

New-Onset Psychosis Associated with COVID-19: A Case Report

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has caused a huge burden across the world. COVID-19 affects not only physical health but also neuropsychiatric health. Reported neuropsychiatric presentations due to COVID-19 include encephalopathy, mood changes, and neuromuscular dysfunction, which may occur during the infection. There have been also reports showing that the COVID-19 could provoke psychosis during the infection. However, there is still no available evidence regarding this event. In this report, three uncommon cases of new-onset psychosis with mild symptoms of COVID-19 admitted to Bali Provincial Mental Hospital in Bangli, Indonesia are described. The patients had presented persecutory delusions and auditory hallucinations. None of the patients had suicidal ideation or behavior. Three of the cases met the criteria for brief psychosis according to Indonesia's guidelines for mental health disorders and classification. This report showed brief psychosis without suicidal ideation. However, clinicians have to be more alert in treating this condition due to its potential emergency risk shown in previous reports.

Keywords: COVID-19, Pandemic, Brief reactive, Psychosis

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Introduction

In late 2019, Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) has emerged as unknown pneumonia in Wuhan, China (1). The pneumonia was later known as Coronavirus disease 2019 (COVID-19). Since then, it has spread rapidly across the world. COVID-19 eventually was declared a pandemic in March 2020 (1). Indonesia is also one of the most affected countries during the pandemic (2).

The dramatic circumstances of COVID-19 affected not only physical health but also neuropsychiatry aspects (3). Many COVID-19-related aspects, such as uncertain prognosis of the infection or financial losses due to pandemic policies, will contribute to developing emotional distress and increased risk for psychiatric disorders (4). Negative emotions such as fear and anxiety about contracting the virus, spreading it to loved ones, and dying because of the disease progression also arise in this kind of situation (5).

Reported neuropsychiatric presentations associated with COVID-19 include encephalopathy, mood changes, and neuromuscular disorders, which may occur during the infection or subsequently (6). However, there is much yet to be investigated about psychosis associated with COVID-19. In this report, three cases of new-onset psychosis with COVID-19 admitted to Bali Provincial Mental Hospital in Bangli, Indonesia are described.

Case Report

Case 1

The first case was a 35-year-old male travel driver. He was brought by his family due to his unusual behavior in the last seven days. For the last three days, he was not able to sleep, looked confused, and talked irrelevantly. Sometimes, he mumbled and looked scared. He has caused public nuisance within his neighborhood by climbing the roof. He looked restless when arrived at the emergency room. There was no history of smoking, consumption of any illicit substances, or alcohol abuse. Also, no history of mental disorders was found in his family. He was unwilling to talk on the first two days of admission and only answered “no” to any questions. On the third day, he said that he was scared of a big man who wanted to hurt him and was only seen by him. He had never seen the man since the last night and felt much better.

That was his first time experiencing this condition.

He lost his job during the pandemic and argued with his wife almost every day. Therefore, he spent most of his time hanging out with his friends without physical distancing and wearing masks. He experienced cough and fever for the last three days before being admitted to the hospital. His vital signs were within the normal limit. His chest radiograph showed no abnormality. The routine blood test showed a white blood cell count (WBC) of $21.86 \times 10^3/\mu\text{L}$ (lymphocyte 3.3%, monocyte 7.9%, and neutrophil 88.7%). Blood biochemical examination showed aspartate aminotransferase (AST) of 218 U/L, alanine aminotransferase (ALT) of 84 U/L, blood urea nitrogen level of 77 mg/dL, and creatinine of 1.74 mg/dL. His reverse transcription-polymerase chain reaction (RT-PCR) test for COVID-19 was positive.

He was diagnosed with brief psychotic disorder, COVID-19 infection, acute or chronic kidney disease, and transaminitis. He was treated with haloperidol (5 mg twice daily) for psychiatric symptoms and oseltamivir, chloroquine phosphate, azithromycin, vitamin C, ambroxol, folic acid, and also, hepatin supplement (curcuminoid and echinacea extract manufactured by Lapi Pharmacy) for his physical symptoms. His psychiatric symptoms improved in three days and disappeared in five days of medication. His fever improved within two days and his cough improved within four days of admission. Physical symptoms disappeared in one week of medication. He also had psychotherapy for his psychiatric condition. His family was given psychoeducation about the patient's psychiatric condition, as well as preventive education on wearing masks, and transmission modes of COVID-19. He was discharged from the hospital on the 15th day.

Case 2

The second case was a 35-year-old married man with a son, who was accompanied by his family and presented to the hospital because he was angry without any reason for three days. He often mumbled to himself and told his brother that they were going to be killed by their uncle. Other symptoms were hearing voices saying that he and his family were in danger. He believed that his uncle attempted to get his late father's property and planned to hurt them. He was more convinced of his belief, saying that his uncle had sent curse spells on them, when he saw his son

woke up in the middle of the night and laughed at him. He looked suspicious and furious when he arrived at the emergency room. He also kept saying that he would be killed. He had a social pattern of drinking alcohol. There was no history of mental disorders in his family.

According to his family, the patient had a fever nine days ago for three days. There were no symptoms of cough, sore throat, or shortness of breath. His vital signs were within the normal range. His chest radiograph showed pneumonia. Routine blood test showed WBC of $21.86 \times 10^3/\mu\text{L}$ (lymphocyte 18.4 %, monocyte 16.7%, eosinophil 2.3 %, basophil 0.5 %, and neutrophil 62.1%). Blood biochemical examination showed total bilirubin of 1.15 mg/dL, direct bilirubin of 0.4 mg/dL, AST of 380 U/L, and ALT of 410 U/L. His RT-PCR test for COVID-19 was positive.

He was diagnosed with brief psychotic disorder, COVID-19, and transaminitis. He was treated with haloperidol (5 mg twice daily) for psychiatric symptoms and had oseltamivir, chloroquine phosphate, levofloxacin, vitamin C, curcuma, and also, Hepatin supplement for physical symptoms. His psychiatric symptoms disappeared in three days of medication. He also got psychotherapy for his psychiatric condition. His family was given psychoeducation about the patient's condition. He was discharged from the hospital on the 15th day.

Case 3

The third case was a 70-year-old widow, living with her son and daughter-in-law. She was accompanied by her family and presented to the hospital for causing public nuisance in her neighborhood by knocking on doors and asking for a cup of coffee. The patient said that her daughter-in-law prohibited her from making coffee and she was angry. For this reason, she went to other houses. She kept making coffee because there were voices in her ears telling her to do so. The patient was talking to herself for a week. She would make 10 cups of coffee each day and rarely drank the coffee. She also did not get any sleep for two days. There was no history of smoking, consumption of illicit drug substances, or alcohol. There was no history of mental disorders in her family.

She had coughed for the last three weeks with no history of fever. She had never gone through a medical check-up. The history of hypertension, diabetes or other diseases was unknown. Her blood pressure was 150/70 mmHg in two

measurements. Her Mini-Mental State Examination (MMSE) score was 27, showing no cognitive problem. Her chest radiograph showed cardiomegaly with aortic sclerosis. The routine blood test showed a WBC of $14.01 \times 10^3/\mu\text{L}$ and the rest were within the normal limit. However, this test showed a random blood glucose level of 239 mg/dL, sodium level of 135.8 mmol/L, potassium of 3.21 mmol/L, and chloride of 87.5 mmol/L. Her RT-PCR test for COVID-19 was positive.

She was diagnosed with brief psychotic disorder, COVID-19, type 2 diabetes mellitus, and hypertension. She was treated with haloperidol (5 mg every 12 hours) and lorazepam (2 mg at bedtime) for psychiatric symptoms. The patient also took metformin, linagliptin, amlodipine, chloroquine phosphate, oseltamivir, levofloxacin, and vitamin C for physical symptoms. Her psychiatric symptoms disappeared in three days of medication. She was discharged from the hospital on the 15th day.

Discussion

Psychosis associated with COVID-19 has been identified in some countries, but it is still unknown whether psychosis is related to coronavirus infection (7). Another finding revealed that mental disorders are among the complications of COVID-19 infection, which are the sequelae of brain damage. Mental disorders could also be caused by other diseases as direct effects of infection in the central nervous system or excessive immune response (8). Poverty, unemployment, and financial insecurity have had serious effects on mental health during the COVID-19 pandemic (9). Mental disorders during the COVID pandemic may include adjustment disorder, worsened obsessive-compulsive disorder, depression, anxiety, and even psychosis (10).

Our cases comprised fully alert patients despite their disorganized thought. All of our cases were presented with auditory and visual hallucination, and one of the cases was presented with a prominent persecutory delusion which met the criteria for brief psychosis according to ICD-10. All of the cases had minor symptoms of COVID-19. These are similar neuropsychiatric symptoms as reported by a previous case report (11). A recent study by Parra *et al.* has reported 10 subjects with psychotic symptoms during COVID-19 infection. The most frequent neuropsychiatric symptoms found in the study were delusions of prejudice, persecutory, and

idea of reference, which are similar to the symptoms of our cases (12).

The pathophysiology of psychosis associated with COVID-19 is still unclear. The increase of IgG antibodies in COVID-19 is hypothesized to be associated with psychotic disorders (13). In addition to the direct viral infiltration, other proposed mechanisms for neuropsychiatry manifestations are hyperinflammatory response against the virus, cytokine dysregulation, and molecular mimicry. The neuro-inflammatory reaction will contribute to microglial cell activation resulting in demyelinating processes as the primary etiology for encephalopathy (14). Previous studies also reported elevated C-reactive protein as a marker for a systemic hyperinflammatory response during severe COVID-19 (11,12). The following peripheral hypercytokinemia could cause the imbalance of neurotransmitters in the central nervous system and result in neuropsychiatry disorders (14). However, in this case report, the individuals were presented with mild COVID-19 symptoms.

It is believed that psychosis in our cases was not caused by iatrogenic factors, since the psychosis had appeared before their hospital admission. In addition, chloroquine psychosis is commonly featured as depersonalization or derealization (15). Another drug in our case, azithromycin, is rarely reported to cause serious adverse neuropsychiatric effects in adults (16). A previous case report has suggested that delirium is associated with levofloxacin. Nonetheless, its occurrence is extremely rare (17). Lastly, oseltamivir was not reported to increase the risk of serious neuropsychiatric events (18). Psychiatric medications including antidepressants, mood stabilizers, antipsychotics, and anxiolytics should be selected with the least possibility of interaction with COVID-19 treatment, and safely used (19).

References

1. He F, Deng Y, Li W. Coronavirus disease 2019: What we know? *J Med Virol.* 2020; 92(7):719-25. doi: 10.1002/jmv.25766.
2. Olivia S, Gibson J, Nasrudin R. Indonesia in the time of Covid-19. *Bulletin of Indonesian Economic Studies.* 2020; 56(2):143-74. doi: 10.1080/00074918.2020.1798581.
3. Byrne A, Barber R, Lim CH. Impact of the COVID-19 pandemic a mental health service perspective. *Prog Neurol Psychiatry.* 2021; 25(2):27-33. doi: 10.1002/pnp.708.
4. Pfefferbaum B, North CS. Mental Health and the Covid-19 Pandemic. *N Engl J Med.* 2020; 383(6):510-12. doi: 10.1056/NEJMp2008017.
5. Hsu ST, Chou LS, Chou FH, Hsieh KY, Chen CL, Lu WC, et al. Challenge and strategies of infection control in psychiatric hospitals during biological disasters-From SARS to COVID-19

In this case report, suicidal ideation or attempt was not present. However, a previous report had presented such symptoms (20). In view of its unknown precise mechanisms, it was assumed that the symptoms may vary due to other factors, including social, genetic, psychological, and cultural factors. This can also be present in future cases since recent government policy measures and changes during the pandemic period could provoke life distress (4). Therefore, physicians should be cautious with psychiatric emergency signs.

All of the aforementioned cases showed brief psychotic events in patients with COVID-19. These patients and their families had no previous history of mental disorders. All of the patients were alert and received similar therapies in the psychiatry and internal medicine departments. The psychiatric symptoms improved within three to five days while the physical symptoms lasted irregularly. According to the COVID-19 protocol of the mental hospital of Bali, asymptomatic and mild COVID-19 cases are discharged after 14 days of treatment.

Conclusion

COVID-19 infection could appear as acute psychiatric symptoms. New-onset psychosis is one of the uncommon presentations in COVID-19 infection. However, clinicians have to be more alert in treating psychosis associated with COVID-19 due to its potential emergency risk. Further studies with bigger samples are required to determine the relationship between these conditions.

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- in Taiwan. *Asian J Psychiatr.* 2020; 54:102270. doi: 10.1016/j.ajp.2020.102270.
6. Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. *Brain Behav Immun.* 2020; 87:34-39. doi: 10.1016/j.bbi.2020.04.027.
 7. Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. *The Lancet Psychiatry.* 2021; 8(2):130-40. doi: 10.1016/S2215-0366(20)30462-4.
 8. Kumar S, Veldhuis A, Malhotra T. Neuropsychiatric and Cognitive Sequelae of COVID-19. *Front Psychol.* 2021; 12:577529. doi: 10.3389/fpsyg.2021.577529.
 9. Posel D, Oyenubi A, Kollamparambil U. Job loss and mental health during the COVID-19 lockdown: Evidence from South Africa. *PLoS ONE.* 2021; 16(3): e0249352. doi: 10.1371/journal.pone.0249352.
 10. Pan KY, Kok AAL, Eikelenboom M, Horsfall M, Jorg F, Luteijn RA, et al. The mental health impact of the COVID-19 pandemic on people with and without depressive, anxiety, or obsessive-compulsive disorders: a longitudinal study of three Dutch case-control cohorts. *Lancet Psychiatry.* 2020; 8(2):121-29. doi: 10.1016/S2215-0366(20)30491-0.
 11. Ferrando SJ, Klepacz L, Lynch S, Tavakkoli M, Dornbush R, Baharani R, et al. COVID-19 Psychosis: A potential new neuropsychiatric condition triggered by novel coronavirus infection and the inflammatory response? *Psychosomatics.* 2020; 61(5):551-55. doi: 10.1016/j.psych.2020.05.012.
 12. Parra A, Juanes A, Losada CP, Álvarez-Sesmero S, Santana VD, Martí I, et al. Psychotic symptoms in COVID-19 patients: A retrospective descriptive study. *Psychiatry Res.* 2020; 291:113254. doi: 10.1016/j.psychres.2020.113254.
 13. Severance EG, Dickerson FB, Viscidi RP, Bossis I, Stallings CR, Origoni AE, et al. Coronavirus immunoreactivity in individuals with a recent onset of psychotic symptoms. *Schizophr Bull.* 2011; 37(1):101-7. doi: 10.1093/schbul/sbp052.
 14. Jasti M, Nalleballe K, Dandu V, Onteddu S. A review of pathophysiology and neuropsychiatric manifestations of COVID-19. *J Neurol.* 2021; 268(6):2007-12. doi: 10.1007/s00415-020-09950-w.
 15. Hamm BS, Rosenthal LJ. Psychiatric Aspects of Chloroquine and Hydroxychloroquine Treatment in the Wake of Coronavirus Disease-2019: Psychopharmacological Interactions and Neuropsychiatric Sequelae. *Psychosomatics.* 2020; 61(6):597-606. doi: 10.1016/j.psych.2020.06.022.
 16. Zareifopoulos N, Panayiotakopoulos G. Neuropsychiatric Effects of Antimicrobial Agents. *Clin Drug Investig.* 2017; 37(5):423-37. doi: 10.1007/s40261-017-0498-z.
 17. Kogan Y, Elias N, Paz A, Odeh M. Acute Delirium Associated With Levofloxacin. *J Clin Med Res.* 2018; 10(9):725-27. doi: 10.14740/jocmr3538w.
 18. Huh K, Kang M, Shin DH, Hong J, Jung J. Oseltamivir and the Risk of Neuropsychiatric Events: A National, Population-based Study. *Clin Infect Dis.* 2020; 71(9):409-14. doi: 10.1093/cid/ciaa055.
 19. Mohebbi N, Talebi A, Moghadamnia M, Nazari Taloki Z, Shakiba A. Drug Interactions of Psychiatric and COVID-19 Medications. *Basic Clin Neurosci.* 2020; 11(2):185-200. doi: 10.32598/bcn.11.covid19.2500.1.
 20. Gillett G, Jordan I. Severe psychiatric disturbance and attempted suicide in a patient with COVID-19 and no psychiatric history. *BMJ Case Rep.* 2020; 13(10):e239191. doi: 10.1136/bcr-2020-239191.