COVID-19 Psychosis: A Potential New Neuropsychiatric Condition Triggered by Novel Coronavirus Infection and the Inflammatory Response?

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BACKGROUND

- COVID-19 (SARS-CoV-2) has caused worldwide anxiety and grief, however, the degree and characteristics of psychopathology and potential virus-specific neuropsychiatric manifestations have yet to be fully described.
- Coronaviruses are neurotropic and can enter the brain through the olfactory neural pathway, peripheral and central nervous system manifestations.1
- SARS-CoV-1 was linked with psychiatric complications in affected patients, and corticosteroid use has been identified as a factor in psychiatric presentations.2,3
- Preliminary COVID-19 studies from China found high levels of anxiety, stress, depression, alcohol use, and decreased mental well-being, as well as severe general psychological distress.3,4
- None of these studies examined COVID-19 positivity in the study population.
- Further research:
  - One study found neurological manifestations in 36% of hospitalized patients with severe COVID-19 infection, including stroke and alterations in consciousness.5
  - Another described encephalopathy and persistent alterations in consciousness among patients who subsequently died of COVID-19 disease.6
  - The patients from the above studies had severe respiratory and systemic complications, and were given multiple medications, including corticosteroids, which could explain the neuropsychiatric symptoms.
- There is prior evidence to suggest that infection with coronaviruses is associated with psychotic symptoms; however, new-onset psychosis in asymptomatic patients infected with COVID-19 has not been described.7,8
- Since the first regional case of COVID-19 on March 1, 2020, just 11 miles from our medical center, we have encountered multiple COVID-19 positive patients in our Emergency Department who were asymptomatic for COVID-19 physical symptoms but who presented with new-onset psychotic symptoms.

CASE 1:

- Mr. C, a 33-year-old white male, with opioid use disorder but no prior history of psychosis, presented to the ED for evaluation of auditory hallucinations, paranoid and persecutory delusions of his ex-wife and “people with knives and guns in a blue van outside” trying to kill him, and severe agitation for 4 days.
- He reported no respiratory or GI symptoms, anosmia, or ageusia, and his vital signs, CBC, CMP, CXR, and brain CT scan were unremarkable.
- CRP was elevated (1.9 mg/dl), but ferritin and d-dimer were normal.
- He was tested in the ED and found to be COVID-19 positive.
- He was provided medical support and started on quetiapine 50 mg twice daily with significant symptom improvement noted.

CASE 2:

- Mr. A, a 30-year-old male without any formal psychiatric history, was brought to ED by his wife with bizarre behavior for several days.
- Symptoms: extreme anxiety, suicidal ideation, agitation, auditory hallucinations, decreased sleep, and drinking excessive amounts of water and Pedialyte.
- On examination, he was guarded, internally preoccupied, and paranoid.
- When left alone momentarily, he fled and hid in a cabinet in the ED.
- He had no respiratory or GI symptoms; no anosmia or ageusia; and vital signs, CBC, CMP, CXR, brain CT were normal.
- Acute phase reactants were mildly elevated:
  - CRP was 0.67 (0.0-0.5 mg/l)
  - Serum ferritin was 421 (180-370 mcg/l).
- Mr. A tested positive for COVID-19 in our Emergency Department.
- He was transferred to the medical service for supportive care and was treated psychiatically with quetiapine 25 mg daily for 4 days.
- His psychotic agitation improved, and he was discharged home with psychiatric follow-up.

CASE 3:

- Mr. B, a 34-year-old single female, with a history of panic disorder, presented to the ED for evaluation after experiencing heightened levels of anxiety.
- She had no respiratory or GI symptoms, anosmia, or ageusia, and her CMP, CXR, and brain CT and all vital signs were normal.
- CRP was elevated, 1.89 mg/dl, while ferritin was normal.
- She was tested and found to be COVID-19 positive.
- After being medically stabilized, she was transferred to our COVID-Positive Psychiatric unit and initiated on aripiprazole 5mg daily + clonazepam 0.5mg BID + melatonin 3mg QHS.
- She was continued on her outpatient medication, Fluoxetine 10mg daily.
- Significant improvement in her symptoms were noted.

REFERENCES


DISCUSSION

- These cases all presented with severe anxiety, agitation, paranoia, disorganized thinking, and without the typical COVID-related symptoms.
- These cases resemble 3 from Boston,10 however, our patients were not expressing COVID-related concerns, and were also diagnosed with COVID-19.
- The symptoms described here may be related to stress due to the pandemic in psychologically vulnerable individuals.
- Lack of COVID-preoccupation in these patients, presence of infection, and elevated inflammatory markers, make this less likely.
- The inflammatory response to COVID-19 infection (“cytokine storm”) has been postulated to produce neuropsychiatric symptoms through immunological mechanisms.12,13
- Immune-based triggers are linked to the pathogenesis of multiple psychiatric illnesses.14,15
- CRP, which was elevated in all 3 of our patients, has been studied as a marker of immune activation, which is thought to have a causal or triggering role in schizophrenia.16
- It is hypothesized that coronaviruses may act as opportunistic pathogens of the CNS as they have been shown to have neuroinvasive qualities.17
- CNS penetration and neuroinflammation from other coronaviruses have been associated with new-onset psychotic disorders.4,11
- It is thought that COVID-19 may produce neuropsychiatric symptoms through viral infiltration of CNS → transmigration into CNS through blood leukocytes → cytokine activation → CNS inflammation and BBB compromise.17
- The discussed cases series describe a potentially novel condition, however, are limited by the small sample and lack of uniform medical and neuropsychiatric workup.
- Future studies should have:
  - More sensitive functional brain imaging studies
  - More detailed neurocognitive testing
  - More thorough and broader array of cytokines and inflammatory markers
  - Measurement of viral RNA in CSF

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