Scleritis Following the booster shot of inactivated COVID-19 (Sinopharm) Vaccine in a 52-year-old Woman

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Abstract

Background : The only way to mitigate the spread of COVID-19 pandemic, were vaccines. Although effective in decreasing the rate and severity of the disease, there has been also considerable adverse events. Since the birth of vaccines, adverse reactions undeniably accompanied vaccines immunity and COVID-19 vaccines are no exceptions. In this report, we aimed to evaluate a rare reaction.

Case presentation : We report a 52-year-old woman, presenting with scleritis following the third dose of Sinopharm vaccinations. She had no significant past history of any disease or any similar reactions after previous doses. No significant positive point was found during evaluations. She was prescribed a tapering dose of prednisolone (30mg at the start), along with azathioprine (50mg/day) to control the episode. After two weeks, the scleritis completely resolved.

Conclusion: Adverse events of vaccines could be a sign of an undiagnosed autoimmune disease. As mentioned in this case, clinicians must carefully assess patients with ocular adverse events as they are highly associated to undiagnosed autoimmune diseases.

Keywords

scleritis; COVID-19; COVID-19 vaccine; adverse events; case report

Key Clinical Message: Although vaccination is necessary to prevent infectious diseases, there are also rare adverse events that could be a sign of an undiagnosed autoimmune disease. Clinicians must carefully assess patients to rule out possible underlying diseases.

Introduction

In December 2019, world faced the outbreak of COVID-19 of which the SARS-CoV-2, was known as the causative pathogen. As the virus found its way world spread, in beginning of march 2020 WHO officially declared the disease as a pandemic (1).

Inevitably, massive vaccination became the only way to prevent and control the unleashed pandemic (2). In almost two years 155 vaccine candidates were developed which 23 of them were authorized fallowing different strategies (inactivated, mRNA, viral vector, nanoparticle-based peptide vaccines, etc.). All authorized vaccines have shown promising efficacy; however, the AEs and SAEs remained an unknown challenge (3). The most common AEs were injection site pain or tenderness, fatigue, headache, rash, fever, chill, as well as myalgia, and arthralgia (4). Moreover, thrombosis and thrombocytopenia, myocarditis or pericarditis, inflammatory myositis, and autoimmune diseases were frequently reported SAEs (4, 5). To date few, studies have reported cases of ocular inflammatory AEs after the first or second dose of vaccination, including white dot syndrome, pan uveitis, choroiditis, along with scleritis and scleritis (6, 7).

Herein, we reported a case of 52-year-old woman presented with simple scleritis following third dose of Sinopharm COVID-19 vaccination.

Case Presentation

A 52-year-old woman presented with redness in both eyes for one week (Figure1). She had no history of hypersensitivity reaction or similar events. The patient first developed right eye redness 3 days following the third dose of inactivated Sinopharm vaccine (BBIBP- CorV), which spread to the left side 3 days after. In physical examination, the patient's vital signs were normal and stable, without respiratory distress and fever. No signs of lymphadenopathy or splenomegaly were detected. The patient's neurological examination was unremarkable. The ophthalmic evaluation showed no signs and symptoms of eye discharge, pain, photophobia, and itching. Besides, the patient had a remarkable past medical history of pterygium on her left eye conjunctiva in the past year, well controlled. The oculist reported her visual acuity to be 20/20 OU before. Slit lamp examination showed anterior diffused scleritis with negative phenylephrine test results. There was no sign of inflammation or the existence of cells.

Laboratory results showed elevated levels of CRP, and ESR to be 9.1 (positive: >9), and 39 (positive>30). Moreover, liver function tests, kidney function tests, albumin, total protein, PANCA and anti-MPO, CANCA and Anti PR3, FANA, ds cryoglobulins, C3, C4, anti-dsDNA, serology tests for HCV, HBV and HIV were negative or normal (Table 1). Also, the results of stool examination and urinalysis did not reveal any findings in favor of renal disorders or infectious diseases.

Radiological evaluation with a CXR and computed tomography scan did not show any notable findings. Echocardiography and electrocardiogram showed no abnormal findings without any systolic or diastolic dysfunction and with normal EF. EMG-NCV were normal.

By merging all the information obtained from the patient's symptoms and clinical evaluations, and the recent COVID-19 vaccine, scleritis as an autoimmune reaction induced by Sinopharm COVID-19 vaccination was approved after all assessments.

She was administered a tapering dose of prednisolone (30mg at the start), followed by azathioprine (50mg/day) to control the episode. After two weeks, the scleritis completely resolved.

Discussion

Episcleritis has been previously found in a patient confirmed with COVID-19 infection (8, 9). In this report, we presented a case of scleritis after the third dose of COVID-19 vaccination with inactivated Sinopharm vaccine. Recently, Pichi and colleagues reported four cases scleritis and episcleritis following the first dose of COVID-19 Sinopharm vaccination (10). There has been few reports of mild scleritis or episcleritis caused by live virus vaccination previously (11).

Regarding various reports of ocular adverse events induced after vaccination, COVID-19 vaccination-associated scleritis would not be exempt in surprising. The pathogenesis and mechanism of this immune response, remains the question. The most frequently proposed mechanism include molecular mimicry between scleral and vaccine peptides as well as hypersensitivity due to antigen-specific cell and antibody reactions (12). Moreover, although safe in most of the population, vaccine adjuvants that were added to achieve the desired protection, led to autoinflammatory syndromes particularly connective tissue disorders due to different nucleic acid metabolism (9, 13, 14). Noteworthy, inactivated COVID-19 vaccines stimulate T helper 2 cell reactions causing an increase in inflammatory (15). The addition of alum as an adjuvant aggravated immunopathologic reactions (16).

The genes for immunity, inflammation, and coagulation are part of X chromosome, so we may suspect that viral interactions associated with human genes could induce an abnormal immune response in COVID-19. Besides, according to Manzo et al., the presence of excess antigen and the formation of relatively resistant soluble antigen-antibody immune complexes after exposure to SARS-CoV-2 may cause persistent inflammation in organs (17). There are several reported cases of ocular inflammation and related conditions following COVID-19 vaccination. These include anterior uveitis (7, 18), scleritis (7), episcleritis (7), multiple evanescent white dot syndrome, Vogt-Koyanagi-Harada disease (19), panuveitis (20), choroiditis (21), and central serous chorioretinopathy (22). Most cases were successfully treated with corticosteroid therapy, including topical, intravitreal, and/or systemic administration, and many patients achieved complete recovery of their baseline visual acuity. A case series of orbital inflammation following mRNA vaccines was also described, with all cases successfully treated with oral prednisolone (23). It is important for healthcare providers to be aware of these potential ocular reactions to COVID-19 vaccination and to monitor patients closely for any signs or symptoms of ocular inflammation or related conditions.

As mentioned, our patient didn't show any serious reaction to previous doses of inoculation until the first booster. These reactions were found to be induced by activation of the secondary immune response; the memory cells (24). Comparing to the first and second doses of vaccinations, Rahmani et al. Reported that booster doses are more probable to stimulate rare AEs including neurological symptoms (25). Moreover, authors suggested hormonal, genetic, and behavioural factors along with the time between the primary cycle to the first booster dose. The more the time between the booster dose and the first administration, the higher the immunogenic effect after the third shot (25). Consequently, further studies could elucidate the proper time of the booster inoculations, particularly for high-risk patients in order to prevent serious reactions.

Vaccine-associated maladaptive immune response becomes more important in patients with autoimmune diseases. A study demonstrated that ocular inflammatory AEs following vaccination could be the first presentation of an undiagnosed autoimmune disease (26). Thus, there should be further assessments in patients presenting with ophthalmologic inflammatory reactions following COVID-19 vaccination.

List of abbreviations

COVID-19: coronavirus disease 2019

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

WHO: World Health Organization

AEs: Adverse Events

SAEs: Serious AEs

PANCA and anti-MPO: perinuclear anti-neutrophil cytoplasmic antibodies

CANCA and Anti PR3: anti-neutrophil cytoplasmic antibodies

CXR: Chest X-ray

EMG-NCV: Electromyography-nerve conduction velocity

AST: aspartate aminotransferase

ALT: alanine transaminase

WBC: White blood cell

RBC: Red blood cell

Hb: hemoglobin

MCV: mean corpuscular volume

MCH: mean corpuscular hemoglobin

MCHC: Mean corpuscular hemoglobin concentration

ESR 1h: Erythrocyte Sedimentation Rate in one hour

CRP: c-reactive protein

Anti B2-GLP1 antibody: anti-b2glycoprotein antibody

ACA: anti-cardiolipine antibody

LA antibody: lupus anticoagulant

dRVVT: Diluted Russell Viper Venom Time

aPPT: activated partial prothrombin time

Anti-dsDNA: anti- double-stranded DNA

C3/C4: complement 3/4

CH50: total hemolytic complement

FANA: fluorescent antinuclear antibody

Anti-Sm/RNP antibody: anti-Smith/antinuclear ribonucleoprotein antibody

HLA: human leukocyte antigen

HCV, HBV and HIV

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the participant in this study for all the information and images.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare no competing interests.

Authors' contributions

K.J analyzed and interpreted the patient data and revised the article critically for important intellectual content, M.R performed associated examinations, F.H and M.S were major contributors in writing the manuscript, M.M drafted the article and approved the version to be published

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	Test, Unit	Result	Reference Range
Blood biochemistry	AST, U/L	17	Up to 35
	ALT, U/L	15	Up to 45
	Uric Acid, mg/dL	4.3	Male 3.4-7 Female 2.4-5.7
Hematology	WBC, µL	8800	4000-11000
	RBC, 10^6/µL	4.84	4.2-6.3
	Hb, g/dL	12.6	12-16
	Hematocrit, %	40.5	30-45
	MCV, fL	83.67	80-100
	MCH, pg	26.03	27-32
	MCHC, g/dL	31.11	33-38
	Platelet, µL	363000	150000-450000
	Neutrophil, %	40%	–
	Lymphocyte, %	25%	–
	Urine 24hr/ Pr, mg/24hr	147	24-141
	Urine 24hr/ Volume, g/24hr	1200	–
	Urine 24hr/Cr, mg/24hr	624	600-1800

	Test, Unit	Result	Reference Range
Serology	ESR 1h	39	positive: >30
	CRP quantitative	9.1	positive: > 6
	Anti B2-GLP1 antibody (IgG)	7	positive: >20
	Anti B2-GLP1 antibody (IgM)	1.7	positive: >20
	ACA IgG	24	positive: >=12
	ACA IgM	1.5	positive: >=12
	LA antibody (dRVVT)	34	direct :25- 45
	LA antibody (aPTT)	30	after mixing: 25-45
	Anti-ds DNA	6.6	positive: >=100
	C3	165	90-180
	C4	54	10-40
	CH50	90	positive: >=90
	FANA	negative	Up to 1/100
	C-ANCA	negative	Up to 1/10
	P-ANCA	negative	Up to 1/10
	Anti-Sm/RNP antibody	0.1	Up to 20
	HLA-B27	negative	–
	HLA-B5	positive	–
	HLA-B51	negative	–

Figures, tables and additional files

TABLE 1 Laboratory Test Results

FIGURE 1: Unilateral anterior scleritis following COVID-19 Sinopharm vaccination three days after the third dose