AstraZeneca COVID-19 vaccine: A possible risk factor for Stroke, Case Series from Sudan

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Case Report

Keywords: COVID-19, Vaccination, AstraZeneca, Stroke, Sudan

Posted Date: November 19th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1090689/v1>

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Abstract

Cerebrovascular accident (CVA) is one of the commonest neurological deficits. There is a well-known association between COVID-19 and stroke. We present a case series of Sudanese patients who developed CVA after receiving the AstraZeneca COVID-19 vaccine suggesting a relationship between the vaccine and CVA.

Introduction

Cerebrovascular accident (CVA) is one of the commonest neurological deficits. Almost 85% of patients tend to have Ischemic infarction and 15% tend to have hemorrhagic infarction (1). The Neurological manifestations depend on the part of the circle of Willis affected (either anterior circulation symptoms or posterior circulation symptoms) (2). CVS has modifiable and non-modifiable risk factors. Non-modifiable risk factors are like age and sex, while some of the famous modifiable risk factors are hypertension, polycythemia and thrombocytopenia (3). There is a well known recognized association between COVID-19 and stroke (4). The relation between thrombotic thrombocytopenia and COVID-19 Vaccine is not established yet.

Cases Presentation

Case 1:

A 45 years old Sudanese male was brought to the casualty (seven days after he received the COVID-19 AstraZeneca Vaccine) with a sudden attack of left sided weakness. The condition was preceded by headache and neck pain. On examination, he was confused. Blood pressure was 180/75. Systemic examination was normal; the abnormalities were confined to the central nervous system where he had neck stiffness and gross bilateral papilledema. Both upper and lower left sided limbs revealed power grade zero, hypotonia and areflexia . On investigations, he had severe thrombocytopenia, platelets were very low (30×10^3), D-dimer was high and Carotid angiography showed total occlusion of the right Carotid artery. Brain MRI and MRV showed sagittal sinus thrombosis and hemorrhagic infarction. During his period of hospitalization he had convulsions in spite of the fact that he received intravenous immunoglobulin, methylprednisolone and platelets transfusion. The patient died two days after admission (Figure 1).

Case 2:

A 57 years old Sudanese female (with no history of hypertension or diabetes) was brought to the casualty with left sided weakness after ten days of receiving the COVID-19 AstraZeneca vaccine. The condition was not preceded by headache, convulsions or loss of consciousness. On examination, she was unwell, not pale, jaundiced or cyanosed. Pulse was 80 beats/minute and blood pressure was 110/70 Hgmm. Central nervous system examination showed evidence of left sided hemiparesis (power was grade three with hypotonia and areflexia in both upper and lower limbs). All modalities of sensation were intact.

Regarding investigations, CT brain showed right cerebral infarction and Carotid angiography showed partial occlusion of the left Carotid artery. Platelets were very low (35×10^3), D-dimer was very high and other blood investigations were normal. During the period of hospitalization she received methylprednisolone, intravenous immunoglobulin and platelets transfusion. She showed remarkable improvement and after two weeks she was discharged home with grade four power and she could walk without support (Figure 2).

Case 3:

A 65 years old Sudanese male, non-diabetic nor hypertensive was admitted because of repeated attacks of transient Ischemic attacks (TIAs). Thirteen days before the appearance of his complaint, he had received the COVID-19 AstraZeneca Vaccine. On examination, there were no abnormalities. Regarding investigations, D-dimer was high, platelets were low (65×10^3) and Carotid angiography was normal. MRI revealed periventricular Ischemia (small vessels disease). The patient received methylprednisolone and platelets transfusion. He showed remarkable improvement and was discharged on aspirin and atorvastatin (Figure 3).

Discussion

Covid-19 is associated with common neurological diseases including stroke. Stroke is the most common neurological disorder. It's the third killer worldwide and is of the commonest causes of disability. There are two main types of stroke: Ischemic stroke (constitutes 85%) and hemorrhagic stroke (constitutes 15%)(5).

COVID-19 infection is an acute inflammatory condition associated with increased incidence of fatty plaques formation and injury of endothelial cells of the vascular wall. Coagulopathy and vascular endothelial dysfunction have been proposed as complications of COVID-19 (6). The coexistence of inflammation, hypoxia and hypercoagulability can lead to formation of micro and macro thrombi in vessels. So, patients with COVID-19 are at an increased risk of venous and arterial thromboembolization leading to cerebrovascular accidents (7).

COVID- 19 viruses have caused increased morbidity and mortality worldwide. To meet this extraordinary challenge, new vaccines have been developed with a speed never seen before in medical history; vaccination against SARS-COV-2 is considered an effective preventive strategy to halt the COVID-19 pandemic. Several vaccines against COVID-19 have been developed (8).

Recently, reports of coagulopathy have appeared associated with COVID- 19 vaccinations and particularly the ChAdOx1 nCoV- 19 vaccine.

Immune thrombotic thrombocytopenia is a rare side-effect of vaccination against COVID-19 referred to as vaccine-induced immune thrombotic thrombocytopenia (VITT). VITT usually occurs 1 to 2 weeks after

vaccination with ChAdOx1 nCoV-19. Cerebral venous thrombosis is more common than arterial thrombosis (9).

Scully and colleagues proposed the following definition for VITT: patients presenting with acute thrombosis and thrombocytopenia with elevated D-dimers, using a D-dimer threshold of $<2000 \mu\text{g/L}$ for VITT-unlikely and $>4000 \mu\text{g/L}$ for VITT-suspected.. They showed that 22 (96%) of 23 patients with VITT had antibodies against platelet factor 4 (PF4) (10).

After the introduction of the adenovirus vector vaccine ChAdOx1 (Oxford–AstraZeneca), we report three cases of thrombosis with thrombocytopenia, each started 8–14 days after administration of the first vaccine dose. To our knowledge this is the first case series done in Sudan regarding this topic. It's important to consider such cases and educate patients about possible side effects of vaccination, in order encourage them to seek medical help if any symptom start to develop after getting vaccinated as early as possible to reduce chances of severe disease.

A mechanism similar to heparin-induced thrombocytopenia was proposed with antibodies to platelet factor 4 (PF4). The thrombosis is likely caused by platelet-activating antibodies against PF4 produced after vaccination. It has been termed as vaccine induced prothrombotic immune thrombocytopenia to differentiate it from heparin induced thrombocytopenia (11).

Further studies are needed to confirm this proposes. We recommend assessing patients for increased risk of thrombosis before getting vaccinated and to follow up with them after vaccination.

Conclusion

According to what was proposed in this study venous thrombosis and especially CVST are the most frequent types of stroke that tend to appear after vaccination. Vaccine related arterial thrombosis in the brain is exceedingly rare. Ischemic stroke was associated with large artery occlusion, both carotid and middle cerebral artery.

Declarations

Ethics approval and consent to participate:

Ethical approval was obtained from each center ethical committee. Both verbal and written consents to publish this information were obtained from the patients.

Consent to publish:

Consent for publication was obtained from all patients and authors.

Availability of data and materials:

The datasets used and \ or analyzed during the current study are available from corresponding author on reasonable request.

Authors' contributions:

All authors participated in planning the study, data collection, results and discussion sections.

Competing interests:

The authors have no conflict of interest to declare.

Funding:

The authors received no funding for this work.

Acknowledgment:

Not applicable.

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Figures

Figure 1

A 45 years old Sudanese male was brought to the casualty (seven days after he received the COVID-19 AstraZeneca Vaccine) with a sudden attack of left sided weakness. The condition was preceded by headache and neck pain. On examination, he was confused. Blood pressure was 180/75. Systemic examination was normal; the abnormalities were confined to the central nervous system where he had neck stiffness and gross bilateral papilledema. Both upper and lower left sided limbs revealed power

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Figure 2

A 57 years old Sudanese female (with no history of hypertension or diabetes) was brought to the casualty with left sided weakness after ten days of receiving the COVID-19 AstraZeneca vaccine. The condition was not preceded by headache, convulsions or loss of consciousness. On examination, she was unwell, not pale, jaundiced or cyanosed. Pulse was 80 beats/minute and blood pressure was 110/70 Hgmm. Central nervous system examination showed evidence of left sided hemiparesis (power was grade three with hypotonia and areflexia in both upper and lower limbs). All modalities of sensation were intact. Regarding investigations, CT brain showed right cerebral infarction and Carotid angiography showed partial occlusion of the left Carotid artery. Platelets were very low (35×10^3), D-dimer was very high and other blood investigations were normal. During the period of hospitalization she received methylprednisolone, intravenous immunoglobulin and platelets transfusion. She showed remarkable improvement and after two weeks she was discharged home with grade four power and she could walk without support.

Figure 3

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