Case Reports in Ophthalmology

Case Rep Ophthalmol 2021;12:944–951
DOI: 10.1159/000520500
Received: October 6, 2021
Accepted: October 27, 2021
Published online: December 2, 2021

Case Report

Ocular Surface Erosion after Suspected Exposure to Evaporated COVID-19 Vaccine

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Keywords
COVID-19 vaccine · Ocular surface erosion · Skin rash · Health worker · Case report

Abstract
The purpose is to report ocular surface erosion of health personnel who were exposed to evaporated CoronaVac during a vaccination campaign. A campaign for CoronaVac vaccination was conducted in a closed space of 11.04 × 5.96 m, partially divided into 6 rooms with interconnected area among the rooms. A total of 20 health personnel worked in the vaccination rooms. On the third day of campaign, a vial, containing a single dose of 0.5 mL, of the vaccine was dropped accidentally onto the floor and broken by an administering nurse. A total of 15 personnel had symptoms and signs of ocular surface erosion at the average time from the accident to the onset of 10.2 ± 7.1 h; 4 personnel also had skin rash. These personnel included all 13 persons who already worked in the rooms when the accident occurred and continued for additional 4–6 h and 2 personnel who presented in the rooms 1–2 h after the accident and stayed for 2–3 h. Proximity and timing suggest CoronaVac correlation with the ocular and skin reactions. Cautions should be taken to avoid broken vials, spills, and aerosolization of CoronaVac during the vaccination.

Trial Registration: this study was registered in the Thai Clinical Trial Registry, Registration No. TCTR 20210510008, URL: http://www.thaiclinicaltrials.org/.

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Introduction

Vaccination for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is expected to lower a number of hospitalizations and deaths from the pandemic of coronavirus disease 2019 (COVID-19) [1, 2]. Strategies to distribute, administer, and select sources of SARS-CoV-2 vaccines vary worldwide [3], whereas health and occupational hazards associated with the vaccination have not been reported. CoronaVac, authorized for emergency use in low-resource settings [4], is a vaccine made of beta-propiolactone inactivated SARS-CoV-2 virus particles with an aluminum hydroxide adjuvant [5]. We report a series of health professionals who developed adverse events after a vial of CoronaVac was broken in an indoor facility during a vaccination campaign.

Methods

A campaign of CoronaVac (Sinovac Biotech, Beijing, China) vaccinations was deployed for health professionals at Rajavithi Hospital, Thailand, for 3 days. A total of 2,296 people were vaccinated.

The vaccination area was a closed space partially divided into 6 small rooms of equal size with interconnected front and back hallways, rooms 1–4 for vaccination and rooms 5–6 for registration (Fig. 1). There was a functioning air conditioning system without additional ventilator or filters for all the rooms.

On the third day, 20 personnel worked in the vaccination rooms. All were vaccinated with CoronaVac on the first 2 days. In each room, the nurse was assigned for preparing and administering the vaccine, and the others were assistants. No protective equipment other than face masks was used. The nurse in room 4 accidentally dropped and broke a vial of the vaccine, causing a spill of its total volume (0.5 mL) onto the floor adjacent to the wall between rooms 3 and 4. She promptly wiped the solution using a piece of tissue paper and disposed in a garbage can in room 4 where it remained for the rest of the day.

Personnel with conjunctivitis were asked to provide conjunctival, nasal, and throat swab samples for SARS-CoV-2 by reverse transcription polymerase chain reaction assay. This study was approved by the Research Ethics Committee, Rajavithi Hospital. The approval number is 64083. All patients gave written informed consent to publish their case including publication of images.

Results

A total of 15/20 (75%) personnel had ocular symptoms (average age, 36.9 ± 12.9 years; females, 86.7%). These 15 personnel include all who worked in the rooms when the accident occurred and continued working for 4–6 h (13 personnel) and those who started working after the accident and continued working for 3 h (2 personnel). The other 5/20 (25%) personnel who were in the rooms after the accident and worked for half an hour had no symptoms.

The symptoms were eye irritation (60%), red eyes (50%), tearing (45%), swollen eyelids (30%), and skin rash (20%). The average time from the accident to the onset of symptoms was 10.2 ± 7.1 h.

All 15 personnel with ocular symptoms had some degree of conjunctivitis without papillae or follicles and positive fluorescein staining according to the Oxford Grading System [6] in the interpalpebral area as punctate epithelial erosion with severity from grade 1 to 3 (Fig. 2). Eye examinations from unaffected personnel were unremarkable.

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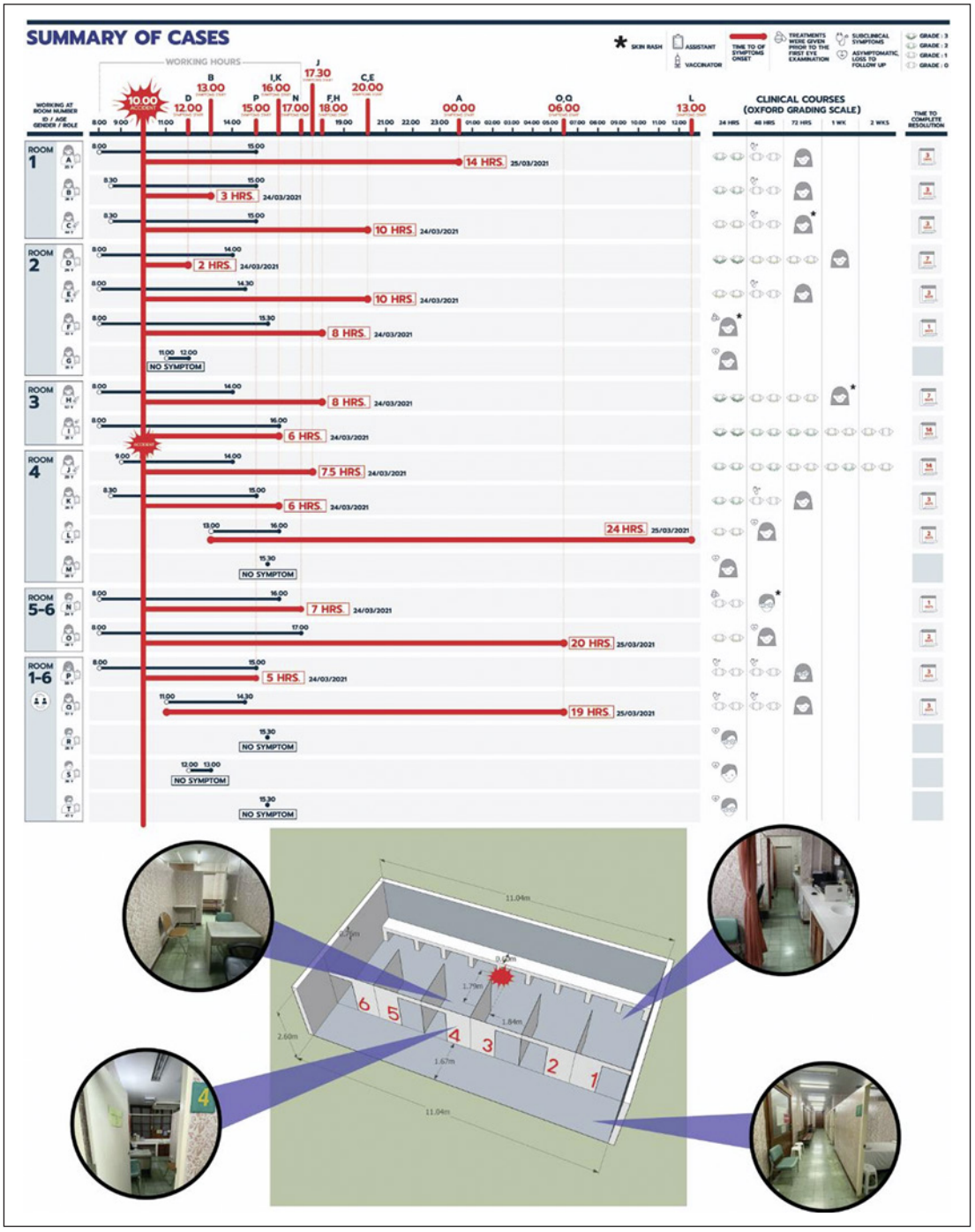

Fig. 1. Infographic of clinical courses of the personnel and a map of the vaccination rooms. Top, the infographic of cases suspected of exposure to evaporated CoronaVac and their clinical courses. A total of 15 personnel were assigned to work in each of the rooms 1–6 as indicated in the figure (persons A to O). There were 4 additional personnel who moved through all 6 rooms during the vaccination (persons P to T). Bottom, the vaccination rooms of 11.04 × 5.96 m and 2.6 m tall, divided into 6 small rooms of 2.5 × 1.84 m. The front and back hallway was 11.04 × 1.67 and 11.04 × 1.79 m, respectively. A washing area of 11.04 × 0.6 m was in the back hallway. There was an open-air space of 0.6 m from the top of each wall. The red splash indicates where the vaccine was accidentally dropped.

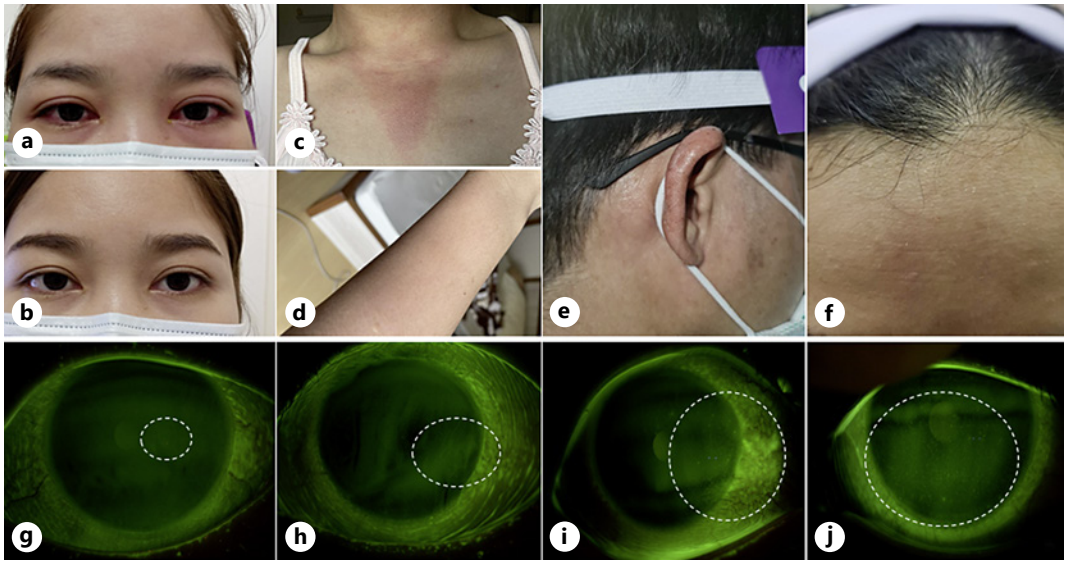

Fig. 2. Clinical evidence of the adverse events. **a**, **b** Pictures of external eyes of person I at initial presentation and complete resolution. **c**, **d** Pictures of skin rash on the upper chest and forearm of person F. **e** A picture of skin rash behind the right ear of person N. **f** A picture of skin rash on the forehead of person H. **g** Fluorescein stain grade 0 of person P. **h** Fluorescein stain grade 1 of person O. **i** Fluorescein stain grade 2 of person K. **j** Fluorescein stain grade 3 of person D. The areas of fluorescein stain in (**g–j**) are circled as shown.

The nurse who accidentally dropped the vaccine in room 4 and the assistant who wore contact lens and worked in room 3 manifested the most severe and longest clinical manifestations for 2 weeks. This person received topical fluorometholone QID for 3 days. The rest of the affected personnel received topical antihistamine or lubricant. All showed full recovery at the last examinations, 46.7% showed full recovery within 72 h. All reverse transcription polymerase chain reaction results were negative.

Neither the 591 vaccine recipients nor the hospital staff who worked near but not in the vaccination area reported similar symptoms. Additionally, there were no symptoms among the 1,705 recipients and 36 staff in the same facility on the first 2 days.

Discussion

We hypothesize, after finding no other likely association, such as contamination of cleaning agents or malfunction of ventilation system, that the evaporated solution of the vaccine was associated with ocular surface erosions of the affected personnel. Supportive evidence included a temporal relation between the accident and the clinical manifestations and a spatial relation between the area of the accident and the severity of the clinical presentations. The physical evidence on the ocular surface and skin supports the hypothesis of exposure to potential volatile substances [7]. The findings might also be related to the duration of exposure in the closed rooms since none of vaccine recipients and personnel who presented in the rooms in a relatively short period of time had the clinical manifestations.

The indoor office environment, like the closed vaccination rooms, may be associated with eye complaints of workers by lowering relative humidity and creating indoor air pollutants. These factors can compromise the integrity of precorneal tear film [8]. Their effects may be accumulated and exacerbated by the evaporated chemicals of the vaccine.

The excipients or aluminum hydroxide adjuvant may be the likely chemicals that associated with the adverse reactions. Safety precautions exist for eye protection for each of the excipients (Table 1) according to databases of hazard substances [9, 10]. However, there have not yet been reports of ocular manifestations by direct or indirect eye contact with these chemicals. Since all the personnel with clinical manifestations were vaccinated with CoronaVac before their symptoms, the sensitized immunity may play roles in inducing reactions to the inactivated virus particles in the CoronaVac.

Given the total volume of the vaccination space (287.61 m^3) and the small volume (0.5 mL) of the spilled vaccine, it was a significant observation that there was a clustered health hazard event in the temporal and spatial proximity of this spill. We estimated that if all the average vapor droplets were 3 μm in diameter [11] (~27 μm^3 or 2.7×10^{-11} mL), then the volume spilled could potentially had distributed up to 1.85×10^{10} droplets into the small, closed vaccination rooms (6.45×10^7 droplets/m^3). We are unaware of data to suggest if this aerosolized concentration is likely to pose significant dose hazards to workers.

Another possible association for this clustering of ocular manifestations may be an outbreak of epidemic viral conjunctivitis. Arguments against this explanation include the absence of similar manifestations among vaccine recipients, among staff not presenting within several hours of the accident, and staff working outside of the vaccination rooms in our large hospital facility.

CoronaVac and other SARS-CoV-2 vaccines are considered safe with few systemic adverse events to the recipients [5, 12–14]. This report highlights the potentially preventable adverse events which may be related to exposure to evaporated CoronaVac. It is not known if similar adverse events may occur with exposure to other vaccines in the same manner. We recommend the following: (1) vaccination should be in an open-air area. (2) Care should be taken in preparation of the vaccine. (3) Consider wearing protective clothing and eye protection for vaccination staff. (4) Meticulous clean-up of any spills and immediate removal of all absorbed and rinsed vaccine material. After revision of vaccination protocols, no similar events were found in other CoronaVac campaigns in the hospital. Recently, there have been some reports on ocular adverse events, which may be associated with COVID-19 vaccines, in persons who were vaccinated [15]. To the best of our knowledge, this may be the first report of a possible ocular adverse event occurred to healthcare workers who were vaccinators in a vaccination area.

Conclusion

We report on a spill of CoronaVac, which was followed by a cluster of adverse events to proximal health care personnel. We recommend caution during vaccine handling and fastidious clean-up of any spills.

Statement of Ethics

This study was reviewed and approved by the Research Ethics Committee, Rajavithi Hospital, on April 20, 2021. The approval number is 64083. Written informed consent was obtained from all patients for publication of the details of their medical signs and symptoms including accompanying images. This study was registered in the Thai Clinical Trial Registry, Registration No. TCTR 20210510008, URL: http://www.thaiclinicaltrials.org/.

Table 1. Excipients of CoronaVac with their properties and toxicities [9, 10]

	Aluminum hydroxide powder EMPLURA® hydrargillite	Disodium hydrogen phosphate anhydrous for analysis EMSURE® ACS,Reag. Ph Eur	Sodium chloride for analysis EMSURE® ACS,ISO,Reag. Ph Eur	Sodium dihydrogen phosphate anhydrous 99.99 Suprapur®
Ambient fire may liberate hazardous vapors	Y	Y	Y	Y
Acute oral toxicity				
Animal	LD50 rat: >2.000 mg/kg	LD50 rat: >2.000 mg/kg	No data available	LD50 rat: >2.000 mg/kg
Human	No data available	No data available	No data available	No data available
Acute inhalation toxicity				
Animal	No data available	LD50 rat 4 h >0.83 mg/L	No data available	LD50 rat 4 h >0.83 mg/L
Human	No data available	No data available	No data available	No data available
Acute dermal toxicity				
Animal	No data available	LD50 rat >2.000 mg/kg	No data available	LD50 rat >2.000 mg/kg
Human	No data available	No data available	No data available	No data available
Skin irritation				
Animal	Rabbit: no skin irritation	Rabbit: no skin irritation 24 h	Rabbit: no skin irritation	Rabbit: no skin irritation 4 h
Human	No data available	No data available	No data available	No data available
Eye irritation				
Animal	Rabbit: no eye irritation	Rabbit: no eye irritation 30 s	Rabbit: no eye irritation	Rabbit: no eye irritation
Human	No data available	No data available	No data available	No data available
Evaporation rate	No data available	No data available	No data available	No data available
Exposure controls				
Eye/face protection	Safety glass	Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN166 (EU). Safety glasses	Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN166 (EU). Safety glasses	Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN166 (EU). Safety glasses
Respiratory protection	Required when dusts are generated. Recommended filter type: filter P 1 (acc. to DIN 3181) for solid particles of inert substances	Respiratory protection is not required	Respiratory protection is not required	Respiratory protection is not required

Conflict of Interest Statement

There are no conflicts of interest.

Funding Sources

There are no funding sources.

Author Contributions

Somporn Chantra, MD, case owner, made substantial contributions to the conception or design of the work, interpretation of data for the work, drafting the work or revising it critically for important intellectual content, and final approval of the version to be published. Pareena Chaitanuwong, MD, case owner, made substantial contributions to the conception or design of the work, interpretation of data for the work, and drafting the work or revising it critically for important intellectual content. Kasem Seresirikachorm, MD, made substantial contributions to the conception or design of the work, interpretation of data for the work, and drafting the work or revising it critically for important intellectual content. Mitchell Brinks, MD, MPH, made substantial contributions to interpretation of data for the work, drafting the work or revising it critically for important intellectual content, and final approval of the version to be published. Onsiri Serirat, MD, case owner, gave final approval of the version to be published. Winston Chamberlain, MD, PhD, made substantial contributions to interpretation of data for the work, drafting the work or revising it critically for important intellectual content, and final approval of the version to be published. Paisan Ruamviboonsuk, MD, made substantial contributions to the conception or design of the work, interpretation of data for the work, drafting the work or revising it critically for important intellectual content, and final approval of the version to be published.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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