Outcome of Parkinson's Disease Patients Affected by COVID-19

There is extensive debate on the neurological consequences of corona virus disease 2019 (COVID-19) and the impact this might have for patients with neurodegenerative conditions, including Parkinson's disease (PD). Older advanced PD patients may represent a particularly vulnerable population, as respiratory muscle rigidity as well as impairment of cough reflex alongside preexisting dyspnoea may lead to increased severity of COVID-19.[1] In addition, there are indirect possible effects, such as the impact of stress, self-isolation, and anxiety, as well as the consequences of prolonged immobility because of the lockdown.[2,3]

Several observations make the link between COVID-19 and PD particularly intriguing. Antibodies against coronavirus were found in the cerebrospinal fluid of PD patients more than 2 decades ago, suggesting a possible role for viral infections in neurodegeneration.[4] Angiotensin-converting enzyme 2 (ACE2) receptors are highly expressed in dopamine neurons, and they are reduced in PD because of the degenerative process; therefore, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–related brain penetration may cause additional harm and worsen symptoms and may increase the requirement of dopamine replacement therapy, as evident in 5 of our cases.[5,6] Interestingly, the ability of coronaviruses to enter the brain through the nasal cavity determines anosmia/hyposmia and ageusia in many infected subjects, a symptomatology that closely resembles one of the most prominent premotor symptom of PD.[7] Finally, the dopamine synthetic pathway is possibly involved in the pathophysiology of COVID-19, as ACE2 and dopamine decarboxylase coexpress and coregulate in nonneuronal cell types, which may indicate dopamine depletion and the need for considering levodopa as treatment.[8]

Outcomes of PD patients infected by SARS-CoV-2 are unknown. We present here the outcome of 10 clinical cases (Table 1) collected from the experience at the Parkinson and Movement Disorders Unit in Padua, Italy, and the Parkinson's Foundation Centre of Excellence at King's College Hospital in London, UK, from the beginning of March to the current period. The PD center in Padua has a catchment of 1022 patients, mainly in the province of Padua, which had 3407 cases of COVID-19, 2 of whom were advanced PD patients. Both were women residing in nursing homes with severe motor manifestations, and both were treated with levodopa therapy (Table 1). One remained asymptomatic, whereas the other, who in the last months had been suffering from deteriorating cognition and hallucinations, developed respiratory problems and died. The King's center has 4000 PD patients in the catchment and is currently following more than 600 patients. In all, thus far, 8 cases have been identified with COVID-19, and clinical details are presented here. The Kings' COVID-19 PD group consists of 6 men and 2 women, all older than 60 years of age with severe motor dysfunction, comorbidities, and most requiring additional levodopa dosing following infection (Table 1). Anxiety and other nonmotor features, such as fatigue, orthostatic hypotension, cognitive impairment, and psychosis, also worsened during the infection. Fatigue was a dominant symptom during the SARS-CoV-2 infection in all cases on advanced therapies. Three patients died from COVID-19 pneumonia.

These findings suggest that PD patients of older age (mean, 78.3 years) with longer disease duration (mean, 12.7 years) are particularly susceptible to COVID-19 with a substantially high mortality rate (40%). Those on advanced therapies, such as deep brain stimulation or levodopa infusion therapy, seem especially vulnerable, and a mortality rate of 50% among our 4 such cases is of concern. Although 2 recent articles have addressed the issue of COVID-19 in PD, none specifically showed cases directly affected by COVID-19, and we believe ours is the first report of this nature.[2,3] The report of Prasad et al focuses on the perceptions of SARS-CoV-2 infection in 100 PD patients and some symptoms listed tally with our observations in a real-life population with COVID-19.[2] Many national and charity guidelines do not list PD or specifically older subjects on advanced therapies as a susceptible group, and this information needs to be amended in light of these new data.[9]

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TABLE 1. Clinical features and outcomes of Parkinson's disease patients with corona virus disease 2019.

Patients	Age	Sex	PD duration (years)	PD therapy	Comorbidities	Clinical picture requiring SARS-CoV-2 testing	Therapeutic interventions(antibiotics and intensive care)	Outcome
1	76	F	28	• Carbidopa-levodopa 25/100 mg 1 table t 3 times daily and ½ tablet once daily • Rotigotine 4 mg 1 patch once daily Safinamide 50 mg 1 tablet once daily	• Dementia • Dysphagia • Severe joint deformities	• Fever	• No intensive care required	Spontaneous recovery
2	79	F	12	• Carbidopa-levodopa 25/100 mg 1½ tablets 4 times daily	• Dementia • Hallucinations	• Fever • Cough • Shortness of breath • Confusion	• CPAP required (no resuscitation was advised)	Died 14 days after onset of respiratory symptoms
3	81	M	10	• Carbidopa-Levodopa CR 25/100 mg 1 tablet once daily • Carbidopa-Levodopa 25/100 mg 2 tab 3 times daily	• Hypertension • Ischemic heart disease • Chronic kidney disease • Dementia	• Fever • Dry cough • Shortness of breath	• Antibiotics (piperacillin/ tazobactam + clarithromycin) • No intensive care or CPAP required • Required increased levodopa dosing	Transferred to rehabilitation ward after 11 days of hospitalization
4	94	M	2	• Carbidopa-Levodopa 25/100 mg 1 tablet 3 times daily	• Angina pectoris • Osteoporosis	• Multiple falls and head injury • Cough • Delirium • Arrhythmia	• Antibiotics (amoxicillin/ clavulanic acid + clarithromycin) • No intensive care or CPAP required	Transferred to rehabilitation ward for respite care; 10 days of hospitalisation
5	87	M	6	• Carbidopa-Levodopa 25/100 mg 1 tablet twice daily • Carbidopa-Levodopa 25/100 mg 1½ tablets twice daily	• Congestive Cardiac failure • Chronic obstructive pulmonary disease • Atrial fibrillation • Orthostatic hypotension • Asthma	• Syncopal episodes • Hallucinations • Fall with facial trauma • Cough	• Antibiotics (amoxicillin/ clavulanic acid) • No intensive care, CPAP not possible because of facial trauma (no resuscitation was advised) • Required increased levodopa dosing	Died after 10 days of hospitalization
6	83	F	3	• Carbidopa-Levodopa 25/100 mg 2 tablets twice daily and 1½ tablets twice daily	• Anxiety disorder	• Worsening of mobility with fall and hyperCKemia • Dry cough • Fatigue • Worsening of anxiety	• No intensive care or CPAP required • Required increase in levodopa dosing	Transferred to neurorehabilitation after 25 days of hospitalization

(Continues)

TABLE 1. Continued

Patients	Age	Sex	PD duration (years)	PD therapy	Comorbidities	Clinical picture requiring SARS-CoV-2 testing	Therapeutic interventions(antibiotics and intensive care)	Outcome
7	61	M	17	• IJLI 1684 mg daily • Carbidopa-levodopa 25/100 mg 1 tablet once daily • Rotigotine 4 mg 1 patch once daily • Opicapone 50 mg 1 tablet once daily	• Traumatic fractures secondary to falls • Orthostatic hypotension	• Fever • Cough • Fatigue	• Antibiotics • CPAP required	Died during hospitalization
8	75	M	10	• IJLI 1262 mg daily • Opicapone 50 mg 1 tablet once daily • Carbidopa-Levodopa CR 50/200 mg 1 tablet once daily • Carbidopa-Levodopa CR 25/100 mg 1 tablet once daily • Levodopa- Benserazide 100/50 mg 1 tablet 3 times daily	• Orthostatic hypotension • Osteoporosis • Benign prostatic hyperplasia • Depression • Neuropathic pain	• Fever • Cough • Fatigue	• Antibiotics • CPAP required	Died during hospitalization
9	72	M	15	• DBS bilateral STN • Subcutaneous Apomorphine infusion 46 mg daily • Rasagiline 1 mg 1 tablet once daily • Ropirinole CR 2 mg 1 tablet once daily • Levodopa-benserazide 50/12.5 mg 1 tablet 4 times daily • Carbidopa-Levodopa CR 25/100 mg 1 tablet 3 times daily	• Asthma • Diabetes mellitus type II	• Fever • Fatigue • Worsening of motor symptoms	• Required increase in levodopa dosing • No intensive care or CPAP required	Spontaneous recovery, waiting for transfer for rehabilitation
10	75	F	24	• IJLI stopped due to recent PEG-J tube malfunctioning • Levodopa-Benserazide 100/25 mg six times daily • Carbidopa-Levodopa CR 25/100 mg once daily	• Atrial fibrillation • Cognitive impairment	• Fatigue • Cough	• Required increase in levodopa dosing • No intensive care or CPAP required	Recovering

CPAP, continuous positive airway pressure; CR, controlled release; DBS, deep brain stimulation; IJLI, intrajejunal levodopa infusion; F, female; M, male; PD, Parkinson's disease; PEG-J, percutaneous endoscopic transgastric jejunostomy; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STN, subthalamic nucleus.

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