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Case Report

Post-COVID Psychosis: A Case Report

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Abstract

Long-COVID syndrome has been characterized by several different symptoms, most commonly including fatigue, cough, palpitations, and myalgia. Post-COVID Psychosis is a relatively uncommon form of Long-COVID syndrome that entails the development of residual psychotic symptoms following COVID-19 infection in a patient with no significant prior psychiatric history. Here, we describe the case of a 49-year-old female with no prior psychiatric history who presented with worsening mental status changes and acute development of delusions following a recent COVID-19 reinfection. She describes experiencing similar psychotic features after her initial COVID-19 infection in March 2020 and was treated by a psychiatrist with the antipsychotic quetiapine and lasted for approximately 11 months before resolving completely. Her reinfection in September 2021 triggered the reemergence of these psychotic features. While further testing is being completed to officially rule out other etiologies, the patient's presenting symptoms in the context of her medical history along with temporal relation to her COVID infections and lack of other outward causes seem to suggest that she was experiencing Post- COVID psychosis.

***Keywords:** post-covid, psychosis, neuropsychiatry, psychotic features, delirium, long covid,*

Introduction

COVID-19 first started late in the year 2019 in the city of Wuhan, China, but rapidly spread across the globe as people traveling through the region were infected and inadvertently began to spread the virus to their home or other visiting countries. Since January 2020, a total of 75,350,359 cases have been confirmed in the United States alone [15]. Over the course of the past two years, circumstances have changed with the introduction of the vaccines which were granted an emergency use approval from the FDA in December 2020 [16, 17]. A study based on data from eight countries with relatively higher vaccination rates was analyzed and found to show that all the vaccines currently being administered "…are highly effective in mitigating the infection of COVID-19…even if the vaccination rate is lower than the immunity threshold" [18].

However, even with the development of these vaccines, there came the development of new variant strains of the virus. The presentation of these variants, the effectiveness of existing vaccines against them, and general treatment protocols for COVID-19 continue to be studied today. An area of COVID-19 related research that is slowly gaining more traction is about the post-infection effects. Termed "long COVID", "COVID Long Hauler's Syndrome" and "Post Covid Syndrome" among several other names, patients have been found to sometimes experience a variety of sequelae following the infection and subsequent resolution of COVID-19 which has been shown to include cardiovascular, pulmonary, hepatobiliary, gastrointestinal, neurological and renal symptoms as well [5].

Neuropsychiatric symptoms with an onset occurring during or after a COVID-19 infection have been increasingly reported, and several case reports have been published describing a variety of patient cases involving the same and interestingly, many of these patients appear to not have any significant history of neuropsychiatric concerns. One report by Chen et al. (2020) indicated that encephalopathy and disorders of consciousness that lasted over 24 hours were found in approximately 20% of individuals who were deceased following their COVID-19 infection in Wuhan, China [19]. While long term neuropsychiatric effects of COVID-19 infection are still being studied with data still being gathered, similar effects have been reported previously with other respiratory syndrome survivors. Lam et al. (December 2009) published their results following an analysis of status post-severe acute respiratory syndrome (SARS) infection [20].

Of their 233 patients, over 40% reported being affected by active psychiatric illness and 40% reported experiencing a chronic fatigue problem with 27.1% meeting the 1994 CDC criteria for chronic fatigue syndrome. These patients were diagnosed with PTSD (54.5%), depression (39%), pain disorder (36.4%), panic disorder (32.5%), and obsessive-compulsive disorder (15.6%) between 31 to 50 months post-infection [20]. While the mechanism for these neuropsychiatric sequelae remains to be elucidated, Troyer et al. (July 2020) have suggested a number of potential mechanisms based on previous studies on post-infectious neuropsychiatric conditions; these potential mechanisms include CNS infiltration by COVID-19, upregulation of proinflammatory cytokines by neurons and glial cells and transmigration of infected peripheral myeloid cells secondary to increased blood brain barrier permeability in stressful conditions [21].

It is worth noting that further study and analysis of these symptoms will require an expanded body of evidence from which to draw these conclusions. The aim of this case report is therefore to help contribute to this body of evidence regarding neuropsychiatric sequelae of COVID-19, while presenting further unique features about the case that do not seem to have yet been reported regarding the duration of the symptoms and repeat symptoms following reinfection.

Here, we report on the case of a 49-year-old female who presented for an evaluation and management of her neuropsychiatric symptoms including delirium, paranoia and hallucinations which began acutely during the time of her second COVID-19 infection and closely mirror her post-COVID infection status following her initial infection. While the patient continues to be followed and worked up, her history and presenting status seem to closely align with what could be described as “post-COVID psychosis”.

Case Summary

In December 2021, a 49-year-old female patient with a medical history significant for hypothyroidism, and irritable bowel syndrome presented to the telemedicine neurology clinic with complaints of delusions that she was experiencing over the past three days. The patient explained that she contracted COVID-19 in September 2021 and since then had been experiencing dementia-like symptoms in the form of memory lapses and brain fog. Three days ago, the patient was especially concerned when she began to experience delusions concurrent with her persisting dementia-like symptoms that she described as being “bad thoughts”. These thoughts frightened the patient, who said that they would revolve around themes of self-harm and occasionally even suicide. She then began to explain that she was having some delusional thoughts during our conversation but denied any current suicidal ideation or thoughts of self- harm. Her husband was also present in the distance. The patient revealed that despite not having any psychiatric or neurological medical history prior, she had a very similar experience in 2020 as well.

The patient revealed that her recent COVID-19 infection in September 2021 was, in fact, a reinfection. She was first infected in March 2020, and reports that soon after her initial infection, she began to experience episodes of delirium and dementia-like symptoms. These delusions had similarly been “bad thoughts” but were not related to self-harm necessarily. She was also able to hear voices that she could not specifically identify, and she could not recall what they were saying. She explained that her altered mental status had continued significantly beyond the course of her COVID-19 infection. After her hospital discharge, she found that her delusions began to worsen. There came a point when these delusions had become so debilitating for the patient that they prompted her to voluntarily admit herself to a psychiatric in-patient ward. She was being seen and managed by the attending psychiatrist, who she continued to work with beyond her in-patient admission. The patient was reportedly also experiencing hallucinations intermittently in the form of shadows and figures that could make her feel paranoid. Eventually, to the patient’s relief, all these symptoms began to improve around December 2020, and effectively resolved approximately 11 months following their initial onset.

Between the time of symptom resolution earlier in 2021 and her current visit, the patient reports that she had returned to her pre COVID-19 cognitive baseline. Her brain fog had cleared, her focus improved, and her delusions were gone. Everything seemed back to normal, until September 2021 when she was reinfected with COVID-19. Once again, those neuropsychiatric symptoms began to present soon after her reinfection. A few days before this visit, the patient also reports having “heard the voice of God”. Her hallucinations were not as frequent as they had been during her initial experience but were still intermittently present. She described that her husband has told her multiple times that she is not “thinking or acting” like herself, even telling the patient that over the course of the night the patient would say “terrible things” to her husband. She says that while she cannot recall what exactly she said, she has made her husband aware that she cares for him and that those words are not truly her own. She emphasized to him that they do not reflect her true feelings or thoughts, and her husband recognizes these instances as being part of her ongoing condition. The patient also explained that she began a course of Elavil (amitriptyline) the night before this visit and found that it seems to have significantly exacerbated her symptoms. She reports feeling anxious continuously and is significantly more aggressive than she used to be.

The patient endorsed headaches, weakness, change in sensation and lightheadedness upon review of symptoms. She previously had a tendon repair as well as cholecystectomy. The patient reports no contributory medical or psychiatric family history. Along with the Elavil, the patient was taking Seroquel (quetiapine), levothyroxine, and trazadone.

While she admits to having tried illicit drugs in her teenage years, she no longer is using any illicit drugs, alcohol, or tobacco at this time. The neurological exam itself was unremarkable and a previous CT Head report that was done from her inpatient hospitalization was reviewed by us and found to be unremarkable as well. Based on her presentation and history, patient was thought to be experiencing a unique form of post COVID long hauler's syndrome, supported by the fact that symptoms mirrored her previous infection and both times, symptom onset coincided with COVID-19 infection. She was advised to take several anti-inflammatory vitamins supplements and given a prescription for low dose prednisone. To further investigate etiology and rule out other causes, an MRI Brain without contrast was ordered along with EEG testing. The patient will be returning to the clinic for follow up in a month's time.

Discussion

Post-Covid syndrome, also referred to as COVID-19 Long Hauler's Syndrome and Long- COVID, has been described in existing literature as presenting with a wide variety of symptoms although a formal definition for it has yet to be established. A review by Yong (May 2021) collected several reports on Post-Covid Syndrome and concluded that the most commonly reported symptoms are fatigue and dyspnea [1]. Other symptoms that have been reported include flushing, ear pain, chills, and visual impairments [2,3,4]. An article by Nalbandian et al. (March 2021) comprehensively discusses the various sequalae manifested in various organ systems, ranging from pulmonary to hepatobiliary, specifying post-COVID syndrome as including any "persistent... delayed or long-term complications beyond 4 weeks from the onset of symptoms" [5]. Among these different systems, Nalbandian et al. (March 2021) also describe the neuropsychiatric sequelae of post-Covid syndrome, explaining that patients have been reported to experience migraine-like headaches, late-onset headaches, persistent loss of taste and smell, as well as cognitive impairments including brain fog (difficulty with concentration, memory, language and/or executive function) [5].While it seems clear that the brain is no exception to the systemic effects of inflammation associated with COVID-19, these neuropsychiatric manifestations have yet to be fully explored and a growing body of evidence will be needed to better characterize and understand them.

Post-Covid psychosis can be loosely defined as the presentation of delirium, dementia-like features, altered mental status, mood changes and/or brain fog among other symptoms that developed at the time of, or immediately following, acute COVID-19 infection with no outward or obvious etiologies contributing to its development or persistence. Since the beginning of Covid-19, several cases of post-Covid psychosis have been described. Lim et al. (July 2020) describe the case of a 55-year-old female with no prior medical history and no personal or familial history of any neuropsychiatric conditions who began to exhibit visual hallucinations, disorientation, agitation, aggression, paranoia, and labile affect two days after her COVID-19 infection. She was admitted and treated for these psychiatric symptoms before being discharged at Day 20, with a prescription of 0.5 mg risperidone. The patient reported stopping the medication by Day 29, and eventually, reported complete resolution without psychotic symptoms by Day 52 [6].

Desai et al. (September 2021) report on a 55-year-old female with a past medical history of hypertension, type 2 diabetes and obesity and no prior mental health issues who presented to the ED with her family members for concerns about her behavior [7]. She had just been discharged a week prior following a COVID-19 infection in which she received oxygen therapy, steroids and remdesivir. She had been discharged without psychotic features, which she also never experienced in the hospital. Desai et al. describe that the patient was having non-command type auditory hallucinations as well as religious delusions, in which the voice of God would ask her to save the Earth. She was reportedly also very anxious and agitated, and would scream at staff members or remove IV lines. MRI and CT scan were unremarkable, urine drug screening was negative and infectious disease work up was negative. On the second day, the patient was also experiencing visual hallucinations of God, and she was admitted to the inpatient psychiatric ward. An improvement was noted after being started on haloperidol 10 mg and sodium valproate 1000 mg for treatment. She was later discharged on aripiprazole 10 mg and sodium valproate 1000 mg daily following her two-week inpatient stay.

Another case was reported by Ariza-Varon et al. (February 2022) in which a 48-year old woman with no past medical, psychiatric or substance use history went to the hospital for a 5-day history of cough, fever, malaise and fatigue that was confirmed to be COVID-19 [8]. Four days following this diagnosis, the patient began to display paranoia and self-referential delusional ideas with fluctuating behavior and sleep-wakefulness inversion. The patient was reported to be disoriented to space and time, had inappropriate anxious mood, unstructured paranoia, religious delusions, auditory command hallucinations as well as motor restlessness. She also lacked appropriate insight or judgment. Except for lymphocytosis and high CRP, most of her lab work (including white cell count, hemoglobin, platelet count, kidney, and liver function test ad electrolytes) were normal. CT skull was found to be normal, but brain MRI revealed asymmetric bilateral hippocampal and parahippocampal cortical hyperintensities with affected amygdala.

The patient's respiratory symptoms had resolved by day 3, but her neuropsychiatric symptoms remained. She also began to display significant aggression that required lorazepam and haloperidol use. This worsening motivated the use of high dose methylprednisolone 1 g for 5 days, starting Day 3 of hospitalization. Three days of steroid therapy led to marked improvement in patient status, with near complete resolution of neuropsychiatric symptoms by the fifth day of treatment. Patient was reported to no longer display any neuropsychiatric symptoms again following discontinuation of the antipsychotics.

The cases summarized above are only a select few of several other cases that were reported and studied with similar presentations of symptoms. More importantly, they are included to represent an important pattern. Each of the cases appear to happen in patients initially presenting for COVID-19 before acutely developing psychiatric symptoms, largely despite any past psychiatric history. While the case reported by Ariza-Varon et al. (February 2022) described notable MRI brain findings, it should be noted that many cases were also seen without any such findings. The development of acute onset neuropsychiatric symptoms in the context of a viral infection is not a novel finding. Reports as early as the 18th and 19th centuries described the onset of symptoms including anxiety, psychosis, suicidality, and mania [9, 10]. Neuropsychiatric sequelae have also been reported during the SARS-CoV-1 epidemic in 2003, the H1N1 influenza pandemic in 2009 and the MERS-CoV outbreak in 2012; these have been described as including seizures, encephalitis, and Guillain -Barre syndrome among others [11,12,13,14]. This pattern of neuropsychiatric symptoms and sequelae in the context of viral infections is therefore a historic one, and bears recognition of its significance.

Conclusion

COVID-19 has been a highly impacting disease that continues to be studied in terms of its manifestation, transmission, and treatment. This viral infection seems to have commanded a systemic inflammation that can lead to unique presenting symptom profiles in infected patients, but also can lead to varying post-infection sequelae. Neuropsychiatric sequelae of COVID-19 infection continue to be reported, and certain observations may be drawn based on existing literature. As briefly summarized in this article as well, many of these patients' report experiencing these symptoms acutely in the context of COVID-19 infection. While some of these patients may carry a previous psychiatric history, cases including the one presented here have been reported in patients without any psychiatric history as well. Neuropsychiatric presentations can differ, but our review of existing case reports seems to have shown that they tend to include descriptions of delirium, personality changes (i.e. increased aggression) and hallucinations (auditory and/or visual). It seems that nearly all these patients tend to have had been hospitalized for their infection, thus potentially suggesting that post-COVID psychosis is more likely in moderate-severe infection cases; however, these neuropsychiatric sequelae in patient with mild- moderate COVID-19 infections not requiring hospitalization is perhaps yet to be seen.

As mentioned earlier, the case we present here has two notable features – its duration of symptoms and reemergence following reinfection. It is also worth noting that several cases, including the three others summarized here, tend to have reported that while there was an acute onset of the disease following COVID-19 infection, the resolution of these symptoms seems to occur earlier than in our patient, who reports having experiences symptoms for 11 months prior to resolution. This could be due to several contributing factors, including but not limited to differing degrees of inflammation, varying psychiatric treatment protocols, differing COVID-19 related hospitalization lengths and past medical history. Another unique feature of our case is the reemergence of these symptoms following reinfection with COVID-19. It is significant that this patient's neuropsychiatric sequelae appear to have been reproducible with reinfection despite reportedly complete resolution of neuropsychiatric symptoms following her initial infection. This seems to strengthen the relationship between these psychotic features and COVID-19 infection, especially since the patient reports that her presenting symptoms closely mirror her initial neuropsychiatric symptoms as well. It must be considered that this is solely based on the patient's reported experience, and influence of perceived insight and the possibility that the initial neuropsychiatric sequalae had not been completely resolved despite the patient's belief could affect the interpretation of the findings. An important question that this patient's reemerging symptoms presents is the possibility of increased vulnerability to neuropsychiatric symptoms or conditions following COVID-19 infection, suggesting a possible future goal of research. These questions can be elucidated as more evidence is gathered and analyzed regarding neuropsychiatric sequelae of COVID-19.

The analysis gleaned from this case report is still restricted by certain limitations. Firstly, the patient continues to be worked up for other potential etiologies for her presentation; despite having symptoms that appear nearly identical to her initial post-COVID infection period, other possibilities that could have led to these symptoms are yet to be ruled out by lab work and imaging that is pending at the time of writing. Additionally, we do not have full confirmation regarding the compliance of the patient to her prescribed antipsychotic medications which could have contributed to her prolonged experience of symptoms. Furthermore, access to documentation from her COVID-19 hospitalizations would be helpful in further studying and strengthening the analysis of our findings.

Overall, this case report adds to a growing body of evidence surrounding the presentation of neuropsychiatric sequelae of COVID-19, here labeled as "post-COVID psychosis", and serves as an added reminder for clinicians to consider regarding the long-term care of patients who experienced COVID-19 infection.

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Ethical Approval

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RY contributed to the study design, data collection, data interpretation, drafting and revising of this article. DJ supervised the study, provided treatment for the patient, revised this article, and provided final approval of this version for submission.

Conflict of Interest

The authors have no conflicts of interest to report.

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