Indian J Lepr 2023, 95 : 305-309

http://www.ijl.org.in

Case Report

Chadox1-S/Ncov-19 Vaccine induced Type 1 Lepra Reaction in a Patient of Borderline Lepromatous Leprosy

Savi[1], A Arora[2], G Sharma[3], J Kaur[4]

Received: 05.07.2023 Revised: 24.09.2023 Accepted: 28.09.2023

Leprosy reactions are immunologically mediated acute inflammatory responses which occur in otherwise chronic course of leprosy. There are mainly two types of lepra reactions. Type 1 reaction (T1R) is a delayed type of hypersensitivity reaction characterized by erythematous edematous appearance of pre-existing skin lesions, appearance of new lesions and neuritis. Type 2 reaction (T2R) or erythema nodosum leprosum is an immune complex mediated hypersensitivity reaction characterized by erythematous tender subcutaneous nodules in addition to systemic features. We present here a case report of a 28-year-old male, resident of Bihar who was diagnosed to be suffering from borderline lepromatous leprosy having hypo-esthetic skin lesions on face, forearms, buttocks, and legs with slit skin smear showing acid-fast bacilli and was on Multibacillary Multi Drug Therapy (MB-MDT) for past 7 months. Four months later, patient received first dose of Chadox1-S/Ncov-19 vaccine after which he developed erythema, edema, and pain over pre-existing skin lesions of leprosy in absence of any other systemic features. Again, on receiving second dose of the vaccine after 3 months, he developed similar complaints within 24 hours of vaccination. He was diagnosed as T1R, and both the episodes were managed with systemic corticosteroids and MB-MDT continued. The increase in cellular immunity following vaccination has been postulated as a possible mechanism for the trigger of T1R and few other reports also mention its occurrence following the Chadox1-S/Ncov-19 vaccine.

Keywords : Leprosy, Borderline Lepromatous Leprosy, Type 1 Reaction, Chadox1-S/Ncov-19 Vaccine, COVID vaccine

Introduction

Leprosy is one of the oldest diseases of mankind, caused by *Mycobacterium leprae*, affecting chiefly skin, peripheral nervous system, and eyes. It is established that leprosy reactions are immunologically mediated acute inflammatory responses that occur in otherwise chronic course of leprosy and are of two types. Type 1 reaction (T1R) is Type IV hypersensitivity reaction associated with activation of cellular immunity against *M. leprae* antigenic determinants characterized by erythematous appearance of pre-existing skin lesions with appearance of new lesions. Type 2 reaction (T2R) or erythema nodosum leprosum is type III hypersensitivity reaction characterized by systemic features along with new erythematous subcutaneous tender nodules (Naafs 1994).

[1] Dr. Savi MBBS, Junior Resident
[2] Dr. Astha Arora MD, Senior Resident
[3] Dr. Geeta Sharma MBBS, Junior Resident
[4] Dr. Jasleen Kaur MD, Associate Professor
Department of Dermatology, Government Medical College and Hospital, Sector 32, Chandigarh-160030, India
Corresponding Author: Dr Astha Arora, **Email**: astharora912@gmail.com

COVID19 pandemic has severely affected leprosy control and prevention activities (WHO 2021). Worldwide vaccination against COVID 19, intended to provide protection against severe illness and hospitalization, may in turn trigger Type 2 leprosy reactions.

We present a case of borderline lepromatous leprosy that developed T1R triggered by Chadox1-S/Ncov-19 vaccine.

Case Report

A 28-year-old male patient, resident of Bihar, welder by profession, presented at the Dermatology OPD of Government Medical College Chandigarh with chief complaints of multiple hypopigmented to erythematous plaques over body with decreased sensation over the lesions in the last 1 year which developed redness and swelling 1 day after administration of second dose of Chadox1-S/Ncov-19 vaccine.

There was no history of fever, malaise, joint pains, headache, epistaxis, pain and redness in eyes and other systemic features. There was no history of nausea, vomiting, diarrhea, sore throat, burning micturition, recent surgery, drug intake, or stress. The patient did not give history of difficulty in doing fine movements such as buttoning of shirt, feeling of walking on cotton wool, decreased sensation over distal extremities, fluid-filled blisters at trauma prone areas.

On examination, the patient had multiple lesions over body in asymmetrical distribution. Few lesions were well-defined erythematous edematous round to oval plaques (Fig. 1) and others were well to ill-defined plaques with well-

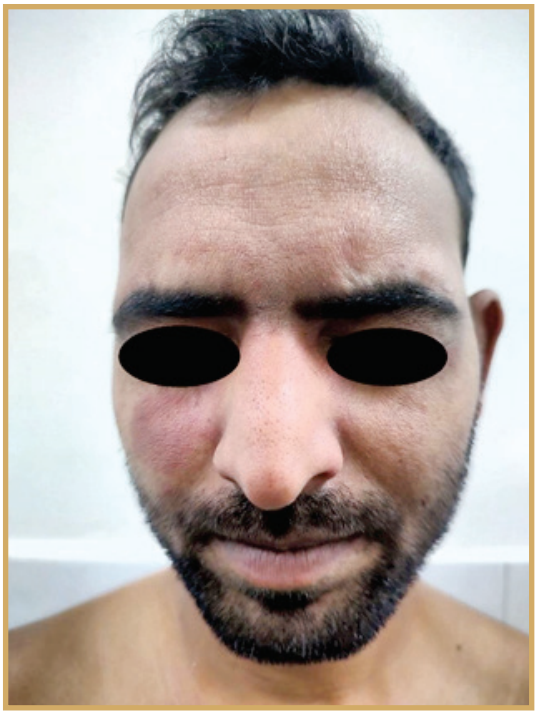

Fig. 1 : Well-defined edematous round to oval plaques on forehead and cheek.

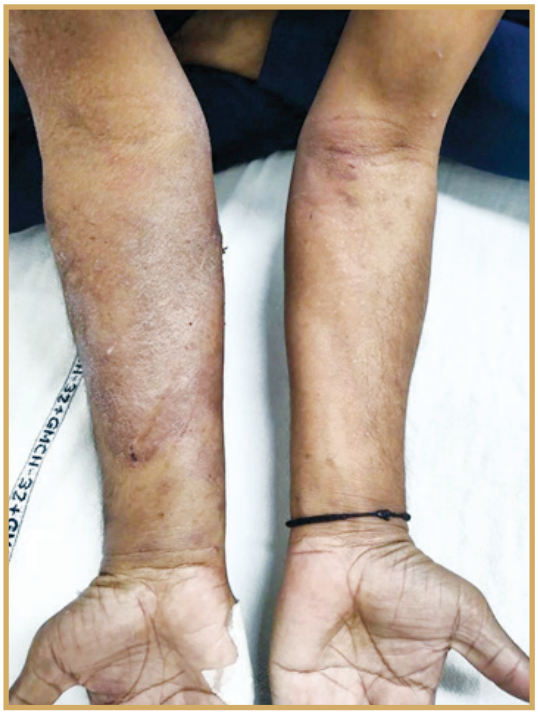

Fig. 2 : Well to ill-defined plaques with well-defined inner and ill-defined outer borders on left forearm.

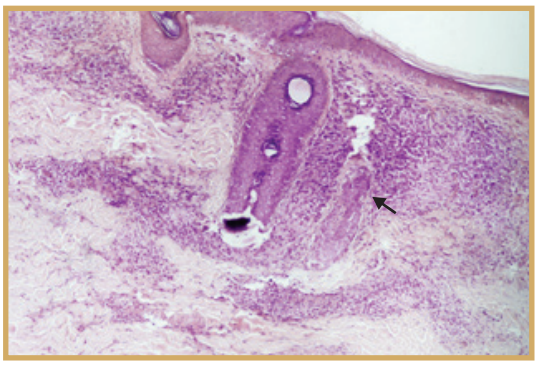

Fig. 3 : Histopathological image showing ill-defined non-caseating epithelioid granulomas (indicated by arrow) with few Langhan cells and prominent lymphocytes with few foamy macrophages in dermis, H&E, 10x.

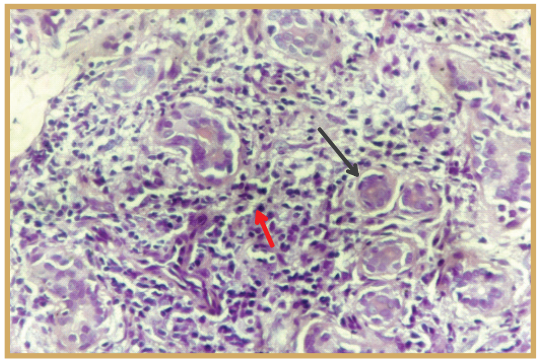

Fig. 4 : Histopathological image highlighting significant findings - Black arrow- giant cells, orange arrow-lymphocytes, H&E 40x.

defined inner and ill-defined outer borders having sloping edges giving inverted saucer appearance and satellite lesions with pseudopods (Fig. 2). The lesions had decreased hair and sweating. Sensation to temperature and fine touch was reduced, whereas sensation to crude touch and pressure was preserved over the lesions. On nerve palpation, ulnar and common peroneal nerves were grossly thickened on both sides with tingling sensation in area of distribution. Tenderness, nodularity and swelling were not present. Motor and cranial nerve function was preserved.

On eliciting past history, patient was on Multibacillary Multi Drug Therapy (MB MDT) for leprosy on as directed under National Leprosy Eradication Programme (including rifampicin, dapsone and clofazimine) since past 7 months. He reported a similar episode of erythema, edema, and pain over pre-existing lesions with edema over hands and feet within 24 hours of first dose of Chadox1-S/Ncov-19 vaccination 3 months back.

Diagnosis of borderline lepromatous leprosy with T1R was made. Slit skin smear showed bacteriological index (BI) as 2+ and morphological index (MI) as 0%.

Biopsy performed from skin lesions showed ill-defined non-caseating epithelioid granulomas comprising of few Langhan cells and prominent lymphocytes with few foamy macrophages in dermis. Perineural fibroblast proliferation showed characteristic onion skinning (Figs. 3 & 4). For the current episode, the patient was treated with oral corticosteroids at 0.5mg/kg/day and tapered according to WHO guidelines and MB-MDT was continued. This episode of T1R resolved in 1-2 weeks of oral corticosteroids which were continued for 8 weeks, and the patient did not experience any other episode of Type 1 reaction while on MB-MDT.

Discussion

Leprosy reactions are distressing complications of disease resulting from host immune response and cause anxiety, discomfort, stigma and financial hardships for patients and their family. The appearance of reactional states may be interpreted as a sign of worsening and may raise doubts about curability of disease to the patient. Repeated episodes of reactions also

affect treatment compliance and may sometimes result in nerve damage leading to deformities/ disabilities.

The pathogenesis and triggers of T1R are not very clear. Roche et al (1991) demonstrated that patients who had positive lepromin reaction and anti-PGL1 (phosphoglycolipid 1) antibodies were at greater risk of lepra reaction. Yamamura et al (1992) demonstrated T helper type-1 (Th1) (Interleukin 1β, Interleukin 2,Tumour necrosis factor α, Interferon γ) cytokines predominance in lesions of T1R, whereas T helper type-2 cytokines were found to be decreased. High levels of TNF-α, IL-2 receptor and adhesion molecules in serology of patients with T1R were demonstrated by Bhattacharya et al (1993) and Parida et al (1992). Studies have also shown increased TNF-α mRNA levels in peripheral nerves and skin of patients in T1R (Khanolkar-Young et al 1995).

Immunohistochemistry analysis shows increased levels of IL-12, TNF-α and oxygen free radicals in T1R which are proinflammatory cytokines of Th1cells. Thereby, it is postulated that T1R are mediated by Th1 cells (Little et al 2001, Kahawita et al 2008). T1R are caused by an increase in cellular immunity; therefore, precipitants may include infections and vaccinations (Nery et al 2013). Antigenic determinants similar to those of *M.leprae* maybe present in Chadox1-S/Ncov-19 vaccine, increased cell mediated immunity against which may trigger T1R. Usually T1R are precipitated after starting MDT, injuries, and puberty, pregnancy, and lactation due to fluctuations in hormonal state (Boggild et al 2004, Ooi & Moschella 2001). The risk factors include borderline group of patients, previous episode of reactions, female gender, older age, large and disseminated patches with multiple nerve involvement (Gupta & Kar 2017).

The ChAdOx1-S/nCoV-19 vaccine is monovalent vaccine, constituted using a single vector recombinant chimpanzee adenovirus, expresses glycoprotein S of SARSCoV-2 (Rebello & Pennini 2021). The other excipients include L-histidine, L-histidine hydrochloride, monohydrate magnesium chloride hexahydrate polysorbate 80, etc. After administration of ChAdOx1-S/nCoV-19 vaccine, SARS-Cov-2 glycoprotein S is expressed locally resulting in stimulation of cellular immune system and neutralizing antibodies along with expression of high levels of TNF-α and IFN-γ. The excipients present in the vaccine may also induce innate immunity. However, the immunologic mechanisms describing the association between vaccines and leprosy reactions have not been fully studied.

The global drive for vaccination against COVID 19 has reduced incidence of serious life-threatening illness, hospitalizations, and death. In leprosy endemic countries such as India, unmasking of leprosy infections, leprosy reaction following vaccination has been reported (Sandre et al 2019). T2R have also been reported following other vaccines, including influenza vaccine (Sandre et al 2019, Bhandari et al 2022). Chadox1-S/Ncov-19 vaccine has local and systemic reactions, however, generally considered safe (Folegatti et al 2020). Although scientific proof is lacking but based on temporality and biological plausibility, it can be hypothesized that T1R may be triggered following Chadox1-S/Ncov-19 vaccination based on increased levels of inflammatory mediators and stimulation of cellular immunity post vaccination. Another possible mechanism could be increase in cell mediated immunity against antigenic determinants of the vaccine. However, this needs to be confirmed at molecular level and in animal models. Leprosy patients should be counseled about the risks and benefits of ChAdOx1-S/nCoV-19 vaccine or other vaccines before being immunized and be kept on regular follow up.

Conclusion

COVID 19 pandemic has affected monitoring and detection of new cases of leprosy. Health care professionals, especially in leprosy endemic countries, need to be aware of the possible risks of reactional states following vaccination for SARS CoV 2.

References

1. Bhandari A, Shilpa, Gupta S et al (2022). Reactions in leprosy cases triggered by COVID-19 vaccination- a cross sectional study from a tertiary care centre in India. *J Eur Acad Dermatol Veneorol.* 10.1111/jdv.18390. doi: 10.1111/dv.18390.
2. Bhattacharya SN, Chattopadhaya D, Saha K (1993). Tumor necrosis factor: status in reactions in leprosy before and after treatment. *Int J Dermatol*. **32:** 436–439.
3. Boggild AK, Keystone JS, Kain KC (2004). Leprosy: a primer for Canadian physicians. *CMAJ*. **170**: 71-78.
4. Folegatti PM, Ewer KJ, Aley PK et al (2020). Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: A preliminary report of a phase 1/2, single-blind, randomized controlled trial. *Lancet*. **396(10249**): 467-478.
5. Gupta R, Kar HK (2017). Management of leprosy reactions. In: IAL Textbook of Leprosy, (Kumar B, Kar HK Eds), Jaypee Digital, New Delhi, Chapter 32, pp 465-477.
6. Kahawita IP, Walker SL, Lockwood DNJ (2008). Leprosy type 1 reactions and erythema nodosum leprosum. *An Bras Dermatol.* **83**: 75–82.
7. Khanolkar-Young S, Rayment N, Brickell PM et al (1995). Tumour necrosis factor-alpha (TNF-alpha) synthesis is associated with the skin and peripheral nerve pathology of leprosy reversal reactions. *Clin Exp Immunol*. **99**: 196–202.
8. Little D, Khanolkar-Young S, Coulthart A et al (2001). Immunohistochemical analysis of cellular infiltrate and gamma interferon, interleukin-12, and inducible nitric oxide synthase expression in leprosy type 1 (reversal) reactions before and during prednisolone treatment. *Infect Immun*. **69**: 3413–3417.
9. Naafs B (1994). Leprosy reactions. *Trop Geogr Med*. **46**: 80–84.
10. Nery JA, Bernardes Filho F, Quintanilha J et al (2013) Understanding the type 1 reactional state for early diagnosis and treatment: a way to avoid disability in leprosy. *An Bras Dermatol*. **88**: 787-792.
11. Ooi WW, Moschella SL (2001). Update on leprosy in immigrants in the United States: status in the year 2000. *Clin Infect Dis.* **32**: 930-937
12. Parida SK, Grau GE, Zaheer SA et al (1992). Serum tumor necrosis factor and interleukin 1 in leprosy and during lepra reactions. *Clin Immunol Immunopathol*. **63**: 23–27.
13. Rebello P, Pennini S (2021). Erythema nodosum leprosum and active leprosy after ChAdOx1-S/nCoV-19 recombinant vaccine. A report of two cases. *Lepr Rev*. **92**: 421-426.
14. Roche PW, Theuvenet WJ, Britton WJ (1991). Risk factors for type-1 reactions in borderline leprosy patients. *Lancet.* **338**: 654–657.
15. Sandre MK, Poenaru SM, Boggild AK (2019). Erythema nodosum leprosum triggered by antecedent influenza vaccine and respiratory tract infection: A case report. *J Cut Med Surg*. **23**: 114-116.
16. World Health Organization (2021), Global leprosy (Hansen disease) update, 2020: Impact of COVID-19 on global leprosy control. *WER.* **No. 36**: 421–444.
17. Yamamura M, Wang XH, Ohmen JD et al (1992). Cytokine patterns of immunologically mediated tissue damage. *J Immunol*. **149**:1470–1475.

How to cite this article : Savi, Arora A, Sharma G et al (2023). Chadox1-S/Ncov-19 Vaccine induced Type 1 Lepra Reaction in a Patient of Borderline Lepromatous Leprosy. *Indian J Lepr.* **95**: 305-309.