CASE REPORT

Episcleritis Followed by COVID-19 Pneumonia after COVID-19 Vaccination

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Abstract

A 56-year-old man presented at the emergency department with bilateral eye pain, itching and watery discharge for 10 days, fever for seven days, and cough for one day. He had been vaccinated against COVID-19 and had developed ocular symptoms two days after receiving the second dose of the vaccine Sinopharm. Investigations revealed that the nasal PCR was positive for COVID-19. We managed him on the lines of episcleritis and critical COVID-19 pneumonia. The patient later deteriorated and was intubated. He died on the sixth day of his hospitalization as a result of a protracted disease course and ST-segment elevation myocardial infarction (STEMI). We report the development of episcleritis and critical COVID-19 infection after COVID-19 vaccination to emphasize the consideration of antibody-dependent enhancement after vaccination.

Keywords: *COVID-19, episcleritis, pneumonia, vaccination.*

INTRODUCTION

SARS COV-2 has become the greatest pandemic of the decade [1]. The disease primarily affects the lungs, resulting in mild to critical COVID-19 pneumonia [2]. Several measures have been implemented to prevent its spread, which includes standard operating procedures (SOPs), personal protective equipment (PPE), safe distancing, isolation and vaccination [3].

Since the publication of the genetic sequence of the SARS-COV 2 virus in January 2020, researchers have been working to develop an effective vaccine to prevent the disease's development and spread. Various factors have been evaluated, including nucleic acid sequence (DNA and RNA), peptide, viral factor, virus-like particle, and recombinant protein. There have been efforts to develop both live attenuated and inactivated vaccines [4]. Research is still being carried out to develop vaccines against different strains of the virus. According to the World Health Organization (WHO), potential vaccines in development include inactivated or weekend virus vaccines, protein-based vaccines, viral vector vaccines, RNA and DNA vaccines [5]. Researchers are gradually introducing these to eradicate or at least control the disease.

The systematic manifestations and disease development post-vaccination have been studied since the introduction of COVID-19 vaccination to people. Symptoms following vaccination could be a side effect of the vaccine, manifestation of the disease development post-vaccination due to antibody-dependent enhancement or immunocompromised status, or it might be incidental. It is critical to take note of them so that appropriate action can be taken if multiple such reports are received. The most frequent symptoms reported after vaccination include headache, fatigue, dizziness, and anaphylaxis [6]. Systemic and local manifestations vary with the first and second doses of vaccination [7]. We report a case of a male patient who developed episcleritis followed by critical COVID-19 pneumonia two days after the second dose of the COVID-19 vaccine. We also highlight the mechanism of antibody-dependent enhancement behind it. As the COVID-19 vaccine is novel, it is essential to note any adverse health outcomes after its administration.

CASE PRESENTATION

A 56-year-old male, known case of diabetes mellitus, hypertension, ischemic heart disease, status-post percutaneous coronary intervention (done 5 years back), presented at the emergency department of a private hospital in Pakistan with the complaint of bilateral eye pain, redness, itching and watery discharge from eyes for 10 days, fever for seven days and cough for one day. He had been using oral antihypertensive drugs (Tablet Amlodipine 5 mg once daily), oral hypoglycemic drugs (Tablet Metformin 500 mg once daily) and dual oral antiplatelet drugs (Tablet Clopidogrel 75 mg once daily and Tablet Ascard 75 mg once daily) for his comorbidities. The patient had received two doses of the COVID-19 vaccine Sinopharm, the first dose twenty-three days before the onset of symptoms and the second dose two days before the symptoms. He had no history of travel but had front-line COVID-19 healthcare workers at home. All the healthcare workers were vaccinated against COVID-19 and followed SOPs strictly. He had no history of exposure to any COVID-19 positive patient.

The family stated that the patient was in his usual state of health before the second dose of receiving the vaccine Sinopharm and developed ocular symptoms after two days of the second dose of vaccine. These were

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Table 1: Laboratory investigations at the time of presentation.

Labs	Result	Normal Range	Unit
Haemoglobin	14.4	(12.3-16.6)	g/Dl (grams per decilitre)
Haematocrit	43.3	(38.4-50.7)	% (percent)
White Blood Cell Count (WBC)	9.8	(4.8-11.3) x10E9	cells/L (cells per Litre)
Neutrophils	94.3	(34.9-76.2)	%
Platelet (PLT)	121	(154-433) x10E9	cells/L
Neutrophil to Lymphocyte Ratio (NLR)	21	(1-4)	Ratio
Red Cell Distribution Width (RDW)	14.5	(12.1-16.9)	%
Lactate Dehydrogenase (LDH)	459	(120-246)	U/L (Units per Litre)
C-REACTIVE PROT (CRP)	175.05	(0-10)	mg/L (Milligrams per Litre)
Prothrombin Time (PT)	12.1	(9.3-12.8)	Seconds
International Normalized Ratio (INR)	1.2	(0.9-1.2)	Ratio
Activated Plasma Thromboplastin Time (APTT)	35.0	(22.9-34.5)	Seconds
D-DIMER	4.0	<0.5	mg/L FEU
Brain Natriuretic Peptide (PBNP)	2018	<125	pg/mL (picograms per millilitre)
Sodium	139	(136-145)	mmol/L (millimoles per Litre)
Potassium	3.4	(3.5-5.1)	mmol/L
Chloride	97	(98-107)	mmol/L
Bicarbonate	18.70	(19-24)	mmol/L
Blood Urea Nitrogen (BUN)	40	(6-20)	mg/dl (milligrams per decilitre)
Creatinine	1.8	(0.9-1.3)	mg/dl
Troponin I	0.127	>0.04	ng/ml (Nano grams per millilitre)

Arterial Blood Gas (ABG) on presentation

Table 2: Shows the arterial blood gas result on presentation (May 6; 2021- 12.53 pm).

Lab	Value	Reference Range	Unit
PH	7.37	(7.35-7.45)	
PCO2	35.10	(35-48)	mmHg (millimetre of mercury)
PO2	48.00	(83-108)	mmHg
Bicarbonate	19.70	(19-24)	mEq/L (milli Equivaents per Litre)
Base Excess	-4.8	(-2-3)	mEq/L
O2 Sat	81.30	(94-98)	%

Arterial Blood Gas (ABG) on presentation

Table 3: Shows his urine detailed report (UDR) (May 6; 2021- 10.45 am).

Labs	Result	Reference Range
Color	Dark Yellow	
Appearance	Slightly turbid	
Specific Gravity	1.033	1.005 - 1.025
pH	5	
Urine Protein	1.5 g/L (3+)	Negative
Glucose	17 mmol/L (3+)	Negative
Ketone	0.5 mmol/L (1+)	Negative
Nitrite	Negative	Negative
Leucocyte Estrase	Negative	Negative
Red Blood Cells	Occasional	0-2 /HPF (per High Power Field)
Leucocytes	Occasional	0-4 /HPF
Epithelial Cell	Nil	/HPF
Non Squamous Cell	Nil	0-4 /HPF
Bacteria	Moderate	nil/HPF
Yeasts	Nil	nil/HPF
Other Casts	NIL	nil/HPF
Crystals	Nil	nil/HPF

Urine Detailed Report

gradual in onset, and progressive in nature, for which he consulted a physician and took eye drops (artificial tears and topical tobramycin) for seven days. Eye symptoms gradually started improving after taking those drops but did not completely resolve. He then developed a continuous fever, relieved by antipyretics and spiked highest up to 38.2°C. He also complained of a cough for one day, which was dry.

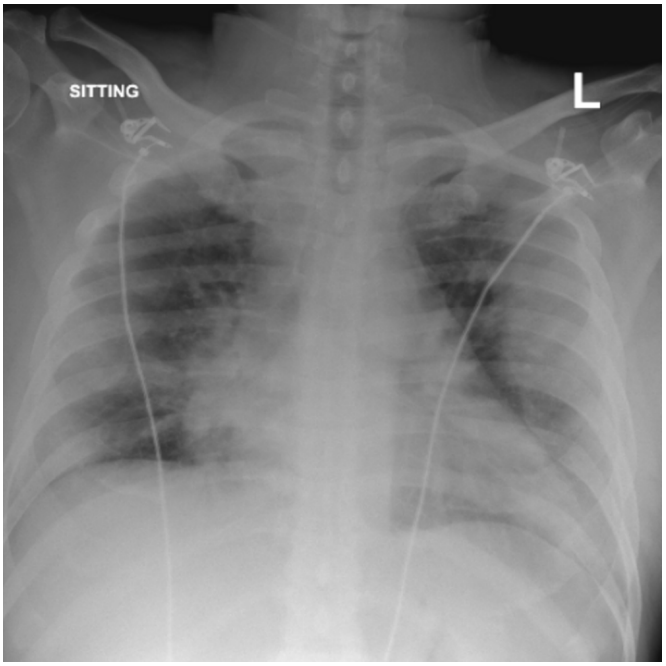

Fig. (1): Chest X-Ray showing bilateral parenchymal opacities in mid and lower zones (done on May 6; 2021- 9.37 am).

On presentation, his blood pressure was 119/65 mmHg, pulse was 117 beats/minute, respiratory rate was 30 breaths/minute, oxygen saturation was 94% on room air, and the temperature was 38.5'C. He had bilateral red-eye with a watery discharge. Chest auscultation revealed bilateral crept. The rest of the systemic examination was unremarkable. The laboratory investigations are shown in Tables **1**, **2**, and **3**.

His Chest X-Ray showed bilateral parenchymal opacities in mid and lower zones, suspicious of infection (**Fig. 1**).

Ultrasound of kidneys was normal.

The patient tested positive for COVID-19 on nasal swab sent for PCR (Polymerase Chain Reaction).

On presentation, the patient had labored breathing so Continuous Positive Airway Pressure (CPAP) ventilation was given. We managed him on the lines of episcleritis, critical COVID-19 pneumonia, and acute kidney injury secondary to an underlying infection, and shifted him to the COVID-19 Special Care Unit. CPAP was intermittently applied. Infectious disease, pulmonology and ophthalmology teams were consulted. Injection (Inj.) paracetamol 1000 mg three times a day, dexamethasone 6 mg once a day, remdesivir 100 mg once a day, and enoxaparin in renal adjusted dose once a day was given. Artificial tears were given and cold compresses were applied to the eyes. Episcleritis was transient and resolved after 12 days of symptom development. The patient's condition deteriorated later, and he was intubated. He died on the sixth day of his hospitalization as a result of a protracted disease course and ST-segment elevation myocardial infarction (STEMI).

DISCUSSION

This case report describes a patient who developed episcleritis followed by critical COVID-19 pneumonia after receiving the COVID-19 vaccine Sinopharm. COVID-19 vaccines were introduced to people in December 2020, and their side effects have been studied since then. Reactogenicity to lipid nanoparticles, production of inflammatory mediators in the body, and antibody-dependent enhancement (ADE) are proposed mechanisms for these negative outcomes [8-11].

The mechanism of reactogenicity to lipid nanoparticles and the production of inflammatory mediators is usually seen in vaccines like Pfizer and Moderna. In these vaccines, lipid nanoparticles (LNPs) encase messenger RNA (mRNA). A neutral phospholipid, cholesterol, polyethylene glycol lipid, and an ionizable cationic lipid are the four main components of LNPs. SARS-CoV-2 viral spike glycoprotein is also encoded by mRNA, so LNPs aid in the uptake of mRNA of COVID-19 into the cytosol following intramuscular injection. In the ribosomes, the mRNA is translated into S protein, which serves as an antigen target for B lymphocytes. Thus, intramuscular administration of these vaccines causes local inflammation in response to lipid nanoparticles, which causes the recruitment of neutrophils and antigen-presenting cells to the site of delivery. This results in side effects, such as pain, swelling, fever and drowsiness [8, 9].

The next major mechanism responsible for adverse outcomes following vaccination is an antibody-dependent enhancement (ADE). It occurs because high-affinity antibodies in the vaccines usually eliminate the infection, while non-neutralizing or sub-neutralizing antibodies bind to the viral antigen without eradicating the infection, resulting in ADE. Chau YC, *et al.* in their study thoroughly explained the extrinsic and intrinsic mechanisms of ADE. Extrinsic enhancement occurs when the Fc region of the antibody-virus immunocomplex binds to Fcy receptor, leading to increased phagocytic cell expression and increased viral uptake by them, which increases a load of virus-infected cells in the body. Intrinsic enhancement occurs due to the immunomodulation of the antibody signaling pathway resulting in excessive viral replication. According to Lee WS, *et al.* ADE in viral infections occurs in two ways: the first one is similar to the extrinsic mechanism described previously and the second, is due to increased inflammation as a result of excessive immune complex formation. Antibody-dependent enhancement is usually seen when multiple strains of the same virus coexist, resulting in the destruction of one by antibodies while sub-neutralization of others. It is more common following the administration of inactivated vaccines, as these have multiple epitopes which increase the production of sub- or non-neutralizing antibodies [10, 11]. As Sinopharm is an inactivated COVID-19 vaccine, we believe this to be the possible mechanism of the development of adverse effects in our case.

Though antibody-dependent enhancement tends to be a major cause behind these side effects, our patient had multiple comorbid conditions, including diabetes mellitus, hypertension, and ischemic heart disease, which we believe may have precipitated the phenomenon. Immunocompromised people are more likely to develop ophthalmological manifestations and the disease itself [10]. The immunocompromised state could be due to the patient's comorbid conditions, immunosuppressive pharmacologic therapy, or the disease process itself. These result in the development of more severe diseases. Our patient died as a result of ST-segment elevation MI, which could have been caused by the previous comorbid conditions compounded by the COVID-19 disease.

We report this case of episcleritis and critical COVID-19 pneumonia after the second dose of inactivated vaccine Sinopharm, raising the possibility of antibody-dependent enhancement following COVID-19 vaccination. Symptoms can be temporary or persistent. In our patient, the symptoms of COVID-19 infection started with episcleral inflammation and progressed to critical COVID-19 pneumonia. A few case reports have shown the development of bilateral choroiditis, vision loss, and

panuveitis following the administration of the COVID-19 vaccine after vaccines Sinopharm, Astra Zeneca and Pfizer [12-15]. In this regard, additional observations and reports are required. The case emphasizes the importance of adhering to SOPs even after vaccination, as ADE increases the risk of developing more severe COVID-19 illness following vaccination. Appropriate patient counselling and public awareness are required.

CONCLUSION

Antibody-dependent enhancement (ADE) is a possibility after the inactivated COVID-19 vaccine Sinopharm. The phenomenon can be precipitated by the patient's immunocompromised status, and the symptoms can be transient or permanent. By virtue of this case report, we hope to encourage others to report any systematic manifestation of COVID-19 illness observed after vaccination, as well as raise awareness of the importance of adherence to SOPs even after vaccination.

CONSENT FOR PUBLICATION

Written Informed consent was taken from the patient for publication and he was informed that none of his personal information will be included in the final publication.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Declared none.

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