



## Letter to the Editor

## Psychosis in a patient with anti-NMDA-receptor antibodies experiencing significant stress related to COVID-19



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## Letter to the Editor

The scale of the impact of COVID-19 pandemic on most aspects of day-to-day life is like never seen before. Not surprisingly, it is leading to significant psychological stress among general population, vulnerable communities, and particularly health care workers (Sani et al., 2020). There are reports of new-onset psychiatric symptoms and exacerbation of pre-existing psychiatric conditions associated with the pandemic related stress coming from across the globe (Majadas et al., 2020). Moreover, there is emerging evidence that the more severe the inflammatory response to SARS-CoV-2, worse the psychiatric outcome (Mazza et al., 2020). This is the first report of new-onset psychosis in a patient with anti-NMDA-receptor antibodies experiencing significant stress related to COVID-19 pandemic.

A 17-year-old boy with no significant past medical or psychiatric history presented with 2-weeks history of abrupt onset fever, urinary incontinence, slurred and incoherent speech, overactivity, mood incongruent crying, unprovoked anger outbursts and screaming, and reduced sleep. Prior to the onset of these symptoms, he was very distressed due to the potential risk of getting infected with SARS-CoV-2 and bullying by a neighbour who scared him that he would contract the infection from his father who had recently returned home from another state and was observing mandatory home quarantine. He was diagnosed with acute and transient psychotic disorder at a local hospital and prescribed oral olanzapine titrated up to 15 mg/day, but he showed no response. When he was brought to our hospital, his mental status examination revealed overfamiliar attitude, increased psychomotor activity, and labile affect. Physical examination showed no neurological deficits. Laboratory evaluation including haemogram, renal function tests, liver function tests, thyroid stimulating hormone, serum calcium and magnesium, C reactive protein, and cerebrospinal fluid study were within normal limits. Brain MRI and EEG did not reveal any abnormal findings that would explain his presentation. He was prescribed oral sodium valproate 500 mg/day and oral quetiapine 100 mg/day, while awaiting the autoantibody test results of his CSF sample, but showed no response during the two days of his hospital admission. Considering poor response to treatment, his family discharged him from the hospital and consulted another psychiatrist who prescribed oral haloperidol 4.5 mg/day. He returned to our hospital a

week later with no change in his symptoms. In the meantime, his CSF anti-N-methyl-D-aspartate (NMDA)-receptor antibodies came positive. He was readmitted and initiated on immunotherapy with steroids (methylprednisolone 1 gm daily for 5 days). He showed gradual improvement in symptoms over a period of 1 week. Search for occult malignancies using USG abdomen was negative. Considering poor response and excessive sedation, the dose of haloperidol was gradually reduced to 1.5 mg/day with no symptomatic exacerbation.

Anti-N-methyl-d-aspartate receptor (NMDAR) antibody encephalitis, an autoimmune encephalitis with auto-antibodies that target the NR1 subunit of the NMDAR, has recently been identified as a form of atypical autoimmune encephalitis with predominant neuropsychiatric manifestations (Pollak et al., 2020). A case series of anti-NMDAR encephalitis in children from India reported neuropsychiatric symptoms, including mood symptoms, inappropriate crying, social withdrawal, and unprovoked anger outbursts and screaming, as the most common initial presentation, leading to delays in diagnosis and appropriate treatment (Basheer et al., 2017). Our patient had an abrupt onset of psychiatric symptoms, consistent with those reported in anti-NMDAR encephalitis, along with movement disorder (dysarthria), autonomic instability (fever and urinary incontinence), and presence of anti-NMDAR antibodies in CSF, which is highly suggestive of a diagnosis of autoimmune psychosis. Poor response to psychotropic medications and a good response to steroids in our patient is consistent with a diagnosis of autoimmune psychosis. However, a normal MRI brain, EEG and otherwise normal CSF preclude a definite diagnosis of autoimmune psychosis (Pollak et al., 2020).

Our patient was experiencing significant stress related to the risk of contracting SARS-CoV-2 and bullying emanating from stigma associated with it prior to the onset of symptoms. Did the stress contribute to his presentation? There is evidence to suggest the role of stress in precipitating autoimmune disorders, including autoimmune psychosis. Song et al. (2018), explored the association between previous history of stress related disorders and the development of subsequent autoimmune diseases in 41 distinct autoimmune diseases in both population and sibling-based comparisons study recently. They found that a clinical diagnosis of stress-related disorders in the past was significantly

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associated with an increased risk of autoimmune disease (Song et al., 2018). One of the potential mechanisms mediating stress and autoimmune disorders is thought to be the activation of autonomic nervous system inducing the dysregulation of immune function and disinhibition of inflammatory response via the inflammatory reflex, which is a centrally integrated physiological mechanism in which afferent vagus nerve signalling is functionally associated with efferent vagus nerve-mediated output to regulate proinflammatory cytokine production and inflammation (Pavlov and Tracey, 2012). However, it is possible, perhaps likely, that the stress in our patient was merely coincidental. Appropriately designed studies to explore the interaction between stress and autoimmune psychiatric disorders, particularly autoimmune psychosis, need to be done. Our case report also underscores the importance of search for potential underlying causes in paediatric psychosis even when there is an apparent potential explanation, like stress precipitating the illness, to avoid misdiagnosis of a treatable condition, like anti-NMDAR autoimmune psychosis, which may result in significant adverse outcomes if left untreated.

#### Financial disclosures

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#### Declaration of competing interest

No conflicts of interest.

#### References

Basheer, S., Nagappa, M., Mahadevan, A., Bindu, P.S., Taly, A.B., Girimaji, S.C., 2017. Neuropsychiatric manifestations of pediatric NMDA receptor autoimmune encephalitis: a case series from a tertiary care center in India. *Prim. Care Companion CNS Disord.* 19 <https://doi.org/10.4088/PCC.17m02110> pii: 17m02110.

- Majadas, S., Pérez, J., Casado-Espada, N.M., Zambrana, A., Bullón, A., Roncero, C., 2020. A case with psychotic disorder as a clinical presentation of COVID-19 [published online ahead of print, 2020 Jul 8]. *Psychiatr. Clin. Neurosci.* <https://doi.org/10.1111/pcn.13107>, 10.1111/pcn.13107.
- Mazza, M.G., De Lorenzo, R., Conte, C., et al., 2020. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. *Brain Behav. Immun.* <https://doi.org/10.1016/j.bbi.2020.07.037>.
- Pavlov, V.A., Tracey, K.J., 2012. The vagus nerve and the inflammatory reflex: linking immunity and metabolism. *Nat. Rev. Endocrinol.* 8 (12), 743–754. <https://doi.org/10.1038/nrendo.2012.189>.
- Pollak, T.A., Lennox, B.R., Müller, S., et al., 2020. Autoimmune psychosis: an international consensus on an approach to the diagnosis and management of psychosis of suspected autoimmune origin. *Lancet Psychiatr.* 7, 93–108. [https://doi.org/10.1016/S2215-0366\(19\)30290-1](https://doi.org/10.1016/S2215-0366(19)30290-1).
- Sani, G., Janiri, D., Di Nicola, M., Janiri, L., Ferretti, S., Chieffo, D., 2020. Mental health during and after the COVID-19 emergency in Italy. *Psychiatr. Clin. Neurosci.* <https://doi.org/10.1111/pcn.13004>. Online ahead of print.
- Song, H., Fang, F., Tomasson, G., et al., 2018. Association of stress-related disorders with subsequent autoimmune disease. *J. Am. Med. Assoc.* 319 (23), 2388–2400. <https://doi.org/10.1001/jama.2018.7028>.

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