

Psychiatric adverse reaction to COVID-19 vaccine booster presenting as first-episode acute mania with psychotic features: A case report

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Case Report

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Abstract

Background

A few case series on psychiatric adverse reactions to COVID-19 vaccines have been reported despite the absence of a history of psychiatric disorders. Herein, we report a case of a first episode of acute mania with psychotic features received the third mRNA-1273 vaccine.

Case presentation

A 37-year-old man developed talkativeness, grandiose delusions, emotional instability, sleeplessness, excitement, hyperactivity and suicidal behavior 4 days after receiving the third mRNA-1273 COVID-19 vaccine. On the 9th days after vaccination, he was diagnosed with first-episode acute mania with psychotic features and admitted to the psychiatric institute for the first time. After olanzapine administration, the psychiatric symptoms improved within 4 weeks.

Conclusions

To our knowledge, this is the first report of a first episode of acute mania with psychiatric features associated with the mRNA-1273 vaccine booster. Psychiatrists should be aware of this possibility and be attentive to such a rare and severe adverse effect that could occur within 10 days of vaccination.

Background

The coronavirus disease (COVID-19) pandemic has compromised public health, societies, and economies globally. Vaccination is considered the most powerful weapon against this worldwide pandemic. The side effects that have been disclosed by the Centers for Disease Control and Prevention include tiredness, headache, muscle pain, chills, fever, and nausea [1]. Nevertheless, the short- and long-term side-effects of the vaccine remain unclear, and a variety of adverse reactions have been continuously reported in individual patients. Thus, Mouliou and Dardiotis conducted a review concerning severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) mRNA vaccines and post-vaccination adverse incidents, suggesting that inflammation is a likely common denominator in some cases and/or diagnoses reported as spontaneous adverse events [2]. Importantly, a few case series of psychiatric adverse reactions to COVID-19 vaccines have been reported despite the absence of a history of psychiatric disorders [3]. Herein, we present a case of a first episode of acute psychotic mania that occurred a few days after receipt of the third mRNA-1273 vaccine.

Case Presentation

A 37-year-old man received the BNT162b2 mRNA vaccine twice, and experienced fatigue after the first booster shot approximately 6 months prior to presenting at our institution. After the third COVID-19 vaccination half a dose of the mRNA-1273 vaccine he complained of mild headache, a floating sensation,

and difficulty concentrating; he did not have fever. Four days after vaccination, he presented with talkativeness, and grandiose delusions, saying that he had won 2 billion yen in horse racing. He also presented with emotional instability, such as crying when saying “Everyone would be happy.” The following day his family brought him to the emergency department of our hospital; he presented with sleeplessness, excitement, hyperactivity, and sexual deviance. Eight days after vaccination, he went to see hospital again, consulted by a neurologist and was not diagnosed with any neurological disorders, such as encephalitis. Thereafter, on the 9th day after vaccination, he jumped from the 2nd floor of his house, and was transported back to the hospital by ambulance. After receiving physical treatment on days 9 after vaccination, he was consulted by emergency medicine doctors and admitted to the psychiatric department with complaints of excitement and hyperactivity. This was his first psychiatric admission; he had no previous medical history. He exhibited flight of ideas, hyperactivity, distraction, hyperthymia, and religious delusions, such as saying “my child is God.” He displayed a lack of insight and became enraged when his actions were restricted. His Young Mania Rating Scale (YMRS) score was 21. Physical and neurological examinations results were insignificant, blood examination 1 day prior to admission showed a C-reactive protein (CRP) concentration of 0.10 mg/dL; white blood cell (WBC) count of 16,600/ μ L; and renal, liver, and thyroid functions within the normal ranges. His COVID-19 PCR, sexually transmitted infection (such as syphilis), and urinary illegal drug test results were negative. His head computed tomography, brain magnetic resonance imaging (MRI), electroencephalography, and cerebrospinal fluid (CSF) examination results were normal. He was diagnosed with first-episode acute mania with psychotic features and treatment was started 5 mg/day olanzapine orally and, after 2 days, 10 mg/day. After 2 weeks, his psychotic symptoms disappeared and his manic symptoms gradually improved. On the 23rd day after admission, his YMRS score improved to 9, and he was tapered off olanzapine by the 41st day after admission. On the 66th day, he was discharged from hospital given that his acute mania had completely resolved without administration of any further medication. Following discharge, the patient remained stable and has not exhibited any manic symptoms during follow-up.

Conclusions

To the best of our knowledge, this is the first report of a psychiatric adverse reaction presenting as first-episode acute mania with psychotic features after the mRNA-1273 vaccine booster. Recently, an association between mood dysregulation and COVID-19 vaccination has been reported in the literature, where both the illness course and potential mechanisms of vaccination have been discussed [2, 3]. For instance, acute mania with psychotic features has been described following mRNA vaccination; it manifested in a 42-year-old man as irritability, sleeplessness, delusions, and finally as amnesia of the whole situation 1 day after receiving the first dose of the BNT162b2 mRNA vaccine [2, 4]. Similarly, it manifested in a 57-year-old man as sleeplessness, irritability, and a suicidal attempt some days after receiving the 2nd dose of the BNT162b mRNA vaccine [2, 4]. It has also been reported in a 52-year-old woman who experienced a rapid relapse in bipolar mania within a few days of receiving another viral vector COVID-19 vaccine (the 1st dose of the ChAdOx1-S/nCoV-19 vaccine) [5]. Overall, symptom onset in all cases was within 10 days of vaccination, likely suggesting the presence of a high-risk period

warranting vigilance [3]. Therefore, it is essential to detect the risk groups [2, 4]. Furthermore, the mechanism that could cause psychiatric symptoms might be driven by the vaccine-derived protein antigen, such as in autoimmune psychosis [4].

Similar to the above-mentioned reports, the most probable explanation of the present case is an immunologic response following vaccination that might have triggered manic symptoms by creating a hyperinflammatory state [5]. The potential link between elevated levels of inflammatory markers and the onset of mania has been presented in previous research [6]. The occurrence of psychosis following vaccination may be also mediated by the immune response of the body against SARS-CoV-2 [3]. Specifically, a previous study suggested that administration of the vaccine elicits a cellular immune reaction which leads to a T-helper cell-mediated outpouring of pro-inflammatory cytokines [7]. In some individuals, this may lead to a cytokine storm and NMDA receptor hypofunction with a resultant increase in dopamine, which may trigger a psychotic state [7]. Another hypothesis is suggested that SARS-CoV-2 damages the central nervous system via an autoimmune mechanism due to the 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 [4]. This protein is a viral antigen that can cause neuropsychiatric symptoms such as autoimmune psychosis (anti-NMDAR, AMPAR, CAPR2 encephalitis) by rapidly exacerbating the pro-inflammatory response and activating the autoimmune mechanism [8, 9]. In the present case, the serum CRP concentration, brain MRI findings, and CSF examination results were within the normal ranges; however, the WBC count was elevated, indicating a potential association between inflammation and acute psychotic mania. Moreover, the mRNA-1273 vaccine booster having been administered after two BNT162b2 mRNA vaccines, together with the heterologous vaccine schedules, might have induced greater systemic reactivity than homologous vaccination [10], resulting in first-episode acute mania with psychotic features.

This case report has some limitations. First, while mentioning the pathogenic mechanisms in the present case, inflammatory marker concentrations (i.e., IL-6, TNF- α , and IL-1) were not measured in the blood and CSF. Second, after 3 months of discharge, this patient had no psychiatric symptoms. However, it cannot be completely ruled out that his manic symptoms may recur and that this first manic episode may have been the starting point of bipolar disorder.

In conclusion, to our knowledge, this is the first report of first-episode acute mania with psychiatric features associated with the mRNA-1273 booster vaccine. Psychiatrist should be aware of this possibility, and attention should be paid to such a rare but severe adverse reaction within 10 days of vaccination. However, this report should never discourage COVID-19 vaccination, as the benefits of vaccination outweigh the rare risk of manic switch in the majority of cases. There is an additional need to develop a consensus on monitoring and managing psychiatric side effects of COVID-19 vaccination.

List Of Abbreviations

COVID-19, coronavirus disease; CRP, C-reactive protein; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WBC, white blood cell; YMRS, Young Mania Rating Scale

Declarations

Ethics approval and consent to participate

Written patient consent was obtained on 03/06/2022. Ethics approval was obtained from the Medical Ethics Commission for Clinical Studies in the Wakayama Medical University (approval no. 3644 on 09/16/2022).

Consent for publication

Written patient consent for publication was obtained on 08/09/2022.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AK, YF, HM, YY, KO and SK contributed to the patient treatment. AK, YF, HM, YY, KO and SK collected data and wrote the first draft of the manuscript. AK, YF, HM, YY, KO and SK supervised the project, were critically involved in its design, and assisted in editing the final manuscript. All authors contributed toward drafting the paper and agree to be accountable for all aspects of the work.

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