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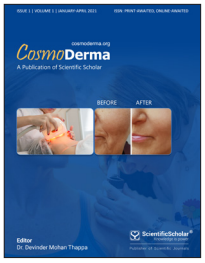

Perspective

A possible viral interference between SARS-CoV-2 and varicella zoster virus

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Received : 17 October 2022
Accepted : 17 November 2022
Published : 16 December 2022

DOI
10.25259/CSDM_122_2022

Quick Response Code:

ABSTRACT

It is not uncommon to observe herpes zoster in severe illnesses. However, its rarity in millions of SARS-CoV-2-infected patients around the world is intriguing. Further, its frequent occurrence following the serological clearance of SARS-CoV-2 infection indicates an unknown mechanism at work. The purpose of this study was to investigate this phenomenon and identify a possible underlying mechanism. The authors believe, there is a powerful viral interference created by SARS-CoV-2 virus during its active phase. This was evident by the paucity of reports of herpes zoster infection as long as COVID-19 disease was active. Therefore, COVID-19 infection does not permit the development of herpes zoster until the infection is serologically negative – due to its powerful suppression of varicella-zoster virus. They speculate that the same active principle of viral interference can be applied by developing a superinfection therapy by introducing a non-pathogenic virus to infect patients harboring a pathogenic virus, to combat serious infections such as COVID-19.

Keywords: SARS-CoV-2, Herpes zoster, Varicella zoster virus, Viral interference, Superinfection therapy, COVID-19

SARS-CoV-2 infection causes a spectrum of symptoms varying from a mild form to a very severe and multiorgan/multisystem fatal disorder. Despite several cutaneous manifestations reported during the course of COVID-19 illness,[1,2] there is not much evidence of other concomitant viral infection except isolated cases of reactivation of varicella zoster virus (VZV). We believe, this might be caused by a powerful viral interference caused by the SARS-CoV-2 virus.

Herpes zoster is an acute dermatological affliction caused by the reactivation of VZV. This human neurotropic virus causes chicken pox. Following this primary infection, this virus migrates to sensory ganglion and establishes a lifelong latent infection. Its reactivation occurs whenever there is an immunocompromised state – trauma, old age, chronic debilitating diseases, malignancy, diabetes, prolonged corticosteroid therapy, etc. This triggers the virus to multiply and spread centrifugally down the sensory nerves to skin and mucosa of that specific area innervated by the affected nerve. Usually, it involves one or a few dermatomes unilaterally [Figure 1]. However, disseminated herpes zoster can be seen infrequently in conditions of extreme immune suppressions.

However, only a few isolated reports of herpes zoster occurring during COVID-19 illness are available [Table 1]. Nofal *et al.*[3] recorded herpes zoster ophthalmicus in four patients within 5 days of the development of COVID-19 infection; two of their patients were children as small

Table 1: Development of HZ in COVID-19 patients.

Authors	No. of patients	Age (in years)	HZ onset after COVID-19 infection (in days)	Site(s) involved	COVID-19 serology	Inference
Nofal *et al.*[3]	Male: 3 Female: 1	Mean: 21.5 (Range: 7–42)	Mean: 4.5 (Range: 4–5)	Herpes zoster ophthalmicus	Positive	HZ is an indicator or complication of COVID-19 infection
Tartari *et al.*[4]	Male: 1 Female: 3	Median: 70.5 (Range: 68–74)	Median: 5.5 (Range: 4–7)	Necrotic HZ of trigeminal nerve (3) Classic HZ (1)	Positive	HZ is precipitated by COVID-19 induced decrease in CD3+ and CD8+lymphocytes
Elsaie *et al.*[5]	Male: 1 Female: 1	Mean: 64 (Range: 60–68)	HZ preceded COVID-19 infection by 2–5 days	Thoracic HZ (1) Lumbar and thigh HZ (1)	Positive	HZ might be an indication for latent COVID-19 infection
Ferreira *et al.*[6]	Male: 1	39	10	Facial HZ involving three divisions of trigeminal nerve	Positive	Retrograde reinfection of HZ in trigeminal area due to local impact of SARS-CoV-2

HZ: Herpes Zoster

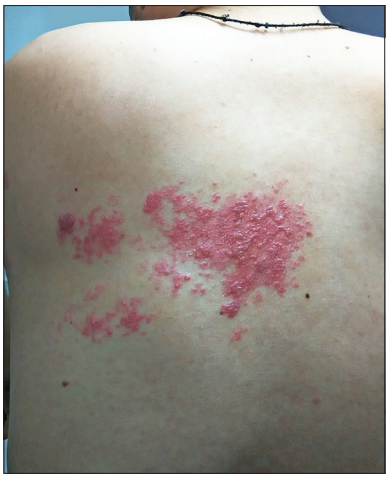

Figure 1: Grouped vesicles on an erythematous base in the left upper back.

as 7–9 years of age. Tartari *et al.*[4] reported necrotic herpes zoster ophthalmicus in four elderly patients who developed the eruptions between 4th and 7th day of COVID-19 infection. On the other hand, Elsaie *et al.*[5] recorded classical herpes zoster in two patients of which one developed COVID-19 infection and herpes zoster simultaneously, while the other had herpes zoster infection 2 days preceding the development of COVID-19 infection. Ferreira *et al.*[6] reported one case of COVID-19 infection developing herpes zoster ophthalmicus on 10th day of illness. SARS-CoV-2 infection is known to cause lymphopenia due to direct affliction of the lymphocytes, impairment of anti-viral responses, and the activation-induced cell death.[7,8] Lymphopenia, in turn, may result in reactivation of dormant VZV virus in those sensory ganglia where its concentration is maximum.[3] Necrotic herpes zoster which is more common in HIV-positive patients was reported by Tartari *et al.*[4] All of their patients were elderly, HIV-negative, and had a decreased CD3+ and CD8+ lymphocytes, a situation that makes them more prone to the reactivation of VZV.[9]

Apart from these reports, there has been a substantial lack of cases where the two viral infections (COVID-19 and VZV) occur simultaneously. It is noteworthy that in "long COVID," a special situation encountered in several of the confirmed SARS-CoV-2 patient who survived, zoster reactivation was conspicuous by its absence among the symptoms of "long COVID."[10] Further, after COVID-19 vaccination two, there is a paucity of reports of herpes zoster.[11] This appears to be in stark contrast to the regularly occurrence of herpes zoster in non-COVID people with other comorbidities.

This brings an interesting hypothesis in light that despite the disease causing an acute physical and psychological stress on the affected individual, SARS-CoV-2 virus did not permit the reactivation of the dormant VZV – probably due to its presence causing a viral interference. This situation makes a strong case for the research workers to think about the development of super infection therapy (SIT), an innovative therapeutic approach of introducing a non-pathogenic virus to infect the patients harboring a pathogenic virus.[10] Such a host-directed therapy strategy could activate endogenous innate immune response through a toll-like receptor. This will exert a post-infection interference through constant presence of an attenuated non-pathogenic viral strain, thus, boosting potent endogenous innate response. Kovesdi and Bakacs[12] stress that SIT can be developed into a biological

platform for "one drug-multiple virus" broad spectrum therapeutic approach. This may open a new vista to combat future viral challenges such as newer mutations of SARS-CoV-2, and thus curtail effectively any virus emergences, which previously used to take shape of an epidemic and pandemic due to limited therapeutic options.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Daneshgaran G, Dubin DP, Gould DJ. Cutaneous manifestations of COVID-19: An evidence-based review. Am J Clin Dermatol 2020;21:627-39.
2. Singh H, Kaur H, Singh K, Sen CK. Cutaneous manifestations of COVID-19: A systematic review. Adv Wound Care (New Rochelle) 2021;10:51-80.
3. Nofal A, Fawzy MM, El Deen SM, El-Hawary EE. Herpes zoster ophthalmicus in COVID-19 patients. Int J Dermatol 2020;59:1545-6.
4. Tartari F, Spadotto A, Zengarini C, Zanoni R, Guglielmo A, Adorno A, *et al*. Herpes zoster in COVID-19-positive patients. Int J Dermatol 2020;59:1028-29.
5. Elsaie ML, Youssef EA, Nada HA. Herpes zoster might be an indicator for latent COVID 19 infection. Dermatol Ther 2020;33:e13666.
6. Ferreira A, Romão TT, Macedo YS, Pupe C, Nascimento O, Fellow of the American Academy of Neurology (FAAN). COVID-19 and herpes zoster co-infection presenting with trigeminal neuropathy. Eur J Neurol 2020;27:1748-50.
7. Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, *et al*. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Cell Mol Immunol 2020;17:533-5.
8. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, *et al*. Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia. J Infect Dis 2020;221:1762-9.
9. Wei L, Zhao J, Wu W, Zhang Y, Fu X, Chen L, *et al*. Decreased absolute numbers of $CD3^+$T cells and $CD8^+$T cells during aging in herpes zoster patients. Sci Rep 2017;7:15039.
10. Aiyegbusi OL, Hughes SE, Turner G, Rivera SC, McMullan C, Chandan JS, *et al*. Symptoms, complications and management of long COVID: A review. J Royal Soc Med 2021;114;428-42.
11. Toscani I, Troiani A, Citterio C, Rocca G, Cavanna L. Herpes zoster following COVID-19 vaccination in long-term breast cancer survivors. Cureus 2021;13:e18418.
12. Kovesdi I, Bakacs T. Therapeutic exploitation of viral interference. Infect Disord Drug Targets 2020;20:423-32.

How to cite this article: Srivastava G, Srivastava G. A possible viral interference between SARS-CoV-2 and varicella zoster virus. CosmoDerma 2022;2:126.