



RESEARCH ARTICLE

A 21-Year-Old Woman with New Onset Tourette Syndrome after Coronavirus Disease 2019 (COVID-19)

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Abbreviations:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

Coronavirus disease 2019 (COVID-19)

Body Mass Index (BMI)

Montreal Cognitive Assessment (MOCA)

Tourette Syndrome (TS)

Chronic tic disorder (CTD)

Gastrointestinal (GI)

Licensed Practical Nurse (LPN)

Central Nervous System (CNS)

Post-acute Sequelae of COVID-19 (PASC)

Polymerase chain reaction (PCR)

Cerebrospinal fluid (CSF)

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019 and has affected millions. Many patients who have had coronavirus disease 2019 (COVID-19) infection develop acute and chronic medical illnesses which can impact every organ system. Those who develop new-onset neurological disorders during the acute phase will often experience long-lasting complications. Although the specific cause is unclear, many mechanisms have been cited, including a direct impact from the virus itself and indirect impacts from inflammation, hypoxia, and hypercoagulability. We present a case of an adult with no neurological or psychiatric history who developed a series of neurological issues ending in the development of Tourette Syndrome (TS) after a COVID-19 infection. The patient has continued to display the symptoms of Tourette Syndrome but has improved with the current treatments available for Tourette Syndrome.

Keywords: Tourette Syndrome; TIC Disorder; COVID-19

Introduction

Individuals who have had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) manifest with a variety of symptoms, the most common being fatigue, dyspnea, and chest pain. Of those patients who have developed coronavirus disease 2019 (COVID-19), 10-30% develop new-onset neurological disorders during the acute phase.¹ Many neurological problems have been reported with COVID-19 from the direct and indirect impacts of the virus. Directly, the virus damages central nervous system (CNS) tissue impairing the blood-brain barrier, and indirectly, it causes cerebrovascular damage from thrombi produced by hypercoagulability.² The virus also causes inflammation of the brain (and other body organs), which may produce secondary CNS toxicity through several mechanisms including cytokine storm activating microglia and astrocytes.³ As a result, several neurological problems may develop including Guillain-Barré syndrome, ischemic and hemorrhagic strokes, encephalopathies, Parkinsonism, migraine headaches, and movement disorders.^{4,5,6}

In addition, many neuropsychiatric disorders have developed secondary to COVID-19 infection. Delirium, psychosis, severe anxiety, and depression have been reported with acute COVID-19.⁷ Post-acute sequelae of COVID-19 (PASC) has been associated with higher levels of anxiety, depression, fatigue, pain interference, pain quality, pain behavior and pain intensity,⁸ especially in those with these preexisting problems before becoming ill with COVID-19.

COVID-19 and other inflammatory viruses are being considered a source of many more neurological and psychiatric disorders due to the biological changes they are producing.⁷ The following case highlights one unusual neuropsychiatric complication, Tourette Syndrome, which developed from infection with COVID-19.

Case Presentation

This is a case of a 21-year-old single licensed practical nurse (LPN) working in a nursing home, with no prior medical, neurological, or psychiatric history in her usual good state of health. In the summer of 2020, she contracted COVID-19, confirmed by polymerase chain reaction (PCR) testing. She experienced fever, upper respiratory symptoms, migraine-like headaches, diffuse pain, and fatigue, loss of taste and smell, and diarrhea. The symptoms resolved within two weeks. She resumed working in the nursing home after resolution of her acute infection but chose to remain unvaccinated against COVID-19.

She was re-infected with COVID-19 (confirmed by PCR testing) in June 2022, presenting with, upper respiratory symptoms and migraine-like headaches which resolved within a week. Shortly thereafter she developed shooting pains down her left side involving face, arm and leg and this was followed by left-sided weakness and facial droop. Her CT/MR brain, laboratory, and EEG at this time were unremarkable. Her symptoms continued and she developed head and facial jerking (tics), followed by lip smacking and then repetitive speech characteristic of Tourette Syndrome.

Despite a trial of guanfacine from her local physician, her symptoms persisted, and she was referred to the Mayo Clinic in February 2023, for a second opinion. On examination, she had head and facial tics and involuntary and repetitive sounds, which were classic for Tourette Syndrome commonly seen in younger people. She was pleasant and cooperative. She experienced mild anxiety about her current symptoms but was euthymic. Her thought processes were normal, although her speech was difficult to understand due to involuntary and repetitive vocalizations. She had no psychotic symptoms or significant cognitive abnormalities from formal screening.

Laboratory tests at this time revealed antibodies to SARS-CoV-2 confirming prior infection and an elevated inflammatory marker, C-reactive protein. A complete blood count, complete metabolic panel, thyroid stimulating hormone, thyroid peroxidase antibody, encephalopathy autoimmune/paraneoplastic panel, viral titers (HSV I/II, EBV, CMV, Parvovirus B-19, West Nile Virus), tick-borne and parasitic pathogen screen, alpha-galactosidase A antibodies, Beta -2 glycoprotein antibodies, coagulation studies including phospholipid antibodies, and rheumatologic laboratory were all unremarkable. ECG, CXR, and EEG were also normal. She had 7Tesla MRI and MRA brain imaging in June 2023 which were unremarkable. Additional testing during an emergency room visit for chest pain and dyspnea, a CT chest angiogram and echocardiogram, were also unremarkable.

However, a movement neurophysiology study to assess her involuntary movements showed findings that could be consistent with tic syndrome. She was then treated with risperidone initially but continued to have lip smacking and repetitive sounds, although her motor tics were better. She began to feel more fatigued on risperidone without further benefit, and the decision was made to switch her to pimozide. On pimozide, her symptoms have improved by 50%.

Discussion

Tourette Syndrome is a neurodevelopmental disorder characterized by motor and phonic tics, which have previously been identified before age 18.⁹ The underlying pathophysiology is not well known for Tourette Syndrome. However, new insights into possible epigenetic changes and alterations in neurophysiology and brain networks are occurring.¹⁰

SARS-CoV-2, which emerged in December 2019, has affected hundreds of millions worldwide. Of those impacted, 10-30% have developed new-onset movement disorders during the acute phase, which is rare compared to pulmonary or cardiovascular

disease.^{1,4} Parkinsonism, dystonia, chorea, ataxia, and myoclonus have commonly occurred.⁴ In a follow-up study, movement disorders began approximately two weeks after the onset of acute COVID-19 (similar to our patient). Ninety-two percent of patients required hospitalization for an average of 23 days, and 22% (average age 66.8 years) had persistence of the neurological symptoms (ataxia, myoclonus, tremor, parkinsonism) after a follow-up of roughly 1 to 3 weeks.¹¹ The severity of COVID-19 and the development of encephalopathy were noted to be weak predictors for the persistence of neurologic disorders, but the prognosis of new-onset COVID-19-associated movement disorders was good.¹¹ In a study of 8 comatose or encephalopathic patients with acute COVID-19, high-titer anti-SARS-CoV-2 antibodies were detected in the cerebrospinal fluid (CSF), demonstrating intrathecal IgG synthesis or blood-brain barrier disruption, which is thought to facilitate the entry of cytokines into the central nervous system enhancing neuroinflammation and neurodegeneration.¹² In a systematic review by Tandon et al., the most common CSF finding in patients with acute COVID-19 was an elevated protein with, very occasionally, mild lymphocyte-predominant pleocytosis.¹³ However, there are no studies evaluating CSF in patients with long COVID neurological complications including tic disorders. Although CT scans and MRIs may detect acute gross brain injuries, they may not detect more subtle brain changes at the cellular level.¹⁴ Additionally, more sophisticated imaging such as 7 TESLA MRI imaging, unless used early in the course of symptoms, may not detect microvascular changes (as in the case of our patient where it was performed a year after the onset of her symptoms). This advanced MRI did rule out cerebrovascular and neurodegenerative causes for her symptoms.

Hassan et al. described a 58-year-old man with chorea, a rare manifestation of COVID-19 infection. Oral umifenovir, procyclidine, risperidone, and amantadine sulfate led to gradual improvement.¹⁵ Children with COVID-19 may also display choreiform

movements.⁵ Other neurological manifestations of COVID-19 include cerebrovascular disorders, including ischemic stroke and macro/microhemorrhages, encephalopathies and meningoencephalitis, parainfectious immune-mediated complications such as Guillain-Barré syndrome, and neuropsychiatric complications.^{6,11,16}

In addition, tic-like behaviors have also been reported following COVID-19 infection.¹⁷ Clinicians have reported a worrying increase in tics in at least eight specialist Tourette clinics worldwide. This phenomenon has affected predominantly girls, particularly those of an adolescent age range, with a higher average age of onset than typical tic disorders.¹⁸ Buts et al. found the average age of onset of these rapid movements to be 13.7 years.¹⁹ The cohort of patients studied by Buts was discovered to have a significantly increased prevalence of comorbid neuropsychiatric disorders (91%), and the majority reported some symptoms of anxiety.¹⁹

The literature supports the occurrence of COVID-19-related movement disorders, which may occur during the acute phase or as potential long-term consequences (PASC). Thirty-four percent of 236,379 survivors of COVID-19 received a neurological or psychiatric diagnosis in the six months after their COVID-19 diagnosis.¹⁷

Permanent cases of movement disorders (such as our patient) may be due to various factors, including inflammation, direct damage from the virus itself, or the unmasking of a previous subclinical neurological disorder or vascular/demyelinating damage.^{11, 20} Additionally, hypercoagulability from COVID-19 may have contributed to her headaches, left-sided weakness and pain. In our patient's case, the lack of preexisting comorbidities, mental or social dysfunction, the timing of symptomatology to her acute COVID-19 infection, the progressive neurological symptoms from headaches to left-sided weakness, facial droop, and then the late age for the onset of Tourette Syndrome suggest a correlation between the virus and her neurological symptoms.

Conclusions

This case report illustrates the impact of COVID-19 on the development of neuropsychiatric disorders, including Tourette Syndrome.²¹ The pathogenesis for COVID-19-associated disorders involves anatomical (e.g., strategic lesions due to hypoxia or microinfarcts), cytokine-mediated, or other inflammatory processes. Accordingly, the prognosis may differ between cases and clinicians should be alert for diverse neurological disorders early and late after the initial infection. Understanding COVID-19 pathogenesis may lead to future innovative research into the underlying cause of many neuropsychiatric disorders.

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