Immune Thrombocytopenic Purpura After Receiving AstraZeneca Coronavirus Disease-2019 Vaccine in A Patient with A Past History of the Same Disease: A Case Report

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June 12, 2023

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key words: AstraZeneca, immune thrombocytopenic purpura, ChAdOx1 nCoV-19, AZD1222, case report, covid-19

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Key Clinical Message: Immune thrombocytopenic purpura (ITP) is an autoimmune disease characterized by a low platelets count, petechiae, purpura, and conjunctival hemorrhage. In this paper, we present a relapse of ITP in an Iranian 31-year-old woman as a potential complication of the AstraZeneca vaccine.

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2)classified in the coronaviridae family is characterized as a pandemic, and the virus is spreading increasingly worldwide (1). Accelerated efforts to develop safe and effective vaccines commenced immediately to control this pandemic (2). AstraZeneca/Oxford's AZD1222, a vaccine candidate that entered phase 1 clinical trial in mid-May 2020, was injected intramuscularly in two doses to the participants aged 18-55 years at least 28 days intervals (3). Early observations insinuate that exposure to the AstraZeneca COVID-19 vaccine might trigger the expression of antiplatelet antibodies, resulting in a condition with thrombocytopenia and venous thrombotic events (e.g., intracranial venous sinus thrombosis) (4). ITP is a rare autoimmune disorder with reduced circulating platelets and occasionally impaired megakaryopoiesis (5). Platelets, as the smallest cell fragments of the human blood,

are central players in the processes of hemostasis and thrombosis (6). The normal human platelets count ranges from 150×10^9 to 450×10^9platelets per liter of blood, and its insufficient count elevates the risk of spontaneous bleeding (7). In this case report, we confer the relapse of immune thrombocytopenic purpura after the first vaccination with "the COVID-19 vaccine AstraZeneca" the first time.

Case history

An Iranian 31 years old female with a previous history of ITP presented with progressive, vast, and diffuse ecchymosis, increased scattered petechia purpura, and fatigue three weeks after receiving the first dose of AstraZeneca. As a result of symptoms persistence, she was referred to an outpatient laboratory to evaluate her complete blood count (CBC) 28 days after vaccine injection. CBC result showed a platelet count of &lt2000 / Mm^3 and demonstrated ITP relapse. Considering her previous medical history, she had experienced a platelet decrease (9000/ Mm^3 platelet count) when she was 25. On that occasion, various tests including autoimmune diseases tests (rheumatoid arthritis, lupus, and antiphospholipid syndrome), and bone marrow aspiration had ruled out other causes of platelets decrease and confirmed ITP. She had been treated with dexamethasone injection for three days in the hospital and taking prednisolone pills for six months. She had periodic checkups of CBCs, and the range of platelets was different between 210-100$\times$ 10^3/ Mm^3. The last CBC monitoring was carried out in 2019.

Differential diagnosis, investigations and treatment

After the COVID-19 pandemic, nevertheless, our case did not perform routine checkups, nor did she have any symptoms of platelet depletion such as scattered ecchymoses and fatigue before receiving the vaccine. Since she previously had ITP, she was given high dose dexamethasone and then saw a physician who recommended hospital admission when her platelet count came back at 25000/ Mm^3. Other hematological, biochemical, and immunological tests did not reveal any other disease except intensive thrombocytopenia (Table 1).

In addition, her CRP was negative, and ESR was normal, ruling out any infection and inflammation existence that could be related to other causes of ITP. In the hospital, she received intravenous immunoglobulin (IVIG)(50gr) and dexamethasone (40mg) for four days, and after her platelet count reached above 100x 10^3/ Mm^3, she was discharged. On completion of treatment, she had been prescribed 40mg per day of dexamethasone for four days at intervals of two weeks with periodic monitoring of her CBC. Figure1 illustrates platelet counts considering before and after disease diagnosis and treatment.

Outcome and follow-up

Considering the persistence of platelet count in the normal range and with due attention to the previous finding that expresses the benefit of vaccination is more than its risks (8), our case received the next dose of AstraZeneca vaccine three months after the first dose and about 1.5 months after treatment completion. Nevertheless, her platelet stability did not collapse (210x 10^3/ Mm^3), nor did she present signs of ITP. Moreover, she got vaccinated with the same vaccine for the third time about six months later and she did not experience any side effects (platelet count: 213x 10^3/ Mm^3).

Discussion

Immune thrombocytopenic purpura is an autoimmune blood disorder characterized by platelet reduction followed by petechiae, purpura, conjunctival hemorrhage, or other types of mucocutaneous bleeding (9). The incidence of the disorder is about 100 in 1milion people each year, and most of the patients are children (9). However, it is developed in acute form lasting about six months in children and adults. It is generally chronic and occurs more in women than men (9). Early detection of ITP is critical because intracranial hemorrhage could be the major cause of fatal bleeding in these patients (9). Immune thrombocytopenic purpura usually appears following autoimmune conditions and viral infections (6). In addition, considering many reports, ITP could be manifested as a result of vaccines (6).

More than 100 COVID-19 vaccine candidates are currently under development, and the number is increasing (10). Various types of vaccines are classified into recombinant protein vaccines, mRNA-based vaccines, DNA-

based vaccines, and vector-based vaccines (10). The AstraZeneca vaccine is from the adenovirus category, and the vaccine candidate is ChAdOx1 nCoV-19 (10). The advantages of this vaccine are a high transfection efficacy, as the viral vector imitates the natural infection process. Disadvantages are that the vaccine may promote thrombocytopenia and intracranial venous sinus thrombosis (4). In addition, there are some reports of post vaccine ITP (11).

Previously, Koch and his colleagues described a 41 years old male with ITP, 14 days after the first dose of vaccination with AstraZeneca from Germany (5). Furthermore, there were other reports of ITP three and two days after receiving AstraZeneca in a Korean 66 years old female and an Iraqi 25 years old male respectively (16, 17). In a case series, 17 cases were reported with secondary ITP related to AstraZeneca. All of them had onset within 28 days after vaccine administration, but one case diagnosed with ITP after 78 days (11).

According to the information from previous vaccines, various mechanisms could trigger ITP after vaccination, such as impairment regulation of T cells, elevated pro-inflammatory cytokine production, and increased macrophage-mediated eradication (12). Although the mechanism of vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) post-AstraZeneca vaccine has been elucidated in some research (13), there isn't much known about the mechanism of immune thrombocytopenia post-AstraZeneca vaccine. It seems IgG antibodies against platelet factor 4 (PF4) are responsible for VITT (14). On the other hand, IgG is the principal antibody in ITP, which is opposed to platelet membrane glycoproteins such as GPIIb/IIIa (15). Moreover, spike protein is the antigenic target for vaccines such as SARS-CoV-1 and MERS (15). But it's unclear whether spike protein and the PF4 have any cross-reactions with each other (15). Altogether, more information is required to determine if the underlying mechanism of other vaccines can be the same as post-COVID19 vaccine ITP.

In this paper we introduced an Iranian 31 years old female with a past history of ITP who developed petechia purpura and ecchymosis following AstraZeneca first dose administration and diagnosed with thrombocytopenia. After completion of treatment the next doses of the same vaccine are injected and there were no side effects. To the best of our knowledge, this paper may be the first case report presenting a patient with a past history of vaccine complication receiving the second and booster doses of the same vaccine without any incident.

Conclusion

Some patients with past history of ITP may be more susceptible to immune thrombocytopenia from drugs or inciting agents as well as AstraZeneca Coronavirus Disease-2019 Vaccine. Physicians should always be cautious administering new agents to ITP patients since that disorder, a prior indicated altered immune response. In addition, measuring platelet count before and after vaccine reception is suggested. Furthermore, it is indispensable to pay attention to any early signs of ITP to primarily manage the condition and prevent disease deterioration that could be life-threatening.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of the Infectious Diseases Center, Gonabad University of Medical Sciences, Gonabad, Iran. (IR.GMU.REC.1400.207).

Author contributions

Saba Seyedi: Conceptualization, Writing – original draft

Shadan Navid: investigation, data curation

Zahra Saadatian: Supervision, writing – review and editing

Acknowledgements

We would like to thank the patient for agreeing to share her clinical information with the readers of this article.

Funding information

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

All authors have approved the manuscript for submission and have no competing interests to declare.

Consent

Written informed consent was obtained from the patient for publication of this case report.

Availability of data and material

Not applicable

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FIGURE1: platelet count x 10 ^{3}/ Mm^{3} based on test date.

Vertical axis denotes platelet count and normal range of platelet is over than 150x 10^{3}/ Mm^{3}. Horizontal axis denotes the date that the tests were performed.

TABLE1: Results of clinical laboratory tests after first spontaneous intravenous injection of dexamethasone 40 mg

Hematology Test CBC

Test	Result	Reference Value/Unit
WBC	11400	4000-11000/Mm^{3}
Neutrophils	10400	3000-5800/Mm^{3}
Lymphocytes	700	1500-3000/Mm^{3}
Platelet	25000	150,000-400,000/Mm^{3}
RBC	4.62	4-5.1/Mm^{3}
Hb	14.0	12.0-16.0/Mg/dl
HCT	40.5	34-44/%
MCV	87.8	80-96/fl
MCH	30.3	27-33/pg
MCHC	34.6	32-36/g/dl
ESR 1st hr	9	0-20/mm/h
PT		
PT patient	14.2	second
PT Control time	12.3	second
INR	1.16	
PTT	30.2	27-45/second
Biochemistry Test	**Biochemistry** Test	**Biochemistry** Test
Blood Biochemistry	Result	Reference Value/Unit
BUN	16	7-21/mg/dl
Creatinine	0.61	0.6-1.2/mg/dl
Na	133	40-220/mEq/L
K	3.7	3.5-5/mEq/L
Ca	8.9	8-11/mg/dl
Bilirubin Total	0.99	1.0-10.5/mg/dl
Bilirubin Direct	0.25	0.1-0.3/mg/dl
AST	46	15-46/U/L
ALT	43	8-45/U/L
ALP	280	64-306/U/L
ALB	4.54	3.5-5.2/g/dL

Immunology Test	**Immunology** Test	**Immunology** Test
Serology	Result	Reference Value
CRP	Negative	Negative

WBC: white blood cells; RBC: red blood cells; Hb: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; ESR1st hr: erythrocyte sedimentation rate first hour; PT: prothrombin time; INR: international normalized ratio; PTT: partial thromboplastin time; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: Alkaline phosphatase; ALB: albumin CRP: c-reactive protein

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