Spontaneous Subarachnoid Haemorrhage After COVID-19 Vaccination; a Rare Case Report

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Abstract

Introduction: Cerebrovascular incidents are considered uncommon but important complications of vaccination against coronavirus disease-2019 (COVID-19). Subarachnoid hemorrhages (SAH) usually occur due to an underlying cerebral aneurysm. In this study, we have reported a subarachnoid hemorrhage incidence in a patient shortly after receiving the COVID-19 vaccine (ChAdOx1-AstraZeneca).

Case Presentation: The patient was a 69-year-old male with no remarkable risk factors, referred to the emergency room with complaints of headache, nausea, and vomiting. The patient had received his first dose of vaccine against COVID-19 four days before symptoms started. An aggravated headache, nausea, elevated blood pressure (180/100), and drowsiness occurred on the second day of admission. Imaging from head computed tomographic (CT) scans implied acute hydrocephalus and increased intracranial pressure (ICP) caused by subarachnoid hemorrhage. The condition was treated by inserting an external ventricular drain (EVD), removed after one week, and the patient was discharged with no permanent deficit. We found no underlying vascular abnormality in primary and follow-up cerebral angiographies.

Conclusions: There are reports of cerebral hemorrhages caused by COVID-19 vaccination, mostly intra-parenchymal. Our study observed a type of cerebrovascular event that has not been reported frequently. Vaccine-associated cerebrovascular events, however rarely, are critical. It is important to demonstrate possible risks and complications, as vaccination programs against COVID-19 have become an essential part of health care in most countries.

Keywords: COVID-19, Vaccine, Subarachnoid Hemorrhage, AstraZeneca

1. Introduction

Coronavirus disease-2019 was reported on September 2019 in Wuhan, China, for the first time (1). Its worldwide spread caused the World Health Organization (WHO) to label it a public health emergency and international concern in January 2020, and in March 2020, it was declared a pandemic disease (2).

The most common symptoms of COVID-19 infection are fever, coughing, and dyspnea, while other symptoms include myalgia, diarrhea, sore throat, headache, fatigue, and anosmia (3, 4).

The physiopathology of this infectious disease is not fully understood (5). Potentially fatal complications could result from severe pneumonia or pulmonary edema (6).

History has proven to us that vaccines are a very effective solution to confront epidemics (7). Thus, the most important step in fighting against the COVID-19 pandemic is vaccines for acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (8, 9).

Most COVID-19 vaccines are designed to induce immune responses and neutralize antibodies against SARS-CoV-2 spike proteins (10).

Several vaccines, including mRNA, adenovirus vectors, protein subunits, and inactivated viruses, have proven effective in phase-III clinical trials and are now being used after emergency approval in many countries. Data from ongoing research suggest that protection might need low levels of neutralising antibodies (NAbs) and may contain other immune modulator mechanisms such as non-NAbs, T cells, and innate immune mechanisms (10).

Coronavirus disease-2019 vaccines that provoke a great amount of virus-neutralizing antibodies might be able to prevent infection. Strict clinical management and a thorough assessment of safety and immune responses are essential in vaccine trials (11).

Fourteen days after the first dose, S-binding antibodies appear and rise between 28 and 128 days later (12). T-cell responses maximized in 14 days after the first
COVID-19 wasn’t higher than in the normal population (21). Patients with no COVID-19. But the risk of SAH in patients with no COVID-19 (21). Also, mortality in patients who suffered from SAH and COVID-19 compared with patients experienced respiratory failure, pneumonia, septic shock, and acute kidney injury were significantly higher among those who suffered from SAH and COVID-19 compared with patients with no COVID-19 (21). Also, mortality in patients with SAH and COVID-19 was remarkably higher than in patients with no COVID-19. But the risk of SAH in patients with COVID-19 wasn’t higher than in the normal population (21).

Wolf et al. suggested that exposure to the COVID-19 vaccine “AstraZeneca” might provoke the expression of anti-platelet factor (PF) antibodies, which leads to thrombocytopenia and thrombotic events (such as intracranial venous sinus thrombosis). The treatment process in those patients must consider immunological phenomena, thromboembolic features, and coagulation disorders (17).

Aneurysmal SAH patients must undergo frequent examinations, tests, and prolonged intensive care. Standard SAH treatment protocols are not properly practical in the current COVID-19 situation due to the requirement for infection control and limitations of critical care resources (22).

Considering that there are limited data on large-scale vaccinations, reliable evidence on the safety of all COVID-19 vaccines is necessary. Especially relations between COVID-19 vaccines, idiopathic thrombocytopenic purpura (ITP), and venous or arterial thromboembolic and haemorrhagic events.

Due to the lack of data on large-scale vaccinations, reliable evidence regarding the safety of COVID-19 vaccines is needed, especially regarding the relationship between COVID-19 vaccines and ITP and venous or arterial thromboembolic and hemorrhagic events (14).

According to the elevated risk of haemorrhagic events due to some COVID-19 vaccines and the highly fatal nature of cerebral haemorrhage (including SAH), it is critical to collect and investigate their relativity, risk factors, and prevention strategies. In the current study, we have reported a subarachnoid hemorrhage after receiving the first dose of the AstraZeneca vaccine in a 69-year-old man in South Khorasan, Iran.

2. Case Presentation

A 69-year-old male with no significant medical history, non-smoking, presented with headache and nausea four days after receiving the first dose of the AstraZeneca vaccine. The patient was fully conscious, and his examination showed no abnormal findings except slightly elevated blood pressure (160/100 mmHg). Primary lab data (including Complete Blood Count, coagulation tests, etc.) were in the normal range (Table 1).

The patient’s headache got aggravated and were unresponsive to medication, followed by vomiting, confusion, lethargy, and high blood pressure (180/100) on the second day of admission. Also, an increase in C-reactive protein (CRP) was detected on the second day.

Head CT showed blood on the subarachnoid surface proximate to Willis circle, associated with ventriculomegaly and periventricular edema, suggesting communicating hydrocephalus due to subarachnoid hemorrhage (Figures 1 and 2).

To control the raised ICP, the patient underwent an external ventricular drain (EVD) placement, leading to re-
solving the loss of consciousness and other symptoms. After seven days, EVD was removed, and the patient was discharged with complete recovery. Both early and delayed (after four weeks) CT angiographies showed no signs of aneurism or vascular anomalies.

3. Discussion

This study reports the occurrence of subarachnoid haemorrhage in a patient who received the first dose of the AstraZeneca vaccine against COVID-19.

Since there are rarely similar cases, it is hard to determine causes or possible relationships between the COVID-19 vaccine and SAH incidence.

There are some reports about the association between spontaneous SAH and COVID-19 infection. The results showed that spontaneous SAH is more likely to occur in the early and late course of infection with COVID-19 (23). However, we haven’t found reports of isolated SAH after receiving the COVID-19 vaccine.
Figure 2. Head computed tomographic (CT) scan showing hydrocephalus

Subarachnoid hemorrhage is responsible for 5 - 10% of all strokes in the United States of America. Almost 10% of non-aneurysmal subarachnoid hemorrhage patients have no vascular abnormalities; thus, no interventional treatment is considered necessary in those cases (19).

A sudden onset thunderclap headache is the hallmark symptom of aneurysmal subarachnoid hemorrhage, which grows to maximal intensity in a few seconds, usually described as the “worst headache ever” (24-26).

Hemorrhage usually occurs during normal activities but also during stressful situations (27) and may be accompanied by symptoms or signs including nuchal stiffness, nausea, vomiting, focal neurologic deficits, photophobia, and loss of consciousness (28).

Average annual SAH incidence varies among different studies and countries, from two per 100,000 population per year in China to 22.5 per 100,000 per year in Finland (29). Some of these variations might be due to differences in diagnosing rates among countries (30, 31). Subarachnoid hemorrhage incidence is more common among
Table 1. Primary Lab Data

| Variables            | Values       |
|----------------------|--------------|
| CBC                  | 4.72 × 10^9 |
| RBC                  | 13.3 × 10^12 |
| WBC                  | 251 × 10^9  |
| Plt                  | 13.7 × 10^12|
| Hb                   | 39.2%        |
| Hct                  | 下标13.7 g/dL|
| BUN                  | 16 mg/dL     |
| Cr                   | 1.0 mg/dL    |
| Na                   | 141 mg/dL    |
| K                    | 3.9 mg/dL    |
| Ca                   | 9 mg/dL      |
| P                    | 3.1 mg/dL    |
| Mg                   | 2.19 mg/dL   |
| Blood sugar          | 157 mg/dL    |
| C-reactive protein   | Negative     |
| ESR                  | ??           |
| D-Dimer              | > 5000       |
| PT                   | 15 sec       |
| PTT                  | 25 sec       |
| INR                  | 1.07         |

women; it increases with age and peaks in the 50 s (31).

A Danish and Norwegian study conducted on people aged between 18 and 65 who received the ChAdOx1 vac-
cine reports elevated rates of venous thromboembolic in-
cidents (32). Also, the European Medicines Agency (EMA) has re-
ceived several reports of thromboembolic events, includ-
ing cerebral venous and arterial thromboses, intravascular coagulation, and hemorrhagic stroke, which require fur-
ther investigations (14).

Bjornstad-Tuveng et al. reported a massive intracranial hemorrhage in a previously healthy young female who had received the first dose of ChAdOx1 one week earlier (33). They found severe thrombocytopenia (37 × 10^9/L), PF4 ant-
obodies, and small thrombi in the frontal lobe, transverse sinus, and pulmonary artery (33). Unlike our patient, coag-
ulopathic events have also been detected in this case.

Simpson et al. found an association between ITP and ChAdOx1 vaccination (14). They realized that the first dose of ChAdOx1 was correlated with slightly increased risks for ITP, with suggestive evidence of risk for arterial thromboembolic and hemorrhagic incidents. They found no rela-
tions between BNT162b2 and thromboembolic, thrombo-
embolic, or hemorrhagic incidents (14). But unlike Simpson et al.’s and Bjornstad-Tuveng et al.’s study, we did not find any coagulopathic disorder in our patient (14, 33).

Although in the current study, we did not observe any coagulopathy or thrombocytopenia, we noticed a slight decrease in platelet count, which may be considered a rel-
ate thrombocytopenia in the first couple of days. Accord-
ing to previous studies, some vaccines are associated with an increased risk of thrombocytopenia, ITP, and elevated levels of anti-platelet antibodies (17, 33). These pathophys-
ologic findings may be associated with leading to damages to cerebrovascular structures that cause incidence or wors-
ening of other haemorrhagic manifestations such as SAH; further studies and investigations on comparable cases will be required to achieve a better understanding of the pathophysiology of this incident.

3.1. Conclusions

There are some reports of ChAdOx1 vaccine-associated thromboembolic and hemorrhagic incidents, but rarely which have led to some countries limiting its use for a while; thus, it is important to demonstrate all possible risks and complications as vaccination programs against COVID-19 have become an important part of health care in almost every country. Public health authorities should noty their jurisdictions about any increased risks related to COVID-19 vaccines.

Footnotes

Authors’ Contribution: All authors contributed equally

Conflict of Interests: Researchers are faculty members of Birjand University of Medical Sciences.

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Informed Consent: The authors obtained written infor-
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