

Commentary

Commentary: Posterior Circulation Ischemic Stroke Occurring after Chadox1ncov-19/AZD1222 Vaccination without Evidence of Vaccine-Induced Immune Thrombotic Thrombocytopenia

Félix Bermejo-Pareja¹, Cristina Ramo-Tello^{2,3} and Julián Benito-León^{1-4,*}

¹Group of Neurodegenerative Diseases, Hospital Universitario 12 de Octubre Research Institute (Imas12), 28041 Madrid, Spain

²Department of Neurology, 12 de Octubre University Hospital, 28041 Madrid, Spain

³Department of Medicine, Faculty of Medicine, Complutense University of Madrid, 28040 Madrid, Spain

⁴*Network Center for Biomedical Research in Neurodegenerative Diseases (CIBERNED), 28031 Madrid, Spain

***Correspondence:** Julián Benito-León, Group of Neurodegenerative Diseases, Hospital Universitario 12 de Octubre Research Institute (Imas12), 28041 Madrid, Spain, E-mail: jbenitol67@gmail.com; DOI: 10.1042/JCTCS.9.2.0060

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Description

Coronavirus disease 2019 (COVID-19) began as an outbreak of pneumonia of presumed viral origin in Wuhan (China) in December 2019, likely originating from a bat-borne virus reservoir [1]. The disease was initially characterized by pulmonary symptoms, fever, cough, and myalgia, attributed to SARS-CoV-2 [1]. Later on, a great variety of clinical characteristic, systemic, and neurological dysfunctions were described with this viral infection.

Probably, the main neurological dysfunction associated by severe COVID-19 has been the increased stroke risk (1.4-5%) compared with some other viral infections, including influenza [1]. The stroke appears in the acute phase (there are systematic reviews, meta-analyses and one umbrella review showing this increase and the main and specific characteristics of these strokes. In addition, in the post covid-19 phase there was an increased risk of stroke and other peculiar neurological dysfunctions including brain fog, cognitive disorders, microvascular clot formation, an endothelial dysfunction [1].

The causal association between SARS-CoV-2 infection and stroke is incompletely understood. Proposed mechanisms include systemic inflammation immune inflammatory mechanisms, a procoagulant state, thrombotic microangiopathy, viral persistence and immune-induced derangements caused by spike protein-related mechanisms.

The rapid spread of the virus and the lack of curative drugs prompted the urgent development of vaccines. COVID-19 vaccine development was scientifically rapid and included attenuated or inactivated-virus vaccines, viral-vector vaccines such as ChAdOx1 nCoV-19/AZD1222, Ad26.COV2. S, Sputnik, and mRNA vaccines such as mRNA-1273 and BNT162b2. The ChAdOx1/AZD1222 vaccine demonstrated efficacy in phase III clinical trials, as did other marketed vaccines. However, very rare adverse events may become apparent only after large-scale population rollout; therefore, real-world adverse events following immunization were primarily characterized in phase IV population-based studies and pharmacovigilance systems.

For viral-vector vaccines, a newly described syndrome termed Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), also referred to as thrombosis with Thrombocytopenia Syndrome (TTS), was identified. VITT may present with venous thrombosis, secondary hemorrhage, and arterial thrombosis, including myocardial infarction and stroke. Notwithstanding, several mechanisms summarized in Table 5 [1], are coagulopathy, endothelial injury, immune dysregulation, microvascular dysfunction, and spike-protein-related effects. These mechanisms differ substantially in evidentiary strength. VITT/TTS and severe COVID-19-associated coagulopathy are well established, whereas non-VITT post-vaccination arterial stroke mechanisms remain incompletely defined, because for non-VITT arterial ischemic stroke the evidence of causality is less consistent because there is not biological support such as VITT, and limited by confounding, background stroke incidence and case ascertainment.

Notwithstanding, several Vaccine Adverse Event Reporting System (VAERS) explicitly that arterial strokes are the main stroke type possible related to vaccination as adverse events of vaccines. In this context, the EudraVigilance analysis by Cari, et al. [2] that analyzed several cardiovascular, neurological, and thrombotic events following viral vector vaccines versus mRNA vaccines detected specifically that arterial strokes had higher frequency with viral vaccines than with mRNA vaccines and introduced the possibility of a possible cause of strokes related to viral vaccines adverse effects.

The described case (summarized): It is the story of a 63-yearold man with well-controlled hypertension and a remote history of smoking developed systemic symptoms within 24 h of first-dose ChAdOx1 nCoV-19/AZD1222 vaccination, followed by severe hypertension and acute posterior circulation neurological symptoms 36-48 h after vaccination. Neuroimaging showed an acute left cerebellar infarct extending into the middle cerebellar peduncle, with approximately 50% stenosis of the intradural left vertebral artery. Platelet counts remained normal, D-dimer and anti-PF4 antibody testing were normal, SARS-CoV-2 Polymerase Chain Reaction (PCR) testing was negative, and cardiac evaluation did not identify a definite cardioembolic source.

The presented case is best interpreted as a posterior circulation ischemic stroke occurring shortly after ChAdOx1/AZD1222 vaccination without evidence of VITT/TTS. The temporal relationship, systemic post-vaccination symptoms, severe hypertension at the onset of neurological symptoms, absence of SARS-CoV-2 infection, and extensive negative etiological evaluation justify pharmacovigilance reporting and hypothesis generation. It is true that individual causality cannot be established from a single case, but no definite alternative etiology was identified despite broad evaluation.

Black, et al. [2], on behalf of the Brighton Collaboration, emphasized that for an individual case, temporal proximity is necessary but not sufficient; recurrence on rechallenge, a distinctive syndrome, specific laboratory evidence, or consistent epidemiological excess would strengthen causal inference. This statement prompted us to include other 13 analogous cases reported (in all over the world) facilitating the clinical plausibility of the possible causal relationship between viral vaccination and ischemic stroke adverse event.

Conclusion

In summary, COVID-19 is associated with increased stroke risk, mainly ischemic stroke, often with cryptogenic etiology and unfavorable prognosis. Several epidemiological data presented in this review indicated that stroke vaccination might determine by similar physiopathology arterial strokes, although it could be very uncommon. The presented case could be an example of the possible adverse effect of Covid-19 viral vaccination (ChAdOx1nCoV-19/AZD1222).

References

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