



Clinical and diagnostic features of long-COVID patients presenting with neurologic symptoms in Chicago

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Abstract

Long COVID, a condition characterized by persistent symptoms after COVID-19 infection, is increasingly being recognized worldwide. Neurologic symptoms are frequently reported in survivors of COVID-19, making it crucial to better understand this phenomenon both on a societal scale and for the quality of life of these patients. Between January 1, 2020, and July 31, 2022, Illinois (IL) had a standardized cumulative death rate that ranked it 24th out of the 51 states in the United States (US). However, the US had one of the highest per capita COVID-19 death rates among large, high-income countries. [Bollyky T. et al. 2023] As a result of the increased number of COVID-19 infections, there was a rise in the number of patients experiencing Long COVID. At our neuro-infectious disease clinic in Chicago (IL), we observed an increasing number of patients presenting with cognitive and other neurologic symptoms after contracting COVID-19. Initially, we needed to provide these individuals with a better understanding of their condition and expected outcomes. We were thus motivated to further evaluate this group of patients for any patterns in presentation, neurologic findings, and diagnostic testing that would help us better understand this phenomenon. We aim to contribute to the growing body of research on Long COVID, including its presentation, diagnostic testing results, and outcomes to enlighten the long COVID syndrome. We hypothesize that the neurological symptoms resulting from long COVID persist for over 12 months. We conducted a retrospective analysis of clinical data from 44 patients with long-COVID. Cognitive symptoms were the most common presenting concern. Abnormalities in Montreal Cognitive Assessment, electroencephalogram, serum autoantibody testing, and cerebrospinal fluid were found in minority subsets of our cohort. At 12 months, most patients continue to experience neurologic symptoms, though more than half reported moderate or marked improvement compared to initial presentation. Although most of the patients in this study did not show a consistent occurrence of symptoms suggesting a cohesive underlying etiology, our clinical data demonstrated some features of Long COVID patients in Chicago (IL) that could lead to new research avenues, helping us better understand this syndrome that affects patients worldwide.

Keywords COVID-19 · Long COVID · Post-COVID syndrome · Neuropsychiatric symptoms · Autoimmunity

Introduction

Persistent multi-organ system symptoms are reported worldwide among those recovered from acute COVID-19. This is commonly referred to as “Long COVID” or “Post-COVID Syndrome.” The reported incidence of long COVID among non-hospitalized adults with COVID-19 varies across the literature but is increasingly reported. A 2022 study by the

United States Centers for Disease Control found that nationally 6.4% of US adults reported experiencing Long COVID symptoms (Ford et al. 2022). Prevalence varied across states, with our state of Illinois falling in the middle (prevalence between 5.4 and 7.1%). Neurologic symptoms are highly prevalent in patients presenting with Long COVID, and contribute to disability worldwide. Fatigue, cognitive dysfunction, headache, psychiatric symptoms, sleep disturbances, dysautonomia, myalgias, and persistent anosmia or dysgeusia are frequently reported (Akbarialiabad et al. 2021; Baig 2020; Brussow and Timmis 2021; Davis et al. 2021; Graham et al. 2021; Hampshire et al. 2024; Martimbianco et al. 2021; Nalbandian et al. 2021; Pavli et al. 2021; Widmann et al. 2021).

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While the clinical features of long COVID are well recognized, the underlying pathogenesis remains poorly understood. Commonly proposed mechanisms for neurologic sequelae of SARS-COV2 infection include prolonged immune activation and secondary damage from the acute hyperinflammatory response, including blood-brain barrier dysfunction, cytokine infiltration of the central nervous system (CNS), microglial activation, and endothelial injury. Other proposed mechanisms include reactivation of a virus reservoir, direct viral infiltration, hypoxic-ischemic damage, and psychologic distress (Akbarialiabad et al. 2021; Baig 2020; Baker et al. 2020; Doykov et al. 2020; Lu et al. 2020; Najjar et al. 2020; Nalbandian et al. 2021; Nuzzo et al. 2021).

To date, no consistent objective finding is diagnostic of long COVID or demonstrative of a distinct underlying etiology. However, there is a growing body of literature demonstrating cases of autoantibody positivity (Monti et al. 2020; Smyth et al. 2021) and abnormalities in cerebrospinal fluid (CSF) (Apple et al. 2022; Bozzali et al. 2021; Valencia Sanchez et al. 2021), electroencephalogram (EEG) (Bozzali et al. 2021; Valencia Sanchez et al. 2021), neuroimaging (Bozzali et al. 2021; Egbert et al. 2020; Lu et al. 2020), cognitive testing (Doykov et al. 2020; Graham et al. 2021), bloodwork, and autonomic testing (Dani et al. 2020; Kanjwal et al. 2020).

As the number of individuals who recovered from COVID-19 continues to increase, so does the number of patients presenting with long COVID. We investigated clinical, demographic, and diagnostic features of long COVID to understand underlying disease mechanisms better.

Materials and methods

Patients and design

We conducted a retrospective analysis of 44 adult patients evaluated by our neuroimmunology team for persistent neurologic symptoms after recovery from acute COVID-19. Any patient 18 years or older, specifically referred for new long COVID neurologic symptoms, with documentation of a positive COVID-19 test result, who experienced a mild to moderate acute illness phase was included. Patient encounters occurred between November 2020 and February 2022.

Acute COVID-19 cases were defined as “mild” if symptoms were managed with home care, “moderate” if a patient required hospitalization with no ICU admission or intubation, and “severe” if a patient required ICU admission and/or intubation.

Symptoms were reported as described by patients in the medical record. Physical and neurologic exams were

reported as documented by the examining neurologist(s). The Montreal Cognitive Assessment (MoCA) was also completed by examining neurologist(s). Laboratory and diagnostic tests were ordered based on clinical indication at the discretion of the examining neurologist(s).

Patients were interviewed about their symptoms after more than 12 months following acute COVID-19 infection. The degree of symptom improvement was recorded using the Targeted Neurologic Deficit (TND) score. TND score was established in previous severe CNS neuroinflammatory studies and focuses on improvement in presenting neurologic deficits as well as functional capacity. (Magaña, S et al., 2011; Fereidan-Esfahani, M et al., 2021)

Results

Demographics

Demographic data is reported in Table 1. A total of 44 patients were included (mean age 51; 65% female). Duration of symptoms at the time of evaluation ranged from 1 to 14 months after acute infection (median 3.5 months). 75% of acute cases were mild, and 25% were moderate in severity.

Symptoms

Cognitive symptoms were the most common clinical presentation, endorsed by 30 patients (68% of the cohort) (Table 1). These included “brain fog,” short-term memory loss, word-finding difficulty, and attentional and executive function impairments. Three of these patients had pre-existing memory concerns with subjective worsening post-COVID-19 infection.

Fatigue was the second most common symptom (59%), followed by headache (52%), sensory complaints (36%), myalgias (27%), psychiatric symptoms (20%), insomnia (15%), gait or balance impairment (15%), weakness (13%), and smell or taste changes (9%). Events involving loss of consciousness or alteration of awareness (including episodes of staring off, confusion, derealization, or syncope) were reported in three patients (6%). Tremors or abnormal movements, vision changes, vertigo/dizziness, and arthralgias each occurred in three patients (6%). Bowel or bladder dysfunction (4%) and autonomic symptoms (2%) were also reported.

Table 1 Demographics

Total <i>N</i>		44	
Age, years: range (mean)		18–89 (51)	
Female, n (%)		29 (65)	
Acute COVID-19 Severity, n (%)	Hospitalized, no ICU (Moderate)	11 (25)	
	Home Care (Mild)	33 (75)	
Duration from onset of acute COVID-19 to presentation, months: range (mean)		1–14 (4)	
Presenting Symptom(s)*, n (%)	Cognitive/Memory Complaints	30 (68)	
	Fatigue	26 (59)	
	Headaches	23 (52)	
	Sensory: Paresthesias, Pain, Numbness; focal or diffuse	16 (36)	
	Myalgias/Muscle spasm	12 (27)	
	Psychiatric/Behavioral Symptoms	9 (20)	
	Insomnia	7 (15)	
	Gait/Balance Impairment	7 (15)	
	Motor Weakness	6 (13)	
	Smell/Taste Impairment	4 (9)	
	Vertigo or Dizziness	3 (6)	
	Loss of Consciousness/Altered Awareness	3 (6)	
	Tremor/Dyscoordination	3 (6)	
	Vision changes	3 (6)	
	Arthralgias	3 (6)	
	Bowel/Bladder complaints	2 (4)	
	Autonomic Symptoms	1 (2)	
	Pre-existing Neurologic or Psychiatric Condition(s)*, n	Yes, any: n (%)	22 (50)
		Migraines/Headache Disorder	6
		Spinal injury or surgery/radiculopathy	4
Neuropathy, Paresthesia		3	
Memory/Cognitive Deficits		3	
Mood or Affective Disorder		3	
Attention-Deficit/Hyperactivity Disorder		3	
Stroke/TIA		2	
Concussion		1	
Bell's Palsy		1	
Cerebral Aneurysm		1	
Pre-existing Autoimmune Condition, n (%)		Yes, any	5 (11)
	Sjogren's Syndrome	1	
	Systemic Lupus Erythematosus	1	
	Psoriatic Arthritis (on Etanercept)	1	
	Crohn's Disease (on Humira)	1	
	Fibromyalgia	1	

Objective findings

Neurologic exam

A neurologic exam was available for all patients, as documented by the examining neurologist in the clinical note (Table 2). Mental status abnormalities were observed in 50% of patients, with impaired recall being the most common. Sensory abnormalities were seen in 29% of patients. Of these, 69% had length-dependent vibratory sense impairment. Reflex abnormalities (15%), gait impairment (13%), muscle weakness (9%), cranial nerve abnormalities (6%), and cerebellar findings (6%) were also noted.

MoCA

MoCA testing was performed on 19 patients with cognitive dysfunction (Table 2). Ten patients (52% of those tested) fell into the range of cognitive impairment with a score of less than 26. Nine of these patients scored in the range of mild cognitive impairment with a score of 18–25 and one in the range of 10–17, consistent with moderate cognitive impairment.

Table 2 Cognitive testing, CSF/serum studies, EEG, and MRI

Test	Patients tested	Results	
MoCA	19	Abnormal total (score < 26): n (% of tested)	10 (52)
		Score Breakdown	
		26–30	9 (47)
		18–25 (mild cognitive impairment)	9 (47)
		10–17 (moderate cognitive impairment)	1 (5)
CSF	4	Abnormal: n (% of tested)	3 (75)
		Albuminocytologic Dissociation (Abnormal proteins ranged 92.2–101.9 mg/dL)	2 (50)
		Elevated CSF IgG synthesis rate	1 (25)
SERUM Autoimmune Encephalopathy Panel	27	Abnormal: n (% of tested)	6 (22)
		Breakdown (n)	
		Anti-GAD 65 Ab positive	5
		Anti-ACh Receptor Ab positive	1
EEG	14	Abnormal: n (% of tested)	5 (35)
		Individual abnormal results	
		Rare anterior left temporal epileptiform activity	
		Intermittent generalized irregular delta-theta slow-wave activity with sharply contoured morphology	
		Intermittent, generalized, irregular delta slow wave activity and abundant beta	
		Intermittent bursts of generalized sharply-contoured delta slow-wave during wake and sleep	
		Multiple electrographic seizures and intermittent spikes, L > R central head regions	
MRI Brain	29	Breakdown	n (% of tested)
		Unremarkable	13 (44)
		Nonspecific Subcortical White Matter Changes	10 (34)
		Diffusion restricting lesion(s)	1 (6)
		Contrast enhancing lesion(s)	3 (10)
		Incidental Findings/ Unclear Significance	8 (27)

Cerebrospinal fluid analysis

Lumbar puncture was performed in four patients with cognitive dysfunction, seizures, and behavioral changes to rule out encephalitis (Table 2). CSF demonstrated elevated protein in two patients. One of these patients also demonstrated elevated intrathecal IgG synthesis rate; the other demonstrated one CSF-specific and four mirror (serum and CSF) oligoclonal bands. None demonstrated pleocytosis.

EEG

EEG data were obtained from 14 patients complaining of cognitive and attentional deficits or stereotyped episodic

symptoms (Table 2). Five patients had EEG abnormalities. One patient was diagnosed with new-onset epilepsy with multiple electrographic seizures arising from the left central head regions. Abnormal findings in other patients included epileptiform discharges arising from the temporal regions and intermittent generalized delta slow wave activity.

MRI

MRI of the brain was completed in 29 patients to investigate vascular causes (Table 2), with 44% interpreted as unremarkable. Nonspecific subcortical white matter changes were commonly seen (34%). Three patients had

contrast-enhancing lesions, and one had diffusion-restricting lesions consistent with subacute infarcts.

Autoimmune encephalopathy panel

The Mayo serum autoimmune encephalopathy panel was performed on 27 patients to investigate the causes of cognitive dysfunction and encephalopathy (Table 2). The panel tested for antibodies including AMPA-R, Amphiphysin, Anti-Glial Nuclear Type 1, Anti-Neuronal Nuclear type 1–3, CASPR2-IgG, CRMP-5-IgG, DPPX Ab IFA, GABA-B-R, GAD65, GFAP, IgLON5, LGI1, mGluR1, Neurochondrin, NIF, NMDA-R, Septin-7, Purkinje Cell Cytoplasmic Ab Type 1, 2, and TR. Antibodies were positive in 22% of those tested. Five patients (18%) were positive for anti-GAD65 antibody, all at low titers (between 0.03 and 0.13; normal ≤ 0.02). One patient was positive for acetylcholine ganglionic receptor antibody, with a titer of 0.16 (normal ≤ 0.02). None of these patients had a history of previous autoimmune disorders.

Bloodwork

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were tested in 28 and 29 patients, respectively (Table 2). ESR was elevated in 14% of these patients and CRP in 20%. The timing of positive tests ranged from 0 to 15 weeks from acute infection. Antinuclear antibodies (ANA) were tested in 16 patients, with 25% resulting positive. Three had titers of $\leq 1:40$ and one of 1:320. Of the patients with positive ANA, two were positive for anti-SSA antibodies alone, one for anti-dsDNA antibodies, and one for SSA, peripheral antineutrophil cytoplasmic antibodies, and antithyroglobulin antibodies.

New autoimmune diagnoses

Two patients (both without pre-existing autoimmune conditions) were newly diagnosed with autoimmune conditions by rheumatologists. One was diagnosed with seronegative rheumatoid arthritis based on radiographic findings and a rheumatologic exam, and another was diagnosed with Sjogren's Syndrome (ANA of 1:320, positive SSA).

Long-term outcomes

Follow-up data on clinical status greater than 12 months from acute COVID-19 infection was collected for 29/44 patients (65%). At the time of follow-up, mild neurologic improvement with no change in functional status (TND score of 2) was reported by 37% of patients. Moderate improvement with a gain of functional independence (TND score of 3)

was reported by 31%. Marked improvement (TND score of 4) was reported by 20%. No gain in neurologic function (TND score of 1) was reported by 37.9% of patients.

Discussion

This retrospective study showed results consistent with other long COVID studies. Most of the patients were women and had mild symptoms of acute COVID-19 infection. The most frequent symptoms reported were cognitive changes, fatigue, and headache. Most notably, we observed that symptoms.

persisted at 12 months or more after initial COVID-19 infection for all patients for whom this longitudinal data was available, though with varying degrees of improvement. The potential impact of chronic ongoing cognitive and neurologic symptoms after even relatively mild infection could be a potentially huge burden on the workforce and productivity of the population at large. This further highlights the importance of better understanding mechanisms and optimizing treatment in our communities.

Abnormal mental status exam findings were present in half of the patients and were without alternative explanation. MoCA results were demonstrative, with 52% of those tested scoring in the range of cognitive impairment. This provides objective evidence using a standardized testing paradigm of otherwise unexplained cognitive deficits in high-functioning individuals. Most of the patients in our cohort were employed and/or had presumptive normal cognitive function before COVID-19 infection. Ferrucci et al. (2021) similarly demonstrated cognitive abnormalities in 60% of patients at five months post-infection, though in a cohort hospitalized for acute COVID-19 infection. Others have reported cognitive testing abnormalities in hospitalized and non-hospitalized cohorts (Apple et al. 2022; Azor et al. 2024; Graham et al. 2021; Widmann et al. 2021). A recent study in the New England Journal of Medicine by Hampshire et al. (2024) with more than 100,000 participants demonstrated objectively measurable cognitive deficits persisting up to one year or more after COVID-19 infection, in comparison with a non-COVID group. Given the prevalence of long COVID, these findings may have significant implications regarding the eligible workforce and productivity worldwide. There are several potential causes for cognitive dysfunction in long COVID, including neuroinflammation, oxidative stress, endothelial dysfunction, and direct injury to neurons. Virus induced neurotoxicity is not isolated to the SARS-COV2 virus, with evidence of multiple viruses potentially triggering cytotoxic neuroinflammatory processes that increase the risk of neurodegenerative disorders such as Parkinson's or Alzheimer's

Disease (Sian-Hulsmann and Riederer 2024). It is also well known that HSV encephalitis increases risk for post-viral development of anti-NMDA encephalitis (Armangue et al. 2018). Furthermore, recent research has found indications of Alzheimer's disease-like signaling in patients with long COVID. (Reiken et al. 2022; Spudich et al. 2022)

Cerebrospinal fluid was analyzed in four patients, with albuminocytologic dissociation in two and abnormal oligoclonal banding in one. Similarly, Apple et al. (2022) demonstrated abnormal protein or oligoclonal banding patterns in 10/17 patients with cognitive complaints in long COVID, and in 0/4 controls. In patients with neurological symptoms of acute COVID-19, Jarius et al. (2022) demonstrated evidence of blood-CSF barrier dysfunction, with albuminocytologic dissociation in 40%, elevated CSF/serum albumin quotient in 50%, and mirror banding in 56% of patients tested. Interestingly, they demonstrated the persistence of findings at repeat sampling 30 days later. Also in acute COVID patients, Franke et al. (2021) found pleocytosis in 3/11 patients, elevated CSF protein in 4/11 patients, and matched oligoclonal bands in 6/9 patients. While more research is needed, our findings add potential evidence of blood-brain barrier dysfunction underlying neurological symptoms of long COVID.

Five patients had abnormalities on EEG. One had new-onset focal epilepsy requiring three anti-epileptic medications for seizure control. Another patient had epileptiform discharges arising from the left temporal region. Bozzali et al. (2021) reported a similar case in a patient 22 weeks from acute infection with EEG findings of bilateral fronto-temporal epileptiform discharges. The EEG findings in our other three patients were unexpected in individuals without neurologic disease. Other authors have similarly demonstrated abnormal findings of unclear significance on EEG in long COVID patients with neurocognitive symptoms (Egbert et al. 2020; Valencia Sanchez et al. 2021). Seizures and EEG abnormalities have frequently been described in acute COVID-19 (Egbert et al. 2020; Najjar et al. 2020), but fewer data exist for long COVID. Future studies are needed to determine the utility of EEG testing in long COVID.

The findings of neuroimaging tests were of unclear significance in our study. The most common findings were non-specific subcortical white matter changes, frequently seen and likely unrelated to the presenting symptoms. MRI findings in the literature are varied, with normal MRI or non-specific findings being the most common results according to studies conducted by Egbert et al. (2020), Valencia Sanchez et al. (2021), and Widmann et al. (2021). However, brain volume measurements and experimental functional MRI testing have demonstrated abnormalities in long COVID patients, as shown by Lu et al. (2020) and Widmann et al. (2021). Another study that examined patients' brains before

and after contracting COVID-19 found a reduction in grey matter thickness in the orbitofrontal cortex and parahippocampal gyrus, as well as a decrease in brain size. (Douaud et al. 2022)

Although the exact cause of long COVID is not entirely understood, many experts believe it may be linked to an immune-mediated, hyperinflammatory response. Our study found that 14% of patients had an elevated ESR, and 20% had an elevated CRP, which suggests that some long COVID patients may have persistent inflammation. Additionally, 25% of patients tested had elevated ANA levels, and two were diagnosed with rheumatologic diseases after COVID-19 infection. COVID-19 may trigger or activate autoimmune disorders in individuals who have a genetic predisposition towards them. Previous studies have also shown evidence of COVID-induced autoimmunity (Salle 2021). The various SARS-CoV-2 strains and vaccination status can affect the likelihood of developing long COVID. A study discovered that double-vaccinated individuals with the Delta variant were 50% less likely to experience long COVID. Additionally, the risk of long COVID was higher in those infected with the Omicron BA.2 variant than BA. (Davis H. et al. 2020)

The positivity rate of autoantibody testing in this study is quite high at 22%. This is unexpected as studies of healthy individuals have shown that the average autoantibody positivity rate is only 0.23% (Lang and Pruss 2017). In healthy individuals, the positivity rate for Anti-GAD65 antibodies is less than 3% (Rolandsson et al. 2015). Per Mayo Clinic Laboratories, positivity can be seen in up to 8% of healthy individuals over the age of 50 (mayocliniclabs.com), still much lower than the rate in our cohort. Although this cohort shows low titers, there may be an indication of an underlying aberrant immune response, but we cannot draw any definitive conclusions. Other studies have reported cases of COVID-19-related antibody-positive autoimmune encephalitis and steroid-responsive encephalopathy (Monti et al. 2020; Smyth et al. 2021; Pugin et al. 2020). Franke et al. (2021) demonstrated high rates of autoantibody positivity in CSF of critically ill acute COVID-19 patients in serum and CSF, with all patients demonstrating autoantibody binding on indirect immunofluorescence assay on mouse brain sections. In addition, known autoantibodies were identified in serum and/or CSF in 7/11 of these patients. In contrast, some studies have shown negative autoantibody testing in acute and post-infectious cases (Foucard et al. 2021; Valencia Sanchez et al. 2021).

On follow-up after > 12 months, 79% of patients continued to experience neurologic symptoms without returning to their pre-COVID-19 baseline. However, 51% of the patients reported moderate or marked improvement. Ali et al. (2022) and Kim et al. (2022) reported minimal

improvement among patients with neurologic symptoms of long COVID around one year after acute infection. By contrast, Servier et al. (2023) found that a majority of patients with long COVID (not restricted to neurologic symptoms) improved over time, reporting “slowly decreasing symptoms” in 91% and “rapidly decreasing symptoms” in 5% of patients within two years after symptom onset. These findings may suggest that the neurologic symptoms of long COVID tend to persist longer than those involving other body systems. Immune dysregulation may be responsible for the prolonged symptoms experienced in long COVID. Several studies have revealed changes in T cells, including PD1 (program cell death protein 1) expression on central memory cells, highly activated innate immune cells, a shortage of naive T and B cells, and constant expression of type I and type III interferons for at least 8–13 months. (Klein, J. et al. 2022; Glynne et al. 2022; Phetsouphanh et al. 2022).

One of the limitations of our study is the absence of pre-morbid diagnostic testing to compare to our results. This limits the interpretation of EEG and MoCA findings. However, a normal baseline is reasonably assumed in individuals with previously normal cognitive function. There was also heterogeneity in laboratory, EEG, and imaging testing locations, though most were done at Rush University Medical Center (RUMC). Another limitation is the heterogeneity in diagnostic testing performed on each patient. This is due to the retrospective nature of the study, with testing done as indicated clinically by the initial evaluating physician. This does limit the ability to assess for cohesive patterns or statistical significance of results in our cohort. Additionally, we do not report data regarding SARS-CoV-2 variants, as this is not obtained with most testing for acute COVID-19. This could help demonstrate differences in long COVID clinical presentation among variants.

Conclusions

The majority of long COVID cases in this study proceeded with mild infection and demonstrated a predominance of cognitive dysfunction. We added to the literature cases of new-onset epilepsy, abnormal cognitive testing, evidence of albuminocytologic dissociation, and new rheumatologic diagnoses underlying neurologic presentations of long COVID. Most of the patients in our study continued to experience neurologic symptoms after 12 months of COVID infection, but more than half of the patients reported moderate or marked improvement. Even though most of the group did not display any clear and consistent occurrence of symptoms that indicated a common underlying cause for their condition, our clinical data revealed various common characteristics of Long COVID patients in Chicago (IL).

These findings can guide clinicians to understand patterns in presentation and diagnostic testing, opening new avenues of research and enabling us to gain a better understanding of this syndrome that affects patients all over the world. Further studies are needed to establish the etiology of long COVID and address this major cause of disability.

Author contributions All authors contributed to the study’s conception and design. Material preparation, data collection, and analysis of the data. Dr. Brandes wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

Declarations

Ethical approval This manuscript has not been submitted to other journals. We declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere. The Corresponding Author confirms that the manuscript has been approved for submission by all named authors. IRB approval was obtained for this study. All identifying information or unique characteristics have been removed to protect the privacy of the patient, therefore, consent was not obtained.

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