COVID Arm After Moderna Booster in Healthcare Worker: A Case Report

Anshari Saifuddin[1], Sukamto Koesnoe[1], Nia Kurniati[2], Sondang Sirait[3], Riesye Arisanty[4], Evy Yunihastuti[1]*

[1] Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[2] Division of Allergy and Clinical Immunology, Department of Child Health, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[3] Department of Dermatovenereology, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[4] Department of Pathology and Anatomy, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Corresponding Author:
Sukamto Koesnoe, MD, PhD. Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Diponegoro no.71, Jakarta 10430, Indonesia. Email: sukamtokoesnoe@gmail.com.

ABSTRAK

Virus SARS CoV-2 telah menginfeksi lebih dari 200 juta orang di seluruh dunia dan lebih 4,4 juta orang di Indonesia. Program vaksinasi menjadi salah satu solusi yang dicanangkan oleh berbagai negara di dunia, termasuk di Indonesia, untuk mengurangi laju transmisi COVID-19. Platform vaksinasi yang diproduksi bermacam-macam, seperti inactivated, viral vector, mRNA dan protein subunit. Program vaksinasi booster dengan platform mRNA (Moderna) direncanakan oleh pemerintah Indonesia untuk melindungi tenaga kesehatan lebih lanjut dari infeksi COVID-19 khususnya varian delta. Pada tulisan ini, kami membahas mengenai salah satu efek samping yang khas didapatkan dari vaksin Moderna, yang disebut sebagai COVID arm.

Kata kunci: *COVID arm, COVID-19, booster, Moderna, vaksinasi, tenaga kesehatan.*

ABSTRACT

SARS CoV-2 virus has infected more than 200 million people worldwide and more than 4.4 million in Indonesia. The vaccination program has become one of the solutions launched by many countries globally, including Indonesia, to reduce the transmission rate of COVID-19. Various vaccination platforms are produced, such as inactivated, viral vector, mRNA, and protein subunit. The vaccination booster program with mRNA platform (Moderna) was launched by the Indonesian government to give better protection for health care workers, particularly from delta variant. In this case report, we discuss one of the typical side effects of Moderna vaccine, which is referred to as the COVID arm.

Keywords: *COVID arm, COVID-19, booster, Moderna, vaccination, healthcare worker.*

INTRODUCTION

SARS CoV-2/ Coronavirus disease 2019 (COVID-19) has been declared a pandemic by WHO since March 2020. As of August 25th 2021, more than 214 million positive cases had been reported worldwide, with more than 4.4 million deaths.[1] There are more than 4 million confirmed cases in Indonesia, with 128 thousand deaths.[2] Many countries compete to develop vaccines in order to reduce the SARS-CoV-2 transmission rate. Indonesia launched the COVID-19 vaccination program to approximately 180 million populations in February 2021. Healthcare workers and first responders are among the first to get vaccinated, which reached approximately 1.7 million people.[3] The vaccine schedule was two doses of inactivated vaccine (CoronaVac) 2 weeks apart. In July 2020, the emergence of the second wave, the majority caused by the new delta variant, raises concern, especially for healthcare workers. The mortality rate of doctors and other healthcare workers significantly increased on the second wave. It raised the idea to give a booster vaccination with an mRNA vaccine platform (Moderna).[4] Side effects that arise after Moderna vaccination are varied, similar to other vaccine platforms. Mild side effects are common, either local or systemic. However, from many studies, Moderna has more severe local side effects than other platforms, referred to as the COVID arm. We will report a COVID arm case manifested early after receiving the booster.

CASE ILLUSTRATION

A 56 years old doctor complained that her left arm had become red, swollen, and tender post-vaccination with Moderna. She received two doses of CoronaVac vaccine four months before without any side effects. The Moderna shot was given in the evening. During the night, she suffered from pain at the site of the injection. The pain disturbed her when she laid on the left side and needed one paracetamol tablet to reduce the pain. The following morning, her temperature increased to 40.2°C. She took another tablet of paracetamol, and a few hours later, the temperature dropped to 38.9°C. She took paracetamol every four hours for the next 48 hours, with temperatures ranging between 38.6 – 39.2°C. Hence, making the patient stay home and miss work. She started to feel her left arm becoming more redd and swollen. On the 3rd day, the fever broke, but she still felt lethargic. RT-PCR SARS-CoV-2 on the nasopharyngeal swab was negative. The upper arm started to swell, redness, and warm to the touch. Her range of motion was reduced due to pain (VAS 3-4). Within the next two days, the swelling extended to the upper part of the lower arm, and she used surface cooling to reduce the symptoms. On the 6th-day post-vaccination, the swelling, redness, and pain were decreased, although the lower part of the upper arm and around the elbow still showed inflammation signs. The next day she used compression stocking to reduce the symptoms further. The symptoms disappeared after the 8th-day post-vaccination. She has a history of breast cancer in 2017 and underwent radical mastectomy on the right mammae. She took tamoxifen 20 mg OD routinely. She has an atopic history in the form of eczema and allergic rhinitis. She also had a thalassemia trait which had not been evaluated for a long time.

A skin biopsy was done to get a proper diagnosis. Histological appearance in the epidermis was mild focal spongiosis with a scattered vacuolar alteration. Histological appearance in the dermis was mild inflammatory infiltrate perivascular on superficial plexus, periadnexal, deep plexus, and subcutaneous fat, consisting of lymphocytes and some histiocytes with few intravascular neutrophils. Eosinophils are not present. No sign of vascular wall damage. The biopsy result is consistent with delayed-type hypersensitivity that can be found in vaccine reactions.

DISCUSSION

COVID arm is one of the side effects that rarely occurs after the administration of the Moderna vaccine. Symptoms usually are swelling, redness, pain, warmth, and pruritus at the location of vaccine injection. COVID arm is used to explain the delayed-type hypersensitivity reaction that occurs approximately one week after using COVID-19 mRNA type vaccine.

In one study of COVID mRNA type vaccine,

persons who received the second dose had a higher incidence of erythema than when receiving the first dose. Participants that used Pfizer-Biontech got erythema at the injection site as much as 4.6% after the first dose and 6.5% after the second dose within seven days. Participants who used Moderna reported moderate to severe degree of erythema: 3.1% after the first dose and 11.9% after the second dose within seven days.[6]

In the third phase clinical trial of Moderna report, the most common local side effect post-vaccination was pain at the injection site. Delayed type reactions at the injection site (with onset in the 8th day or later) were experienced by 244 subjects (0.8%) after the first dose and 68 subjects (0.2%) after the second dose from the total of 30,420 subjects. The reactions were marked by erythema, induration, and pain that usually improved spontaneously within 4-5 days.[7]

In this case, the patient had signs of COVID arm in the form of an erythema, swollen, and pain at the injection site appeared three days post-vaccination. The symptoms of swelling, pain, and erythema began to improve spontaneously on the 4th day after the onset. She only took paracetamol for a few days post-vaccination because of the fever that arose. She did not take any antibiotics. The description of the disease course and the symptom was matched with the COVID arm. Skin biopsy result confirmed COVID arm diagnosis. As reported in previous studies, generally COVID arm appeared approximately one week after the administration of Moderna vaccine.[5,7] In this case, the onset of symptoms was relatively fast compared to COVID arm cases in general. Whether it was related to the patient's history of receiving two doses of inactivated vaccine still needs to be investigated.

With current evidence, it is still unknown how many people are experiencing the delayed-type hypersensitivity due to COVID arm after the first dose and whether they have the same reaction or are even more severe after the second dose.[7] In one study, patients who had symptoms after the second dose experienced symptoms with faster onset than the first dose (1-3 days). Six patients did not experience recurrence of severe reaction as they have experienced at the first dose. In comparison, three patients experienced the same reaction as the first dose, and three patients experienced a lighter reaction than the first dose.[8]

A delayed-type hypersensitivity reaction mediated by T cell occurred due to a reaction to the vaccine component. The reaction will be self-resolving, which will not extend systemically and will not be a contraindication for the next vaccination in the future.[9,10] Reactions reported are against substances such as thimerosal, neomycin, aluminum, but there is no composition from those substances contained in the Moderna or Pfizer vaccine.[11,12] Pfizer and Moderna have polyethylene glycol (PEG2000). Both vaccines also have salt, sugar, acid, and acid stabilizer[13] PEG2000 was the only ingredient in these vaccines that previously known to cause delayed-type hypersensitivity reaction. Further studies are needed to prove that PEG2000 plays a role in the occurrence of the COVID arm.[14]

Local skin reactions after vaccination, especially if accompanied by systemic symptoms, are often incorrectly interpreted as cellulitis. Differences between the COVID arm with cellulitis are following. First, pruritus that is commonly found in the COVID arm usually occurs within a week after vaccination. Second, the symptoms improved spontaneously within 4-5 days and responded well using topical steroids or oral antihistamines.[5]

Halperin, et al.[15] define the diagnosis criteria to differentiate between cellulitis and local reaction post-vaccination. Criteria for cellulitis is a reaction in the injection site with at least 3 of these symptoms: local pain, erythema, induration/swelling, and warmth. The median time from onset of cellulitis is approximately five days post-vaccination compared to delayed-type hypersensitivity reaction that occurs in 7 days or more post-vaccination. In addition to that, the role of bacteria in cellulitis, such as *Staphylococcus aureus* or *Group A Beta Hemolytic Streptococcus* could be found from the injection site. The antibiotic response is one of distinction. If the patient has cellulitis and is not given antibiotics, it could cause the formation of an abscess. While in local reaction post-vaccination, the symptoms will improve

spontaneously.[16]

The growing population that got COVID-19 vaccines, particularly mRNA platforms, will increase COVID arm cases that consulted to primary care doctors. Primary care doctors should be able to distinguish between the delayed-type hypersensitivity reaction post-vaccination with other differential diagnoses, including cellulitis. In the United States, misdiagnosed cellulitis causing 50,000 – 130,000

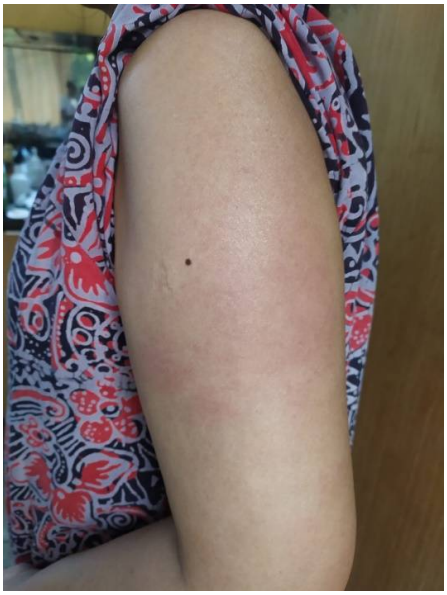

Figure 1. Clinical picture from patient's left arm, 4 days after vaccination.

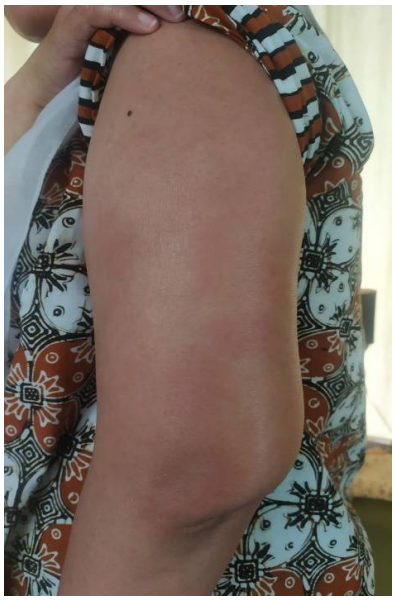

Figure 2. Clinical picture from patient's left arm, 5 days after vaccination.

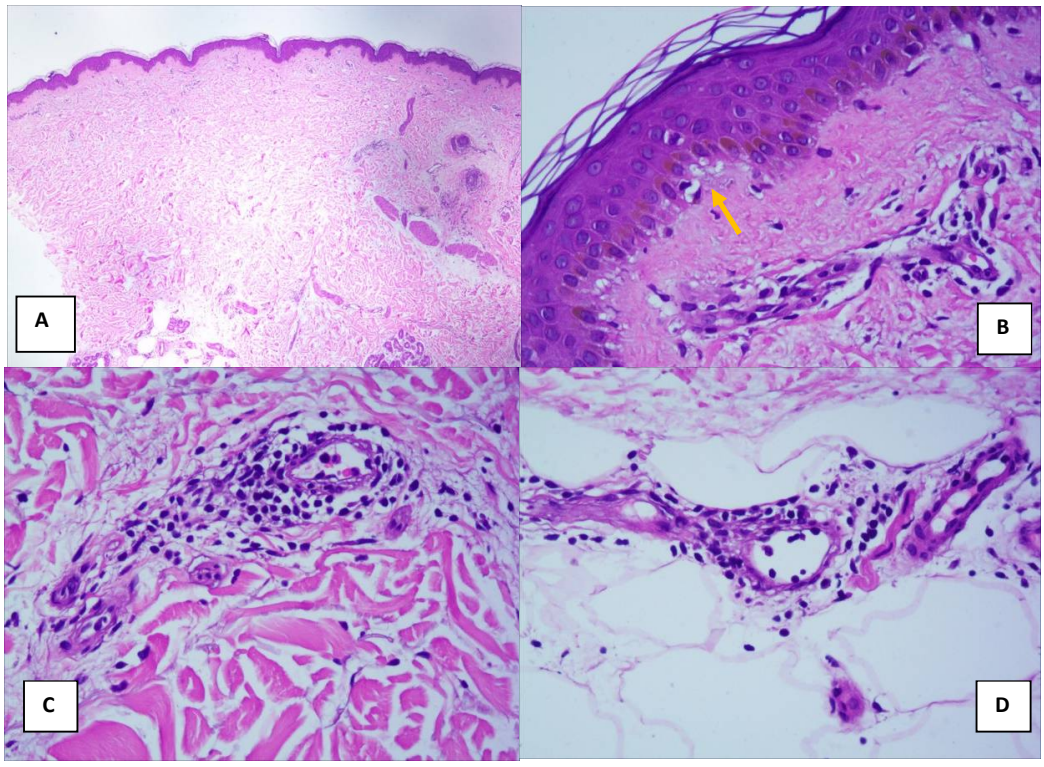

Figure 3. A). Skin biopsy result (100x magnification). B). Vacuolar degeneration in epidermis (400x magnification). C). Mid dermis (400x magnification). D). Subcutaneous (400x magnification).

individuals hospitalized and 195-515 million dollars spent every year[17] In addition, the use of antibiotics in misdiagnosed cellulitis cases could cause increased risk to antibiotic resistance and related to 9,000 nosocomial infection cases every year in the United States.[16]

CONCLUSION

COVID arm is one of the adverse events that can occur after Moderna vaccination. This side effect is self-resolving. Clinicians should be able to differentiate the COVID arm from other differential diagnoses, such as cellulitis. It is essential to give appropriate and effective treatment to the patients.

REFERENCES

1. Worldometers. Coronavirus cases in world. [cited 2021 August 26]. Available from https://www.worldometers.info/coronavirus/
2. Kementerian Komunikasi dan Informatika. Sebaran kasus COVID-19 di Indonesia. [cited 2021 August 26]. Available from https://covid19.go.id/
3. Kementerian Kesehatan RI. Materi Penanganan COVID-19. Kemenkes. Desember 2020.
4. Tim mitigasi Ikatan Dokter Indonesia. Data kematian dokter di Indonesia akibat COVID-19. IDI. 2021
5. Lingren AL, Austin AH, Welsh K. COVID Arm: Delayed Hypersensitivity Reactions to SARS-CoV-2 Vaccines Misdiagnosed as Cellulitis. J Primary Care Comm Health. 2021;12:1-5
6. Allergic Reactions. Centers for Disease Control and Prevention. [cited 2021 August 26]. Available from https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/allergic-reaction.html
7. Baen LR, Sahly E, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384:403-16.
8. Blumenthal KG, Freeman EF, Saff RR, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2.N Engl J Med. 2021;384:1273-7.
9. Kelso JM, Greenhawt MJ, Li JT, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol. 2012;130:25-43.
10. McNeil MM, DeStefano F. Vaccine-associated hypersensitivity. J Allergy Clin Immunol. 2018;141:463-72.
11. U.S. Food and Drug Administration. Fact Sheet for Recipients and Caregivers. Emergency Use Authorization (EUA) of the Pfizer-BioNTech COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 16 Years of Age and Older [fact sheet]. [cited 2021 August 26]. Available from https://www.fda.gov/ media/144414/download#page=2
12. U.S. Food and Drug Administration. Fact Sheet for Recipients and Caregivers. Emergency Use Authorization (EUA) of the Moderna COVID-19 Vaccine to Prevent Coronavirus Disease 2019 (COVID-19) in Individuals 18 Years of Age and Older [fact sheet].[cited 2021 August 26]. Available from https://www.fda.gov/ media/144638/download#page=2
13. Allergic Reactions. Centers for Disease Control and Prevention. [cited 2021 August 26]. Available from https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/allergic- reaction.html
14. Fisher AA. Immediate and delayed allergic contact reactions to polyethylene glycol. Contact Dermatitis. 1978;4:135-8.
15. Halperin S, Kohl KS, Gidudu J, et al. Cellulitis at injection site: case definition and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2007;25:5803-20.
16. Davies HD, McGeer A, Schwartz B, et al. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. N Engl J Med. 1996;335(8):547-54.
17. Weng QY, Raff AB, Cohen JM, et al. Costs and consequences associated with misdiagnosed lower extremity cellulitis. JAMA Dermatol. 2017;153(2):141-6.