

FIRST EPISODE PSYCHOSIS FOLLOWING COVID-19 VACCINATION: A CASE REPORT

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SUMMARY

Vaccines are crucial to ending the COVID-19 pandemic. An mRNA-based COVID-19 vaccine can cause mild to moderate side effects. A number of cases of cardiac, gastrointestinal, and psychiatric side effects have been reported as rare side effects associated with the COVID-19 vaccine.

This article presents a patient, who after the second injection of the mRNA-based COVID-19 vaccine, immediately developed anxiety, nonspecific fear, and insomnia as the prodromal phase of psychosis. Starting from the second week, the patient manifested delusions of persecution, delusions of influence, thoughts insertion, and delusional behaviour, culminating in the suicide attempt. The duration of psychosis was eight weeks, and symptom reduction was observed only after the gradual administration of antipsychotics over four weeks.

The investigations of the patient did not support any structural changes of the brain, any severe medical conditions, a neurological abnormality, a confusion or a state of unconsciousness or alterations in laboratory tests. Psychosis due to the use of alcohol or psychoactive substances was excluded. The psychological assessment of the patient demonstrated the endogenous type of thinking, and the patient had schizoid and paranoid personality traits strongly associated with schizophrenia.

This case indicates a strong causal relationship between the mRNA-based COVID-19 vaccine injection and the onset of psychosis. We intend to follow up this case for possible development of schizophrenia and understand that the COVID-19 vaccine could possibly play a trigger role in the development of primary psychosis. Longer-term supporting evidence is needed to estimate the prevalence of psychosis following vaccination with the mRNA-based COVID-19 vaccine.

Key words: COVID-19 - first episode psychosis - COVID-19 vaccine

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INTRODUCTION

The World Health Organization (WHO) reported that as of February 20, 2022 there were more than 422 million confirmed COVID-19 cases and more than 5.8 million deaths worldwide. In addition, it was highlighted that Omicron has largely replaced all other variants of the virus and accounts for more than 99% of presented sequences (WHO 2022a). Vaccines are crucial to ending the COVID-19 pandemic, and the WHO is working tirelessly with partners to develop safe and effective vaccines. By the end of September 2021, almost 6 and a half billion doses had already been administered worldwide (WHO 2022b).

Like any vaccine, COVID-19 vaccines can cause side effects, mostly mild to moderate, that disappear within a few days. Typical side effects include pain at the injection site, fever, fatigue, headache, muscle pain, chills, and diarrhoea. Less common side effects reported for some COVID-19 vaccines include severe allergic reactions such as anaphylaxis. However, there are several case reports demonstrating possible association of the mRNA-based COVID-19 vaccine with the development of cardiac, gastrointestinal, and psychiatric disorders (Boivin & Martin 2021, Østergaard et al. 2021, Parkash et al. 2021, Roberts et al. 2021).

CASE DESCRIPTION

A 45-year-old single Caucasian male without past medical and psychiatric history visited the outpatient psychiatric clinic accompanied by his parents because of bizarre behaviour and an attempted suicide by hanging in the early morning of the visit day. An outpatient psychiatrist referred him for inpatient treatment due to psychosis and a high risk of self-harm.

There is no family history of mental illness to suggest any genetic predisposition to psychiatric morbidity. There were no perinatal complications or neurodevelopmental delays in his infancy. His early life experiences were good; he lived in a full family, as an honest child, without significant traumatic experiences. The patient graduated from secondary school and began working as a worker.

At the age of 20, he was episodically using amphetamine and alcohol when going to nightclubs with friends. The patient is unmarried, single, and does not have children but has been in a close relationship with a woman for 5 years in the past. Now he lives with his father. The patient characterizes his personality as shy and withdrawn, it is difficult for him to make new contacts and relationships.

A month before the hospitalisation, he received the second dose of the mRNA-based COVID-19 vaccine

and immediately developed total insomnia, unreasonable anxiety, and tremor. As a result, he contacted his family doctor who prescribed metoprolol 50 mg a day, phenibut 250 mg a day, zolpidem tartrate 10 mg a day, but this therapy did not help, insomnia and fear remained.

After 2 weeks, he realized that he has been jinxed as he found some white powder under the carpet in his apartment. From that moment, he became cautious, did not leave the apartment, and reported persecution. On the last day before his visit to the psychiatric clinic, the patient saw a man walking past the windows of his apartment and watching him. The patient described the thoughts in his head as not his own, giving him commands to observe the person on the street. He did not sleep that night and had a strong belief that he should commit suicide. He attached a rope, tried to hang himself, but his father stopped him.

In the psychiatric department, he was found to be emotionally withdrawn, immersed in his experiences, hypomimic (he sat in one position, spoke very quietly, did not actively participate in the conversation, answered questions in monosyllables or in short sentences after a long pause). Correctly said his name, age, location but was disoriented to time. He reported that he was scared and full of fear. The patient had a decrease in concentration ability, his memory was not altered. The patient demonstrated poor insight but after an explanation agreed to proceed with the investigation and treatment.

Neurological and somatic statuses were without abnormalities. Evaluation for substance use disorders did not reveal any dependence syndrome. The patient's vital signs, biochemical blood test, C-reactive protein, glucose level, total bilirubin, alanine aminotransferase, urea, and urinalysis were within normal limits except for leukocytosis (White's leukocytes 12.8-103/ μ l with a reference interval of 4.00-9.80). A rapid plasma reagin test and a PCR test for COVID-19 were negative. A magnetic resonance imaging (MRI) scan showed no pathology of the brain but found a nonspecific expansion of the cortical sulci in the parietal lobe, the frontal lobe, and the upper surface of the cerebellar hemispheres. No paroxysmal activity was registered on the electroencephalogram (EEG). A chest x-ray showed no abnormalities in the lungs.

A psychometric psychological assessment revealed signs of the organic type of brain disorder. The type of thinking process is characterized as concrete, abstract reasoning is based on insignificant facts. Dynamics and memory volume are reduced. The principles of generalization do not exclude an endogenous process. Explanations are based on the presence of paralogy. The personality is characterized by passive social withdrawal, emotional and social isolation, signs of alexithymia, and periods of detachment from other people, reality, and one's surroundings.

Haloperidol 5 mg three times a day, trihexyphenidyl 2 mg once a day, diazepam 10 mg a night, and quetiapine 50 mg a night were administered. During the hospitalisation, the patient did not have any suicidal thoughts or ideation. The acute psychotic symptoms gradually resolved within four weeks, and the patient was discharged from the hospital on the same medication regime with a good insight about his condition.

DISCUSSION

This case indicates a strong causal relationship between the mRNA-based COVID-19 vaccine injection and the onset of psychosis. After the second vaccination, the patient immediately developed anxiety, nonspecific fear, and insomnia as the prodromal phase of psychosis. Starting from the second week, the patient manifested delusions of persecution, delusions of influence, thoughts insertion, and delusional behaviour, culminating in the suicide attempt.

The investigations of the patient did not support any structural changes of the brain; the patient did not have any severe medical conditions, neurological abnormalities, or alterations in laboratory tests with the exception of mild leucocytosis. The patient did not demonstrate clear confusion or a state of unconsciousness. These data rule out an organic cause of psychosis. Psychosis due to the use of alcohol or psychoactive substances was excluded.

After receiving the vaccine, the patient did not experience the typical side effect in the form of flu-like symptoms. The duration of psychosis was eight weeks, and symptom reduction was observed only after the gradual administration of antipsychotics over four weeks. The psychological assessment of the patient demonstrated the endogenous type of thinking; additionally, the patient had schizoid and paranoid personality traits strongly associated with schizophrenia.

Based on the patient's history, clinical presentation, and investigations, we have classified this case as an acute and transient psychotic disorder (F23; ICD-10) according to the International Classification of Diseases 10. We intend to follow up this case for possible development of schizophrenia and understand that the COVID-19 vaccine could play a trigger role in the development of primary psychosis. However, this is not a typical age of onset, and the patient did not have additional risk factors for the development of primary psychosis such as psychological, socio-demographic, or economic ones: birth in winter, beyond childhood trauma, social adversity discrimination, ethnic minority status, immigrant status (Brasso et al. 2021, Varchmin et al. 2021).

Literary data provide limited publications on the psychoses caused by the COVID-19 vaccine. Some case reports highlight the possible association of orga-

nic etiology, autoimmune encephalitis, and the onset of schizophrenia. Roberts et al. presented a case of a short-term psychosis following the first dose of the AstraZeneca COVID-19 vaccine. This patient had flu-like symptoms after vaccination; psychotic symptoms were accompanied by confusion and developed on the 10th day after the vaccination. The psychosis resolved without antipsychotic treatment and was classified as complications associated with the COVID-19 vaccination (Roberts et al. 2021). Reinfeld et al. demonstrated a new case of psychosis after the administration of the first dose of the mRNA-based COVID-19 vaccine and worsening of psychotic symptoms after receiving the second dose. Hallucinations and delusions were presented within four weeks and resolved in three days after the administration of antipsychotics (Reinfeld et al. 2021).

There are several hypotheses that discuss possible interactions between the onset of psychosis and the mRNA-based COVID-19 vaccine. An informative ribonucleic acid is used in the mRNA-based COVID-19 vaccines, which triggers an immune response with the production of antibodies in case of infection. The mRNA molecules are taken up by antigen presenting cells and begin to prime cluster of differentiation CD4 and CD8 T lymphocytes in the lymph nodes and induce the production of cytotoxic T lymphocytes. Memory B cells and antibody-secreting long-lived plasma cells start to form at the germinal centre, which is activated by T follicular helper cells (Bettini & Locci 2021).

Many studies have focused on the role of immunity in the pathophysiology of psychosis and have found abnormalities affecting the innate (mediated by macrophages, neutrophils, and cytokines) and the adaptive immunity system (mediated by T and B-lymphocytes as well as antibodies secreted by B-lymphocytes) (Abdelghaffar et al. 2022, Müller 2018). Additionally, numerous studies have provided evidence that during the first episode of psychosis and schizophrenic psychosis activation of the inflammatory cascade persists, which leads to the activation of T and B-lymphocytes as well as the production of inflammatory cytokines such as Interleukin (IL)-6, IL-1 β , IL-1 receptor antagonist, soluble IL-2 receptor, IL-4, IL-8, IL-12, tumour necrosis factor- α , transforming growth factor- β , and interferon- γ (Dahan et al. 2018, Dawidowski et al. 2021, Ding et al. 2014, Momtazmanesh et al. 2019, Romeo et al. 2018, Zhu et al. 2018).

Moreover, the alteration in ILs leads to the development of oxidative stress, which causes neuronal damage and dysregulation of the metabolism of neurotransmitters associated with schizophrenia such as dopamine, serotonin, and glutamate.

In accordance with this, the immune system is activated in the vaccinated and in the case of genetic vulnerability and other multiple environmental risk

factors there is a risk of developing schizophrenic psychosis.

Longer-term supporting evidence is needed to estimate the prevalence of psychosis following vaccination with the mRNA-based COVID-19 vaccine. It is extremely important to follow up patients after the administration of each dose of the vaccine in order to collect information on side effects and adverse events of the vaccine, which will make it possible to assess their severity in a timely manner and if necessary start symptomatic or pathogenetic treatment. In turn, when diagnosing a psychotic disorder we consider it important to continue monitoring patients for a longer period, taking into account the possibility of developing a schizophrenic process.

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Contribution of individual authors:

Lubova Renemane: literature search and analysis, collecting the clinical data, interpretation of data, writing of the first draft.

Jelena Vrublevska: literature search and analysis, interpretation of data, revision and editing.

Ingrida Cera: collecting the clinical data and clinical interpretation of data.

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