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CASE REPORT

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

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**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.

**KEYWORDS**

COVID-19, COVID-19 vaccination, toxic epidermal necrosis



## 1 | 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.[2,3] 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.[4]

Toxic epidermal necrolysis is an idiosyncratic drug reaction that is associated with high mortality and morbidity rates.[5,6] 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, and mucositis, in both the pulmonary and gastrointestinal tract.[6,7] 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.[6,8]

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.

## 2 | 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 6 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 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 discharge, oral and genital ulceration with 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 were negative. He has been treated with dexamethasone 8 mg daily and cyclosporine 200 mg daily for 6 days. Then, dexamethasone dose was tapered and converted to oral prednisolone. His lesions stopped developing after 4 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 a ventilation and perfusion scan was carried out. The patient is currently under observation and the lesions have been completely cured.

## 3 | 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 could not 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.

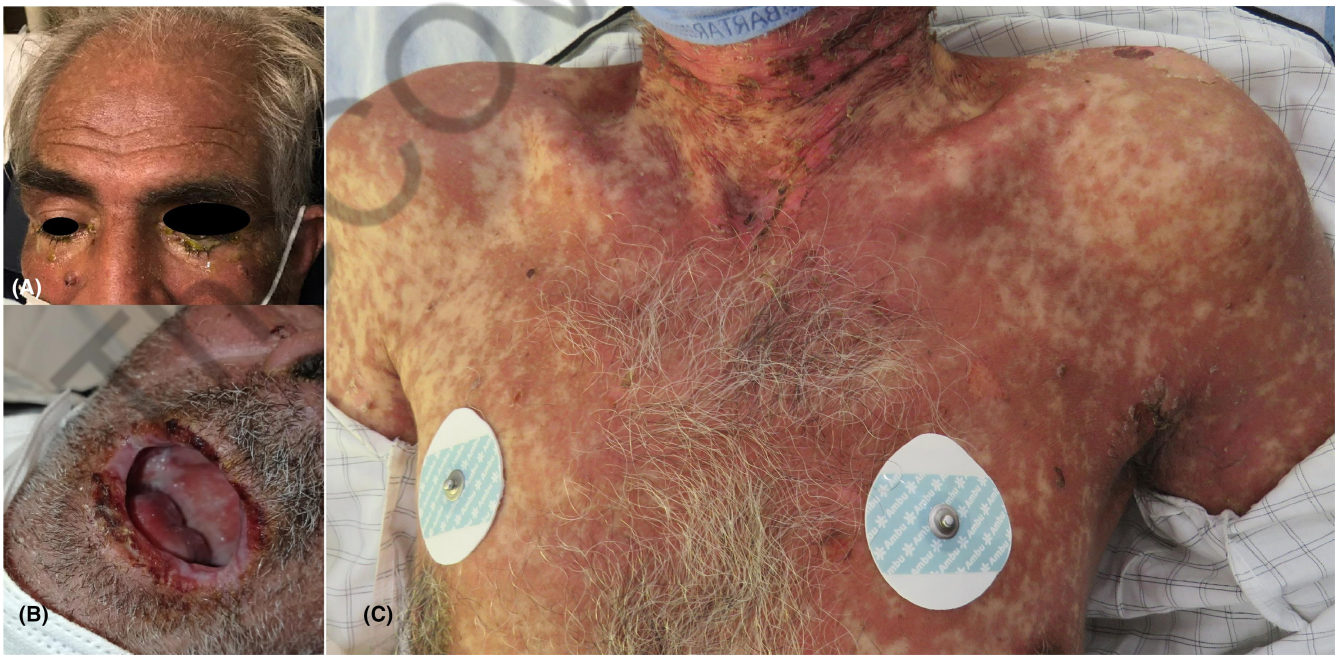


FIGURE 1 (a): Bilateral conjunctivitis with purulent secretion, and (b): oral lesions and hemorrhagic crusting over his lips. (c): Numerous purpuric and dusky patches involving the chest, abdomen, both extremities, and face, with flaccid bullae and areas of epidermal detachment

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.[8] 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 cytotoxic T cells cause damage by releasing enzymes such as granulysin and perforin.[6] It has been suggested that cytotoxic T cells cause damage by releasing enzymes such as granulysin and perforin. TEN/SJS are medical emergencies that require intensive and urgent intervention. This intervention includes the prompt withdrawal of the offending agent along with wound care, systemic immune modulating medication, and prevention of infectious complications with antibiotics. The diagnosis in this case was made using both histopathologic results and observation. Sepsis and organ failures are serious side effects among TEN complications; if these patients are suspected of such difficulties, prompt preventive measures should be taken. In a recent study, it has been suggested that the use of TNF-alpha inhibitors could significantly reduce lesion formation and could lessen the levels of granulysin and TNF-alpha.[9–11] It has been suggested that this group of biologic drugs along with IVIG and plasmapheresis could remove drugs and their metabolites; however, these concepts are still controversial.[9,7,11] Meanwhile, a study conducted in Sweden found no benefit in the use of plasmapheresis.[12] Ergo, currently, there is not enough evidence to support the use of these adjunctive methods. Our case was treated with systemic corticosteroids and cyclosporin and is currently in full recovery. According to the concurrent initiation of cyclosporine for him and the patient's condition, a dose of 0.5–1 mg of prednisolone (equivalent to dexamethasone) was enough for his treatment.

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

**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[13] | Iran | Sinopharm | 49 | woman | 3 d | second dose | 2 weeks | Fexofenadine<br>Topical violet gentian |
| M. Elboraey[14] | Saudi Arabia | Pfizer | Middle-aged | Woman | 5 d | first dose | 2 weeks | prednisolone (30 mg/d),<br>Oral corticosteroids in the form of a mouthwash. |
| L. Boualila[15] | Morocco | Sinopharm | 32 | Man | 6 hours | second dose | 30 days | eye drops and ointment, oral doxycycline. |
| S. Dash[16] | India | AstraZeneca | 49 | Woman | 3 d | First dose | 7 days | Cyclosporine 300 mg |
| M. Bakir[17] | 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[18] | Australia | AstraZeneca | 48 | Woman | 14 d | First dose | 28 days | adalimumab |
| M. Mardani[19] | Iran | Sinopharm | 76 | Man | 1 d | First dose | 2 weeks | prednisolone and prepared mouthwash. |
| C. Aimo[20] | Italy | AstraZeneca | 65 | Man | 3 d | Second dose | 8 weeks | prednisolone 1 mg/Kg/day |
| P. Mansouri[21] | Iran | Sinopharm | 63 | Woman | 1 d | N/A | 2 weeks | Oral prednisolone (40 mg) daily |
| s.shakoei | Iran | Sinopharm | 67 | Man | 6 d | First dose | 2 weeks | Dexamethasone, Cyclosporine |

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 2weeks 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 proven 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.

## AUTHOR CONTRIBUTIONS

S.S contributed to the development of research idea, data gathering, and manuscript draft and revision. A.H contributed to data gathering, manuscript preparation, drafting, and revision.

## ACKNOWLEDGMENT

None.

## CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

## DATA AVAILABILITY STATEMENT

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

## ETHICAL APPROVAL

The patient has given their informed consent to publish this case.

## CONSENT

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

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