports on psoriatic exacerbations during COVID-19 infection, so local literature is still lacking, with little to no available published data detailing its response to antivirals such as Molnupiravir. This report thus aims to present a case of a 67-year-old female with psoriasis who was noted to have an acute psoriatic flare during COVID-19 infection. She was diagnosed with psoriasis 26 years prior and was maintained on topical steroids. Her last severe psoriatic flare was 14 years prior, and since then, she has been in remission. She developed influenza-like symptoms 3 days prior to admission. Thereafter, erythematous maculopapular rashes coalescing into plaques appeared. She tested positive for SARS-CoV-2 infection and was managed as a confirmed mild COVID-19 case along with a psoriatic flare. Molnupiravir, which is an orally bioavailable cytidine analog with antiviral activity, was used in the COVID-19 treatment on the first hospital day with a csDMARD (Methotrexate) administered on the third hospital day. No documented adverse events occurred; fever lysed and lesions began clearing by the fifth day. This report provides additional input in establishing optimal treatment and helps drive the therapeutic approach for psoriatic exacerbations during COVID-19 infection, including the effect of Molnupiravir with csDMARDs in mitigating flare-ups, the possibility of side effects, and the probability of drug-to-drug interactions.

Keywords: acute psoriatic flare, COVID –19 infection, Molnupiravir, case report

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has afflicted the population since the pandemic began in March 2020. As of February 2022, over 409 million cases have been confirmed worldwide, with over 3 million of these cases in the Philippines (1, 2). This global health concern does not only affect those in the medical field and other allied health professionals but also those with pre-existing immune- mediated diseases and/or receiving therapies. It is said that factors such as old age, the use of immunosuppressive drugs, and persons with other underlying comorbidities predict COVID-19 hospitalization and will likely affect the disease outcome (3, 4). This was, however, refuted by other studies, such as the study of Gisondi et al. (4, 5). This acute viral syndrome usually presents with influenza-like symptoms such as cough, fever, and fatigue. There have also been reported cases of cutaneous manifestations such as rash or exacerbation of underlying dermatologic disease. Since the start of the COVID-19 pandemic, there have been few case reports and studies on psoriatic flare- ups being triggered (6, 7). The likely explanations are the prevalent utilization of hydroxychloroquine, cessation of traditional antipsoriatic agents, and the usage of oral corticosteroids while managing COVID- 19 disease or after COVID- 19 infection itself (8, 9).

Psoriasis is a systemic inflammatory condition that presents as well-demarcated erythematous lesions with silvery plaques. Stress and infections are some of the triggering factors in these flare- ups (5). Treatment includes immunosuppressive/immunomodulatory drugs that include the conventional synthetic disease- modifying anti-rheumatic drugs (csDMARDs) such as methotrexate and cyclosporine, and the biologic agents DMARDs such as Adalimumab and Etanercept. There is still, however, little evidence on the effect of taking these aforementioned therapies in the event of being treated for COVID-19 infection (6). Molnupiravir's anti-inflammatory effects, its safety and efficacy for the treatment of mild to moderate cases of COVID-19, are continuously being evaluated (13). No clinical drug-drug interaction studies of Molnupiravir have been conducted; thus, a careful approach should be observed.

Here, I report a case of a 67-year-old female with an acute psoriatic flare- up during a COVID-19 infection who has been treated with Molnupiravir and a csDMARD.

CASE PRESENTATION

Patient Information

A 67- year- old, female, was admitted due to febrile episodes with a maximum temperature of 38 ^{0}C, a productive cough with yellowish sputum, and the presence of an erythematous maculopapular rash coalescing into plaques, which started a week prior to admission. The patient had chronic plaque psoriasis for 26 years and was only on topical Calcipotriol and Betamethasone treatment. There was no history of using any oral systemic therapy. Her last severe psoriatic flare was 14 years prior, and since then, she has been in remission. She is also known to be hypertensive for 10 years, has had hypothyroidism for 20 years and has not received any COVID- 19 vaccinations. Heredofamilial diseases include psoriasis on the maternal side and hypertension on both sides.

Clinical Findings

On admission, she was afebrile, tachycardic at 105 bpm, and tachypneic at 22 cpm, with an oxygen saturation of 97% on room air. Using the psoriasis area severity index (PASI) as the gold standard measurement tool in assessing severity, she was noted to have well-circumscribed erythematous lesions with silvery scales on her scalp, extensor areas, and back, having a PASI of 17, a body surface area (BSA) of 36%, and a physician global assessment of 3. There were no noted joint symptoms, nor limitations of movement or swelling. Upon auscultation, clear breath sounds were heard, with no noted rales or wheezing.

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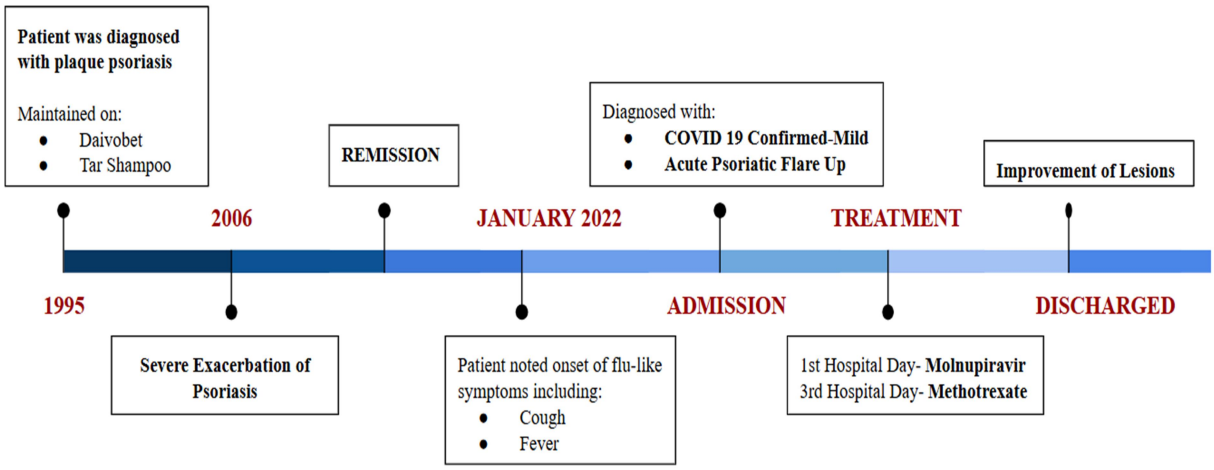
Timeline

Figure 1 presents a summary of the clinical and laboratory characteristics of the patient from the diagnosis of plaque psoriasis to the improvement of lesions (discharged).

Figure 1.

Chronology of the Patient Clinical and Laboratory Characteristics



Diagnostic Findings

Reverse transcription-polymerase chain reaction study of nasopharyngeal and oropharyngeal swab specimens was positive; hence, the diagnosis of COVID-19 infection, mild in severity (4). All relevant laboratories are shown in Table 1.

Therapeutic Intervention

Treatment included Calcipotriol + Betamethasone topical ointment, which was applied once daily, and Tar shampoo, which was commenced every bath. Due to the possibility of drug-to-drug interactions, the Infectious Diseases specialist and Rheumatologist were cautious about starting the csDMARDs and Molnupiravir. The Molnupiravir was initiated as soon as the diagnosis was done, 200 mg/tablet, 4 tablets twice daily on the 1st hospital day, and was continued for 5 days. As methotrexate can be given once weekly, it was administered on the 3rd day after starting Molnupiravir, at a dosage of 4 tablets once weekly, along with folic acid 5 mg/capsule on the day before and after giving Methotrexate. Fever lysed and lesions began clearing by the fifth day. Vital signs were stable and repeat inflammatory markers were noted to decrease.

Follow-up and Outcomes

The patient was subsequently discharged after a week of hospitalization and continued home isolation with resolving lesions. The patient followed up after 2 weeks, noting improvement in the psoriatic flare-up.

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Table 1

Laboratory Results of the Patients

Laboratory Test	Patient's Results	Units	Reference Ranges	Interpretations
Complete Blood Count				
White Blood Cell	15.16	10^9/L	4.0-10.50	↑
Neutrophil	92	%	50.0-70.0	↓
Lymphocytes	5	%	18.0-42.0	↓
Monocytes	2	%	2.0-11.0	↔
Eosinophils	1	%	0-6.0	↔
Basophils	0	%	0.0-2.0	↔
Red Blood Cell	4.80	10^{12}/L	4.2-5.40	↔
Hemoglobin	139	g/dL	125-160	↔
Hematocrit	0.40	Volume %	0.37-0.48	↔
Platelet	264	10^9/L	150-450	↔
Uric Acid	6.60	mg/dL	2.50-6.20	↑
Blood Urea Nitrogen	12.00	mg/dL	7.90-20.20	↔
Creatinine	1.20	mg/dL	0.70-1.20	↔
Sodium	132.00	mmol/L	137-145	↓
Potassium	3.50	mmol/L	3.5-5.1	↔
Alanine Aminotransferase	48.00	U/L	<35	↑
Thyroid Stimulating Hormone	0.010	UIU/mL	0.34-4.22	↓
Free Thyroxine	51.90	pmol/L	10.6-19.4	↑
Ferritin	764.70	ng/mL	14-260	↑
Procalcitonin	0.46	ng/mL	<0.5	↔
D-Dimer	2851.56	ng/mL	<500.00	↑
C-reactive protein	39.46	mg/L	<6.45	↑
Lactate Dehydrogenase	349	U/L	120-246	↑

Note. *The values are in International System of Units (SI Units): Elevated (↑); Low (↓); Normal (↔)*

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DISCUSSION AND CONCLUSION

Since the start of the COVID-19 pandemic, there have been studies on psoriatic flare- ups being actuated during COVID-19 infection. Though the exact mechanism is still poorly understood, it may be due to the host being in a hyperinflammatory state. This is noted especially for those who are at higher risk of developing the infection, such as mentioned in the study by Mroz, which may probably include age, environmental causes such as stress, infections, co-existing comorbidities, or maintenance medications being taken (11). In psoriasis, there is a hyperinflammation of a T-cell-driven autoimmune response with overproduction of cytokine proteins such as IL-23, IL-17, and TNF-α that may be triggered by COVID-19 infection (12). Acute phase reactants such as C- reactive protein and ferritin have also been found to be significantly elevated (13). Therefore, interleukin inhibitors are also used to manage the symptoms. Biologics like TNF inhibitors and interleukin inhibitors, however, may increase the risk of infections and lower the body's ability to fight them (14).

So far, there are only a handful of case reports on the exacerbation of psoriasis during COVID-19 infection, and most of them involved systemic therapies or a history of systemic therapies prior. In this case report, the patient had not taken any oral systemic drugs prior to the infection. The underlying comorbidities may also have increased the risk of acquiring the infection, but this may also be an independent aspect of the severity of the COVID-19 infection or its disease outcome (3,4). The patient observed a severe exacerbation of psoriasis at the time that cough and febrile episodes started. Despite the fact that the patient was unvaccinated and had other comorbidities such as psoriasis and hypertension, the respiratory symptoms were deemed mild. There is still no established optimal treatment for managing patients with psoriasis during COVID-19 infection and its impact on immunosuppressive drugs as part of treatment. As mentioned in the study by Kridin, the use of immunosuppressive therapy may interfere with the use of antiviral drugs, as these may contribute to the worsening of the COVID-19 course (3). For these reasons, Molnupiravir and the csDMARDs were strategically started, and the likelihood of adverse effects was monitored.

Methotrexate is a known safe, readily available, and inexpensive option for the treatment for psoriasis. It is also considered an anti-inflammatory agent against COVID-19 infection, as it mitigates the severity and ameliorates its prognosis (15). There have been studies indicating that low doses of Methotrexate, along with daily folate is used for mild to moderate COVID-19 cases and that it is appropriate to be used as treatment (16, 17). These gathered data indicate that methotrexate has certain protective effects on SARS-CoV-2 infection by downregulating ACE2 (18).

Molnupiravir is a promising broad-spectrum antiviral drug that targets the RdRp, which inhibits the cytidine and uridine triphosphates (19). An issue of possible drug- to- drug interaction between Methotrexate, as a systemic therapy, and Molnupiravir, which is an antiviral drug for COVID-19 infection, has been entertained while managing the patient but still needs further investigation (20). A course of Molnupiravir consisting of 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days and the aspect of timing, was considered upon initiation of Molnupiravir and csDMARD (21,22). A 5- day course seems to be safe without any obvious short-term side effects (23, 24).

Preliminary clinical trials demonstrated that the use of Molnupiravir early in the disease process, when viral loads are high, generated maximum benefit and reduced the risk of prolonged hospitalization and/or death (25, 26). Phases 1, 2, and 3 clinical trials showed that Molnupiravir remarkably reduced the risk of hospitalization or death in adults experiencing mild or moderate COVID-19 infection (27). It is also effective against newer COVID-19 variants, and is more practical and convenient during administration (28, 29, 30). Thus, Molnupiravir was started earlier in our patient on hospital day 1, and Methotrexate was given on the third hospital day, with no complications or onset of new symptoms observed. Improvement of the lesions was observed and was evident upon discharge and during follow- up.

In conclusion, patients with psoriasis may be treated with immunosuppressive drugs or any other systemic therapy during SARS-CoV-2 infection. These therapies may not directly affect outcomes in the clinical course but may help in mitigating the hyper-inflammatory state of the patient; however, caution should be exercised in considering the timing of medications. Drug-to-drug interactions between Methotrexate and Molnupiravir should be further evaluated. Further studies are still needed to formulate optimal treatment, which may vary on a case-by- case basis and require joint decision- making between the physician and the patient.

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Patient Perspective

I experienced an exacerbation of psoriasis at the time when the cough and fever started, 3 days prior to admission. I have a history of psoriasis for 26 years and was able to control it with the use of topical steroid ointment. I have not taken any oral systemic therapies for psoriasis. The last time I had a severe exacerbation of psoriasis was 14 years ago. By the time I was admitted, my body was erythematous with silver scales on my extremities and scalp, associated with cough and intermittent fever. I consented to the use of Molnupiravir and noted no adverse effects or worsening of my cough or my lesions. Improvement of my lesions was noted on the 5th hospital day.

Informed Consent

Informed consent was obtained for the case report including images, and the patient's perspective included herein.

List of Abbreviations

ACE2- Angiotensin- Converting Enzyme 2
COVID-19: Coronavirus Disease 2019
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2
csDMARDs: conventional synthetic Disease Modifying Anti-Rheumatic Drugs
PASI: Psoriasis Area Severity Index
BSA: Body Surface Area
Mg: Milligrams
RdRp: Ribonucleic Acid – dependent Ribonucleic acid polymerase
Bpm: beats per minute
Cpm: cycles per minute

Declarations

Ethical issues
None

Availability of Data and Materials
The data relevant to this study are presented within the article.

Competing Interests
The author declares that she has no known financial or other forms of interest that could potentially influence the work presented.

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Author's Contributions
This work is the sole authorship of the author.

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