Psychosis After SARS-CoV-2 in a Patient With Stable Schizophrenia and Allograft Kidney Transplant

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The coronavirus disease 2019 (COVID-19) pandemic has uprooted the lives of many individuals in its wake. Two reported groups of patients with increased vulnerability to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are those with schizophrenia[1] and solid organ transplant (SOT).[2] We present the case of a patient with stabilized schizophrenia who was status post–renal transplant who subsequently acquired COVID-19. We highlight how all the conditions interacted on the course of each other.

Case Report

Ms A was a 64-year-old black woman who presented to the emergency department (ED) stating multiple paranoid delusions. Notably, she had a history of schizophrenia, insulin-dependent diabetes mellitus, and chronic kidney disease with deceased donor kidney transplant 4 years prior to presentation. By history, Ms A was fastidiously adherent to her home medication regimen, including haloperidol, mycophenolate, tacrolimus, prednisone, and insulin. She had no reported relapse of psychotic symptoms for the past 10 years, which covered pre- and post-SOT and SOT rejection. Laboratory evaluation in the ED included unremarkable complete blood count and metabolic profile except for blood urea nitrogen/creatinine = 53/3.6 mg/dL, hemoglobin A_{1C} = 8.2%, and undetectable mycophenolic acid and tacrolimus levels. Both blood alcohol level and urine drug screen were negative.

Upon admission to the general medical floor, Ms A refused all medications except for insulin. After 2 weeks, court-committed medication treatment, including antipsychotics, was granted. At this time, the psychiatric consultation service was contacted.

Figure 1[3–9] details Ms A's hospital course and posited pathophysiology of her psychosis. Notably, 9 months prior to this incident hospitalization, she developed delusions following acute COVID-19 pneumonia. The latter, which was treated on the general medical floor, required oxygen supplementation and intravenous antibiotics but no admission to the intensive care unit or mechanical ventilation. Subsequently, she became nonadherent to transplant pharmacotherapy and antipsychotics, resulting in recurrent hospitalizations for renal transplant rejection.

On our evaluation, Ms A lacked insight into her history of SOT or psychopathology, despite reporting delusions. She denied auditory or visual hallucinations, depressed or elated mood, and alcohol or substance misuse. She scored 43 and 29 on the Brief Psychiatric Rating Scale (BPRS)[10] and Mini-Mental State Examination,[11] respectively. Magnetic resonance imaging (MRI) of the brain demonstrated no acute brain abnormalities but increased amount of T2/fluid-attenuated inversion recovery (FLAIR) hyperintense signal abnormalities in the bilateral periventricular to deep hemispheric white matter and increased amount of patchy T2/flair hyperintensities in the central pons (Figure 2). There was no evidence of opportunistic infections by serum or cerebrospinal fluid examination.

On day 1 of treatment, Ms A began intravenous haloperidol titrated to 5 mg 2 times/d over 5 days. After 3 weeks of taking haloperidol, her delusions mildly attenuated, with a BPRS score of 39. At this time, intravenous haloperidol was transitioned to oral haloperidol 5 mg 2 times/d. After an additional 2 weeks of oral haloperidol, her BPRS score was 35. She was discharged on her home regimen, including haloperidol.

On monthly follow-up for 2 consecutive months, Ms A's insight and judgment returned to her pre–SARS-CoV-2 infection level, and her final BPRS score was 18.

While initially posited as a respiratory illness, COVID-19 has demonstrated its ability to affect multiple organ systems, including the central nervous system. Potential mechanisms contributing to the pathophysiology of post/acute COVID-19 psychosis include (1) virus-specific pathophysiologic changes, including augmentation of angiotensin II signaling and prothrombotic pathways—the latter could result in microvascular ischemia and injury[12] (see Figure 1); (2) immunologic aberrations and inflammatory damage in response to the acute infection[13] (see Figure 1); and (3) psychosocial impacts of SARS-CoV-2 infection and increased risk of relapse of schizophrenia. Regardless of the exact etiology, Ms A's delusions contributed to nonadherence of immunosuppressants and antipsychotics, leading to

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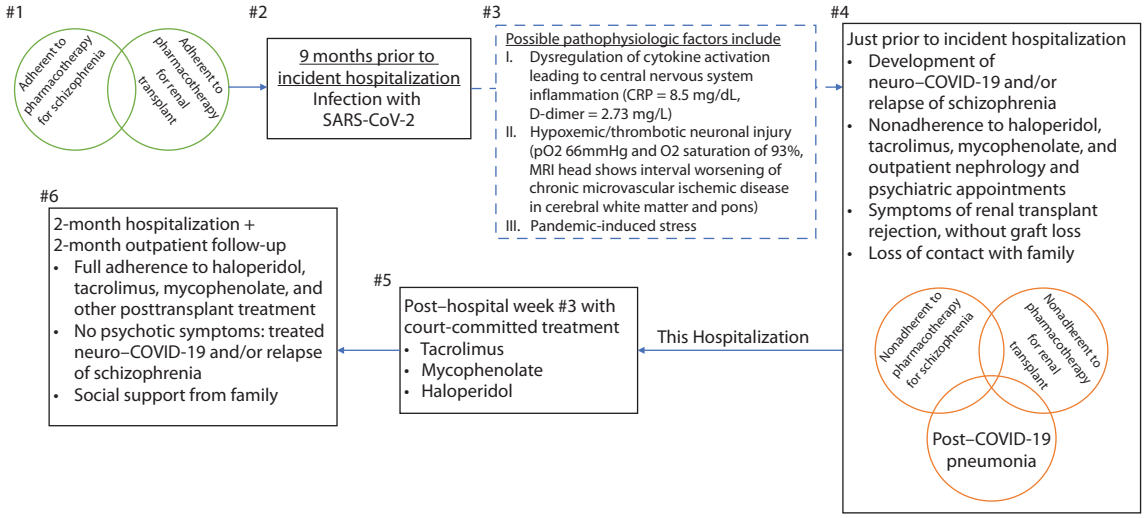
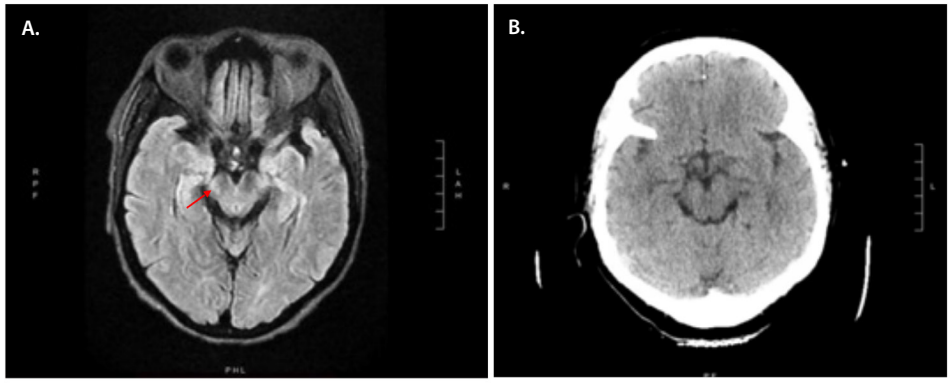
Figure 1. Longitudinal Course of the Patient's Medical and Psychiatric History[a,b]



[a]Values in parentheses represent findings in our patient.
[b]Description of the steps in the figure:
(1) Our patient was adherent to both antipsychotic and transplant pharmacotherapy at baseline, prior to infection with SARS-CoV-2.
(2) Our patient's described hospitalization occurred 9 months after active COVID-19 pneumonia.
(3) Possible pathophysiologic factors inducing psychosis, peri-infection with SARS-CoV-2 include (a) dysregulation of cytokine activation leading to central nervous system inflammation,[3] (b) hypoxemic/thrombotic neuronal injury,[3] and (c) pandemic-induced stress.[4] This patient did have elevated CRP and D-dimer. The former, a potential peripheral marker of immune activation, is postulated to have a causal/triggering role in schizophreniform psychosis,[5] while the latter indicates activation of coagulation pathways and thrombosis.[6] Notably, our patient's head MRI did demonstrate advancing white matter disease as well as new hyperintensities in pons. Reportedly, typology of brain abnormalities on MRI in adults with COVID-19 in the acute/subacute phase involved white matter hyperintensities on MRI (observed in 76% of affected cases).[7] Finally, it is possible that this patient's symptoms could be unrelated to direct/indirect effects of SARS-CoV-2 and rather due to stress itself. For instance, it is known that stressful life events and increased anxiety level negatively affect the course and cause relapse in patients with schizophrenia.[8]
Abbreviations: COVID-19 = coronavirus disease 2019, CRP = C-reactive protein, MRI = magnetic resonance imaging, pO2 = partial pressure of oxygen, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Figure 2. (A) Magnetic Resonance Imaging of the Head Without Contrast During the Current Hospitalization and (B) Computed Tomography of the Head 3 Years Earlier[a]



[a]Magnetic resonance imaging with increased amount of patchy T2/fluid-attenuated inversion recovery hyperintensities in periventricular white mater and central pons.

renal transplant rejection and prolongation of psychosis, respectively.

Ms A, as others with COVID-19, presented with psychotic symptoms.[14–18] It is possible that her increasing amount of T2/FLAIR hyperintense signal abnormalities in bilateral periventricular to deep hemispheric white matter and pons could have precipitated her psychotic phenomenology. For instance, it has been shown that white matter integrity is disrupted in schizophrenia.[19] Additionally, in metachromatic leukodystrophy, a rare autosomal recessive disorder wherein normal myelin integrity is interrupted, the progressive demyelination of periventricular white matter has been proposed to cause overt psychotic symptoms.[20] Regardless, our case provides further evidence for the leading hypotheses of SARS-CoV-2–induced psychosis. Nonetheless, further studies are warranted to better understand both the pathophysiology and treatment of psychosis due to SARS-CoV-2 infection.

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