Acute Psychosis After Immunization With Whole-Virion Inactivated COVID-19 Vaccine; A Case Report From Central India

To the Editors:

The beginning of the coronavirus disease 2019 (COVID-19) pandemic was associated with the beginning of a simultaneous mental health pandemic. Increasing restrictions on travel, limited social interaction, fear of getting infected, and isolation at quarantine centers and hospitals were some of the reasons for the worsening of mental health status.[1] Studies have reported increased rates of neuropsychiatric manifestations in people affected with COVID-19. This includes depression (12.9%), anxiety disorders (19.1%), sleep disorders (27.4%), posttraumatic stress (15.7%), and cognitive impairment (20.2%), among others.[2] A recent review also reports the occurrence of psychiatric adverse events like altered mental status, psychosis, depression, mania, and functional neurological disorders after immunization with the COVID vaccine.[3] Although the data regarding such adverse events are scarce, the existing literature reports these adverse events with messenger RNA (mRNA)–based[4–6] and viral vector COVID vaccines.[7–10] Here we report the case of a 17-year-old adolescent girl who developed psychosis after the second dose of the Covaxin vaccine, a whole-virion inactivated SARS-CoV-2 antigen vaccine. The patient and her parents provided consent for publication of this case report.

CASE REPORT

A 17-year-old adolescent girl presented at the mental health clinic of our referral hospital with an acute onset illness of 1-month duration. The presenting complaints were being restless, fearful, suspicious, talking to herself, poor self-care, disinhibited behavior, decreased food intake, and decreased sleep of 1-month duration. These symptoms appeared within 48 hours of receiving the second dose of the COVID vaccine at a primary health center in February 2022. There was no history of fever postvaccination, and no history of mental illness or substance use was reported. No adverse events were reported after the first dose of the vaccine received in January 2022. There was no history of any mental illness in the family. On examination, she was uncooperative, restless, and fearful, and hallucinatory behavior was observed. She refused to answer questions. No neurological abnormalities were observed. She was rated on Brief Psychiatric Rating Scale with a total score of 55. Investigations including complete blood count, liver function test, renal function tests, serum electrolytes, and thyroid profile were within normal limits for her age. Rapid antigen test screening for COVID-19 was negative. Computed tomography scan of the brain (plain and contrast) did not reveal any abnormality. After discussion with the parents, it was decided to manage the patient on an outpatient basis. The patient was started on olanzapine (5 mg) and clonazepam (0.5 mg) PRN and was followed up after 2 weeks. On follow-up, the patient had shown improvement in self-care, social interaction, hallucinatory behavior, and sleep. She remained fearful and reported auditory hallucinations in the past, which had decreased in severity. Brief Psychiatric Rating Scale score during this visit was 39. Because there was a significant improvement, olanzapine (5 mg) was continued, and a follow-up after 2 weeks was scheduled. On 4-week follow-up, the patient reported that auditory hallucinations had stopped; improvement was noted in other symptoms like fearfulness, self-care, and social interaction; and she was performing routine activities. Brief Psychiatric Rating Scale score had further reduced to 21. She was advised to continue olanzapine and follow up regularly.

DISCUSSION

India started the COVID-19 vaccination program for adolescents aged 15 to 17 years January 3, 2022. Covaxin vaccine, a whole-virion inactivated SARS-CoV-2 antigen vaccine, is the only approved vaccine for this age group. To date, more than 100 million doses of vaccine have been given across the country to children of this age group.[11]

Psychiatric adverse events following the COVID-19 vaccine appear to be a rare occurrence. Adverse events like psychosis,[4,5,9] mania,[6] depression,[7] acute confusional state,[8] and functional neurological disorders[10] have been previously reported. These adverse events were reported in the adult population with mRNA and viral vector vaccines.[3] To the best of our knowledge, this is the first case report of a whole-virion inactivated SARS-CoV-2 vaccine-associated psychiatric adverse effects in an individual younger than 18 years.

Messenger RNA vaccines are associated with fewer systemic adverse events when compared with viral vector vaccines.[12] It is hypothesized that inoculation with the COVID-19 vaccine may result in a proinflammatory response and an autoimmune reaction, which may lead to autoimmune encephalitis.[9] The immunogenic response due to the vaccine is less than that of SARS-CoV-2 infection itself.[3] However, it may be severe enough to trigger a cytokine storm. Elevated levels of interleukin (IL)-1, IL-6, IL-10, and tumor necrosis factor α in turn affect the levels of monoamine neurotransmitters and dysfunction of N-methyl-D-aspartate receptors. This leads to an increased level of dopamine and may trigger psychiatric manifestations in the affected individuals.[13]

Precipitation of symptoms within 48 hours of inoculation, exclusion of other probable causes, and absence of genetic predisposition to mental illness indicate the psychiatric adverse event may be related to the vaccine. This case report presents a rare adverse event associated with the whole-virion inactivated SARS-CoV-2 antigen vaccine. This by itself should not deter individuals from getting vaccinated against a deadly infection that brought the world to a standstill. This should rather generate awareness and accentuate surveillance for the possible adverse events postvaccination.

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A Case of Acute Conditioned Dyspnea During Tracheostomy Weaning Treated Successfully With Adjunctive Mirtazapine

To the Editors:

Approximately 15% of patients undergoing mechanical ventilation receive a tracheostomy as part of their care. A commonly used test to determine whether a critically ill patient with a tracheostomy tube is ready for decannulation is a capping trial, in which a cap is placed over the tracheostomy tube for a period of time to see whether the patient is able to breathe around the tracheostomy tube (or through a fenestration in the tube) through the nose and mouth. Protocol-based capping trials have led to readiness criteria with high specificity and a positive predictive value for successful decannulation.[1] In cases where extubation or decannulation are prolonged because of anxiety, dysfunctional breathing (changes in breathing in the absence or in excess of medical pathology) often warrants specific treatment.[2]

Mirtazapine, a noradrenergic and specific serotonergic (5HT)-ergic antidepressant, is associated with enhancement of 5HT-ergic and noradrenergic systems in the central nervous system. The noradrenergic effect is attributed to the blockade of inhibitory presynaptic α (α)2-autoreceptors. In addition, mirtazapine antagonizes α2-heteroreceptors in 5HT-ergic nerve terminals, thereby increasing serotonin release. Because it also blocks 5-HT2 and 5-HT3 receptors (R), only 5-HT1AR–mediated serotonergic transmission is enhanced. Mirtazapine also has a high affinity for histamine H1 receptors.[3] Although mirtazapine is indicated for the treatment of major depressive disorder, its efficacy in anxiety/disorders has been demonstrated, albeit mainly based on observations from case reports or data from open-label studies.[4]

We present a care report of a patient who experienced unsuccessful capping trials, purported because of anxiety, who was successfully extubated/decannulated with off-label use of mirtazapine. Written and verbal consent for publication of this article has been obtained from the patient. Information has been deidentified to protect anonymity.

The patient is a 56-year-old woman with a past medical history of chronic heart failure and chronic obstructive pulmonary disease who presented to the emergency department with worsening lower extremity edema and shortness of breath becoming hypotensive and hypoxemic, with a blood pressure of 86/66 mm Hg and oxygen saturation of 86%, despite 2 L of oxygen via nasal cannula. Her chest x-ray revealed increasing bilateral lower lung opacity possibly secondary to pleural effusion. Her echocardiogram showed an ejection fraction of 30% and troponin of 44 ng/L.

The patient was admitted to the intensive care unit on furosemide and milrinone. Because of "increasing anxiety," she received lorazepam and experienced worsening hypoventilation with pH of 7.29 on arterial blood gas and placed on mechanical ventilation. As the patient became hemodynamically stable, she was extubated and received a tracheostomy on ventilation, ultimately switched to spontaneous mode with stable vital signs and respiratory rate of 16 to 20 breaths/minute. Despite spontaneous breathing, she could not be weaned off the ventilator for more than 10 minutes because of "anxiety." The patient was breathing with an endotracheal tube and ventilator at night, whence transferred to an extended recovery unit.

On day 1, the patient attempted 2 wean trials. During both trials, she became diaphoretic and tachypneic, describing a feeling of "inability to breathe," requesting to go back on the ventilator. During these trials, the patient's oxygen saturation was 85%. We were consulted at this time "to treat the patient's severe anxiety and assist in completion of a 12 hour wean."

On our evaluation, the patient denied any prior psychiatric history, including alcohol or illicit/prescription substance use. She did report being extremely "anxious" in both anticipation and especially when the endotracheal tube was capped. Her initial Hospital Anxiety and Depression Scale[5] score was 19, with a Depression subscale score of 2 and an Anxiety subscale score of 17 (severe), whereas her Dyspnea-12 Questionnaire[6] (measuring the severity of breathlessness, quantified to cover both physical and psychological dimensions) score was 27. Our patient's mental status examination was unremarkable save an anxious mood, as she denied depressed mood, psychosis, or suicidality. Her mini-Mental State Examination[7] score was 29. Notably, complete blood count, complete metabolic profile, thyroid function tests, and infectious serologies were essentially unremarkable. In addition, aeration on chest x-ray significantly improved from admission.

Please see Figure 1, with regard to all medications used and the first 21 days of longitudinal course of successful weaning. By day 21, the patient reached 12 hours on the tracheostomy collar. On day 27, the patient transitioned to bilevel positive airway press nocturnally. On days 21 and 27, Hospital Anxiety and Depression Scale—Anxiety/Dyspnea-12 Questionnaire scores were 6/12 and 4/7, respectively. The patient was discharged to skilled nursing on both mirtazapine and lorazepam, as prescribed, 30 days after our initial consultation.

DISCUSSION

Similar to the multidimensional conception of pain, dyspnea can be consisted of perceived intensity (SI) of breathing discomfort, immediate nonreflective experience of unpleasantness (A1), and a stage of cognitive evaluation and emotional response (A2). A2 is characterized by prominent emotional reactions such as depression, anxiety, and fear and is susceptible to differences in individual personality traits and life situations. Thus, in the case of our patient, we surmise that sensations of breathlessness led to immediate negative affect, conditioned dyspnea, and avoidance of weaning trials, thereby resulting in multiple failed weaning trials.[8]

As for the potential rationale for using mirtazapine in our patient's phenotype, mirtazapine has been shown to reduce the expression of conditioned anxiety dose