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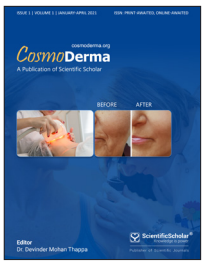

Letter to the Editor

COVID vaccines inciting lepra reaction: An observation in a referral centre

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Dear Sir,

COVID-19 pandemic has put the world in a stand still and, with the current vaccination drive globally to combat the disease, many adverse effects have been reported in the literature. Numerous clinical trials and registry-based studies for COVID vaccines have reported a spectrum of vaccine induced dermatological manifestations, apart from being a trigger of various pre-existing dermatoses.[1-3] However, the literature is scanty in relation to lepra reactions following COVID vaccination.

We came across 14 adult patients with pre-existing Hansen's disease in a background of COVID vaccination, out of which nine cases were in Type 1 lepra reaction and five cases in Type 2 lepra reaction, over a period of 1 year.

We observed 14 patients (10 males and four females) with a mean age of 36.71 years diagnosed earlier with Hansen's disease and presenting to OPD with lepra reaction [Table 1]. Out of the 14 cases, nine patients were borderline tuberculoid leprosy while five were in borderline lepromatous pole of the Ridley-Jopling classification. It was observed that two different types of COVID vaccines were administered to the patients in the study, that is, ten patients had received Covishield (Recombinant ChAdOx1-S) vaccine manufactured by the serum institute of India and four patients were given Covaxin (the whole virion inactivated vaccine NIV-2020-770 strain) by Bharat Biotech, India. The duration between the administration of the vaccine and the onset of leprosy reactions ranged from 4 to 10 days (average being 5.92 days). There was no prior history of any superadded infection, trauma, or any other vaccination other than COVID vaccine in the subjects.

On clinical examination, all the patients in Type 1 lepra reaction had erythema and edema over the pre-existing leprosy patch with seven patients having ulnar neuritis (77.7%) and four patients with neuritis of common peroneal nerve (44.44%). The patients in Type 2 lepra reaction presented with erythema nodosum leprosum (ENL) lesions associated with constitutional symptoms such as fever, myalgia, and arthralgia. No nerve abscess, deformity, or systemic involvement was seen in any of the cases.

Along with MDT, all the cases were treated with tapering doses oral prednisolone (0.5–0.75 mg/kg) and two cases of ENL were given thalidomide at tapering doses. Each patient had a stable course of disease and were counseled not to defer the next vaccination.

Saraswat *et al.* recently published a series of four cases in lepra reaction (three in Type 1 lepra reaction and one in Type 2 lepra reaction) 5–11 days following COVID vaccination with Covishield (three cases) and Covaxin vaccine. They were treated with tapering doses of

prednisolone and thalidomide (in Type 2 lepra reaction). They stated that CXCL10 and IL-6 along with cortisone-cortisol shuttle enzymes are potential laboratory markers of Type 1 lepra reactions, and IL-17 and platelet-derived growth factor BB are for Type 2 lepra reactions and further suggested large scale studies to understand versatility of clinical presentation of lepra reactions following COVID-19 vaccination and its exact pathogenesis.[4]

Panda *et al.* reported a case of Type 2 lepra reaction after COVID vaccination with a proposed hypothesis of increased neutrophil to lymphocyte ratio and a change in neutrophil counts in peripheral blood and tissues which may be closely associated with pathological injury in COVID-19 patients triggering lepra reactions following COVID-19 vaccination.[5]

Rebello and Pennini reported two cases of Hansen's disease that were released from treatment since variable months. They developed ENL lesions 2–3 days following the first dose of the ChAdOx1-S/nCoV-19 vaccine and were managed with thalidomide (100 mg/day). It was discussed that the SARS-CoV-2 glycoprotein S is expressed locally by stimulating the cellular immune system, with high levels of tumour necrosis factor (TNF-α) and interferon (IFN)-γ which are also the main mediators for ENL.[6]

Bhandari *et al.* surveyed 35 patients with leprosy visiting leprosy clinic from July 2021 to December 2021. All the patients had received the Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine. Twenty-one of 35 patients (60%) had received two doses. Two of them developed ENL, and one developed Type 1 lepra reaction shortly after receiving the

Table 1: Patient profile of lepra reaction triggered by COVID vaccination.

Patient no.	Age/sex	Hansen's spectrum	Duration of MDT	Reaction type	Vaccination history	Avg duration of onset of lesions	Treatment
1	37 yr/M	Borderline tuberculoid	6 months	Type 1	Covishield- 1st dose	5 days	Prednisolone (40 mg/day) tapered in 3 weeks
2	45 yr/M	Borderline tuberculoid	8 months	Type 1	Covaxin- 1st dose	4 days	Prednisolone (30 mg/day) tapered in 3 weeks
3	30 yr/F	Borderline tuberculoid	4 months	Type 1	Covishield- 1st dose	5 days	Prednisolone (30 mg/day) tapered in 4 weeks
4	32 yr/M	Borderline tuberculoid	7 months	Type 1	Coviaxin- 2nd dose	6 days	Prednisolone (30 mg/day) tapered in 3 weeks
5	44 yr/M	Borderline lepromatous	6 months	Type 2	Covishield- 2st dose	4 days	Prednisolone (30 mg/day) tapered in 4 weeks with Thalidomide 300mg in divided doses for 6 weeks and then tapered
6	34 yr/F	Borderline lepromatous	4 months	Type 2	Covishield- 1st dose	4 days	Prednisolone (40 mg/day) tapered in 3 weeks
7	33 yr/M	Borderline tuberculoid	3 months	Type 1	Covishield- 1st dose	6 days	Prednisolone (30 mg/day) tapered in 3 weeks
8	36yr/F	Borderline tuberculoid	4 months	Type 1	Covaxin- 2nd dose	5 days	Prednisolone (30 mg/day) tapered in 3 weeks
9	40 yr/F	Borderline tuberculoid	5 months	Type 1	Covishield- 1st dose	7 days	Prednisolone (30 mg/day) tapered in 3 weeks
10	38yr/M	Borderline lepromatous	2 months	Type 2	Covishield- 2nd dose	6 days	Prednisolone (40 mg/day) tapered in 3 weeks
11	42 yr/M	Borderline tuberculoid	5 months	Type 1	Covishield- 1st dose	4 days	Prednisolone (30 mg/day) tapered in 3 weeks
12	46 yr/M	Borderline lepromatous	3 months	Type 2	Covaxin- 2nd dose	8 days	Prednisolone (30 mg/day) tapered in 3 weeks Thalidomide 300mg in divided doses for 6 weeks and then tapered
13	30 yr/M	Borderline lepromatous	2 months	Type 2	Covishield- 1st dose	6 days	Prednisolone (40 mg/day) tapered in 3 weeks
14	43 yr/M	Borderline tuberculoid	5 months	Type 1	Covishield- 1st dose	9 days	Prednisolone (30 mg/day) tapered in 3 weeks

first dose of the vaccine. All the three patients were managed by tapering doses of oral prednisolone.[7] The triggered reaction could be explained by the high immune alteration and SARS-CoV-2 spike-specific effector T-cell response with first dose of the adenovirus-vectored ChAdOx1 nCoV-19 vaccine beginning by day 7 and maximizing by day 14.[8]

COVID-19 vaccines also causes inflammatory cascade through neutrophilia and increased Th1 T cell responses (due to increased TNF-α and IFN-γ production by CD4+T cells) leading to raised cell-mediated immunity toward leprosy bacilli, thereby possibly causing both spectrum of lepra reactions.[9]

The IADVL Special Interest Group on leprosy have recommended safe use of oral prednisolone, methotrexate, minocycline, pentoxifylline, colchicine in supervised doses in the management of lepra reactions in the context of COVID pandemic with consistent re-evaluation.[10]

COVID infection as well as vaccination has been reported to induce or exacerbate lepra reactions. Our observation reflects COVID vaccination as a triggering event for initiation of lepra reaction. However, COVID vaccination did not have any deleterious effect on the course of disease *per se*, mortality rate, or the outcome of treatment for lepra reactions. We have treated all the patients with the minimum therapeutic dose of steroids and thalidomide. Fluctuation of the immunological pole of Hansen's disease was not observed in any of the subjects during follow-up visits.

We present this observation of lepra reactions in which all the patients had a triggering factor of COVID-19 vaccination for reaction. Each patient had a stable course during the reaction and were being treated promptly once the features of lepra reaction were seen. No major complications were observed during the treatment and in follow-up visits.

Hence, we conclude that both Type 1 and 2 lepra reactions may be triggered by COVID vaccination however that does not invalidate vaccine's safety or efficacy. Further large scale studies are needed to understand versatility of clinical presentation of leprosy reactions following COVID-19 vaccination and its exact pathogenesis.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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