

Non-infective granulomatous dermatitis following *Mycobacterium w* injections

Sir,

The recent COVID-19 infection caused a worldwide pandemic, the effects of which have not still subsided even after the development of vaccines, due to various mutations in the virus. Coronaviruses are enveloped non-segmental positive-sense RNA viruses, belonging to the *Coronaviridae* family and *Nidovirales* order. COVID-19 infection causes mild to severe respiratory illness. A severe acute respiratory syndrome due to this infection results in critical illness with intensive care unit admission and mortality.¹ Several measures were tried to revive such patients, one of which was the administration of *Mycobacterium w* injections. We report a case presenting as an exaggerated local side effect of this vaccine.

A 45-year-old woman presented with multiple asymptomatic lesions on the abdomen and both upper arms for six weeks. She had taken several antibiotics without any benefit. There was a history of intensive care unit admission two months back for severe COVID-19 infection. On enquiry, she revealed that she was given certain injections at the site of lesions during

her hospital stay. As per her discharge summary, it was found that these were *Mycobacterium w* injections. On cutaneous examination, there were multiple non-tender, erythematous ulcerated plaques, with some oozing and crusting on the surface. They were distributed mainly on the abdomen and both upper arms [Figure 1]. A provisional diagnosis of atypical mycobacterial infection, deep fungal infection and ecthyma were considered. Skin biopsy revealed granulomatous dermatitis with tuberculoid granulomas in the upper reticular dermis and suppurative granulomas in the lower reticular dermis [Figures 2 to 4] Specials stains like periodic acid-Schiff, Ziehl-Neelsen stain and Fite stain did not demonstrate any organisms. She denied a second biopsy for culture study. A diagnosis of non-infective granulomatous dermatitis was given based on the histopathology features and side effects mentioned in the literature.² She was started on 20 mg prednisolone and the lesions subsided within one month leaving behind post-inflammatory scarring [Figure 5]. She is on regular follow up with no recurrence. *Mycobacterium w* or *Mycobacterium indicus pranii* injections are immunomodulatory injections which contain heat-killed organism and it is given intradermally at three different sites daily for three days in 0.1 mL dose to



Figure 1: Multiple erythematous ulcerated plaques, few showing crusts on surface at injection sites

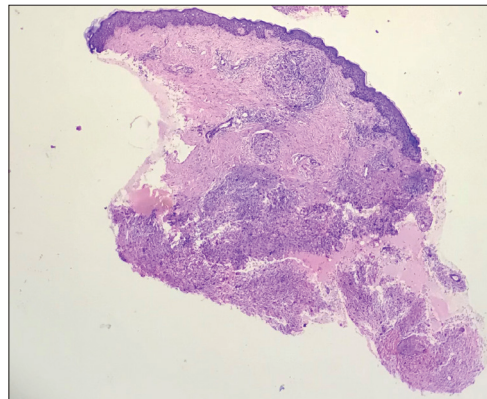


Figure 2: Tuberculoid and suppurative granulomatous dermatitis (H&E ×40)

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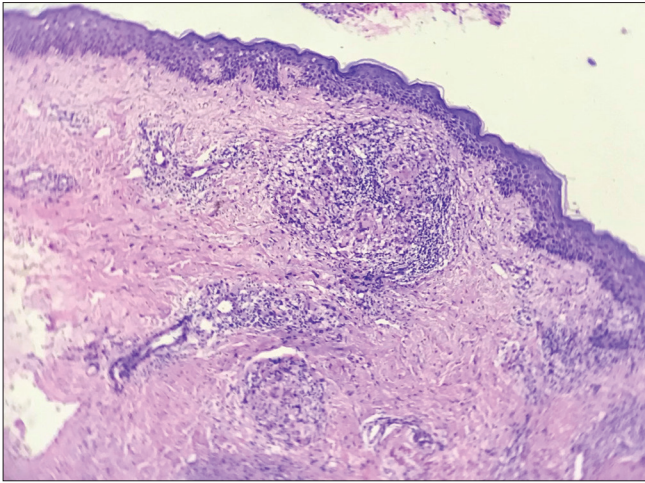


Figure 3: Tuberculoid granuloma in upper dermis (H&E ×100)

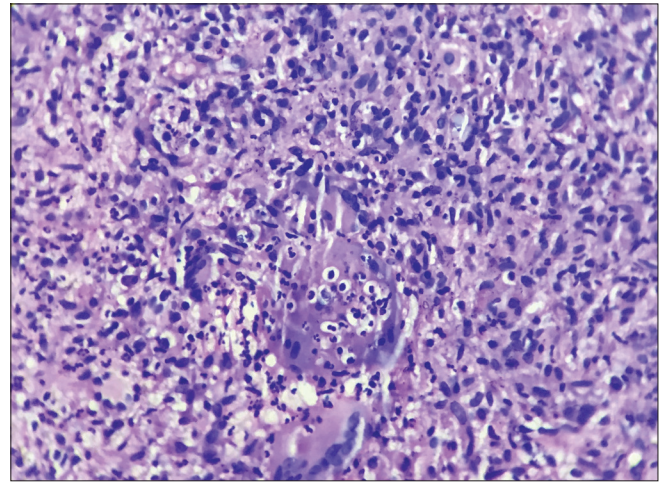


Figure 4: Suppurative granuloma in lower dermis (H&E ×400)



Figure 5: Lesions healing with treatment

severely ill patients with gram-negative sepsis admitted in the intensive care unit. Other indications include lepromin-negative leprosy and non-small cell lung cancer patients along with paclitaxel and cisplatin regimens.

At the advent of the second wave, *Mycobacterium w* injections were given to severely ill COVID-19 infected patients admitted to the intensive care unit. This was in accordance with the guidelines laid down by the Global Research Collaboration for Infectious Disease Preparedness and the World Health Organization, which suggested that adjuvant therapy is one of the methods to save patients infected with severe COVID-19 infection.² Mechanism of action of *Mycobacterium w* vaccine as studied in leprosy was via toll-like receptors, thus enhancing the host T cell responses. It is known to be safe and well-tolerated in gram-negative sepsis and the recent report also suggests the same for severe COVID-19 infection.³

Ingale *et al.* in their study on the use of *Mycobacterium w* vaccine for severely ill COVID-19 patients, reported local site reaction in 85.4% of patients, out of which the majority (54%) were mild and a few (14%) were severe. It comprised erythema and induration, followed by pustule formation and

ulceration which healed by scarring. Mild reactions did not require any major treatment, however severe reactions required oral anti-inflammatory agents and topical steroids.³

Injection site granulomatous reaction to immunotherapeutic agents like interferons⁴ and vaccines⁵⁻⁷ is a known phenomenon. The usual injection site side effect of *Mycobacterium w* vaccine is the formation of asymptomatic papule/plaque or tender nodule which later ulcerates and heals with atrophic scarring. Khullar *et al.* have reported a generalised granulomatous dermatitis in two of their lepromatous leprosy patients with *Mycobacterium w* vaccine. In their cases, the lesions were seen distant to the injection site, with the persistence of ulceration. They hypothesise that the generalised lesions could be a manifestation of haematogenous spread or strong delayed-type hypersensitivity to *Mycobacterium w* antigens⁶. Sharma *et al.* in their study evaluating the safety and efficacy of usage of *Mycobacterium w* vaccine as adjunctive therapy in category 2 pulmonary tuberculosis reported injection site reaction in 82.4% of the patients. About 68% of the patients experienced a mild intensity of the reaction whereas 12.9% had moderate to severe reaction at the local site. These reactions healed spontaneously, without active treatment.⁷

In our case, typical history, characteristic clinical features, no organisms found on special staining and response to anti-inflammatory agents clinched the diagnosis. There are relatively fewer reports in the literature demonstrating the histopathology features of this side effect when *Mycobacterium w* vaccine was used as adjunctive therapy in COVID-19 patients. Our purpose of reporting this case was to create awareness among the dermatologists and pathologists about the local side effects of these injections and to avoid unnecessary treatment with multiple antibiotics.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflict of interest

There are no conflicts of interest.

Chirag Desai, Shalu Gala¹

Divya Sparsh Skin and Hair Clinic, Dadar, ¹Dr. Shalu Gala Skin, Hair & Cosmetology Clinic, Mumbai, Maharashtra, India.

Corresponding author:

Dr. Chirag Desai,
Dadar, B21, Krishnalaya Society, 6th Floor, N.S.Mankikar Marg,
Chunabhathi-west, Mumbai, Maharashtra, India.
chirag@gmail.com

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Mercury-induced cutaneous poisoning with generalised erythema and pruritic blister

Sir,

A 73-year-old woman presented with a three-month history of generalised erythema and scattered blisters. These were accompanied by pruritus, oral ulcers, vulval mucosal erosions, swelling of lower limbs, loss of appetite, insomnia and apathy. Three months ago, she was diagnosed with toxic epidermal necrolysis in another hospital and treated with 40 mg of methylprednisolone per day for two weeks. There was partial improvement followed by a rapid flare after withdrawing methylprednisolone. On further questioning, the patient reported that she had been taking compounded pills from a local clinic for chronic urticaria since four months.

Physical examination revealed erythema and pigmentation in a livedoid pattern on the torso, arms and legs [Figure 1a], with clear, flaccid blisters on the chest and abdomen [Figure 1b]. Nikolsky sign was negative. There were erosions on the lips, gingivae and vulva [Figures 1c and d] with swelling of the lower limbs. A skin biopsy demonstrated lichenoid tissue reaction with a subepidermal blister accompanied by a mixed-cell infiltrate in the superficial dermis [Figures 2a and b]. Direct immunofluorescence showed a granular deposit of IgG, IgA and C3 at the dermo-epidermal junction [Figure 3]

and indirect immunofluorescence to BP180, BP230, DSG1 and DSG3 was negative. Anti-nuclear antibody was positive (1:320) while other autoimmune antibodies were all negative. Results of other routine laboratory investigations were unremarkable.

Patient showed poor response to oral methylprednisolone administered with a diagnosis of suspected lichenoid eruption. The real etiology remained hidden until we found occasional mercury beads within her homemade pill [Figure 4]. Urine mercury concentration was 62 µg/L (normal range <10 µg/L) which confirmed mercury toxicity. Methylprednisolone was discontinued and patient was administered 3 intramuscular injections of 2,3-dimercaptopropane sulfonate (5 mg/kg) to chelate the mercury.¹ She was told to stop taking the homemade pills which led to normalization of the concentration of mercury in urine. At the two-month follow-up, the bullae and ulcers had nearly resolved with post-inflammatory hyperpigmentation.

Mercury poisoning, can present with multi-organ systemic involvement such as neural, renal, gastrointestinal and skin. Mercury in all forms is toxic to the body and clinical

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