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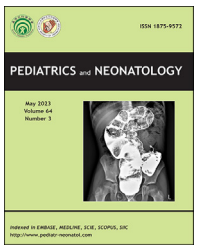

Letter to the Editor

Acute psychosis induced by mRNA-based COVID-19 vaccine in adolescents: A pediatric case report

1. Introduction

Coronavirus disease 2019(COVID-19) is a pandemic, and vaccination has been used as a preventive measure to control the outbreaks through herd immunity. BNT162b2 (Pfizer-BioNTech) is a lipid nanoparticle formulated nucleoside-modified messenger RNA (mRNA) that encodes severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike protein stabilized in the prefusion conformation. It has demonstrated 95% efficacy in preventing COVID-19, which is currently the only one receiving Emergency Use Authorization in adolescents aged 5—17 years from the Food and Drug Administration.[1] Irrespective of the favorable safety and the side-effect profile of the BNT162B2 vaccine in 12-17-year-old recipients, some rare yet significant adverse effects, such as myocarditis other than injection site pain, fatigue, myalgia, and headache, as defined by the Centers for Disease Control and Prevention, are being reported in individual cases.[2] Here, we have reported the case of a male adolescent patient manifesting acute psychosis 2 days after receiving the second dose of the BNT162B2 vaccine.

2. Case presentation

A 15-year-old boy presented to the emergency department of our hospital with the chief complaint of agitation, involuntary limb stretching, and screaming 2 days after receiving his second dose of the BNT162B2 vaccine. He was healthy without any specific medical history before the vaccination. His vital signs and neurological examination were all within normal limits. Moreover, his hematology, blood chemistry, and urine toxicology results were within normal limits. However, we recorded elevated CPK levels of 792U/L and CK-MB levels of 28 U/L. His COVID-19 PCR test was negative. Brain magnetic resonance imaging revealed no abnormally enhanced lesions.

After admission, he was observed to demonstrate bizarre behaviors, including sitting up and lying down frequently and taking up the mannerism of praying in bed. We also noted auditory hallucinations and delusions. Accordingly, a psychiatrist was consulted, and aripiprazole and biperiden were prescribed for acute symptom control. An electroencephalography (EEG) study performed a week after his symptom onset showed negative findings. Lumbar puncture with basic cerebrospinal fluid (CSF) analysis and extensive CSF workup for autoimmune encephalitis (including anti-NMDAR, anti-AMPAR1, anti-AMPAR2, anti-CASPR2, anti-LGI1, and anti-GABAR) were conducted 1 week after the onset of the symptoms and revealed negative finding. Simultaneously, antibodies for paraneoplastic neurological syndrome were examined, which also showed negative results. Subsequently, his acute symptoms improved to some extent, and he was discharged with aripiprazole and biperiden. However, his hallucinations and bizarre behavior persisted for >1 month after his discharge. Accordingly, we decided to reschedule his admission for 3-day intravenous methylprednisolone (1 g/day) treatment. The oral form steroid (30 mg/day) was prescribed after discharge, after which the dosage was tapered if the symptoms improved. The total course of steroid treatment was 3 weeks, and the patient's psychiatric status gradually improved within the 2-month follow-up. His thinking capacity and emotional expression also showed significant improvement. EEG was performed during the outpatient follow-up with negative findings.

3. Discussion

Although the safety and effectiveness of the m-RNA COVID-19 vaccine have been tested, the short-term and long-term

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side effects of this vaccine remain unknown, especially in the pediatric group. Cases of psychosis following vaccination with the COVID-19 vaccine are rare. Acute psychosis induced by vaccine administration has only been reported for vaccines against rabies[3] and yellow fever.[4] One possible explanation for neuropsychiatric symptoms as in the present report is that SARS-CoV-2 causes an increase in the levels of pro-inflammatory factors, particularly IL-1, IL-6, and TNF-α, which damages the central nervous system.[5] The mRNA vaccine encoding the SARS-CoV-2 spike protein may trigger an immune response that is milder than that of COVID-19 infection, resulting in neuropsychiatric symptoms through an inflammatory condition. The perturbation of inflammatory markers could be found in the first-episode psychosis to manifest a pro-inflammatory imbalance.[6] In a more recent case, a 32-year-old man presented with acute confusion, auditory hallucinations, and memory disturbance after receiving the mRNA-based COVID-19 vaccine. He displayed dramatic improvements after methylprednisolone pulse therapy.[7] In the present case, as the CSF study was invasive, we could not follow his CSF regularly. Moreover, the inflammatory factors such as IL-1, IL-6, and TNF-α could not be evaluated in our laboratory. Although no significant evidence of inflammation was recorded in the CSF examination; however, based on the chronology of events and the improvement in the patient's symptoms after the steroid pulse therapy, it is believed that this adverse effect may be related to the vaccine and caused as a result of an inflammatory response. Our case report thus highlights the rare neuropsychiatric side effect of psychosis in adolescents elicited by the BNT162b2 vaccine. Further studies are, however, warranted to determine the pathogenesis of the COVID-19 mRNA vaccine-related neuropsychiatric complications and to assess the role of the detection of antigens, antibodies, and immune complexes in the CSF of patients.

Acute psychosis caused by the COVID-19 mRNA vaccine is not easily diagnosed, such as myocarditis, which has supporting diagnostic laboratory data. However, it can still be detected through detailed clinical observation and can be treated effectively. The degree of post-COVID-19 vaccination side effects can vary across cases. Our case report highlights the need for awareness regarding the possible neuropsychiatric complications of the mRNA COVID-19 vaccine in children. Psychosis associated with the COVID-19 mRNA vaccine can be treated with steroids when traditional antipsychotic medicines are found ineffective. However, long-term follow-up of the patient's cognitive functions and behavior is necessary.

Declaration of competing interest

None.

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