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Letter to the Editor

A novel adverse effect of the BNT162b2 mRNA vaccine: First episode of acute mania with psychotic features

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Dear Editor;

A vaccine against SARS-CoV2, which is causing the global COVID-19 pandemic, was developed for the first-time using mRNA technology. Although the short- and long-term side-effects of the vaccine were unknown, emergency use authorization (EUA) was granted by the Food and Drug Administration (FDA) in December 2020(Parkash et al., 2021). Adverse effects such as tiredness, headache, muscle pain, chills, fever, and nausea were defined by the Centers for Disease Control and Prevention (CDC); nonetheless, other adverse effects are continuously being reported in individual patients(Edriss et al. 2021). Here, we describe two patients displaying first episode of acute mania with psychotic features one day after the administration of the BNT162b2 mRNA vaccine.

1. Case 1

A 42-year-old male was admitted to the psychiatric emergency department five days after being vaccinated with the first dose of the BNT162b2 mRNA vaccine with complaints of irritability and sleeplessness. Although the patient did not have any symptoms outside of weakness on the day of vaccination, the complaints started one day after receiving the vaccine. The patient had delusions that his family was being followed by the deep state and that they were in danger. This was the patients first psychiatric admission. The medical history of the patient showed absence of any illnesses or regular use of medication. In addition, the patient was vaccinated voluntarily and did not have extreme anxiety about vaccination. At the clinical examination, the patient's cooperation and orientation were intact; however, his speech output, speed as well as psychomotor activity were increased. The patients affect was anxious and the mood was dysphoric. He exhibited a loosening of associations, described persecutory and reference delusions and displayed a lack of insight. The Young Mania Rating Scale (YMRS) score was 45. Physical and neurological examinations were non-significant, blood screening results at admission showed a C-reactive protein (CRP) level of 4.2 mg/dL, the white blood cell (WBC) count was 8.8mg/dL and thyroid, liver and renal functions, as well as creatine kinase (CK), ferritin, D-Dimer and electrolytes were in the normal range. Brain magnetic resonance imaging (MRI) was also unremarkable. The patient was hospitalized for treatment. 5mg/day olanzapine per oral (p.o.) was initiated for psychiatric symptoms. At the 7th day of olanzapine treatment, agitated behavior was improved (YMRS: 15). At the routine psychiatric evaluation 15 days after discharge, the patient declared that he was unable to remember the initiation of psychiatric symptoms.

2. Case 2

A 57-year-old male was admitted to the psychiatric emergency department with complaints of irritability, sleeplessness, talking to himself and suicidal attempt with thoughts of extinction three days after receiving the second dose of the BNT162b2 mRNA vaccine. While firstly the patient only had local myalgia on the arm on the day of vaccination, psychiatric symptoms started at night on the day he was vaccinated. The patient did not have a history of any diseases that required the use of medication, was vaccinated voluntarily and did have any anxiety about vaccination. Clinical evaluation suggested intact cooperation and orientation while speech output, speed as well as psychomotor activity were increased. The patient was anxious, and his mood was dysphoric. Nihilistic delusions with no insight were recorded. The YMRS score was 42. This patient also did not have any history of psychiatric illnesses. Physical and neurological examinations. Brain MRI results were also normal. The patient was hospitalized for treatment. 2 mg/day risperidone p.o. treatment was initiated for the management of psychiatric symptoms. At the 5th day of risperidone treatment, manic symptoms were improved (YMRS: 11) and the patient was discharged with risperidone 2 mg/day p.o.

To the best of our knowledge, this is the first report of adverse neuropsychiatric side-effects of the BNT162b2 mRNA vaccine. One hypothesis is that SARS-CoV-2 can damage the central nervous system via autoimmune mechanisms due to excessive production and release of pro-inflammatory chemokines and cytokines, particularly TNF-α, IL-1 and IL-6. mRNA vaccines contain nucleotides from the genetic code of the virus that encode a viral protein. This protein is a viral antigen that can cause neuropsychiatric symptoms such as autoimmune psychosis (anti-

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NMDAR, AMPAR, CAPR2 encephalitis) by rapidly increasing a pro-inflammatory response and activated autoimmune mechanism (Pollak et al., 2020; Sen et al. 2021). Another hypothesis suggests that the inflammatory mechanisms caused by COVID-19 can trigger neuropsychiatric symptoms via thiamine deficiency. Therefore, vaccination may also lead to neuropsychiatric symptoms by damaging thiamine metabolism (Branco de Oliveira et al., 2021; de Oliveira et al., 2021).

The current letter has some limitations. Inflammatory markers such as IL-6, TNF alpha and IL-1 were not investigated in the blood and CSF. In addition, because the patients were clinically agitated and restless, consent for LP could not be obtained from their relatives. CSF values could not be measured in the patients.

The BNT162b2 mRNA vaccine, which is very important to end the pandemic, nonetheless may have such rare but severe side effects. Risk groups should therefore be carefully determined.

Declaration of competing interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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