

# COVID-19 Induced New-onset Psychosis: A Case Report from Oman

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## ABSTRACT

Neurobehavioral impairment associated with COVID-19 infection has been recently documented in the literature. COVID-19 infection has also been associated with an increased risk for developing psychiatric symptoms, including rare reports on psychosis. We report a case of a 46-year-old male with no significant medical, family, and psychiatric history admitted to the hospital with COVID-19-related psychosis. Possible contributory factors for his condition are discussed, including the relationship between infections and the brain circuitry, inadvertent iatrogenic effects of pharmaceuticals used to manage COVID-19, as well as diathesis-stress associated with the tribulation of the prevailing pandemic.

Coronavirus disease-19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) triggered “a once-in-a-century pandemic” in 2020.<sup>1</sup> The pandemic was managed worldwide by enforced social isolation and lockdowns leading to serious socioeconomic disruptions. A less visible fallout has been the rising mental health consequences, the etiology of which is still unclear. Viral infections have been hypothesized to precipitate and exacerbate various neurobehavioral symptoms, including dizziness, headache, anosmia, and hypogeusia as well as heightening the risk for certain somatic and psychiatric conditions.<sup>2,3</sup> Psychosis has also been implicated to be triggered by COVID-19, though the literature is still patchy. To add to the emergent literature, we report the first case from the Arabian Gulf region where psychotic-like symptoms were precipitated within a short period of recovery from COVID-19 infection.

## CASE REPORT

A 46-year-old male, previously physically and mentally healthy, was brought to the emergency department (ED) presenting with distressing shortness of breath, cough, fatigue, anorexia, and

myalgias for three days during September 2020. The patient tested positive for COVID-19. Following World Health Organization guidelines,<sup>4</sup> his symptoms were deemed to be bordering “moderate to severe” and he was admitted. Mechanical ventilation and routine treatment for COVID-19 related pneumonia were instituted. The administered drugs included intravenous antibiotics ceftriaxone and azithromycin, hydroxychloroquine (600 mg twice daily), and dexamethasone (8 mg once per day) for five days. The patient made a rapid recovery and was discharged from the COVID-19 ward.

Two weeks later, he was brought to the ED with marked mental and psychomotor disturbances. He had reportedly jumped down from the window of the first floor, without sustaining physical injuries or loss of consciousness. The attending clinical team at the ED reported that the patient presented with altered or disturbed consciousness but with normal vital signs—respiration, blood pressure, pulse, skin, and pupils. The accompanying family member reported that he had jumped off the window as “commanded by God” who had ‘assured’ him that he would not suffer injuries from the jump. He did not have a family history of psychiatric disorders. The family denied that he was consuming any psychoactive substances such as tobacco, alcohol, or illicit drugs.

He also had no history of high-risk hobbies, suicide attempts, loss of consciousness, or traumatic life experiences. He had a university degree, was married with children, and held a steady career.

In the ED, because of his agitation and suspiciousness, haloperidol (10 mg) and promethazine (25 mg) were administered. Further exploration of his post-COVID-19 conduct revealed that he had lately developed a sense of exaggerated self-importance. He made statements to the effect that God had verbally praised him as being 'special' and endowed him with 'extraordinary skills'. In addition to his hallucinatory/delusional symptomatology, the patient also expressed emotional instability and psychomotor irritability. He did not seem to have any insight into his condition. However, he remained oriented to time and space.

Investigations included a full blood count, complete metabolic panel, and thyroid function, all of which were within the normal range. The urine drug screen was negative and his brain computed tomography (CT) and chest X-ray showed no structural abnormality. No arrhythmias and ischemic heart disease were noted. Neurological and fundoscopic examinations also yielded normal results.

Therefore, a tentative diagnosis of COVID-19-related psychosis was made. The patient was admitted and was started on olanzapine (5 mg) by mouth at bedtime. After discharge, he was advised for follow-up after two weeks. During the first follow-up, the accompanying family member endorsed that the patient had reverted to his premorbid self. The interview did not reveal the presence of abnormal perceptual experiences or abnormal thoughts including any suicidal or homicidal ideation or action. The quantity and quality of sleep were adequate. He returned to his former occupation despite the constraint of social distancing and lockdown. Overall, the patient's functionality as reflected by his reported daily activities was at par with his premorbid level. Approximately four months after the onset of clouded consciousness and altered state, he continued to function well. He admitted to voluntarily stopping the prescribed medication because it "made me feel heavy and lazy".

Based on the patient's collateral history and rapid remission of presenting symptoms, the clinical team deliberated on the tentative diagnosis of acute psychosis or transient psychotic disorders (ICD-10: F23).<sup>5</sup>

## DISCUSSION

To the best of our knowledge, this is the first reported case of acute COVID-19-related psychosis among the Gulf population. Premorbid, the patient was reported to be physically and mentally healthy, with no significant personal or familial psychiatric history. After eliminating other causative factors, what remained was a temporal relationship between contracting COVID-19 and the development of a psychosis-like state. The range of symptoms exhibited by the patient such as thought echo, auditory hallucinations, delusions of grandeur, and supernatural control are among the core features of acute psychosis as derived by Keks and Blashki.<sup>6</sup> The acute nature of this case is testified by the rapid dissolution of psychotic symptoms in response to antipsychotic medications.

The etiology of psychosis is still an enigma, despite being in the focus of psychiatric practice and research for centuries.<sup>7</sup> While the link between COVID-19 and the development of psychotic symptoms remains uncertain, recent case reports do suggest a link. Most emerging data suggest such psychosis to be limited to acute-type<sup>3,8-10</sup> unless there are preexisting risk factors. There are several mechanisms by which COVID-19 could trigger psychiatric symptoms.<sup>11</sup> Some infective agents already linked to psychosis include HIV, *Toxoplasma gondii*, *Treponema pallidum*, *Chlamydia trachomatis*, and *Brucella*.<sup>12,13</sup> SARS-CoV-2 is neurotropic and can be directly toxic to the brain.<sup>11</sup> In the present case, psychosis might have developed if the virus had infiltrated the central nervous system. The second proposed mechanism for COVID-19 induced psychosis is indirect, due to an abnormal immune response to this new and unfamiliar pathogen, triggering deregulation of cytokines network.<sup>14</sup> The immune system goes haywire resulting in a cascade of self-harming processes including the undue release of excitatory amino acids. Such events have the potential to impair brain circuitries, perhaps leading to psychosis.<sup>15</sup> The iatrogenic effects of the antibiotics ceftriaxone and azithromycin administered to this patient may also have had a role, as the occurrence of psychosis associated with antibiotics is known to vary between 0.3–3.8%.<sup>16</sup> A similar view has emerged regarding the two key COVID-19 medications, hydroxychloroquine<sup>17</sup> and dexamethasone,<sup>18</sup> which were administered to the patient in tandem or rapid succession.

The potential of drug interactions causing psychosis in COVID-19 patients is still speculative as available information is derived from case reports in the absence of controlled studies. Glucocorticoids such as dexamethasone are known to provoke psychiatric symptoms such as depression, irritability, euphoria, increased motivation, psychosis, mania, hallucinations, emotional instability, anxiety, sleep disorders, and suicidal thoughts.<sup>19</sup> Compounds with affinity to glucocorticosteroids such as dexamethasone, have been widely discussed to play critical roles in myriad pathological and adaptive processes. Dexamethasone has the potential to modulate the immune system and is often employed to mitigate inflammatory, autoimmune and lymphoproliferative diseases. According to the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial,<sup>20</sup> mortality among patients from COVID-19 was significantly lower among those treated with dexamethasone compared to those given standard care. For these reasons, dexamethasone is often used to prevent or mitigate factors leading to the commonly observed complications among COVID-19 patients, namely, lung pathology and multisystem organ failure. The present patient received dexamethasone (8 mg once daily) for five days. In the literature, dexamethasone has been recommended once daily for 7–10 days. It is not clear whether the duration of dexamethasone or abrupt withdrawal could have triggered the transient psychotic episode in the present case. Vigilance is needed against the widespread use of dexamethasone by COVID-19 patients.<sup>20</sup>

In addition to biological mechanisms, it is possible that the externally imposed social distancing and lockdown affects the habitual interpersonal interactions, which could lead to stresses that may cause some people to succumb to poor mental health. It is, therefore, a possible combination of high levels of COVID-19-related stress and social isolation that could trigger the breakdown of one's mental faculties and, in turn, manifest as erratic behavior and altered state of consciousness. There is evidence in preclinical literature to suggest that social isolation could trigger schizophrenia-related behaviors.<sup>19</sup>

As the COVID-19 infection continues to grip the world, cases have emerged in the literature to suggest the temporal relationship between the onset of infection and the occurrence of psychotic-

like symptoms.<sup>3,8-10</sup> If there is an emerging case for COVID-19 infection triggering psychosis, more research is needed on whether it is warranted to label such cases as "COVID-19-related psychosis". In most cases, the patients were oriented to time and place, which diminishes the possibility of delirium-induced psychosis. At the same token, the work-up investigation did not reveal any veneer of encephalomalacia or brain insult. This, therefore, excludes any underlying medical or neurological condition that might explain patient manifestation. Differential diagnoses that have to be considered in current or former COVID-19 patients presenting with psychotic symptoms include delirium, medication-induced psychosis, stress-related, and neuropathology. On this basis, new-onset psychosis in suspected or confirmed COVID-19 cases should undergo further medical work-up including all laboratory investigations, brain scan, and lumbar puncture.

## CONCLUSION

The present case supports the emerging evidence that COVID-related psychosis has heuristic value. We have reported a 46-year-old male patient with new-onset psychosis which manifested after he recovered from COVID-19 infection. It is not clear whether the acute psychotic symptoms were triggered by neuro-inflammation intimately tied with COVID-19 infection, the iatrogenic effect of medication, or tribulation triggered by the pandemic. The clinicians should be vigilant to the onset of psychosis among COVID-19 infected people who otherwise have no prior history of mental health issues.

### Disclosure

The authors declare no conflicts of interest

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Written informed consent for publication of this case report was obtained from the patient.

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