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LETTERS TO THE EDITOR

# Recurrent herpes zoster after COVID-19 vaccination in patients with chronic urticaria being treated with cyclosporine—A report of 3 cases

To the editor,

Ever since the novel COVID-19 infection wreaked havoc throughout the globe, nations across the world have been trying to contain the disease with no stone left unturned. Prevention from acquiring the disease is the quintessential need of the hour. Currently, in India two vaccines are under circulation for disease prevention, namely, Covishield™ (recombinant ChAdOx1 nCoV-19 coronavirus vaccine) and Covaxin (The Bharat Biotech COVID-19 vaccine).[1] Both have demonstrated a staggering success rate of efficacy and safety profile, with many other similar vaccines under process of being launched in India. The nationwide mass vaccination campaign launched by the government of India has been accepted with open arms by the masses, and till date more than 87 million Indian of the population have received both doses of vaccination.[2]

Although various guidelines have been laid down for the use of COVID-19 vaccination with concurrent use of immunosuppressives, a real-life experience of the vaccines with many immunomodulators is still lacking in the literature.[3,4] Herein, we present a series of 3 such cases of chronic urticaria being treated with cyclosporine, who developed reactivation of recurrent herpes zoster following COVID-19 vaccination.

Three patients present to us with development of herpes zoster within a week of receiving the first dose of COVID-19 vaccination (Figure 1) (recombinant ChAdOx1 nCoV-19 coronavirus vaccine also known as Covishield™). All patients were known case of chronic spontaneous urticaria being treated with capsule cyclosporine for at least one month. While the thoracic dermatomes were involved in 2 patients, 1 had cervical dermatomal involvement. Interestingly, on seeking a detailed history of medical records were discovered that all 3 patients had developed similar lesions consistent with HZ, in the past over a distant or same site (Table 1).

In case 1, a 34-year-old male, a similar episode of HZ had happened 7 months back over the same site. On examination there was presence of necrotic ulceration confined to the right T1-T2 dermatome. The lesions had erupted as vesicles with painful stabbing pain 7 days after vaccination. The lesions soon evolved to cause erosion and ulceration in the surrounding skin.

Case 2, a 57-year-old male, had herpes zoster ophthalmicus with painful vesicular eruptions and purulent discharge from right eye with intense swelling of unilateral eyelid. His previous episode of HZ had happened 5 years back on right side of the thorax. Similarly, Case 3, a 38-year-old male had HZ of the T4-T5 dermatomes which had erupted after 4 days of immunization. The patient was already being treated for residual post-herpatic neuralgia which had developed from an episode of HZ involving the left thorax that occurred 1 year back.

In our series the mean duration between vaccination and development of HZ was 5.3 days. None of the patients had any lymphadenopathy. The cases were made to undergo COVID-19 PCR test which turned out to be negative. There were no complaints of development of any other acute adverse events following immunization. The patients were diagnosed as cases of recurrent herpes zoster (RHZ) reactivated by concurrent COVID-19 immunization and cyclosporine. All 3 patients had negative serological profile for any acquired immunosuppression. The patients were treated with T. Valacyclovir 1gm TDS for 7–10 days, along with Cap pregabalin and nortryptaline or cabamazepine followed by complete recovery in skin lesions. Case 1 and 2 was also given tablet prednisolone 60 mg in tapering dose for over 14 days. In case 2 it was done so to avoid development of facial nerve palsy or Ramsey-Hunt Syndrome, while in case the use of steroids helped in rapid recovery of inflammation at the site of ulcer. There was no post-herpetic neuralgia after the ensuing follow up period of 1 month in the three cases.

In past various authors have reported the association between herpes zoster and a handful of viral vaccines like hepatitis B, A, antirabies, influenza, and Japanese encephalitis vaccines.[5] A few cases have recently reporting a temporal association between herpes zoster and COVID-19 vaccination. The aforementioned reports indicate a possible mechanism of immunomodulation by the vaccination antigens.[6] The varicella zoster virus has a predilection for the peripheral nerves. Following a primary infection, it can lie in dormant in the dorsal root ganglia of the spinal cord for years, and get reactivated following any stressful event to the body, namely surgeries, high grade fever, prolonged illness, immunosuppression, vaccination, etc. Lately, a sudden resurgence of HZ is being reported in COVID-19 infected individuals, even in absence of any immunosuppression. This has been attributed to the lymphopenia and CD4 T cell impairment induced by viraemia. Vaccination induced cellular immune suppression and up regulation of alloreaction can play a role in triggering the reactivation of VZV in the same way.[5] Additionally, the cyclosporine

  


FIGURE 1 A, Hemorrhagic crusting and necrotic ulceration confined to the right T1-T2 dermatome. B, Multiple grouped vesicles over erythematous based with hemorrhagic crusting involving right ophthalmic branch of trigeminal dermatome with ipsilateral eyelid edema, conjuctival erythema and discharge. C, Multiple grouped vesicles with hemorrhagic crusting over right T4-T5 dermatome

TABLE 1 Details of patients with recurrent herpes zoster

| Parameters | Case 1 | Case 2 | Case 3 |
|---|---|---|---|
| Age in years/sex | 34 years/male | 57 years/male | 38 years/male |
| Site | Right side of chest, scapular area, axilla and a small strip of medial aspect of arm and forearm | Right forehead, eyelid, extending to adjacent scalp | Right side of chest, nipple areola complex and scapular area |
| Dermatomes involved | T1, T2 | Ophthalmic branch of trigeminal dermatome (V1) | T4-T5 |
| Associated features | Pain, burning, superficial ulceration | Purulent discharge from right eye with intense swelling of unilateral eyelid | Pain |
| Lab investigations | Leukocytosis | Dyslipidemia, hypercholestrolemia | - |
| History of primary episode of herpes zoster | 7 months back, Over same site | 5 years back, Over right side of thorax | 1 year back, Left side of thorax |
| History of varicella zoster in childhood | + | + | + |
| Treatment given for RHZ | T. Valacyclovir 1gm TDS x 10 d, T. Prednisolone 30 mg in tapering dose x 3 weeks, Pregabalin, carbamazepine | T. Valacyclovir 1gm TDS x 10 d T prednisolone 60mg in tapering dose for 14 days, Pregabalin, carbamazepine | T. Valacyclovir 1gm TDS x 7 d, Pregabalin, Nortriptyline |
| Time taken for resolution (in days- d) | 20 d | 10 d | 12 d |
| Duration of Cyclosporine therapy before onset of RHZ | 5 weeks | 8 weeks | 6 weeks |
| Post herpatic neuralgia | No | No | No |

induced T cell suppression could play a major contributory role in this reaction.

All the cases in our series were patients of chronic spontaneous urticaria having gone a battery of investigations in the past to rule out any possible triggers of inducible urticaria. Prior to starting capsule cyclosporine, cases 2 and 3 had failed to show any persistent response with high dose of antihistaminics and steroids, and case 1 had also received autologous serum therapy with little to no improvement, Therefore, these cases were being treated with cyclosporine as an established immunomodulator with a good disease control and a good reduction in urticaria severity score.

The duration of consumption of cyclosporine in our cases prior to onset of RHZ ranged from 5 to 8 weeks. In all 3 cases the symptoms of herpes zoster were mild to moderate, with complete resolution of HZ within a month.

The recurrence rates of HZ have been reported to range between 0.2% to 12.5%.[6] The observation of recurrent herpes zoster made by us is contrasting with the commonly reported literature which stated HZ recurrence to be more common in elderly patients. Other risk factors for recurrence include immunosuppression induced by chronic infections, medication and malignancies. Various concurrent chronic inflammatory illnesses like systemic lupus erythematosus,

renal failure, metabolic syndrome, thyroid and pulmonary dysfunctions have also been attributed to high recurrence rates.[6]

To our knowledge, this is the first case series of recurrent VZV following COVID-19 vaccination. Although we acknowledge that it is not feasible to establish a direct correlation between the vaccination and recurrence of HZ, there was a strong clinical suspicion of iatrogenic immunosuppression due to cyclosporine in our cases which could be a major contributory factor. However, in order to establish this theory further, larger case studies conducted over longer periods of time is the call of the hour, as the virus and vaccines evolve.

**KEYWORDS**

COVID-19, COVID-19 vaccination, Leukocytoclastic Vasculitis, SARS-CoV-2

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None.

**ETHICS STATEMENT**

A formal ethical approval was taken. Written informed consent was taken from all the patients for using their data and clinical images.

**CONFLICT OF INTEREST**

Nil.

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