COVID-19 Vaccine-associated Thrombosis (Disseminated Intravascular Thrombosis) with Rare Cutaneous Involvement

Sharmili Sinha¹⁰, Satyabrata Tripathy²⁰

Abstract

Many COVID-19 vaccines have been used on the population all over the world. Not much is known about the vaccines and their adverse effects. A middle-aged lady got fever, body ache, and cutaneous lesions suggestive of disseminated intravascular thrombosis (DIC) almost immediately after COVID vaccination with very high D-dimer level in blood. She was successfully managed with timely initiation of treatment with steroids, anticoagulation, and antibiotics.

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INTRODUCTION

Most of the COVID-19 vaccines have been approved under Emergency Use Authorization (EUA). These have been largely safe with majority reporting minor reactions. The reports of serious side effects have been extremely rare. We, in this report, describe a case with a complication rarely described in the literature.

CASE DESCRIPTION

A 57-year-old lady presented with the chief complaints of fever, body ache, and painful red spots over both legs and thighs for 5 days. Five days prior, she was given COVID vaccine (Covaxin) in the morning (11 am), and on the same day at about 11 pm she started to have fever (102°F) along with body ache. Next day morning, she noticed red spots over both her legs and thighs. She consulted the local doctor and was prescribed with antibiotic (amoxyclav) and antipyretics (tramadol and paracetamol) which she took for next 4 days without much relief. New red rashes continued to develop in crops (Fig. 1) almost daily during these 4 days and the older one turned purplish brown (Fig. 2) with considerable pain over the limbs restricting her mobility. Fever and body ache were



Fig. 1: Red to purplish macules over both legs and perianal region

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Fig. 2: Large purplish to brown lesion on posterior aspect of leg

only partially relieved for 3–4 hours after taking paracetamol. There was no breathing difficulty, cough, or sore throat. She had a past history of psoriasis for which she was not on any systemic medications. She was non-diabetic, non-hypertensive, and no past history of any allergic reactions to any drugs and food.

© The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons. org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated. On examination, multiple oval red to purplish macules varying in size from 0.5 mm to 3 cm were noted over both legs and thighs (Fig. 1). The lesions were more concentrated over the posterior aspect of the thighs and legs and there was a tendency of smaller macules to coalesce with each other forming larger macules or patches. These macular lesions were hot and tender and did not blanch under firm pressure. There were associated erosions over the tongue (Figs 3A and B) and perianal area (Fig. 1) which were painful. Her systemic examination did not reveal any other positive finding. Blood reports are mentioned in Table 1.

Based on the clinical and biochemical findings, a diagnosis of vaccine associated DIC induced by the COVID-19 vaccine was made. Cutaneous vasculitis is a differential diagnosis in which clinical presentation is of erythematous dermal or subcutaneous nodules pustulation and/or ulceration. In this case, none of the lesions had a palpable nodular component and all the lesions were non-blanchable purplish red macules of varying size. Although biopsy was not done, we could exclude vasculitis based on the typical clinical presentation. The patient did not consent for hospitalization and skin biopsy and was treated on outpatient basis. She was started on tablet, methylprednisolone, 32 mg daily for 1 week which was gradually tapered to 16 and 8 mg, respectively, for the subsequent 2 weeks and then reduced to 8 mg alternate days for the fourth week and finally stopped. Also, she was also put on newer oral anticoagulants (dabigatran, 75 mg twice daily) and antibiotics (linezolid, 600 mg twice daily, and levofloxacin, 500 mg once daily), which she continued for 10 days. At day 10, during the follow-up, she was afebrile, free of pain, and no new lesions were appearing with old lesions starting to fade with post-inflammatory pigmentation. Her quantitative C-reactive protein (CRP) level was 7.5 mg/L and D-dimer was 2,000 ng/mL. Antibiotics were stopped and she was advised to continue methylprednisolone and dabigatran for 1 month.

DISCUSSION

Among all side effects of COVID-19 vaccine, cutaneous reactions are usually quite varied reported both from trials and practitioners. Among the trial data of 11 authorized COVID-19 vaccines, injection site pain was the most prevalent cutaneous feature in up to 88% participants and was self-limiting. Erythema, swelling, induration, and itch were less common.¹

Less than 0.2% of Moderna's vaccinated cohort developed rashes, eczema, papular urticaria, and vesicular rash, etc.,² and less than 0.1% of Sputnik V's vaccinated participants experienced minor reactions. Unspecified rash has been described in the BBIBP-CorV vaccine trial and Covaxin trial. Vaccine-related buccal ulceration and oral herpes were also noted in the Convidecia vaccine cohort.³

Three cases of serious cutaneous reactions were observed among these 11 vaccines. One participant in the CoronaVac trial developed a severe, acute hypersensitivity reaction with urticaria 48 hours after the first dose.⁴ Among the 11 recipients of the ZF2001 vaccine who developed unspecified rashes, one case was labeled as severe (grade 3 or higher).⁵ The AZD1222 trial reported one case of severe cellulitis in addition to one case each of vaccine-induced psoriasis, rosacea, vitiligo, and Raynaud's phenomenon.⁶

It is noteworthy that female patients younger than 65 years of age consistently composed the majority of these delayed large

Table 1: Blood test reports at onset of lesions	
Total leukocyte count	16,400/mm ³
Hb	11.7 gm%
Platelet count	4.09 lakh/μL
Blood cell morphology	Normal and no immature cells
AST	54 IU/L
ALT	66 IU/L
ALP	399 IU/L
Bilirubin	0.9 mg/dL
Albumin	4.1 gm/dL
TSH	7.09 IU/L
T3, T4 level	Normal
CRP	32.8 mg/L (normal <6 mg/L)
Serum ferritin	211 μg/mL (18–160 μg/mL)
D-dimer	>10,000 ng/mL (normal <500 ng/mL)
INR	1.3
aPTT	29 s (21–35 s)
Urea	27 mg/dL
Creatinine	1.0 mg/dL
Sodium	134 mmol/L
Potassium	4.7 mmol/L



Figs 3A and B: Erosions over the tongue



local reactions. Women also comprise a majority of the healthcare workforce and vaccination campaigns initially targeted healthcare professionals.⁷ The research supports the fact that women exhibit a greater immune response to vaccines and also higher adverse events.⁸

Most of the delayed large local reactions were mild and transient with few recurrences after the second dose. In McMahon et al., only 11 subjects developed reactions after both doses; all were mRNA-1273 vaccine recipients. Six of the twelve patients who received the mRNA-1273 vaccine, as discussed in Blumenthal et al., had recurrent reactions that were of lesser severity than those after the first dose.⁹ Most delayed large local reaction reports in non-trial literature occurred with the mRNA-1273 vaccine. Of the 103 patients, as discussed in Fernandez–Nieto et al., who developed delayed large local reactions after the first dose of BNT162b2; half of them experienced similar recurrent reactions after the second dose.¹⁰

However, none of the vaccine trials did report any significant vascular event related to the COVID-19 vaccine. It is well known that moderate-to-severe COVID-19 infection induces a hypercoagulable state with increased microvascular thrombotic complications. In this case, the diagnosis of non-overt DIC was made based on clinical characteristics of skin lesions and biochemical parameters with a DIC score of 4.¹¹ COVID-19 vaccines in use have been largely proven safe. This is perhaps the first report from India with such an extremely rare COVID-19 vaccine related complication confined to skin.

CONCLUSION

Many vaccines have been marketed after EUA by drug-controlling agencies during the COVID-19 pandemic. So, hitherto, unknown complications are not unusual, and in our view, COVID-19 vaccine-associated cutaneous thrombotic manifestations could be one of them.

LEARNING POINTS

Features of DIC mainly with predominant cutaneous involvement have been rarely reported in literature as a reaction to COVID-19 vaccination. The patient responded well to steroids and anticoagulants. It was self-limiting.

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