



## Before blaming a COVID vaccine for cytotoxic lesions of the corpus callosum all other differentials must be ruled out

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We read with interest the article by Ohara et al. about two patients developing a cytotoxic lesion of the corpus callosum (CLOCC) about 1 week following the first dose of the Biontech Pfizer vaccine (BPV) [1]. Both patients were treated with methyl-prednisolone and partially recovered at the last reported follow-up [1]. The study is promising but raises concerns that should be discussed.

We disagree with the notion that side effects of SARS-CoV-2 vaccinations are not life-threatening, as stated in the introduction [1]. Several fatal adverse reactions to SARS-CoV-2 vaccinations have been reported. In a recent systematic literature review according to PRISMA standards, about fatalities after SARS-CoV-2 vaccinations, 38 patients were found who died due to a SARS-CoV-2 vaccination [2]. Causes of death were vaccine-induced immune thrombotic thrombocytopenia (VITT) ( $n = 32$ ), myocarditis ( $n = 3$ ), ADEM ( $n = 1$ ), myocardial infarction ( $n = 1$ ), and rhabdomyolysis ( $n = 1$ ) [2]. A 63-year-old female developed fulminate myocarditis after the second dose of the AstraZeneca vaccine (AZV), required heart transplantation, and died 54 days after onset of myocarditis [3]. There are also cases which experienced fulminant, fatal cerebral venous sinus thrombosis (VST) in association with VITT [4]. In a single case, vaccination with the BPV caused fatal autoimmune hepatitis.

A shortcoming of the study is that the cause of CLOCC in patient 2 was not clarified. The patient did not undergo cerebrospinal fluid (CSF) investigations, had no ophthalmologic investigations, and no blood coagulation tests had been carried out [1]. Serum levels of B-vitamins, including B1 and B12, should have been carried out. Also missing are a magnetic resonance angiography (MRA), contrast-enhanced

MRI, magnetic resonance venography (MRV), and perfusion-weighted imaging (PWI). An MRI of the spinal cord is necessary to rule out myelitis. Differentials that should have been ruled out include ischemic stroke (the patient was a smoker), focal encephalitis, vasculitis, venous sinus thrombosis, acute disseminated encephalo-myelitis (ADEM), systemic autoimmune disorders, and Marchiafava-Bignami disease. CLOCC has been particularly reported in association with influenza infections [5].

Overall, the interesting study has limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. It is crucial to associate a morphological entity such as CLOCC with a pathophysiological or etiological concept. The diagnostic management of patients with CLOCC should be broadened and therapy should rely on the most plausible etiology.

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### Declarations

**Disclosures** The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Compliance with ethics 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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