Parkinson's Disease and Post–COVID-19 Syndrome: The Parkinson's Long-COVID Spectrum

Implications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Parkinson's disease (PD), particularly worsening of motor and non-motor symptoms and possibly higher mortality in those with advanced disease, comorbidities, and frailty have been reported in several case series and observational studies.[1-5] As time has evolved, the issue of long-term sequelae in patients affected by coronavirus disease 2019 (COVID-19), often referred to as "long COVID", has emerged, and recently, in the United Kingdom, the National Institute for Health and Care Excellence has defined the "post–COVID-19 syndrome" as "signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis."[6] Here we present the prevalence of post–COVID-19 syndrome in 27 patients with PD who were affected by COVID-19 across several centers in the United Kingdom, Italy, Romania, and Mexico from the beginning of March 2020 to present (Table 1). As some of the post–COVID-19 symptoms may be part of the PD clinical phenomenology, we considered symptoms part of the clinical manifestations of a post–COVID-19 syndrome only if these occurred after a confirmed SARS-CoV-2 infection or in case of an acute or subacute worsening of a preexisting symptom that had been previously stable. In addition, we report on motor worsening and increased levodopa equivalent daily dose requirements within the long-COVID spectrum. In our series, 23 (85.2%) patients with PD developed post–COVID 19 symptoms (Table 1). We report that the most common long-term effects of COVID-19 are worsening of motor function (51.9%) and increased levodopa daily dose requirements (48.2%) followed by fatigue (40.7%); cognitive disturbances (22.2%), including "brain fog", loss of concentration and memory deficits; and sleep disturbances (22.2%), such as insomnia. Broadly these symptom complexes concur with the existing literature on long COVID in the general population.[7] Interestingly, the severity of COVID-19, as indicated by a history of hospitalization, did not seem to be the *condicio sine qua non* for the development of a post–COVID-19 syndrome in patients with PD. We also believe that in some cases the stress of

TABLE 1 *Demographics, PD-related information, and prevalence of post–COVID-19 syndrome (n = 27); Data is presented as mean ± standard deviation, median (interquartile range) or number (percentage)*

Outcome measures	Results
Sex, male	16 (59.3%)
Race/ethnicity	
White	9 (33.3%)
Black	2 (7.4%)
Other	16 (59.3%)
Age at PD diagnosis, years	59.0 ± 12.7
PD disease duration at time of COVID-19 diagnosis, years	9.2 ± 7.8
H&Y stage at COVID-19 diagnosis	2.0 (1.0)
LEDD at COVID-19 diagnosis, mg	1053.5 ± 842.4
Hospitalization due to COVID-19	6 (22.2%)
Charlson Comorbidity Index at COVID-19 diagnosis	2.0 (1.5)
Post–COVID-19 syndrome	23 (85.2%)
Respiratory symptoms	
Breathlessness	1 (3.7%)
Cough	3 (11.1%)
Cardiovascular symptoms	
Chest tightness	0 (0%)
Chest pain	1 (3.7%)
Palpitations	0 (0%)
Generalized symptoms	
Fatigue	11 (40.7%)
Fever	5 (18.5%)
Pain	3 (11.1%)
Neurological symptoms	
Cognitive disturbances[a]	6 (22.2%)

(Continues)

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Key Words: COVID-19; Parkinson's disease; SARS-CoV-2; Long COVID; Post–COVID-19 syndrome

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TABLE 1 *Continued*

Outcome measures	Results
Headache	5 (18.5%)
Sleep disturbances	6 (22.2%)
Peripheral neuropathy symptoms[b]	3 (11.1%)
Dizziness	4 (14.8%)
Delirium	2 (7.4%)
Gastrointestinal symptoms	
Abdominal pain	0 (0%)
Nausea	2 (7.4%)
Diarrhea	0 (0%)
Reduced appetite	1 (3.7%)
Musculoskeletal symptoms	
Joint pain	3 (11.1%)
Muscle pain	2 (7.4%)
Psychological/psychiatric symptoms	
Depression	2 (7.4%)
Anxiety	4 (14.8%)
Ear, nose, and throat symptoms	
Tinnitus	0 (0%)
Earache	0 (0%)
Sore throat	0 (0%)
Loss of taste or smell	4 (14.8%)
Dermatological	
Skin rashes	0 (0%)
PD-specific aspects	
Motor worsening	14 (51.9%)
Increased LEDD requirement	13 (48.2%)

[a]Brain fog, loss of concentration, or memory issues.
[b]Pins and needles and numbness.
Abbreviations: PD, Parkinson's disease; COVID-19, coronavirus disease 2019; SD, standard deviation; IQR, interquartile range; H&Y, Hoehn and Yahr Scale; LEDD, levodopa equivalent daily dose.

a prolonged lockdown due to the pandemic and the reduced access to health care and rehabilitation interventions may contribute to the burden of the post–COVID-19 syndrome in PD. Therefore, post-COVID clinical manifestations may result from a combination of new symptoms and lockdown as well as viral illness-related worsening of preexisting PD features.

In conclusion, this is the first multicenter case series investigating the occurrence of post–COVID-19 syndrome in patients with PD. The small sample size and the lack of a controlled group make it challenging to draw any firm conclusions; nevertheless, we believe our case series is meaningful as it highlights the possibility of the existence of a post–COVID-19 syndrome in most patients with PD recovering from acute COVID-19. There is a clear need for greater awareness of this issue among health care professionals, and further studies are required with longitudinal follow-up of a larger cohort of patients with PD to address the natural history of the reported symptoms and with a view to developing personalized management strategies.

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