

# **Brief Communication**

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# Long post-COVID vaccination syndrome

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#### Abstract

Evidence is accumulating that not only SARS-CoV-2 infections but also anti-SARS-CoV-2 vaccinations can be complicated by long-term side effects (long post-COVID-vaccination syndrome (LPCVS)). We here report a patient with LPCVS after the second dose of an mRNA-based anti-SARS-CoV-2 vaccine. The patient is a 45yo female, who developed headache, impaired concentration, vertigo, insomnia, fatigue, exhaustibility, palpitations occurring spontaneously or during exercise, unstable blood pressure, and loss of appetite with bloating immediately after the second dose of an mRNA-based anti-SARS-CoV-2 vaccine. Except for vertigo all other manifestations were previously unknown to the index patient. Extensive work-up by means of instrumental investigations did not reveal a plausible cause for her complaints. Depression was excluded as cause of her complaints. Though improved, symptoms were still present at the 6-months follow-up. It is concluded that anti-SARS-CoV-2 vaccinations can be followed by long-term compromise, which is challenging to substantiate but needs to be taken serious as affected patients can be severely compromised and unable to regain their pre-vaccination status. Whether LPCVS more frequently occurs in patients with comorbidities remains unknown but there are indications that certain pre-morbid conditions favour its development.

### **Brief communication**

From infections with SARS-CoV-2 it is known that the disease course may not only extend over an acute phase (1-4 weeks) but also over a subacute phase (5-12 weeks), and even a chronic phase (>12 weeks) [1]. The chronic phase is also known as post-COVID-syndrome and the subacute phase and the chronic phase are summarised under the term "long-COVID" syndrome [1]. From SARS-CoV-2 vaccinations it is known that they may be complicated by several adverse reactions, which can be mild, moderate, or severe [2]. There is now increasing evidence that such complications can last >4 weeks and thus can be classified as subacute respectively chronic adverse reactions. We here report a patient with a myriad of long-term adverse reactions to the second dose of a SARS-CoV-2 vaccine in more than a single organ (long post-COVID-vaccination syndrome (LPCVS)).

The patient is a 45yo Caucasian female, height 165cm, weight 56kg, who developed chills and fever up to 39°C immediately after the second dose of an mRNA-based SARS-CoV-2 vaccine (Moderna) in July 2021. These manifestations resolved spontaneously within a few hours. Since the vaccination she additionally developed headache, impaired concentration, vertigo, insomnia, fatigue and exhaustibility, palpitations occurring spontaneously or during exercise, and unstable blood pressure values, and loss of appetite with bloating. Headache was previously unknown to the patient, projected to the right frontal area, took an undulating course, and began to improve five months after vaccination. Impaired concentration was described as brain fog or as being drunk and did not improve earlier than four months after onset but was still present at the 6m follow-up. She described vertigo as drowsiness which lasted for four months and began to improve thereafter. Loss of appetite was still present at the 6m follow-up and resulted in a weight loss of 6kg. Insomnia did not improve before three months after onset but was still present at the 6m follow-up. Fatigue and exhaustion persisted for four months and improved thereafter. Palpitations and unstable blood pressure values partially resolved four months after the vaccination but were still present at the 6m follow-up. Work-up for loss of appetite and bloating on an emergency ward revealed an uterus myomatosus but was otherwise normal. One day after the vaccination she complained about dyspnoea. Routine work-up for dyspnoea at an emergency ward on the same day was non-informative. One and a half months after the vaccination she experienced an undulating bulb pressure over the right bulb and blurred vision on the right eye which persisted for three months to decrease thereafter. At the same time she experienced ear pressure bilaterally which persists until today.

Her pre-vaccination history was positive for vertigo since age 21y, smoking, multiple allergies (penicillin, iodine-containing contrast medium, orchad grass), and allergic asthma. She had not experienced any side effects after the first jab of the same vaccine. Her history was negative for any type of headache. Her family history was positive for lung cancer (mother, father).

Clinical neurological exam 6 months after vaccination revealed sore neck muscles exclusively. She denied any severe conflicts with her husband or tensions in her job as a stewardess. Depression was excluded upon her previous history, extensive exploration, and only 2 points on the HDRS<sub>17</sub> depression scale.

Work-up for the patient's complaints included investigations such as blood tests, cardiologic exam (ECG, 24h-ECG, 24h blood pressure monitoring, echocardiography, stress test, spiral CT of lungs), oto-laryngological exam, neurological investigations (carotid ultrasound, cerebral MRI), ultrasound of the collum, swallowing act, thyroid ultrasound, and mammography, which were all non-informative. Only

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the abdominal MRI revealed a cyst/hemangioma in segment 7 of the liver, and a small cyst in the left kidney. Ophthalmologic investigations revealed astigmatism, myopia, presbyopia, fusion weakness and lack of convergence, and a bulb pressure of 19 on the right side. X-ray of the cervical spine revealed mild spondylosis and kyphosis. MRI of the orbita revealed an empty sella. There was mild hypercholesterolemia. She benefited from physiotherapy, tizanidine, and analgesics on demand.

The patient is interesting for multifocal LPCVS. LPCVS is not well defined but patients report similar complaints as in long-COVID syndrome. These include fatigue, post-exertional malaise, headache, dizziness, altered mental state, disorientation, anosmia, myalgia, exertional dyspnoea, or dysgeusia [3]. Clinical neurologic examination and instrumental investigations are usually non-informative, as in the index patient. The type and degree of clinical manifestations of LPCVS may depend on the frequency and type of comorbidities [4]. Some of the manifestations of LPCVS can be attributed to immune thrombocytopenia, hypercoagulability, and the immune response triggered by the vaccination [5]. Another pathophysiological factor that could explain the syndrome could be the decline of titers of neutralising antibodies after vaccination [6,7]. There are also indications that previous immunosuppression may favour the development of side effects from anti-SARS-CoV-2 vaccinations [8]. Which of these suspected pathophysiologic mechanisms was relevant for the index patient remains speculative but the clinical presentation suggested that she could suffer from a hereditary metabolic disease. Arguments in favour for such a disorder are the short stature, the pituitary adenoma, the liver and renal cysts, the ophthalmologic abnormalities, and the history of malignancies in her mother.

In conclusion, this case shows that anti-SARS-CoV-2 vaccinations can be followed by long-term compromise, which is challenging to substantiate but needs to be taken serious as affected patients can be severely handicapped and unable to attend and regain their prevaccination abilities, positions and tasks. Whether LPCVS more frequently occurs in patients with comorbidities remains unknown but there are indications that certain pre-morbid conditions favour its development.

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Code availability: Not applicable

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