

CASE REPORT

Herpes Zoster in COVID-19 patient: A Coexistence or Coincidence?

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ABSTRACT

Varicella-Zoster Virus (VZV) reactivation has been identified during the acute or subacute stages of COVID-19 infection. This phenomenon may be attributed to immune changes in COVID-19 patients, such as dysregulation and fatigue of the cellular immunity. We report a case of COVID-19 patient with herpes zoster (HZ). A 26-year-old woman was consulted for painful red patches and blisters on her right cheek. She has previously been diagnosed with and treated for COVID-19 and mild pneumonia 10 days prior. A herpetiform distribution of vesicles was observed spreading according to the branch of the trigeminal nerve innervation. The findings led to a clinical diagnosis of HZ. We recommended the standard acyclovir regimen in addition to the oseltamivir prescribed by the pulmonologist. The symptoms were completely resolved after seven days of acyclovir treatment, with no further complications. This was to our knowledge, the first case of HZ in COVID-19 reported in our country.

Keywords: COVID-19, Herpes zoster, Immune response

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INTRODUCTION

Coronavirus Disease-19 (COVID-19) is an acute respiratory syndrome caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)(1). Initially, COVID-19 infection was believed to be exclusive to the respiratory system. However, as the disease progresses, further research reveals that COVID-19 can manifest in variety of ways(2). The skin is one of the non-pulmonary organs involved in COVID-19 infection. Exanthematous, maculopapular, or morbilliform rashes and urticarial lesions are the most widely known cutaneous symptoms of COVID-19(3). Moreover, some studies have discovered an increasing trend in viral skin infection, including the reactivation of *Varicella-Zoster Virus* (VZV) during the COVID-19 pandemic(3)(4). The presence of HZ raises the question of whether COVID-19 is an effect or a cause. In this paper, we present a case of herpes zoster infection in a COVID-19 patient.

CASE REPORT

A 26-year-old woman consulted to the dermatology department with a one-day history of painful red patches on her right cheek. The complaints were accompanied by

a burning feeling. The red patches quickly transformed into vesicles, multiplying in number, and spread to her upper eyelid and lower cheek. The patient was uncertain whether she has ever had varicella.

The patient had previously been hospitalized in an isolation room for ten days. She had a fever, a cough, a loss of smell, and shortness of breath. PCR test for COVID-19 yielded a positive result and chest CT-scan showed pulmonary infiltration. Her complete blood count was within normal ranges. The quantitative CRP level was 3.61 mg/L, and D-dimer level was 0.4 ug/mL. Dermatological examination of the right face revealed a group of vesicles with a herpetiform distribution and well-defined erythematous base. Erosive lesions were observed in some places. The lesion was found to correspond to the distribution of the 2nd branch of the trigeminal nerve (as shown in Figure 1). Based on the clinical presentation, a diagnosis of herpes zoster of the right maxillary branch of the trigeminal nerve was established.

The patient was treated with acyclovir 800 mg five times daily for 7 days, cefixime 100 mg twice daily, pregabalin 75 mg twice daily, and 2% sodium fusidate cream twice daily on the lesion. Meanwhile, oseltamivir, N-acetylcysteine, paracetamol, and multivitamin were prescribed by the pulmonology department to treat her COVID-19 infection. Her skin lesions improved significantly three days after treatment (Figure 2 – Figure



Fig. 1

Figure 1: 1st day a group of vesicles with a herpetiform distribution with an erythematous skin base



Fig. 3

Figure 3: Progress of patient's lesions from the 2nd until 3th day

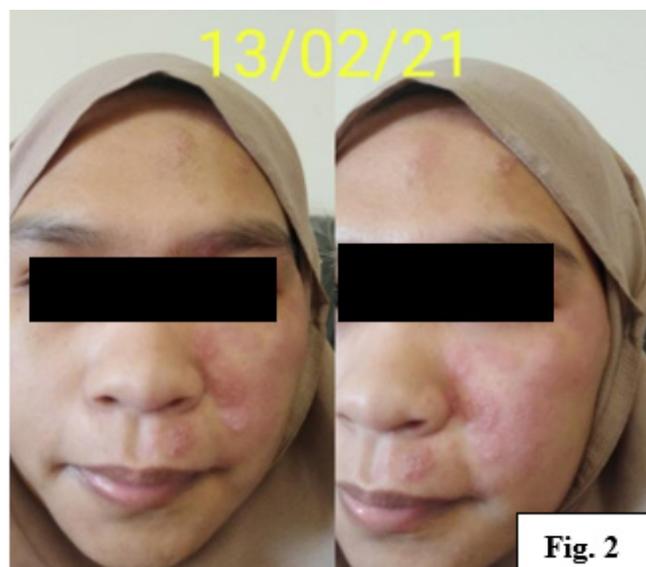


Fig. 2

Figure 2: Progress of patient's lesions from the 2nd until 3th day



Fig. 4

Figure 4: Stage of crusting and resolution in 4th day

3). The lesions on the skin then began to crust and heal (Figure 4). There were no new vesicles, and the old lesions had become hyperpigmented.

DISCUSSION

Herpes zoster (HZ) is characterized by the abrupt onset of unilateral vesicular eruptions and radicular pain confined to a specific dermatome. After a previous varicella infection, *Varicella-Zoster Virus* (VZV) remains latent in the posterior root ganglia and could be reactivated as HZ(3). HZ develops when there is a failure in cell-mediated immunity during iatrogenic or pathologic conditions. After being infected with VZV, T-cell immunity begins to decline over time, resulting in decreased protection against HZ(1). Immunocompromised conditions, HIV infection, advance age, trauma, radiation, certain medication and

stress can increase the risk of HZ (1).

We established a clinical diagnosis based on the patient's typical rash and symptoms. There were herpetiform vesicles distributed on the right side of the patient's face, exhibiting the classic sign and distribution of HZ in the trigeminal area. The lesion begins with erythematous macules and papules in a dermatomal distribution. Later, the vesicles evolve into pustules before drying and crusting in 7 to 10 days (1).

Recent researches suggest that COVID-19 does not only affect the respiratory tract but can also manifest in other organs systems, including the skin. The dermatological signs associated with COVID-19 are morbilliform rash, chilblain-like lesion, urticaria, erythematous macular, and retiform purpura. This may be caused by an immune response to the viral nucleotide or by a systemic

complication in vasculitis and thrombotic vasculopathy (2).

There is a doubling of HZ cases during the COVID-19 outbreak in Turkey compared to the same period last year(4). Several reports of HZ have been identified prior to, during, or following COVID-19 infection(1)(3)(5). Although the relationship between COVID-19 and HZ is not well established, some authors propose that HZ is a possible COVID-19 complication. The major hypothesis is direct SARS-CoV-2 effect on cell-mediated immunity. SARS-CoV-2 can attack lymphocytes directly, reducing and impairing T-cell activity(1). COVID-19 has also been related to lower levels of CD4+, CD8+, CD3+, B-cells, Natural Killer (NK) cells, as well as monocytes and eosinophils, when compared to controls (3). As the result, SARS-CoV-2 infection increases the likelihood of HZ reactivation by suppressing the cell-mediated immune response to viral infections(1). Furthermore, patients with COVID-19 suffer from significant emotional distress and anxiety. Psychological stress may also play a role in overall immune functions and promote HZ in COVID-19 patients (4).

As previously mentioned, COVID-19 patients typically have lower lymphocyte cells count. However, in our patient, the absolute lymphocytes count (ALC) was within normal ranges. On the other hand, normal ALC cannot always indicate a sufficient cellular immunity response as it does not describe overall specific T cell subpopulations. Hence, changes in the proportion of T-cell subsets and activities is more relevant to determine cellular immunity properties than the ACL (3).

We prescribed our patient with oral acyclovir as well as oral antibiotics to prevent secondary bacterial infection. The patient responded well to treatment, as evidenced by the reduction of rashes and the absence of new lesions. Despite all of that, we realize that this article has several limitations. Firstly, Tzanck smear and PCR testing were hard to performed, so we had to rely solely on clinical manifestations to establish diagnosis. Second, because we only reported one patient, it is difficult to conclude that there is a strong relationship between HZ and COVID-19. Lastly, the specific subtypes and expression of T-cells, as well as cytokine activity, were not measured to support our hypothesis.

CONCLUSION

COVID-19 patients have a lower cell-mediated

immunity response, which puts them at greater risk of viral infection, including herpes zoster, as they tend to have a higher risk of *varicella-zoster virus* reactivation. Herpes zoster could be an alarming indicator of undiagnosed COVID-19, as asymptomatic or mild COVID-19 infection with minor downgrading of immunity may only present as *Varicella-Zoster Virus* reactivation. There have been few studies in this context demonstrating the direct relationship between herpes zoster and COVID-19 and in Indonesia, the present case is the first case reported to date. Future studies need to focus in the cellular immunity response of herpes zoster and COVID-19. In addition, a larger number of patients and more thorough investigations are required to establish direct relationship between herpes zoster and COVID-19.

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REFERENCES

1. Saati A, Al-Husayni F, Malibari AA, Bogari AA, Alharbi M. Herpes Zoster Co-Infection in an Immunocompetent Patient With COVID-19. *Cureus*. 2020;12(7):4–9.
2. Freeman EE, McMahon DE, Lipoff JB, Rosenbach M, Kovarik C, Desai SR, et al. The spectrum of COVID-19-associated dermatologic manifestations: An international registry of 716 patients from 31 countries. *J Am Acad Dermatol* [Internet]. 2020;83(4):1118–29. Available from: <https://doi.org/10.1016/j.jaad.2020.06.1016>
3. Maia CMF, Marques NP, de Lucena EHG, de Rezende LF, Martelli DRB, Martelli-Junior H. Increase in the number of Herpes Zoster cases in Brazil related to the COVID-19 pandemic. *Int J Infect Dis*. 2021;104:732–3.
4. Ertugrul G, Aktas H. Herpes zoster cases increased during COVID-19 outbreak. Is it possible a relation? *J Dermatolog Treat* [Internet]. 2020;0(0):1. Available from: <http://dx.doi.org/10.1080/09546634.2020.1789040>
5. Voisin O, Deluca N, Маһй А, Lelorc'h E, Hubert S, Мһnage E, et al. Disseminated Herpes Zoster During COVID-19. *Infect Dis Clin Pract*. 2021;29(2):e109–10.