Accepted Artic

Article type: Letter to editor

Title: Post herpetic granulomatous dermatitis and herpes zoster necroticans triggered by Covid-19

vaccination

Keywords: herpes zoster, covid-19, vaccination, granulomatous

**Short running title:** Atypical herpes zoster post covid 19 vaccination.

Word count: 620

Figure count- 1

Table count- 0

**Reference count-** 6

**Authors** 

Dr Durga Madhab Tripathy, \*MD, DNB

Dr Sushil Kumar, @MD

Dr Neerja Saraswat, \*MD, DNB

Dr Shobhit Goel, \*\*MD

Dr Eeshaan Ranjan, \*MD, DNB

dmt5861@gmail.com

greatsushil77@gmail.com

neerjaneerja007007 @gmail.com shobhitgoel167@rediffmail.com

eeshaan.ranjan@gmail.com

**Corresponding Author** – Dr Neerja Saraswat, Associate Professor, Dermatology, Armed Forces Medical College, Pune, India

Address for Correspondence - Department of Dermatology, Military Hospital, Agra, India

Email – neerjaneerja007007@gmail.com

**Telephone** – (+91) 7217671378

Source(s) of support, funding- Nil

Presentation at meeting- Nil

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dth.15707

<sup>\*</sup>Assistant Professor, Dermatology, Military Hospital, Agra, India

<sup>&</sup>lt;sup>®</sup>Associate Professor, Dermatology, Motilal Nehru Medical College, Allahabad, India

<sup>&</sup>lt;sup>+</sup> Associate Professor, Dermatology, Military Hospital, Agra, India

<sup>\*\*</sup>Assistant Professor, Pathology, Military Hospital, Agra, India

<sup>#</sup> Associate Professor, Dermatology, Military Hospital, Jammu, India

**Acknowledgement**: The patient in the manuscript has given written informed consent to the publication of case details and photographs.

**Author contribution statement:** The manuscript has been read and approved by all the authors. The requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Conflicts of Interest: None for all authors.

## Manuscript

Postherpetic granulomatous dermatitis and herpes zoster necroticans triggered by Covid-19 vaccination

The severe acute respiratory syndrome coronavirus -2 (SARS CoV-2) pandemic since its onset in Jan 2020 has affected medical practice like a kaleidoscope. To combat the rampant surge of cases, a vigorous vaccination drive was undertaken on a global scale. Covishield (recombinant monovalent vaccine by Serum Institute of India) and Covaxin (Whole virion inactivated vaccine by Bharat biotech, India) are the two different kinds of vaccines which are manufactured in India and almost one-fourth of the population were vaccinated within the first six months. A plethora of dermatological adverse effects of the vaccine have been reported so far amongst which reactivation of herpes zoster (HZ). Vaccine-induced immunomodulatory effects are hypothesized for reactivation. <sup>1,2</sup> We report a series of two cases of the entity, firstly, an atypical acute presentation in the form of herpes zoster necroticans and secondly, post-herpetic granulomatous dermatitis, an uncommon sequelae, both triggered by covid-19 vaccination.

## Case 1

54-year-old Indian male developed multiple grouped vesicles and bullae with severe burning and hyperalgesia over the right half of the upper face and scalp 05 days after administration of the first dose of Covishield vaccine. Over the next 48 hours, spontaneous rupture of lesions resulted in a large ulcer. On examination, there was a large ulcer spanning the right side of the face and scalp with a sharp cut-off at the midline emanating serosanguinous discharge and surface necrotic crust throughout. (Figure 1A&B) Associated conjunctival congestion was noted but herpes zoster ophthalmicus (HZO) was ruled out by the ophthalmologist. Tzanck smear from the erosion showed multi-nucleated giant cells and acantholytic cells. The patient was managed as HZ necroticans with parenteral acyclovir and broad-spectrum antibiotics to which he showed a good response.

52-year-old healthy Indian male developed multiple asymptomatic erythematous to violaceous raised lesions over the previous healed scar of herpes zoster on the left side of the face. The onset of the lesions was three weeks after administration of the first dose of Covaxin vaccine and six months from acute lesions of HZ. On examination, multiple violaceous to erythematous coalescing indurated plaques were noted along the scar of the previous HZ across V3, C2 & C3 dermatome on the left side of the face. (Figure 1C&D) Serum calcium and Angiotensin conversion enzyme (ACE) level were normal. Evaluation for any focus of tuberculosis was also non-contributory. Histopathology revealed multiple epithelioid cell granulomas with lymphocyte cuffing in the dermis which were periappendageal. (Figure 1E&F) Special stains of tissue for Acid fast bacilli (AFB) and fungal elements were negative. The patient was diagnosed with post herpetic granulomatous dermatitis and managed with lesion directed therapy with a gradual response and is under regular follow up.

Reactivation of Varicella-Zoster virus (VZV) due to Covid-19 infection can be explained by the fact that lymphopenia occurring in febrile conditions are an ideal setting for the VZV reactivation, however this can't be an explanation in case of Covid-19 vaccine. Vaccine-induced T cell activation and release of TNF-α and IFN-γ causes an exaggerated immune response and possibly resulting in HZ necroticans, a severe form of the condition to occur in the case reported. <sup>3</sup> Also hypothesized that immunomodulation brought about by viral spike protein (glycoprotein S) of the vaccine causes pleiotropic effects on the host cells. A clonally activated syncytium mediated lymphocytic elimination and poor phagocytic capability of macrophage-like cells result in granuloma formation. <sup>4</sup> Postherpetic granulomatous dermatitis is regarded as Wolf's isotopic response that occurs within weeks to months after acute lesions of HZ. Although mostly reported in settings of malignancy, chemotherapy, and immunodeficiency, it occurred in the index case post-Covid-19 vaccination. <sup>5,6</sup> As the pathogenesis of many vaccination-induced adverse effects remain elusive, we report two uncommon presentations associated with VZV reactivation induced by Covid-19 vaccination and propose possible mechanisms

## References

- 1. Ayatollahi A, Hosseini H, Firooz R, Firooz A. COVID-19 vaccines: What dermatologists should know? Dermatol Ther. 2021 Sep;34(5):e150-156.
- Arora P, Sardana K, Mathachan SR, Malhotra P. Herpes zoster after inactivated COVID-19 vaccine: A cutaneous adverse effect of the vaccine. J Cosmet Dermatol. 2021 Nov;20(11):3389-3390.
- Martín-Carrasco P, Pérez-Ruiz C, de Zulueta-Dorado T, Conejo-Mir J. Postherpetic Granulomatous Dermatitis in a Man Treated With Nivolumab. Actas Dermosifiliogr. 2017 Oct;108(8):783-784. English, Spanish.
- McCoy WH 4th, Otchere E, Musiek AC, Anadkat MJ. Granulomatous dermatitis as a
  postherpetic isotopic response in immunocompromised patients: A report of 5 cases. JAAD
  Case Rep. 2018 Sep 14;4(8):752-760.
- 5. Alpalhão M, Filipe P. Herpes Zoster following SARS-CoV-2 vaccination a series of four cases. J Eur Acad Dermatol Venereol. 2021 Nov;35(11):e750-e752.
- Ferenczi K, Rosenberg AS, McCalmont TH, Kwon EJ, Elenitsas R, Somach SC. Herpes zoster granulomatous dermatitis: histopathologic findings in a case series. J Cutan Pathol. 2015 Oct;42(10):739-745.

Legends

Figure 1A & 1B: A large ulcer spanning the right side of face and scalp with a sharp cut-off at the midline emanating sero-sanguinous discharge and surface necrotic crust throughout associated with conjunctival congestion.

Figure 1C & 1D: Multiple violaceous to erythematous coalescing indurated plaques were noted along the scar of previous HZ along V3, C2 & C3 dermatome on the left side of the face.

Figure 1E & 1F: Histopathology shows multiple epithelioid cell granuloma with lymphocyte cuffing in the dermis which were peri-appendageal and peri-neural. (H&E, 10x & 40x)



DTH\_15707\_Figure 1.tiff