Isolated intracranial hypertension following COVID-19 vaccination: A case report

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Abstract
Increased intracranial pressure in cerebral venous sinus thrombosis or metabolic disease has been reported. We present a case of new-onset chronic headache and bilateral papilledema in the setting of elevated intracranial pressure in strong temporal association to vaccination against COVID-19 with AstraZeneca. After repeated drainage of cerebrospinal fluid and conservative drug therapy, pathological findings were regredient. Even in absence of typical risk factors, increased intracranial pressure should be considered in case of clinical suspicion after COVID-19 vaccination.

Keywords
chronic headache, COVID-19, intracranial hypertension, papilledema, vaccination

Introduction
Headache is one of the most frequent and heterogeneous features in SARS-CoV-19 and can also occur after COVID-19 vaccination. Typically, cephalgia after COVID-19 presents with pressing or pulsating quality with severe intensity, sometimes accompanied with nausea vomiting, or other migraine-like symptoms. A large percentage complains about persistent headaches. Here, we report on a patient with increased intracranial pressure after COVID-19 vaccination.

Case presentation
A 23-year-old man without history of headache was referred to our neurological clinic for bilateral papilledema (Frisén grade II) and headache 1 week after vaccination with ChAdOx1-nCoV-19 (AstraZeneca) on March 10th. On the day of vaccination, the patient directly experienced high fever (40°C) and chills lasting for 48 h following headache (2 days after vaccination). After the remission of fever, persistent headache remained as a prominent symptom, described as pressing and pulsating primarily in the (sub-)occipital region with an intensity of seven to eight in the numeric rating scale (NRS) and missing accompanying symptoms e.g. photo- or phonophobia. In addition, the patient had flashing without any visual impairment and pulsating tinnitus. Despite papilledema II, visual acuity (0.9 bilateral) and visual field testing were unremarkable. Further neurological examination, vitals (blood pressure: 140/100 mmHg, heart rate: 77/min, temperature: 37.1°C) and weight (BMI: 25 kg/m²) were also normal. In a subsequent lumbar puncture, the cerebrospinal fluid (CSF) opening pressure in lying position was 62 cm H2O, which was lowered to 17 cm H2O after extracting 20 ml leading to direct headache improvement. CSF analysis was normal (cell count 1/μL, protein 31 mg/dL, CSF/serum glucose ratio > 0.5). Magnetic resonance imaging (MRI) and MR venogram of the brain did not reveal any intracranial mass, edema nor cerebral venous sinus thrombosis. However, there were radiologic signs of intracranial hypertension.
such as swelling of optic nerve sheaths and tortuosity of both optic nerves as well as slight flattening of both eyeballs.

**Discussion**

This is to the best of our knowledge the first case presenting intracranial hypertension temporally associated with COVID-19 vaccination and without signs of other secondary underlying causes for this disease such as obesity, recent weight gain, sinus-venous thrombosis, sleep apnea, endocrinologic abnormalities, history of taking vitamin A derivatives or tetracycline, tumor or meningitis.

Even though causality cannot certainly be assumed, the following factors make the association of COVID-19 vaccination and intracranial hypertension likely. First, there was a strong timely relationship between the vaccination and begin of the headache and the other symptoms such as pulsating tinnitus and proven papilledema. Secondary causes such as sinus-venous thrombosis, meningitis, hormone intake and changes and medication (e.g. tetracyclines) were thoroughly excluded in our patient. Second, there are now several reports of persistent headache after COVID-19 infection. And, intracranial hypertension was reported in association to COVID-19 infection. Headache intensity and quality in these cases was comparable to our patient with pressing quality and bilateral manifestation. Even though causality cannot certainly be assumed, the following factors make the association of COVID-19 vaccination and intracranial hypertension likely. First, there was a strong timely relationship between the vaccination and begin of the headache and the other symptoms such as pulsating tinnitus and proven papilledema. Secondary causes such as sinus-venous thrombosis, meningitis, hormone intake and changes and medication (e.g. tetracyclines) were thoroughly excluded in our patient. Second, there are now several reports of persistent headache after COVID-19 infection. And, intracranial hypertension was reported in association to COVID-19 infection. Headache intensity and quality in these cases was comparable to our patient with pressing quality and bilateral manifestation. A secondary cause as venous thrombosis, meningitis, hormones, and medication was excluded in our patient by the described diagnostic work up. Furthermore, intracranial hypertension was reported after vaccination against measles, DTP and polio in children. However, a definite explanation how vaccination can lead to intracranial hypertension as in our patient cannot be given. Neuroinflammation seen in COVID-19 infection secondary leading to endothelial dysfunction, hypercoagulopathy and hyperviscosity thus resulting in venous stasis and subsequent increased intracranial pressure as well as increases in certain key cytokines such as interferones and TNF-α could also be discussed as possible mechanisms for COVID-19 vaccines. However, despite the strong temporal association, causality cannot be concluded with certainty. The absence of (partial) empty sella as typical finding in chronic intracranial hypertension argues against long-standing intracranial hypertension in our patient. In contrast, the disease course with a complete remission of headache and papilledema accompanied by a normalization of the intracranial pressure (e.g., 20 cm H₂O) after 3 months with altogether four lumbar tapes as well as specific medication (e.g. acetazolamide, torasemide) according to further supports an association with the vaccination.

**Conclusion**

One cause for a persistent headache after COVID-19 vaccination can be an increased intracranial pressure. In order to proof or definitely exclude that a lumbar puncture with measuring the opening pressure has to be done in these patients.

**Clinical implications**

- COVID-19 infection or vaccination may be an important factor for developing raised intracranial pressure.
– These conditions can lead to new-onset chronic headache.
– Clinicians should consider further diagnostic work-up in new persistent headache and visual impairment.

Author contributions
All authors have read and approved the manuscript before submission. D.C.T. drafting/revising of the manuscript for content, including medical writing. A.S. revising manuscript for content, including medical writing. F.S. drafting/revising of the manuscript for content, including medical writing, study concept, design, interpretation of data, acquisition of data, development of clinical algorithm.

Informed consent
The written informed consent was obtained from the patient for publication of this case report and including images.

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