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

Amira Siddig1, Abbashar Hussein2, Khabab Abbasher Hussien Mohamed Ahmed**3**, Abdallah M. Abdallah4, Mohamed Malekaldar5, AlHussien Abbasher6, Mohammed Abbasher7, Abubaker Alsedig Abbasher8

1. MD, PhD, AlNeelain University, Faculty of Medicine, Khartoum, Sudan, [amirasiddig121@gmail.com](mailto:amirasiddig121@gmail.com)
2. MD, MD, PhD, University of Khartoum, Faculty of Medicine, Khartoum, Sudan, [abbashar59@yahoo.com](mailto:abbashar59@yahoo.com)
3. Final year MBBS student, University of Khartoum, Faculty of Medicine, Khartoum, Sudan, [Khabab9722@gmail.com](mailto:Khabab9722@gmail.com)
4. MBBS, MRCP 1, University of Bahri, Faculty of Medicine, Khartoum, Sudan, abdallah.mustafa1738@gmail.com
5. MD, MD, Omdurman teaching Hospital, Khartoum, Sudan, [Malekaldar1973@gmail.com](mailto:Malekaldar1973@gmail.com)
6. AlYarmouk college, Khartoum, Sudan, [Hussienabbashar93@gmail.com](mailto:Hussienabbashar93@gmail.com)
7. AlNeelain University, Faculty of Medicine, Khartoum, Sudan, [mohabbasher01@gmail.com](mailto:mohabbasher01@gmail.com)
8. Zamzam University College, Khartoum, Sudan, [amirasiddig121@hotmail.com](mailto:amirasiddig121@hotmail.com)

**Correspondence Author:**

Khabab Abbasher Hussien Mohamed Ahmed

Email: [Khabab9722@gmail.com](mailto:Khabab9722@gmail.com)

Mobile: 00249907712134

ORCID: 0000-0003-4608-5321

Sudan, Khartoum State, Postal code: 11111

**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.

**Keywords:**

COVID-19, Vaccination, AstraZeneca, Stroke, Sudan

**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 stroke (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 (30×103), 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 Hmm. 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 (35×103), 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 (65×103) 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.

**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 μg/L for VITT-unlikely and >4000 μg/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 sever 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). But we don't have to unnecessary alert patients if there are no high levels of suspension. We recommend assessing patients for increased risk of thrombosis before getting vaccinated and to follow up with them after vaccination. Further studies are needed to confirm this proposes.

**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.

**References**

1. Tadi P, Lui F. Acute Stroke. [Updated 2021 Sep 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535369/?report=classic>
2. Kuriakose D, Xiao Z. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. International Journal of Molecular Sciences. 2020;21(20):7609.
3. Boehme A, Esenwa C, Elkind M. Stroke Risk Factors, Genetics, and Prevention. Circulation Research. 2017;120(3):472-495.
4. Stein L, Mayman N, Dhamoon M, Fifi J. The emerging association between COVID-19 and acute stroke. Trends in Neurosciences. 2021;44(7):527-537.
5. Sidig, A., Salah-Eldien, M., Mohamed Ahmed, K., Abbasher, H., Alhusseini, R., Abbasher, M. and Hussien, A., 2021. COVID-19 as a Risk Factor for Ischemic Stroke, A Case Report, Khartoum, Sudan, 2020. *Acta Scientific Neurology*, 4(11), pp.18-21.
6. Del Turco S, Vianello A, Ragusa R, Caselli C, Basta G. COVID-19 and cardiovascular consequences: Is the endothelial dysfunction the hardest challenge?. Thrombosis Research. 2020;196:143-151.
7. Wijeratne T, Gillard Crewther S, Sales C, Karimi L. COVID-19 Pathophysiology Predicts That Ischemic Stroke Occurrence Is an Expectation, Not an Exception—A Systematic Review. Frontiers in Neurology. 2021;11.
8. Kyriakidis N, López-Cortés A, González E, Grimaldos A, Prado E. SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. npj Vaccines. 2021;6(1).
9. Kelton J, Arnold D, Nazy I. Lessons from vaccine-induced immune thrombotic thrombocytopenia. Nature Reviews Immunology. 2021;.
10. Perry R, Tamborska A, Singh B, Craven B, Marigold R, Arthur-Farraj P et al. Cerebral venous thrombosis after vaccination against COVID-19 in the UK: a multicentre cohort study. The Lancet. 2021;398(10306):1147-1156.
11. Huynh A, Kelton J, Arnold D, Daka M, Nazy I. Antibody epitopes in vaccine-induced immune thrombotic thrombocytopaenia. Nature. 2021;596(7873):565-569.