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Case Report

Reversal reaction in a borderline lepromatous leprosy patient after COVID-19 vaccine: Prevention or risks?

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Abstract Reversal reaction in leprosy is an immunologically mediated response due to alteration of cell-mediated immunity associated in leprosy spectrum. In COVID-19 pandemic era, leprosy patient is susceptible to the infection. According to guideline, vaccination should be given to leprosy patients. This case reported a 33-year-old male with reversal reaction after COVID-19 vaccination. On examination, patient had erythematous plaque of the face, trunk and extremities, also multiple ulcers of the trunk and extremities. Treatment was commenced immediately with prednisone and second vaccination was delayed. Within our follow-up, marked improvement were obtained after 6 weeks.

Key words
Reversal reaction, borderline lepromatous leprosy.

Introduction

Leprosy is a chronic infection, included in Neglected Tropical Diseases (NTD) caused by *Mycobacyterium leprae*, primarily affecting peripheral nerves and skin.[1,2] For centuries, leprosy remains a major public health problem in many developing countries, including Indonesia which was reported to be the third highest number of new cases each year. Reversal reaction is a delayed hypersensitivity reaction, occurs in borderline patients related to changes in cellular immune response.[1] In the COVID-19 pandemic era, an increasing trend of multibacillary cases seems to be reported, signalling a serious effect of the pandemic on leprosy control.[3] Along with COVID-19 spread, leprosy patient will also receive COVID-19 vaccination according to the guideline.[4,5]

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Case report

A 33-year-old male was admitted in the Department of Dermatology and Venereology, with chief complaint of erythematous plaque, numbness and swelling of the face, trunk, upper and lower extremities in the past 2 weeks ago.

He exhibited these symptoms, in combination with fever and arthralgia, approximately 2 weeks after receiving the first dose of the COVID-19 vaccination. He was a diagnosed case of borderline lepromatous leprosy and treated with routine multibacillary (MB) multidrug therapy (MDT) regimens for 6 months. Prior to vaccine, there were no r noticeable signs or symptoms.

Physical examination showed/revealed diffuse infiltrates and edema in both ear lobes, erythematous plaque and edema of the face, trunk and both upper and lower extremities, concomitant with multiple ulcers covered with crusts over trunk and lower extremities (**Figure 1 and 2**). Greater auricular nerve and peroneal

Figure 1 Ear edema and infiltration.

nerve were thickened. Nerve pain and tenderness were also present in the examination. Impaired sensory function of touch, pain and temperature in lesions were observed.

Slit skin smear from the lesions showed increased bacterial index (BI) compared to the previous result. Nevertheless, skin biopsy was not obtained in this patient.

According to our findings, patient's clinical manifestation, physical examination and slit skin smear concordant with severe reversal reaction in leprosy. As he received COVID-19 vaccine approximately 14 days prior to the reaction with no other possible cause, thus vaccination can be considered as the triggering factor.

Finally, patient treated with routine MDT MB, in combination with prednisone 40 mg daily subsequently tapered off every 2 weeks, and other symptomatic medication. Skin lesions was improved visibly along with nerve tenderness or pain after 6 weeks of treatment (**Figure 3**).

Figure 2. Erythematous plaque and edema of the face, trunk and both upper and lower extremities; multiple ulcers covered with crusts of trunk and lower extremities.

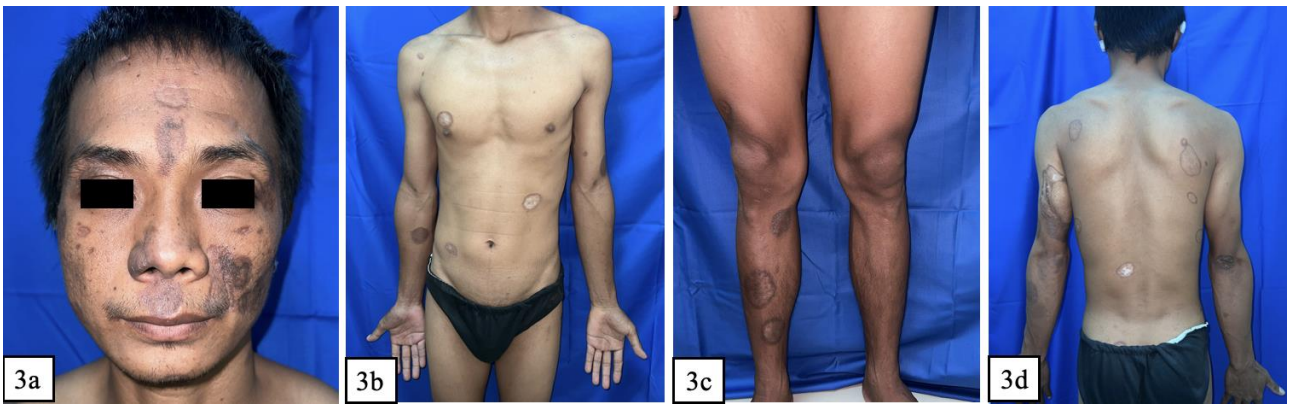

Figure 3 Hyperpigmentation macules and plaque of the face, trunk and both upper and lower extremities.

Discussion

Reversal reaction or type 1 reaction in leprosy is considered as delayed type hypersensitivity reaction mediated by reaction of T helper 1 (Th1) cells to mycobacterial antigens. It occurs in borderline patients, associated with patient's cellular immunity.[1,6] At the end of 2020, according to epidemiological report by World Health Organization (WHO) showed a 37.1% reduction in new cases compared with 2019. Conversely, the drop in total new cases were not coherent with an increasing trend in MB new cases,[7,8] This presumed an indication of more infective cases had been detected and highlights the possibility of possibility of health seeking behaviour disruption rather than true reduction in cases.[2,8] In the context of COVID-19 pandemic era, leprosy patient are vulnerable to the infection.[5,9] Therefore, according to the guideline, all measures implemented to contain the COVID-19 infection was made including vaccination.[10]

Type 1 reactions are caused by an alteration in cellular immunity, thus eliciting factors may include MDT use, infection and vaccination.[6,11,12] Patient received Sinovac-CoronaVac vaccine, which is a cell-based, aluminium hydroxide-adjuvanted, β-propiolactone-inactivated vaccine against SARS-CoV-2 virus.[13] Vaccine contain a pathogen-specific immunogen, which can trigger innate immune system and T cell activation. Vaccination may induce production of neutralizing antibodies for months.[10,14,15] In addition, other study using ELISpot analysis proved vaccine can stimulate cellular responses against SARS-CoV-2 spike protein, caused an increase in interferon gamma (IFN-γ) and Granzyme-B-producing cells.[14]This reaction are associated with activation of cytokines derived from Th1 cells including interleukin-1β (IL-1β), tumor necrosis factor-alpha (TNF-α), interleukin-2 (IL-2), and IFN-γ.[6,12] Increase in cytokines such as TNF-α, IFN-γ, ILβ, IL-6, IL-8, and Granzyme B-producing cells play an important role to reversal reaction after vaccination as reported previously.[14] Therefore, it seems that these pro-inflammatory cytokines stimulated by COVID-19 vaccine can also worsen the clinical manifestation related to pre-existing leprosy infection.[2,4,16] Aponso *et al*. from Singapore also reported similar case in a 24-year old Indian man who was diagnosed with reversal reaction, unmasked in 10-15 days after COVID-19 vaccination.[4]

Clinical manifestation in this patient was in accordance to severe reversal reaction as characterized by the involvement of pre-existing and new inflamed skin lesions, nerve pain and tenderness, erythematous plaque with swelling of the face, also multiple ulcers of the trunk and extremities.

The treatment commenced as soon as possible to reduce the complication. According to guideline for severe reversal reaction, prednisone 40 mg daily was given with 1-2 weeks tapering off.[12] Successful treatment is achieved after 6 weeks of therapy, yet the prednisone was still maintained at 5 mg until 12th week. No other complication was noted in this patient.

Conclusion

Reversal reaction occurs with an increase in cell-mediated (Type IV) immune response, which can be triggered by several factors, including vaccination as reported in this case. Activation of Th1 and increased expression of pro-inflammatory cytokines such as TNF-α, IFN-γ, ILβ, IL-6 play a prominent role in stimulating reversal reaction. Therefore, the upregulation of T-cell mediated immune response caused by COVID-19 vaccine may elicit type 1 leprosy reaction.

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