

CASE REPORT

Cariprazine Treatment of Shared Delusional Disorder in the Age COVID -19: A Case Report

Hani Raoul Khouzam^{1,2*}, and John Tran^{2,3}

¹ *Mental Health Clinic, VA Central California Health Care System (VACCHCS), Fresno, California, USA*

² *Health Sciences, UCSF-Fresno Department of Psychiatry, Fresno California, USA*

³ *Fresno County Department of Behavioural Health, Chief, Department of Psychiatry, UCSF-Fresno, Vice Chair, Department of Psychiatry and Behavioural Sciences, UCSF*

Correspondence should be addressed to Hani Raoul Khouzam, Mental Health Clinic, VA Central California Health Care System (VACCHCS), Fresno, California, USA

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ABSTRACT

This case report describes the occurrence of persecutory delusions in a close friend of a patient who developed delusions as a complication of an acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The person infected with the SARS-CoV-2, commonly referred to as COVID-19, and experienced a first episode of psychosis manifested by fears and delusions. His paranoia is that his neighbours were plotting to kill him and his family by using the nerve gas sarin which was supplied by terrorists. These persecutory delusions subsided with the recovery from COVID-19. The patient's family had communicated to one of his close friends whom he has known since high school about the developing of these delusions. Consequently, that friend developed the same delusions and took extreme precautionary actions by barricading himself in his apartment and barb wired his front door entrance. He also ordered various chemicals online to presumably manufacture antidotes to the nerve gas sarin. These delusions persisted leading to an emergency room visit and psychiatric hospitalization where he was treated with the antipsychotic medication cariprazine (Vraylar®).

This case summarizes the possible occurrence of psychosis as a psychiatric complication of COVID- 19. It also reveals clinical features of shared delusional disorder and provides the opportunity to explore the pharmacological action of cariprazine.

KEYWORDS

COVID-19; Delusional disorder; Cariprazine treatment; Psychosis

INTRODUCTION

Psychosis as a Complication of SARS-CoV-2 Infection

COVID-19 is a novel type of highly contagious infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which is manifested by several serious medical complications and death. Several psychiatric complications of COVID-19 have begun to emerge including new onset of psychosis [1].

Psychosis usually refers to a group of symptoms that include disturbances in perception of reality manifested by hallucinations and/or illusions, delusions of paranoia, and suspiciousness [2]. In some cases, cognitive deficits may exist and correlate with the severity of the psychosis [2]. Current available clinical findings suggest the incidence of psychosis to be in the range of 0.9% to 4% in COVID-19 patients [2]. Because all reported cases of psychosis have been based on observational data and case studies with very limited sample sizes, they cannot be generalized until larger case-controlled studies and/or prospective studies are conducted. However, these types of studies are difficult to initiate amid the unprecedented global pandemic.

Shared Delusional Disorder (SDD)

Among the psychotic disorders, SDD was reclassified in the latest edition of the diagnostic and statistical manual of mental disorders (DSM-5) under other specified schizophrenia spectrum and other psychotic disorder with three diagnostic criteria [3]:

1. A delusion that develops in the context of a close relationship with an individual with an already established delusion.
2. The delusion must be very similar or even identical to the one already established one that the primary case has.
3. The delusion cannot be better explained by any other psychological disorder, mood disorder with psychological features, a direct result of physiological effects of substance abuse or any general medical condition.

In general, SDD is difficult to diagnose due to its rare occurrence. The afflicted individuals often do not seek out treatment because they do not realize that their delusions are abnormal. Moreover, as the delusion becomes more severe, the recognition and insight of its existence will be weakened over time [4].

Cariprazine (Vraylar®)

Cariprazine is an atypical antipsychotic or a second-generation antipsychotic (SGA) medication. It has been approved by the Food and Drug Administration (FDA) for the treatment of schizophrenia, treatment of acute manic or mixed episodes of bipolar I disorder, and treatment of depressive episodes associated with bipolar I disorder [4-6].

Cariprazine (Vraylar®) is a partial dopamine D2 and serotonin 5-HT1A receptors agonist, and a serotonin 5-HT2A receptor antagonist [5,7]. It exhibits high affinity for dopamine (D2 and D3) and serotonin (5-HT1A) receptors and has low affinity for serotonin 5-HT2C and alpha1A-adrenergic receptors [8]. Cariprazine functions as an antagonist for 5-HT2B (high affinity) and 5-HT2A receptors (moderate affinity). It binds to histamine H1 receptors but has no affinity for muscarinic (cholinergic) receptors [6].

Cariprazine is available as oral capsules of 1.5 mg, 3 mg, 4.5 mg and 6 mg doses. It is given orally once daily and can be taken with or without food [4,7]. Side effects may first appear on the first day after starting cariprazine. The most prevalent side effects include akathisia, insomnia, nausea and weight gain [6,9]. Cariprazine does not appear to impact prolactin levels, and unlike many other antipsychotics, it does not increase the QT interval on the electrocardiogram (ECG) [9]. The recommended dose range for this medication is 1.5 mg to 6 mg once daily. It is recommended to start the medication at 1.5 mg once daily and increase to 3 mg once daily on Day 2. Depending upon clinical response and tolerability, further dose adjustments can be made in 1.5 mg or 3 mg increments [6,9,10]. Dosages above 6 mg daily do not confer sufficient increase in effectiveness to outweigh dose-related adverse reactions [9,10].

CASE REPORT

Mr. A was a 41-years-old gentleman, who is a construction worker, with no known current or past history of mental illness., He was admitted to the hospital for symptoms suggestive of SARS-CoV-2 infection, including fever with chills, cough, difficulty breathing, fatigue with muscle aches, headache, sore throat and runny nose. His diagnosis was eventually confirmed by a positive COVID-19 testing. He was discharged from the hospital after receiving 9 days of medical support and oxygen therapy. A week later, Mr. A's wife reported that he was behaving very strangely. He became delusional and suspicious. He firmly believed that his neighbours were plotting to kill him and his family using the nerve gas, sarin, which he felt was supplied by terrorists. He began to implement extreme precautionary actions by barricading himself in their apartment and barb wired his front door entrance. He also ordered various chemicals from online dark websites with the intention to use them as antidotes to sarin.

As a result of these sudden behavioural changes, his wife begged him to visit his primary care physician. He had a complete physical examination which did not reveal any abnormal findings. He had no symptoms or signs of SARS-CoV-2, reinfection, inflammation, head injury, bone fractures or joint problems. His lab tests, includes complete blood count (CBC), chemistry profile urine analysis, urine screen for illicit drugs and thyroid function test, were all normal. Due to his healthy physical condition, no further medical work up or imaging study was recommended. He was not offered any treatment. His wife and his two 12-years-old twin daughters tested negative for SARS-CoV-2 infection. His wife sought help and support from several of his family members and friends. They reside out of state and unable to come to help and persuade him to abandon his strange behavior and bizarre delusions.

Mr. A had a very close friend, Mr. B, whom he had known since they were on the baseball team in high school. Mr. A and Mr. B shared a very strong friendship, and many of their classmates had mistakenly thought that they were biological brothers. They have kept close contact throughout the years, and they were each other "best men" in their respective weddings. Their families travelled together and camped in national parks every summer and special anniversary dates. Due to COVID-19 pandemic restrictions and social distancing precautions, the two families have not gathered for a long time and only kept in touch via social media and face time. Mr. A's wife reached out to Mr. B and pleaded with him to intervene and persuade his lifelong friend to "gain back his sanity." Mr. B agreed to help but want to carefully analyse and study the "whole situation" before he intervened, Mr. A has no knowledge of his wife's arrangement with Mr. B. As this process began, Mr. A miraculously and

dramatically changed his behaviours for unknown reason. He apologized for his unusual behaviours and reported that all his fears and suspiciousness were kind of “a bad dream.” His symptoms continued to improve over the course of the following three weeks, and he regained his normal level of physical and psychological functioning. In the meantime, Mr. B ‘s wife contacted Mr. A to inform him that her husband has lost his mind and acting very strangely over the past three weeks. She described him as being suspicious and fearful. He exhibited bizarre belief about a terrorist plot planned by their neighbours to spread the nerve gas sarin in their place of residence. He barricaded himself and barb wired their front door entrance. He also checked the online dark websites for chemicals and antidotes to the nerve gas sarin.

Mr. A became extremely concerned about his friend’s wellbeing and tried to convince Mr. B that Mr. B is having the exact same “bad dream” that he has gone through. In response, Mr. B became very angry, hostile and threatened to retaliate as well as to harm Mr. and his whole family.

Mr. B was a 41-years old, married, medium built and healthy gentleman who owned a hardware store. He had no known current or history of medical or mental illness. He had a complete physical and neurological examinations which yielded no abnormal findings. He did not smoke or used any caffeine, alcohol, illicit or recreational drugs. He tested negative for COVID-19 but was deemed a potential danger for self and others. Mr. B was involuntarily hospitalized in a psychiatric emergency unit. He did not respond to trials of various anxiolytics or antidepressants. He developed intolerable sedation, nausea and increased appetite when treated with the antipsychotics, including olanzapine, risperidone and quetiapine. His wife requested that he should be treated with the novel antipsychotic cariprazine based on a recently seen television advertisement. A therapeutic intervention was initiated with cariprazine at the starting dose of 1.5 mg once daily, and it was increased to 3 mg once daily on the following day. Mr. B tolerated the medication well without developing any adverse effect. His delusion completely subsided after 12 days of treatment on cariprazine. He regains his insight and could not believe that he acted and behaved in such bizarre manners. He was then discharged from the psychiatric unit and scheduled for outpatient follow-up. It is not known at the time of writing this report if Mr. B will be maintained on the daily 3 mg dose of cariprazine.

Mr. B reached out and apologized to his friend Mr. A, and they rekindled their enduring and cherished friendship.

DISCUSSION

The link between viral infection and psychosis was documented in some accounts of the Spanish influenza pandemic of 1918 where some infected individual developed hysteria, melancholy, and insanity, which later led to the descriptive term in other influenza pandemics, of "psychoses of influenza" [11]. Several etiologies have been suggested correlating the effects of a viral infection on inducing psychosis such as the virus itself causing the psychosis, or its devastating medical complications inducing the psychosis [12]. Additionally, some reports of COVID-19 infection have been associated with delirium and psychosis [11,12]. The psychosocial disturbances, including social isolation, increasing fear, the dread of losing loved ones, loss of employment, vanishing of financial assets, and the confusing political views on limiting and combating the virus spread, have also been postulated as factors that could precipitate a psychotic break in vulnerable individuals [12].

While some individuals develop psychotic symptoms in association with COVID-19 infection such a in Mr. A, other individuals without the infection could also display psychotic symptoms such as Mr. B, who developed SDD

as a consequence of his close ties and long-life friendship with Mr. A. The prevalence of psychosis in non-infected individuals is rare and seems to correlate with extreme social isolation, living in quarantine, excessive vigilance about hand-washing and personal health, conspiracy theories regarding the etiology of the virus, and the general and global fears in response to the pandemic [13].

While SDD is considered a rare psychiatric disorder, it was historically described as Folie à deux ('madness for two'), also known as shared psychosis or induced delusional disorder [14]. When it affects more than two people, it may be called folie à... trois ('three') or quatre ('four'); and further, folie en famille ('family madness') or even folie à plusieurs ('madness of several'). The disorder was first conceptualized in France in the 19th century by Charles Lasègue and Jean-Pierre Falret, hence also known as Lasègue-Falret syndrome [9]. This disorder is most commonly diagnosed when two or more individuals live in proximity, may be socially or physically isolated, and have little interaction with other people.

As a psychiatric syndrome, SDD is characterized by symptoms of delusional beliefs, and sometimes hallucinations that are transmitted from one individual to another [14].

The treatment of SDD usually require the isolation of the individuals who share the same delusions and monitoring if the delusion resolves or lessens over time [15,16]. This intervention was not indicated since Mr. A and Mr. B were already geographically separated from each other. It is also recommended to treat SDD with a combination of psychotherapy and pharmacotherapy [16]. Individual and family therapy are usually implemented to involve the individuals and their entire families to work on interpersonal relations and family dynamics with the hope of developing mutual trust [17].

Additionally, minimizing social isolation could play a role in disproving the delusions [18]. When the delusions continue to persist then pharmacological treatment with an antipsychotic medication would be recommended [16,19].

Given the circumstances and friendship between of Mr. A and Mr. B, individual and family psychotherapy were not warranted. Mr. A did not require treatment with an antipsychotic medication since his delusions were spontaneously resolved. Conversely Mr. B's persistent delusions, if left untreated, could become chronic and led to the development of anxiety, depression, aggressive behavior, and future psychosocial, economic, and vocational complications [20].

It is postulated that Mr. A developed his first psychotic episode as a complication of SARS-CoV-2, social isolation and decreased human interactions imposed by the COVID-19 guidelines, or possibly the combination of the infection and social isolation following his recovery. While these measures are necessary to prevent infections spread and are lifesaving, living in quarantine and socially distancing oneself has been known to trigger psychotic episodes, particularly in vulnerable individuals. However, both Mr. A and Mr. B were emotionally and psychologically stable prior to the COVID-19 pandemic; they did not have any family history of psychiatric or emotional disorders; and at the time, they were not living in close proximity. So, it is still unclear if their psychotic symptoms were direct consequence of COVID-19 impact on their mental stability.

Pharmacological intervention with an antipsychotic medication was clinically indicated and urgently warranted to prevent the complications that are associated with an untreated delusional disorder. The treatment with the atypical and SGA antipsychotic cariprazine (Vraylar®) led to the remission of the Mr. B's SDD without the development of any adverse effect.

It is not clear if Mr. B's SDD would have resolved spontaneously with the passage of time. Clinical data about the prognosis of SSD, as a rare condition, are lacking, and it is expected that the majority of cases go unreported. However, in Mr. B's case, the treatment with cariprazine, seemed to have achieved a desirable clinical outcome and could thus predict a very good prognosis of his SDD.

CONCLUSION

The unprecedented medical and psychiatric complications of SARS-CoV-2 are being daily observed, updated and documented during the global COVID-19 pandemic. At the present time the psychiatric complications of developing psychosis during and post viral infection is still unclear and debatable. In this case report, the development of SDD in a close friend of a person who was infected with COVID-19 remains an anecdotal finding until more rigorous large sample randomized clinical trials are conducted to establish a link between COVID-19, the development of psychosis, and its possible treatment. In the meantime, it is hoped that this case report will provide clinicians with information about the possible psychiatric complications of this global pandemic, summarize the diagnosis of SDD, and show its response to treatment with the atypical SGA antipsychotic cariprazine (Vraylar®).

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DISCLAIMER

The views described in this manuscript are those of the author and do not reflect the official policy of the VACCHCS or The Department of Veterans Affairs or Fresno County Department of Behavioural Health or UCSF-Fresno Department of Psychiatry.

The chronological events, demographic characteristics and personal information of the described case report have been changed to protect patients' confidentiality medical records information.

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