



Case Report

“Psychosis Triggered by Lyme Disease and Coronavirus Disease 2019 (COVID-19): A Case Report”

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Citation: Farooq F, Farooqi M, Qadir T, Ferrando SJ (2023) “Psychosis Triggered by Lyme Disease and Coronavirus Disease 2019 (COVID-19): A Case Report”. Ann Case Report. 8: 1402. DOI: 10.29011/2574-7754.101402

Received Date: 08 August 2023; **Accepted Date:** 12 August 2023; **Published Date:** 15 August 2023

Abstract

We present here the case of a young man who had two discrete episodes of psychotic illness concurrent with infectious etiologies: First, Lyme disease and then, 2 years later, Coronavirus Disease 2019 (COVID-19). We discuss the clinical presentation, illness course and the potential for common or divergent underlying pathogenesis. Both the literature and the case mentioned indicate that physicians must maintain a high degree of suspicion for an infectious process as a potential underlying cause of emergent psychosis, particularly in the age of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS Co-V2).

Keywords: Coronavirus Disease 2019 (COVID-19), Lyme disease, Neuropsychiatric illness, Psychosis, Inflammatory cytokines.

Introduction

It is well documented that infectious pathogens can be associated with psychiatric complications, both acutely and chronically. It is also posited that infections may trigger underlying psychiatric disorders, including schizophrenia, bipolar disorder, and major depression [1]. Because the psychiatric symptoms caused by infectious illness may be indistinguishable from a new onset psychiatric disorder, the pathogenesis is not always clear. The psychological stress of an infectious illness, concurrent psychosocial factors, the physiological effects of the infection, including inflammation or neuro-invasion, or some combination of these factors, may all play a role. It is always a question as to whether psychiatric symptoms are a manifestation of underlying biological vulnerability, as in the stress-diathesis model, or an

expectable reaction in a subset of patients with infectious illness [2]. Moreover, in the presence of concurrent infectious illness and psychiatric symptoms, it is impossible to determine the course and prognosis. This is further complicated because psychiatric symptoms may persist after the treatment and resolution of the acute infectious illness. We present here the case of a young man who had two discrete episodes of psychotic illness concurrent with infectious etiologies: First, Lyme disease and then, 2 years later, Coronavirus Disease 2019 (COVID-19). We discuss the clinical presentation, illness course and the potential for common or divergent underlying pathogenesis.

Case Presentation

The Patient is a 21-year-old male with a diagnosis of schizoaffective disorder, presented to the outpatient clinic, stable on olanzapine 10 mg PO daily and sodium valproate 500 mg PO three times a day. Past psychiatric history was notable for two hospitalizations, in May 2018 and May 2020.

May 2018:

- In May 2018, he presented to the Emergency Department with symptoms of catatonia, selective mutism, thought disorganization, frontal pressure-like headaches, postural hypotension, and gait ataxia.
- Positive Lyme titers were found, and he was admitted to the neurology service for IV ceftriaxone to treat Lyme encephalitis, confirmed by CSF analysis. MRI and EEG were normal.
- He was concurrently treated with high dose lorazepam, with gradual resolution of catatonic symptoms after several days.
- Lorazepam was tapered in the hospital and he manifested symptoms of depression, for which he was started on duloxetine.
- It remained unclear if his catatonic presentation was secondary to Lyme disease or an early manifestation of a psychiatric condition.
- He was reported by family to have been psychiatrically stable over the ensuing two years.

May 2020:

- Two years later, in May 2020, the patient was admitted to the inpatient unit for erratic and disorganized behaviour.
- He was found to be Coronavirus Disease 2019 COVID-19 positive, hypothermic, and required medical stabilization.
- The patient was transferred for inpatient psychiatric treatment, where he was preoccupied with internal and religious thoughts, mutism then later hyper sexuality and grandiose delusions.
- He reported he previously stopped duloxetine at least a year prior due to improved mood.
- QTc was noted to be prolonged, leading to a recommendation of avoiding antipsychotic medication.
- He was treated with sodium valproate 500 mg three times daily and lorazepam, which was eventually tapered.
- During his 28 days on the inpatient unit, he remained delusional, believing he was sent by God for a higher purpose.
- QTc subsequently normalized, and he was treated with Lurasidone with minimal benefit.
- Ultimately, Olanzapine 10 mg daily was initiated, and his mood and psychotic symptoms stabilized.

June 2020-July 2021:

- On an outpatient basis, he was continued on olanzapine 10 mg daily and sodium valproate 500 mg three times a day.
- He progressively improved and did not express any delusional thoughts or bizarre behaviour, though his low mood and anhedonia lingered.
- Over the course of 1 year, olanzapine was tapered off due to

excessive sedation, and he was switched to aripiprazole 5 mg daily, with good effect. Valproic acid was decreased to 500 mg twice daily.

- After 1 year, the patient returned to normal baseline function, being able to hold a steady job and socialize appropriately. There was no indication of recurrent psychosis or major affective symptoms.

Discussion

In this case report, the patient suffered from two psychotic episodes concurrent with two infectious diseases, Lyme and COVID 19. There is ample data to support the emergence of new-onset psychiatric symptoms after diagnosis of an infectious disease; therefore, physicians should always maintain a high index of suspicion [1]. A nationwide study of mental disorders and suicidal behaviours following Lyme borreliosis revealed elevated rates of affective disorders, suicide attempts, and suicide in individuals with a history of Lyme borreliosis compared to those without. The study couldn't establish causality, but it suggested possible mechanisms linking Lyme borreliosis to mental disorders, including inflammation, immune activation, and autoimmunity. The findings indicate that Lyme borreliosis may be associated with psychiatric manifestations, but it is not a major contributor to the overall frequency of mental disorders or suicide in the general population [3]. It is presumed the parasite *Borrelia burgdorferi* responsible for Lyme disease causes three types of infections resulting in neuropsychiatric symptoms: First is meningovascular form causing cerebrovascular infarcts. The second is Lyme meningoencephalitis, the atrophic form, which is associated with gliosis, cortical atrophy, and dementia. The third type is caused by Central Nervous System (CNS) immune response [4]. The direct entry of the spirochete into the host may result in neuronal injury, but the most significant contributor to neuronal and glial cell injury is the induction of cytokine-mediated inflammatory cascade [4]. *B. burgdorferi* strains specificity plays a crucial role in its ability to infect the nervous system by entering through the bloodstream or peripheral nervous system, leading to inflammation in the brain. The host immune response is vital in the early stages of Lyme neuroborreliosis (LNB), as *B. burgdorferi* triggers immediate brain inflammation and neuronal death, affecting glial cells, cytokine, and chemokine markers [5]. Evidence also points towards the role of both nonspecific and specific immune response associated with Lyme disease. The specific immune mediated response includes formation of specific antibodies against neural tissue, cross-reactivity between *B. Burgdorferi* specific antibodies and neural tissue, and production of T cell complexes and *B. b* specific humoral immune response [6]. Nonspecific immune responses also play an interesting role in persistent inflammation by provoking metabolic changes including oxidative stress, mitochondrial dysfunction, altered homocysteine metabolism and tryptophan

catabolism, excitotoxicity, decrease in serotonin, and increase in quinolinic acid [6].

The patient presented with another episode of psychosis after two years in association with COVID-19. This episode was somewhat different from the first. He did have mutism, consistent with catatonia, but also had more overt psychotic and manic symptoms. Psychiatric symptoms have been associated with coronavirus infection since the onset of the pandemic. Coronaviruses have been previously associated with recent-onset psychosis [7], similar to influenza virus, which has been associated with Schizophrenia [8]. Psychosis, in particular, has been described by multiple authors. Ferrando, et al. first described 3 cases in which patients with no prior history of psychosis presented with new onset of psychosis ranging from auditory hallucinations to paranoid or persecutory delusions to bizarre somatic sensations after supposedly contracting COVID-19 [7]. Multiple case reports and systematic reviews have identified multiple patients with no prior psychiatric or psychosis history who developed psychosis concurrent with COVID-19 [9]. Compared to other coronaviruses, there is a suggestion that Covid-19 may have greater association with psychiatric symptoms. In a meta-analysis comparing psychiatric symptoms associated with Covid-19 and SARS, all ten symptom domains of the SCL-90 were more prevalent and severe in the acute phase of Covid-19 as compared to SARS [10]. It is believed that multiple environmental and biological factors play a role in the development of neuropsychiatric symptoms associated with Covid-19 infection. These include electrolyte abnormalities, impaired lung, liver and kidney function, vascular insults including stroke, decreased oxygen saturation, hyper inflammation and social isolation to limit its spread [11]. SARS CoV2 enters the brain after penetrating the nasal mucosa, often resulting in loss of smell, then migrating through the olfactory tract and the cribriform plate, or through trigeminal or vagal pathways. It also crosses the blood-brain barrier (BBB) that is compromised by cytokine-mediated inflammation [12]. Patients infected with SARS CoV2 experience a massive cytokine storm, which results in a high concentration of proinflammatory cytokines in the serum. These cytokines also cross the BBB, activating astrocytes and microglia, which cause phagocytosis of the damaged cells and further secretion of inflammatory mediators. Quinolinic acid release by activated CNS immune cells increases glutamate at high concentrations by inhibiting the enzyme glutamine synthetase in the glutamate-glutamine cycle and activates NMDA receptors, causing excitotoxicity [12].

Upon reviewing the mechanisms described above, it becomes evident that there is a significant commonality between the proposed mechanisms of psychiatric effects caused by Lyme disease and SARS CoV2. While both pathogens may reach the brain, the primary mode of neuropathology seems to be mediated by

CNS inflammation. Both infections may lead to neuropsychiatric symptoms, blood-brain barrier breakdown, immune system activation, cytokine release, CNS immune activation, and neurotransmitter dysfunction. In this case, the patient was diagnosed with Lyme-induced catatonia, schizoaffective disorder, and depression, highlighting the diagnostic challenges when neuropsychiatric symptoms present with infectious illness. However, our longitudinal observation of the patient suggests that he does not have a chronic psychotic illness, as his psychotic presentations occurred solely in association with acute infection. His most prominent ongoing psychiatric symptoms appear to be depression, and he has been capable of maintaining employment and normal social function.

Conclusion

Both the literature and the case discussed above emphasize the importance of physician's vigilance about infectious processes being potential triggers for emergent psychosis and other psychiatric disorders, especially in the context of SARS-CoV-2. Patients who experience psychosis and other psychiatric disorder due to an infection might be at risk of developing them again following another infection. However, distinguishing between primary and secondary psychopathology without longitudinal follow-up may prove challenging.

Footnotes

Declaration of Conflicting Interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Consent: Written informed consent was obtained from the patient for publication

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