

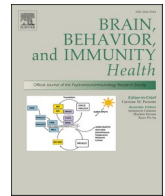


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Cognitive deficits and memory impairments after COVID-19 (Covishield) vaccination

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ABSTRACT

Vaccination is an essential public health strategy to control the 2019 Coronavirus (COVID-19) pandemic. While the benefits of the COVID-19 vaccines far outweigh the risks, side effects continue to be reported in the literature. We report a 65-year-old man who developed cognitive deficits and memory impairments following his first dose of Oxford AstraZeneca vaccine (Covishield). The onset of acute cognitive deficits and memory impairments could be another complication to COVID-19 vaccination that physicians and neurologists need to be warned to. Monitoring the safety of COVID-19 vaccines and describing side effects associated with them is essential to improve safety profiles and enhance public trust.

1. Case presentation

We report a 65-year-old man who developed cognitive deficits and memory impairments following his first dose of Oxford AstraZeneca vaccine (Covishield) against 2019 Coronavirus disease (COVID-19). Patient was admitted to Bhawani Hospital and Research Centre after sudden memory loss lasted for a day. He was not oriented to time, place and person. He was unable to describe both short and long-term memory previously acquired. He received Oxford AstraZeneca vaccine 6 days back with no clinical neurological sign for first 5 days after vaccination. On examination his speech was of a non-fluent type characterized by isolated words. He was completely unaware of his presence in the hospital. Non-contrast CT was essentially normal with no evidence of hemorrhage or focal lesion. All routine blood tests were normal. Acute cognitive deficits and memory impairments following vaccination were probably due on a cerebrovascular basis. Patients fully recovered within 24 h.

2. Discussion

COVID-19 infection is straight implicated in neurological invasion through diverse possible pathway as hypoxia brain injury, direct brain infection, autoimmune demotion, ACE2 pathway alteration, leading to

impairments in cognition and neurogenesis (Xiong et al., 2020; Di Carlo et al., 2021; Marin and Kipnis, 2013; Montemurro, 2021). We are extremely convinced of the usefulness of vaccination and epidemiological data from several studies indicated an excellent efficacy and safety profile for COVID-19 vaccines (Vitiello et al., 2021). However, while the benefits of the COVID-19 vaccines far outweigh the risks, side effects continue to be reported, some of which are common, such as headache (Sekiguchi et al., 2021) and others are much rarer (Chan et al., 2022; Lazaro et al., 2022). Complications most frequently reported with Covishield vaccine (Oxford –AstraZeneca) are injection site pain (91.0%), asthenia (74.3%), headache (68.7%), soreness (55.0%) and fever (47.5%) (Konu et al., 2021). Chan et al. (2022) reported two patients who developed aseptic meningitis after vaccination. Similarly, Lazaro et al. (2022) reported an acute disseminated encephalomyelitis (ADEM) four weeks after vaccination. After vaccination headaches are usually common and self-limiting, however possible differential diagnosis of acute neurological symptoms needs to be investigated in patients with severe symptoms. The onset of cognitive deficits and memory impairments following his first dose of Oxford AstraZeneca vaccine (Covishield) is uncommon. Several differential diagnoses were considered in our single case. Based on blood tests, infectious and noninfectious endocarditis was unlikely, as well septicemia or antiphospholipid syndrome. Oxford AstraZeneca vaccine has been linked to an increase in

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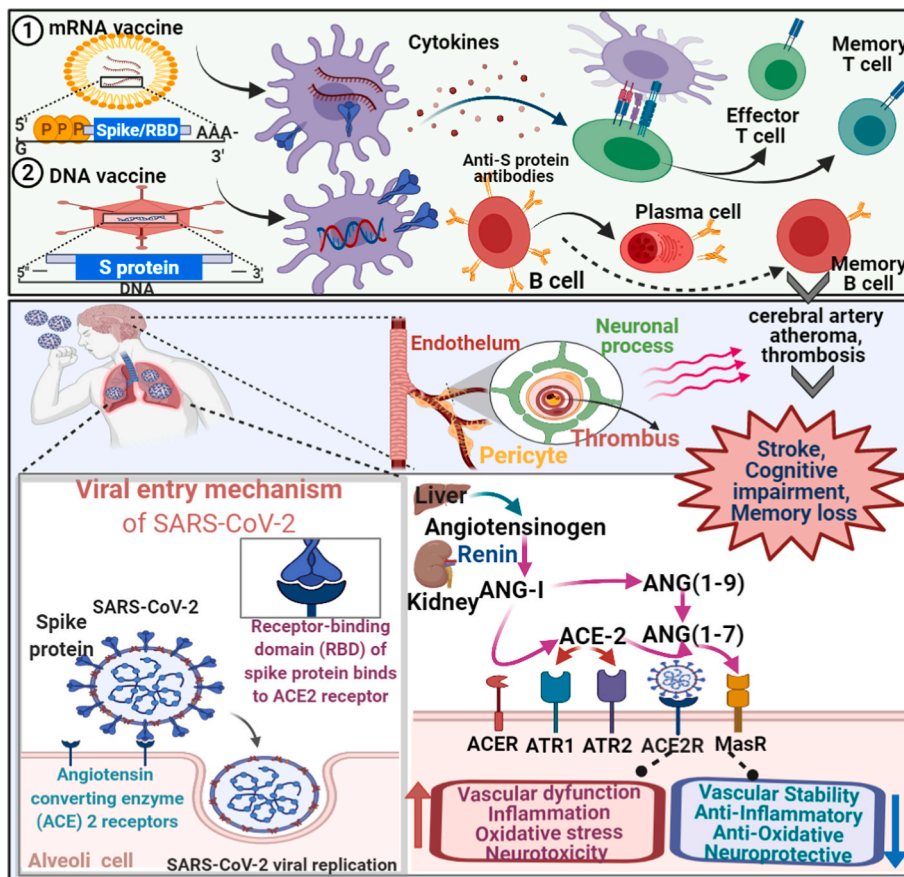


Fig. 1. Illustration represents the possible hypothesis and molecular mechanism of memory loss associated with cognitive decline in COVID-19 infection. **A:** Administration of mRNA vaccines triggers cytokine cycle which communicates with memory T cell. **B:** Administration of DNA vaccine triggers cytokines leading to Anti-S protein antibodies, B cell and memory B cell. **C:** It shows the pathological mechanisms of COVID-19 infection in which affected B and T Cell plays a vital role in thrombosis leading to stroke and associated cognitive decline.

complaints of neurological complications (Finsterer, 2022). Stroke and Guillain-Barré syndrome are the most prevalent neurological side effects documented (Finsterer, 2022). Pre- and post-stroke environments are linked to different levels of pro and post-inflammatory inflammation, which leads to memory cells and cognitive impairment (Eldahshan et al., 2019; Shrotri et al., 2021). In the reported case, our 65-year-old patient was healthy before the immunization, but he developed mild to moderate cognitive impairment afterward. The effects of vaccination after the first or second dosage are still poorly known, which is why there is so little literature on cognitive and memory deficits after vaccination (Ali Awan et al., 2021). COVID-19 vaccine may destroy few lymphocytes. This idea for cognitive impairment after vaccination was supported by pre-stroke mechanisms of COVID-19 vaccine studies (Eldahshan et al., 2019; Finsterer, 2022; Blauenfeldt et al., 2021; Esba and Al Jeraisy, 2021). Similarly, Mehta et al. (2021) reported two cases of young males who developed severe thrombocytopenia and fatal cerebral venous sinus thrombosis (CVST) following the first dose of Vaxzevria vaccine (previously named COVID-19 vaccine AstraZeneca), emphasizing the importance of close collaboration between clinicians of diverse specialties when managing challenging cases of CVST with thrombocytopenia. Vaxzevria and Covishield have the same chemical composition but are subject to different proprietary and licensing arrangements.

Covishield vaccine contains Adenovirus vaccine vector which reported to have diminished the response of type-1 T-helper lymphocytes cells (Madhi et al., 2021). Over the last 2 years, COVID-19 virus produced a good number of mutations and was associated with the invading mechanisms with immune cells, as it directly binds with the spike protein of memory B Cells and T cells. T and B cells play a vital role in normal neuronal function associated with normal immune response in body. The imbalanced or altered immunity (B and T cell) may cause cognitive decline (Xiong et al., 2020). The main hypothesis is that Covishield Adenovirus vaccine vector binds with the mutated virus

vector and upregulate cytokine function. This may cause a significant inflammatory reaction in the immune cells associated with the mutated virus vector, leading to lose B and T memory cells and a consequently immunologically activated cognitive decline (Xiong et al., 2020) (Fig. 1). Memory loss has not been reported after COVID-19 vaccination, although it is a possibility. For of its often-devastating clinical presentations, ischemic stroke following vaccination are common reported in literature (Blauenfeldt et al., 2021; Luisa et al., 2022; Malik et al., 2021), whereas transient ischemic attack (TIA) after COVID-19 vaccination is probably undervalued, in our opinion. TIA can be associated with hypercoagulable state and attributed herein to the uptake of the vaccination, as also Malik et al. (2021) reported. As tuberothalamic territory strokes produce impairments of arousal and orientation, learning and memory and executive function (Schmahmann, 2003), it is possible that a hypercoagulable state due to vaccination may have given a TIA in this tuberothalamic vascular territory in our patient. In addition to ischemia in the setting of TIA, hypoxia inducing events with vaso-spastic, vasoconstrictive or arterial insufficiency etiologies have been described in the literature as causes of transient global amnesia-like symptoms (Spiegel et al., 2017). Patients with central nervous system pathologies should be investigated about recent vaccinations for a quick and accurate diagnosis to initiate treatment and prevent serious sequelae.

Monitoring the safety of vaccines is essential to improve safety profiles and enhance public trust. Shrestha et al. (2020) described adverse events associated with COVID-19 vaccines and discussed why it is essential to have a functional adverse event monitoring system in this context. Pharmacovigilance and telemedicine are essential aspects of surveillance to ensure the safety of COVID-19 vaccines (Paudyal et al., 2020; Montemurro, 2022; Shrestha et al., 2020). The rapid development of COVID-19 vaccines has raised concerns about their safety, contributing to vaccine hesitancy (Ullah et al., 2021). Esba and Al Jeraisy

(2021) emphasized the importance of a close real time safety monitoring and scientific analysis by pharmacovigilance experts. Similarly, Lacroix et al. (2021) showed the importance of a French Pharmacovigilance Network, in which a multiple approach associated with a close collaboration of all entities involved and the optimization of the pre-existing pharmacovigilance organization allows this complete analysis to the French and the authorities in real time. Indeed, such efficiency is necessary to manage a careful and acute surveillance of these new COVID-19 vaccines for and against the pandemic at the same time (Lacroix et al., 2021). This reported case wants to remind the importance of neurological side effect reporting, particularly cognitive and memory deficits, because cognitive assessment is often not well noticed after vaccination.

3. Conclusion

The onset of acute cognitive deficits and memory impairments could be another complication that physicians and neurologists need to be alerted to, although larger and further studies are needed to determine whether post-vaccination rates of memory impairment are common or not. Our patient fully recovered within 24 h, with no residual neurological deficits. At present, as the benefits of administering the vaccine outweigh the risks of fewer adverse events, vaccination against COVID-19 should be encouraged.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Ali Awan, H., Najmuddin Diwan, M., Aamir, A., Ali, M., Di Giannantonio, M., Ullah, I., et al., 2021. SARS-CoV-2 and the brain: what do we know about the causality of 'cognitive COVID'? *J. Clin. Med.* 10 (15), 3441. <https://doi.org/10.3390/jcm10153441>.
- Blauenfeldt, R.A., Kristensen, S.R., Ernsten, S.L., Kristensen, C.C.H., Simonsen, C.Z., Hvas, A.M., 2021. Thrombocytopenia with acute ischemic stroke and bleeding in a patient newly vaccinated with an adenoviral vector-based COVID-19 vaccine. *J. Thromb. Haemostasis* 19 (7), 1771–1775. <https://doi.org/10.1111/jth.15347>.
- Chan, A.C., Tan, B.Y., Goh, Y., Tan, S.S., Tambyah, P.A., 2022. Aseptic meningitis after BNT-162b2 COVID-19 vaccination. *Brain Behav. Immun. Health* 19, 100406. <https://doi.org/10.1016/j.bbih.2021.100406>.
- Di Carlo, D.T., Montemurro, N., Petrella, G., Siciliano, G., Ceravolo, R., Perrini, P., 2021. Exploring the clinical association between neurological symptoms and COVID-19 pandemic outbreak: a systematic review of current literature. *J. Neurol.* 268 (5), 1561–1569. <https://doi.org/10.1007/s00415-020-09978-y>.
- Eldahshan, W., Fagan, S.C., Ergul, A., 2019. Inflammation within the neurovascular unit: focus on microglia for stroke injury and recovery. *Pharmacol. Res.* 147, 104349. <https://doi.org/10.1016/j.phrs.2019.104349>.
- Esba, L.C.A., Al Jeraisy, M., 2021. Reported adverse effects following COVID-19 vaccination at a tertiary care hospital, focus on cerebral venous sinus thrombosis (CVST). *Expert Rev. Vaccines* 20 (8), 1037–1042. <https://doi.org/10.1080/14760584.2021.1940145>.
- Finsterer, J., 2022. Neurological side effects of SARS-CoV-2 vaccinations. *Acta Neurol. Scand.* 145 (1), 5–9. <https://doi.org/10.1111/ane.13550>.
- Konu, Y.R., Gbeasor-Komlanvi, F.A., Yerima, M., Sadio, A.J., Tchankoni, M.K., Zida-Compaore, W.I.C., et al., 2021. Prevalence of severe adverse events among health professionals after receiving the first dose of the ChAdOx1 nCoV-19 coronavirus vaccine (Covishield) in Togo, March 2021. *Arch. Publ. Health* 79 (1), 207. <https://doi.org/10.1186/s13690-021-00741-x>.
- Lacroix, C., Salvo, F., Gras-Champel, V., Gautier, S., Massy, N., Valnet-Rabier, M.B., et al., 2021. French organization for the pharmacovigilance of COVID-19 vaccines: a major challenge. *Therapie* 76 (4), 297–303. <https://doi.org/10.1016/j.therap.2021.05.003>.
- Lazaro, L.G., Perea Cossio, J.E., Luis, M.B., Tamagnini, F., Paguay Mejia, D.A., Solarz, H., Fernandez Liguori, N.A., Alonso, R.N., 2022. Acute disseminated encephalomyelitis following vaccination against SARS-CoV-2: a case report. *Brain Behav. Immun. Health* 20, 100439. <https://doi.org/10.1016/j.bbih.2022.100439>.
- Luisa, V., Valentina, P., Alessia, G., Valeria, G., Francesca, C., Chiara, C., et al., 2022. Ischemic stroke shortly after vaccination against SARS-CoV-2: a case-control study. *J. Neurol. Sci.* 436, 120209. <https://doi.org/10.1016/j.jns.2022.120209>.
- Madhi, S.A., Baillie, V., Cutland, C.L., Voysey, M., Koen, A.L., Fairlie, L., et al., 2021. Efficacy of the ChAdOx1 nCoV-19 covid-19 vaccine against the B.1.351 variant. *N. Engl. J. Med.* 384 (20), 1885–1898. <https://doi.org/10.1056/NEJMoa2102214>.
- Malik, B., Kalantary, A., Rikabi, K., Kunadi, A., 2021. Pulmonary embolism, transient ischaemic attack and thrombocytopenia after the Johnson & Johnson COVID-19 vaccine. *BMJ Case Rep.* 14 (7), e243975. <https://doi.org/10.1136/bcr-2021-243975>.
- Marin, I., Kipnis, J., 2013. Learning and memory and the immune system. *Learn. Mem.* 20 (10), 601–606. <https://doi.org/10.1101/lm.028357.112>.
- Mehta, P.R., Apap Mangion, S., Bengler, M., Stanton, B.R., Czuprynska, J., Arya, R., Sztrihai, L.K., 2021. Cerebral venous sinus thrombosis and thrombocytopenia after COVID-19 vaccination - a report of two UK cases. *Brain Behav. Immun.* 95, 514–517. <https://doi.org/10.1016/j.bbi.2021.04.006>.
- Montemurro, N., 2021. Intracranial hemorrhage and COVID-19, but please do not forget "old diseases" and elective surgery. *Brain Behav. Immun.* 92, 207–208. <https://doi.org/10.1016/j.bbi.2020.11.034>.
- Montemurro, N., 2022. Telemedicine: could it represent a new problem for spine surgeons to solve? *Global Spine J.* 21925682221090891. <https://doi.org/10.1177/21925682221090891>.
- Paudyal, V., Al-Hamid, A., Bowen, M., Hadi, M.A., Hasan, S.S., Jalal, Z., et al., 2020. Interventions to improve spontaneous adverse drug reaction reporting by healthcare professionals and patients: systematic review and meta-analysis. *Exp. Opin. Drug Saf.* 19 (9), 1173–1191. <https://doi.org/10.1080/14740338.2020.1807003>.
- Schmahmann, J.D., 2003. Vascular syndromes of the thalamus. *Stroke* 34 (9), 2264–2278. <https://doi.org/10.1161/01.STR.0000087786.38997.9E>.
- Sekiguchi, K., Watanabe, N., Miyazaki, N., Ishizuchi, K., Iba, C., Tagashira, Y., et al., 2021. Incidence of headache after COVID-19 vaccination in patients with history of headache: a cross-sectional study. *Cephalalgia* 18, 3331024211038654. <https://doi.org/10.1177/03331024211038654>.
- Shrestha, S., Danekhu, K., Kc, B., Palaian, S., Ibrahim, M.I.M., 2020. Bibliometric analysis of adverse drug reactions and pharmacovigilance research activities in Nepal. *Ther. Adv. Drug Saf.* 11, 2042098620922480. <https://doi.org/10.1177/2042098620922480>.
- Shrotri, M., van Schalkwyk, M.C.I., Post, N., Eddy, D., Huntley, C., Leeman, D., et al., 2021. T cell response to SARS-CoV-2 infection in humans: a systematic review. *PLoS One* 16 (1), e0245532. <https://doi.org/10.1371/journal.pone.0245532>.
- Spiegel, D.R., Smith, J., Wade, R.R., Cherukuru, N., Ursani, A., Dobruskina, Y., et al., 2017. Transient global amnesia: current perspectives. *Neuropsychiatric Dis. Treat.* 13, 2691–2703. <https://doi.org/10.2147/NDT.S130710>.
- Ullah, I., Khan, K.S., Tahir, M.J., Ahmed, A., Harapan, H., 2021. Myths and conspiracy theories on vaccines and COVID-19: potential effect on global vaccine refusals. *Vaccines* 22 (2), 93–97. <https://doi.org/10.1016/j.vacuum.2021.01.001>.
- Vitiello, A., Ferrara, F., Troiano, V., La Porta, R., 2021. COVID-19 vaccines and decreased transmission of SARS-CoV-2. *Inflammopharmacology* 29 (5), 1357–1360. <https://doi.org/10.1007/s10787-021-00847-2>.
- Xiong, W., Kwan, P., Zhou, D., Del Felice, A., Duncan, J.S., Sander, J.W., 2020. Acute and late neurological complications of COVID-19: the quest for evidence. *Brain* 143 (12), e99. <https://doi.org/10.1093/brain/awaa294>.