

LETTER TO THE EDITOR**Stroke after COVID-19 vaccination**

To the Editor,

de Mélo Silva Jr and Lopes suggest a potential association of COVID-19 vaccination with a risk of developing a brain hemorrhage. I report a case of COVID-19 vaccine-associated ischemic stroke.¹

An 87-year-old woman presented with dysarthria, right gaze deviation, and complete left hemiplegia 24 h after receipt of the second dose of the RNA-based COVID-19 vaccine, BNT 162b2. No symptoms or signs of local or systemic reactogenicity occurred within the 21-day window of the first dose. Previous history was remarkable for ischemic heart disease, hypertension, and dyslipidemia that were managed with aspirin, bisoprolol, ezetimibe, and rosuvastatin. Imaging studies showed a large right infarction, a clot sign indicating an occluding wall-adherent thrombus of the right middle cerebral artery, and no significant atherosclerosis or any other abnormalities of the cervical and intracranial vessels. Aortic, cardiac, and paradoxical embolism was ruled out. Blood count, including platelet count, and coagulation profile were normal. C-reactive protein was 12 mg/dl (normal <5 mg/dl). Thrombolysis or thrombectomy was not performed, and anti-platelet therapy was changed to clopidogrel. The patient was ultimately discharged to a rehabilitation facility 32 days after admission. At that time, she had left hemiplegia and dysarthria.

This woman presented with cerebral thrombosis after receipt of the second shot of the BNT 162b2 vaccine. The timing of the event, with onset of symptoms as early as within 24 h after vaccination, was consistent with a vaccine-related cause. However, the patient was at risk for stroke independently of vaccination because of cardiovascular profile, past medical history, and the presence of comorbidities. Accordingly, scoring on the Naranjo scale was 2, which suggests to consider alternative causes and only a possible relationship between vaccination and the adverse event.² As opposed to these confounders, imaging studies did not show significant atherosclerosis or any other abnormalities of the cervical and intracranial vessels and work-out ruled out aortic, cardiac, and paradoxical embolism and other causes of stroke. Of interest, the patient had none of the qualifying features for vaccine-induced thrombotic thrombocytopenia, no thrombocytopenia, and no other coagulation and prothrombotic disorders.³⁻⁵ Furthermore, she was taking anti-platelet therapy, and biomarkers of inflammation were elevated at the onset of stroke after the second shot of the vaccine, in contrast to the lack of any clinical or laboratory evidence of active local or systemic inflammation during the 3 weeks subsequent to the first

vaccination. Altogether, these findings suggest that inflammation and immune activation driven by the second vaccine shot were the triggers of the thrombosis rather than atherosclerosis.

A safety signal of thromboembolism is not by now established in the context of COVID-19 vaccination, and the risk of stroke is not increased with RNA-based COVID-19 vaccines.⁶ However, arterial and venous thromboembolic events have been reported, and few cases of ischemic stroke have been linked mostly with not RNA-based COVID-19 vaccines.⁷⁻¹²

Multifactorial pathways may contribute to the onset of cerebral thrombosis after COVID-19 vaccination. On first principles, we could not differentiate atherosclerotic thrombosis as opposed to immune-mediated primary inflammatory arterial thrombosis upon clinical, laboratory, and imaging findings. These two mechanisms, however, are not mutually exclusive. We may hypothesize that the immunoinflammatory response to the vaccine could lead to systemic hypercoagulability, dysfunction, activation, and disruption of the endothelium, complement and platelet activation, and inflammatory cell infiltration of the atherosclerotic plaque. Ultimately, activated platelets amplify inflammation locally and may trigger thrombosis of the plaque. This fits with the view that any inflammatory condition could trigger a stroke or other thrombotic events, particularly in the context of atherosclerosis.¹³ However, it is unclear if characteristics of currently available COVID-19 vaccines such as being viral vector- or RNA-based, different RNA content, different dosing schedules, or other factors could be at play and influence the risk of stroke after receipt of a COVID-19 vaccine. It is reasonable that the transient arterial wall inflammation driven by vaccination might be one underlying mechanism contributing to the pathogenesis of cerebral hemorrhage in the case reported by de Mélo Silva and Lopes.¹

Clinicians should be on the lookout for the onset of cerebral thrombosis after COVID-19 vaccination, particularly in patients with severe atherosclerosis. Nonetheless, this is a rare complication that is greatly outweighed by the benefit of vaccination, and the risk of stroke remains higher with COVID-19 itself than with vaccines.

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CONFLICT OF INTEREST

Author have no conflict of interest.

CONSENT

Consent for publication was obtained from the patient.

KEYWORDS

COVID-19 vaccines, stroke, thrombosis

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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