Alternative pathophysiologies must be ruled out before right middle cerebral artery ischemic stroke can be attributed to SARS-CoV-2 vaccination

Dear Editor,

We read with interest the article by Pandey *et al.* who reported on a 23-year-old female who developed recurrent focal seizures on the left side 20 days after the first dose of the ChAdOx1 nCoV-19 anti-SARS-CoV-2 vaccine.[1] Oral antiseizure drugs were ineffective, but intravenous lacosamide stopped seizure activity.[1] Subsequent magnetic resonance imaging revealed an acute ischemic stroke involving the right middle cerebral artery.[1] Blood tests revealed thrombocytopenia and a significantly elevated D-dimer value.[1] The patient made an incomplete recovery after aspirin and rehabilitation. The study is impressive but has limitations that should be discussed.

The main limitation of the study is that the pathophysiology of the ischemic stroke in the right middle cerebral artery area has not been elucidated. It remained unclear whether the stroke was atherothrombotic, cardioembolic, artery-embolic, due to vasospasm, due to dissection, or secondary due to venous sinus thrombosis (VST). Since the antiplatelet antibodies were negative,[1] another pathophysiological explanation must be provided. Was there arterial hypertension? Did the stroke precede the seizure or vice versa? Did the patient receive heparin during the seizures? Were heparin-induced thrombocytopenia antibodies elevated? Knowing the pathophysiology and time course is critical for minimizing the risk of future strokes and for applying the most effective treatment.

Another limitation of the study is that a VST could not be sufficiently ruled out by magnetic resonance venography (MRV) with contrast medium in the acute stage of the stroke. VST can be secondarily complicated by ischemic stroke. Arguments for VST in the index patient are that the patient had seizures, a common clinical manifestation of VST,[2] and that D-dimer was markedly elevated.[1] A normal MRV 6 weeks after stroke onset could be due to the spontaneous dissolution of the clot prior to MRV.[3]

A third limitation is that no reference limits were given. Therefore, the interpretation of the reported values of the laboratory parameters is unreliable. According to reference limits from the literature, the D-dimer was significantly increased and the platelet count was significantly reduced.

A fourth limitation is that the patient did not undergo thrombolysis or thrombectomy in the acute stage of stroke.[1] When was hemiparesis first recognised? Was left hemiparesis initially interpreted as Todd paresis? How many hours after onset of hemiparesis was the cerebral computed tomography performed? How many hours after the onset of hemiparesis was the first magnetic resonance imaging performed?

It is incomprehensible why the patient showed normal function of the cranial nerves as described.[1] Due to the extensive cytotoxic oedema, at least a central facial palsy is to be expected in the clinical neurologic examination.

There is no discussion as to why thrombocytopenia did not result in cerebral or extracerebral bleeding. Was there evidence of abnormal platelet function? Particularly in cases where platelet function is abnormal, thrombosis may occur due to intra-arterial clot formation rather than bleeding.

In summary, the interesting study has limitations that call the results and their interpretation into question. Addressing these issues would strengthen the conclusions and could improve the status of the study. Before attributing right middle cerebral artery ischemic stroke to SARS-CoV-2 vaccination, alternative pathophysiologies must be ruled out.

Author contribution

(1. Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript: A. Writing of the first draft, B. Review and Critique): author JF: 1A, 1b, 1C, 3A, 3B.

Data access statement

All data are available from the corresponding author.

Ethical compliance statement

The authors confirm that the approval of an institutional review board or patient consent was not required for this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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