

Toxic epidermal necrosis following Sinopharm COVID-19 vaccine (BBIBP-CorV): A case report and literature review

Safoura Shakoei¹ and Alireza hadizadeh¹

¹Tehran University of Medical Sciences

June 2, 2022

Abstract

This study reports a patient developing TEN after the first dose of (BBIBP-CorV). He developed numerous purpuric and dusky patches with flaccid bullae and areas of epidermal detachment covered more than 30% of the body area within 6 days. After treatment with dexamethasone and cyclosporin, he recovered within 14 days.

Introduction

In 2019 the novel coronavirus started a pandemic and ever since millions have been affected in the respiratory system and other organs like the skin. Ever since the first vaccines got authorized for use, many people have become immune to severe forms of infection and many lives have been saved [1]. However, complications and side effects of the vaccines were also reported [2]. Even though cutaneous reaction to vaccines is not a novel concept and many reactions are known to have happened, some reactions are more severe and require intensive care. COVID-19 Vaccine-induced TEN is a rare incidence on its own and only a few cases have been reported [3].

Toxic epidermal necrolysis is an idiosyncratic drug reaction that is associated with high mortality and morbidity rates [4 5]. This spectrum of diseases is heralded by an acute fever which is followed by a generalized dusky rash, crusting, extensive erosion, conjunctivitis, necrolysis of the epidermis, mucositis, In both the pulmonary and gastrointestinal tract [5] [6]. It is estimated that the mortality of TEN is around 30%. Several drugs such as sulfonamides, anti-convulsive medications, and even influenza vaccines are known to be chiefly associated with this reaction; however, vaccines are among the least associated causes [5] [7].

In this article, we report a case of TEN following the administration of the Sinopharm COVID-19 vaccine. TEN is an important entity even though it has rarely been reported with COVID-19 vaccines. The current report will also provide a brief review of the literature concerning the reported TEN/SJS cases that are induced by a COVID-19 vaccine.

Case presentation

Our patient is a 67-year-old man with a history of hypertension who presented to our clinic with a history of fever and cutaneous eruptions.

He had received the first dose of Sinopharm COVID-19 vaccine (BBIBP-CorV) with a dose of 0.5 mL given intramuscularly six days before the development of his lesions. His manifestations started with fever and erythema patches on his back followed by bullous lesions on the lower extremities. He was seen in another health care center and was given acetaminophen, cetirizine, and vitamins and did not notice any improvement. Seven days after vaccination, lesions developed on his body, and the genital mucosa was involved.

He had no history of taking any new medication in the past one month before the development of the skin lesions and he had a history of COVID-19 infection 3 months ago.

On physical examination, all mucosal surfaces were involved. Bilateral conjunctivitis with purulent and oral and genital ulceration and hemorrhagic crusting over his lips.

He had numerous purpuric and dusky patches involving the back, chest, abdomen, both extremities, and face, with flaccid bullae and areas of epidermal detachment. He had positive Nikolsky's sign. His body surface area (BSA) involvement is estimated to be more than 30%. Laboratory findings showed elevated D-dimer [2626], erythrocyte sedimentation rate (ESR)[64 mm/h], C-reactive protein (CRP)levels [70 mg/l]. (Figure 1)

The Severity-of-Illness Score for Toxic Epidermal Necrolysis (SCORTEN) score was two on the day of her admission since she was older than 40 and detached body surface more than 10%. Viral markers and COVID-19 (polymerase chain reaction) PCR was negative. He has been treated with dexamethasone 4 mg twice daily and cyclosporine 200 mg daily for 6 days. His lesions stopped developing after four days, and complete healing was noted after 14 days.

Ophthalmic antibiotics and corticosteroids eye drop was used for conjunctivitis treatment. On the other hand, elevated D-Dimer levels prompted the clinicians to evaluate and rule out Deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE). No signs of DVT were found in ultrasonographic evaluations of lower limbs, PTE was also ruled out as ventilation and perfusion scan was carried out. The patient is currently under observation and the lesions have been completely cured.

(Figure 1)

Discussion

This study reports a case who suffered from toxic epidermal necrolysis following COVID-19 vaccination with Sinopharm COVID-19 vaccine (BBIBP-CorV). It is highly suspected that the offending agent is the vaccine since other causes such as medications couldn't cause this phenomenon in the aforementioned timetable.

SJS/TEN is a spectrum of delayed hypersensitivity skin reactions that are potentially fatal. The most prominent cause for these reactions is medications and drugs such as sulfonamides and antiepileptics such as lamotrigine. Infectious diseases such as mycoplasma pneumonia and HIV infections are also known to have caused this reaction. Vaccine-related TEN/SJS is a relatively rare concept and even though multiple cases of MMR, DTP, and influenza vaccine-induced TEN/SJS have been reported, the relation between the vaccines and TEN/SJS has not been established [7].TEN/SJS usually starts the presentation with flu-like symptoms which are consecutively followed by a dusky rash, crusting, targetoid lesions, purpuric macules with full-thickness epidermal necrosis, and extensive erosion. This spectrum of reaction can involve mucus membranes which could impair oral intake. It has been suggested by several studies that a hypersensitivity reaction with cytotoxic T cells which is mediated by CD8+ lymphocytes could be the cause. It has been suggested that the cytotoxic T cells cause the damage by releasing enzymes such as granulysin and perforin [5].

COVID-19 vaccines are designed to combat the infection via different methods. Some such as the AstraZeneca vaccine uses vectors while the Pfizer vaccine uses mRNAs to introduce spike proteins to immune cells. In this case, the Sinopharm vaccine is an inactivated virus vaccine [1]. Up to now, COVID-19 vaccine-related SJS and TEN have also been reported (Table 1). The majority of cases are women with 6 cases. Reactions occurred after both the first dose and second (6 and 3 cases), respectively (in one case it was not defined as to whether the first or the second dose was responsible for the reaction). The mean age of patients was 56.5 (sd:13.23) years old. Meanwhile, the time to the onset of the presentation ranged from 6 hours to two weeks but most of them happened within 4.32 (SD:4.05) days. The reaction resolved on average in 21.3 (SD:14.14) days.

COVID-19 vaccinations are widely used and are proved to protect against severe infection and such instances

are considered rare complications. However, reporting these severe side effects should not prevent the vaccine from being injected, and the fact that should be mentioned is doctors and health care providers should be vigilant to such adverse outcomes and must provide immediate care.

(Table 1)

Key clinical message

COVID-19 vaccinations are safe and effective methods for prevention of infection albeit with few instances of complication. The patients who develop TEN/SJS following vaccination which might have led to mortality if they were misdiagnosed.

Declarations

Ethics approval and consent to participate

This study was approved by the research and ethics committee of Tehran University of Medical Sciences. The patients and their families have given their informed consent to publish this case.

Consent for publication

Written informed consent was obtained from the patients and their next of kin for publication of this case series and any accompanying images. A copy of the written consent is available

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

The authors have no conflict of interest to declare.

Funding

None

References:

1. Xia S, Duan K, Zhang Y, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. *Jama* 2020;**324** (10):951-60
2. Saeed BQ, Al-Shahrabi R, Alhaj SS, Alkokhardi ZM, Adrees AO. Side effects and perceptions following Sinopharm COVID-19 vaccination. *International Journal of Infectious Diseases* 2021;**111** :219-26
3. Riad A, Hocková B, Kantorová L, et al. Side Effects of mRNA-Based COVID-19 Vaccine: Nationwide Phase IV Study among Healthcare Workers in Slovakia. *Pharmaceuticals* 2021;**14** (9):873
4. Loboda J, Dudzik A, Chomyszyn-Gajewska M. Stevens-Johnson Syndrom and Toxic Epidermal Necrolysis–based on literature. *Przegląd lekarski* 2015;**72** (1):35-37
5. Schwartz RA, McDonough PH, Lee BW. Toxic epidermal necrolysis: Part II. Prognosis, sequelae, diagnosis, differential diagnosis, prevention, and treatment. *Journal of the American Academy of Dermatology* 2013;**69** (2):187. e1-87. e16
6. Fernando SL. The management of toxic epidermal necrolysis. *Australasian journal of dermatology* 2012;**53** (3):165-71
7. Grazina I, Mannocci A, Meggiolaro A, La Torre G. Is there an association between Stevens-Johnson syndrome and vaccination? A systematic review. *Ann. Ig* 2020;**32** :81-96
8. Mansouri P, Chalangari R, Martits-Chalangari K, Mozafari N. Stevens-Johnson Syndrome due to COVID-19 vaccination. *Clinical Case Reports* 2021;**9** (11):e05099

9. Elboraey MO, Essa EESF. Stevens-Johnson syndrome post second dose of Pfizer COVID-19 vaccine: a case report. *Oral surgery, oral medicine, oral pathology and oral radiology* 2021;**132** (4):e139-e42
10. Boualila L, Mrini B, Tagmouti A, El Moubarik N, Boutimzine N, Cherkaoui L. Sinopharm COVID-19 vaccine-induced Stevens-Johnson syndrome. *Journal Francais D'ophtalmologie* 2022
11. Dash S, Sirka C, Mishra S, Viswan P. COVID-19 vaccine-induced Stevens–Johnson syndrome. *Clinical and Experimental Dermatology* 2021;**46** (8):1615-17
12. Bakir M, Almeshal H, Alturki R, Obaid S, Almazroo A. Toxic Epidermal Necrolysis Post COVID-19 Vaccination-First Reported Case. *Cureus* 2021;**13** (8)
13. Kherlopian A, Zhao C, Ge L, Forward E, Fischer G. A case of toxic epidermal necrolysis after ChAdOx1 nCov-19 (AZD1222) vaccination. *The Australasian Journal of Dermatology* 2021
14. Mardani M, Mardani S, Asadi-Kani Z, Hakamifard A. An Extremely Rare Mucocutaneous Adverse Reaction Following COVID-19 Vaccination: Toxic Epidermal Necrolysis. *Dermatologic Therapy* 2022:e15416
15. Aimo C, Mariotti E, Corrà A, et al. Stevens-Johnson syndrome induced by Vaxvetria (AZD1222) COVID-19 vaccine. *Journal of the European Academy of Dermatology and Venereology* 2022
16. Mansouri P, Farshi S. A case of Steven-Johnson syndrome after COVID-19 vaccination. *Journal of cosmetic dermatology* 2022

Table 1. Cases of COVID-19 vaccine-induced TEN/SJS

author	country	Vaccine	Age	sex	onset	First or second dose	resolution of lesions	treatment
P. mansouri[8]	Iran	Sinopharm	49	woman	3 d	second dose	2 weeks	Fexofenadine Topical corticosteroids violet gentian violet prednisolone (30 mg) Oral corticosteroids in the form of a mouthwash eye drops and ointment, oral doxycycline Cyclosporin 300 mg
M. Elboraey[9]	Saudi Arabia	Pfizer	Middle-aged	woman	5 d	first dose	2 weeks	
L. Boualila[10]	morocco	Sinopharm	32	man	6 hours	second dose	30 days	
S. Dash[11]	India	AstraZeneca	49	woman	3 d	First dose	7 days	

author	country	Vaccine	Age	sex	onset	First or second dose	resolution of lesions	treatment
M. Bakir[12]	Iran	Pfizer	60	woman	7 d	First dose	22 days	Etanercept 50 mg/ml, 2 doses on the first and second day of admission marked healing in 22 days
A. Kherlopian [13]	Australia	AstraZeneca	48	Woman	14 d	First dose	28 days	adalimumab
M. Mardani [14]	Iran	Sinopharm	76	man	1 d	First dose	2 weeks	prednisone and prepare mouthw
C. Aimo [15]	Italy	AstraZeneca	65	Man	3 d	Second dose	8 weeks	prednisone 1mg/Kg
P. Mansouri [16]	Iran	Sinopharm	63	Woman	1 d	N/A	2 weeks	Oral prednisolone (40mg) daily
s.shakoei	Iran	Sinopharm	67	man	6 d	First dose	2 weeks	Dexamethasone Cyclosporin



Figure 1. 1a: Bilateral conjunctivitis with purulent secretion, and 1b: oral lesions and hemorrhagic crusting over his lips. 1c: Numerous purpuric and dusky patches involving the chest, abdomen, both extremities, and face, with flaccid bullae and areas of epidermal detachment.

