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Case report

Neurological complications in infection with the SARS-COV-2 virus: Parkinson's disease and the impact on professional reintegration - case study

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Abstract

Complications of the SARS-CoV-2 infection have significantly impacted the affected people's quality of life and professional activity. Neurological manifestations may be present from the onset of infection but also in the course of the disease. The most common neurological symptoms are headache, anosmia/hyposmia, ageusia/dysgeusia, and myalgia. The studies also mention severe complications such as stroke, cerebral hemorrhage, meningitis, encephalitis, Guillain-Barré syndrome, acute transverse myelitis, convulsions, and movement disorders, as the infection with the SARS-CoV-2 virus is affecting both central and peripheral nervous systems. SARS-CoV-2 can worsen the symptoms of Parkinson's disease, increasing the mortality rate in patients with advanced disease.

The potential risk of inducing Parkinson's disease has also been suggested, with the virus penetrating the brain where it can trigger cellular processes involved in neurodegeneration. We present you with the case of a nurse in the medical field, without comorbidities, who developed Parkinson's disease after infection with the SARS-CoV-2 virus. Establishing a cause-and-effect relationship between the onset of Parkinson's disease and viral infection may be possible, but the mechanisms by which it affects the nervous system and the involvement of the immune system in the pathogenesis of these manifestations are still under study. The progression of the disease, functional status, and ability to work can have a negative impact on professional activity.

Keywords: *SARS-CoV-2, Parkinson's disease, ability to work, health personnel*

Introduction

Parkinson's disease is a degenerative neurological condition consisting of a motor syndrome characterized by bradykinesia (slow movements with reduced amplitude), tremors, hypertonia (muscle stiffness), and difficulties in performing certain physical activities such as walking or maintaining balance [1]. Motor disorders cause progressive disability with impaired daily activities and a decreased quality of life. Studies conducted in the context of the COVID-19 pandemic suggest a possible

link between COVID-19 and the increased risk of developing Parkinson's disease in the short and long term, a few years after the viral infection [2].

Brundin et al. [2] discuss three possible mechanisms that may explain the association between parkinsonism and SARS-CoV-2 infection:

1. Damage to the nigrostriatal system through vascular lesions.
2. Damage to nigral neurons through local inflammatory mechanisms generated by the cytokine storm associated with COVID-19.
3. The possible neurotropism of SARS-CoV-2.

This paper presents the case of a nurse in the medical field, without comorbidities, who was diagnosed with Parkinson's disease a few months after infection with the SARS-CoV-2 virus.

Case presentation

We are reporting the case of a 52-year-old nurse who presented herself in the occupational medicine specialist's office for insomnia caused by an important algic syndrome in the right shoulder, nocturnal paresthesias in the right upper limb, increased daily fatigue, and fine tremor in writing. She has no significant heredocolateral and personal history, and she didn't get immunized with a vaccine against covid-19. She works in an emergency hospital on 7-hour shifts, including night shifts. In September 2021, she tested positive for SARS-CoV2 infection. The symptomatology started with a fever that persisted for five days (maximum 39° C), chills, important myalgia, hyposmia, insomnia, and cough, initially dry and subsequently slightly productive, with a significantly altered general status. Treatment at home was symptomatic (ibuprofen, paracetamol) and antibiotic (combination of levofloxacin 500mg/day and trimethoprim/sulfamethoxazole 480mg x 2/day) for seven days.

Two months after the SARS-CoV2 infection, control chest computer tomography showed a normal lung picture.

Four months after the SARS-CoV2 infection, she approached a neurology ambulatory for the appearance of resting tremor in the right hand, pain in the right shoulder, predominantly nocturnal paresthesia, a change in tonicity in the right upper limb, and writing (micrography). Craniocerebral MRI detected several brain lesions of demyelinating type of vascular-ischemic origin, cerebellar neuro-vascular contact, levo-convex cervical scoliosis, cervical arthrosis changes, and tiered disc protrusions. The decision was to carry out the challenge test with levodopa (250/25mg/day) and dopamine agonist (50 mg/day), significantly reducing the tremors.

At the neurological examination, a resting and intentional tremor in the right hand was observed, more noticeable at the end of the period of action of levodopa treatment, normal oculomotricity, slightly hypomimic symmetrical facies, Romberg test with unsystematic lateral deviations, bilateral fixation fine shaking, without swallowing disorders for solids and liquids. The patient is walking without support, muscle strength is diminished at the level of the right upper limb due to accentuated pains at mobilization, slight plastic hypertonia is present at the level of the right upper limb and right lower limb, the Noica sign is evident on the right (in extrapyramidal lesions the alternating flexion/ extension movements of the wrist blocked during consecutive raise of the ipsilateral lower limb), the cogwheel sign is present on the right, without coordination disorders, osteotendinous reflexes at the level of the upper limbs are more vivid on the right, osteotendinous reflexes at the level of the lower limbs more accentuated bilaterally, Achilles reflexes present bilaterally, plantar cutaneous reflex determining bilateral normal plantar flexion (Babinsky sign absent), the hand-chin reflex is present bilaterally, paresthesia at the level of the upper right limb predominantly distal that is accentuated during the night, mild hypoesthesia at the level of the upper and lower right limb.

The right shoulder ultrasound detected at the supraspinous tendon level a calcification of 6.5 mm at the enthesis, normally mobilizable in abduction, without subacromial-subdeltoid conflict, and with normal position and fibrillar structure for the long biceps brachial head, subscapular, infraspinatus tendons. On ultrasound the acromioclavicular joint, humeral head and subacromial-subdeltoid bursa were normal.

During the hospitalization, the patient followed antiparkinsonian treatment (levodopa 250/25 mg/day, dopaminergic agonist- piribedil 50 mg/day), neurotrophic, anti-inflammatory, gastroprotective, and a combination of balneotherapy, physiotherapy, and kinesiotherapy with favorable evolution.

The diagnosis at discharge was of Parkinson's disease stage I, cervical discal spondyloarthropathy tiered with right C5-C6 radiculopathy.

The recommendations of the neurologist specialist at discharge were to avoid psycho-emotional stress, intense physical effort, and working night shifts.

The patient continued at-home treatment with levodopa 250/50 mg/day, dopamine agonist 50mg/day, neurotrophic, anti-inflammatory during algic

periods associated with proton pump inhibitors.

Six months after the diagnosis of Parkinson's disease, the worker presented herself in the occupational medicine cabinet accusing of significant pain in her right shoulder and nocturnal paresthesia, significant insomnia, increased diurnal fatigue that evolved to exhaustion, fine tremor, unnoticeable, in writing.

We also considered possible side effects of drugs containing levodopa, carbidopa, and dopaminergic agonists: sleep disorders, nausea, hypotonia, arrhythmias, and dyskinesias.

We issued an aptitude sheet with special supervision and conditional "fit for work" status and the recommendations: no working night shifts, reassessment after three months with medical documents from the neurologist and the specialist in medical recovery and rehabilitation.

At the reassessment, following the recommendations, she presented in good general condition, with a minimal right-hand tremor on rest and intentional, with the same neurological findings on clinical examination, diminished paresthesia at the level of the right upper limb, yet accentuated at night, but with fewer episodes of insomnia and lesser daytime fatigue.

We performed paraclinical antibody panels to exclude some autoimmune pathologies, all of which were negative. Recommendations to avoid psycho-emotional stress, intense physical exertion, and avoiding night shifts for another three months were maintained.

Discussion

Parkinson's disease is a movement disorder that associates a variety of non-motor symptoms encountered in almost all patients, such as hyposmia, constipation, urinary dysfunction, orthostatic hypotension, memory loss, depression, pain, and sleep disorders. [3] The onset occurs, in most cases, between 50-60 years, twice more frequently in men. [4] The etiology of Parkinson's disease is not entirely understood. The main symptoms of the disease develop predominantly due to injury or death of nigrostriatal neurons in the brain and depletion of striatal dopamine reserves. One of the leading hypotheses suggests that the aggravation of oxidative stress with the excessive accumulation of reactive oxygen species leads to an accumulation of the alpha-synuclein protein in the form of cytoplasmic aggregates (Lewy bodies). A recent hypothesis proposes a mechanism of brain damage in two steps: (i) the penetration of an "unknown pathogen" into the brain through the olfactory system or gastrointestinal tract and (ii) the activation of glial cells by the pathogen with increased susceptibility of the brain to oxidative stress which accelerates the aging process of the brain and stimulates neurodegeneration. [5]

Although the symptoms of Parkinson's disease do not frequently occur in patients with post-COVID syndrome, [6] data from the literature support the association between SARS-CoV-2 infection and Parkinson's disease. Goertler et al. [6] analyzed the association between the onset of Parkinson's disease and COVID-19 in six patients with new motor symptoms of parkinsonism. In five of the six patients, nuclear imaging proved impaired dopaminergic absorption in the basal ganglia. Symptomatology in these cases began acutely with stiffness, bradykinesia, and tremor after SARS-CoV-2 infection. [6] Ages ranged from 35 to 72 years. COVID-19 symptoms were mild to moderate in three instances: one patient had a short three-day hospitalization, while the other two did not need hospitalization or treatment. In the other three cases, treatment in intensive care was required, with mechanical ventilation or oxygen therapy. The symptoms of Parkinson's disease started from 5 days to 10 weeks after the positive SARS-CoV-2 test. In our case, the symptomatology appeared later, the patient reaching the neurologist only four months after the SARS-CoV2 infection. Symptoms also included resting tremors in the right hand, paresthesia, and changes in tone in the upper right limb accompanied by a change in writing. A tremor in the right hand with the modification of writing and speaking difficulties was also highlighted in the case presented by Cohen et al. [7] It should be noted that even in this case, the onset of neurological symptoms was faster in the first month after the diagnosis of COVID-19. In the first two weeks after the diagnosis of COVID, rapid onset and a more severe evolution, with a rigid akinetic syndrome, were described by Faber et al. [8]

It should also be mentioned that the favorable response to levodopa is common to both the case presented by us and the cases in the literature. Méndez-Guerrero et al. [9] report a paper on a patient with a severe form of COVID-19 in whom the neurological symptomatology started more than a month after the SARS-CoV-2 infection. The patient experienced asymmetric hypokinetic-rigid syndrome with fine resting and postural tremor, myoclonus, and opsoclonus, with a significant but incomplete symptomatic improvement after 14 days without any specific treatment. The case presented by us is different regarding the clinical picture and long-term evolution.

Rao and collab. [10] wrote on several instances of parkinsonism occurring post-COVID-19. One of the patients, diagnosed with persistent parkinsonism with an excellent response to levodopa-carbidopa, showed a late onset of neurological symptoms more than two months after infection with SARS-CoV-2. [10]

As evidenced by the data published so far, cases with late onset of Parkinson's disease after COVID-19 are relatively fewer. In the case we described, the symptomatology started late and evolved slowly, so the patient requested neurological consultation only four months after the SARS-CoV-2 infection. Despite the positive evolution and the favorable response to treatment, the patient's work capacity as a proficient medical nurse remains affected even more than six months after the diagnosis of COVID-19. As a result, the occupational medicine doctor recommends removing the participation in the ward schedule and reassessment every three months. The onset of Parkinson's disease may result from numerous minor neural lesions (for example, in viral respiratory infections similar to SARS-CoV-2) that occur throughout life. It is well known that anosmia and ageusia are common nonmotor traits of Parkinson's disease. [11]

The role of the SARS-CoV-2 virus in the pathophysiology of Parkinson's disease can be explained by its penetration into different types of cells to reproduce in the human body. SARS-CoV-2 uses the type 1 transmembrane receptors of the angiotensin-converting enzyme 2 (ACE2) located on epithelial and endothelial cells of the respiratory system, immune cells, and cells of the central nervous system (CNS), which may explain the neurological symptoms occurring in COVID-19. [10]

There are two possible ways in which SARS-CoV-2 ends up invading brain tissue:(i) by blood and (ii) by olfactory route using retrograde axonal transport. [6] Interaction with ACE2 receptors of vascular endothelial cells in the CNS increases the permeability of the blood-brain barrier and causes cerebral edema with consecutive microhemorrhages. SARS-CoV-2 can also act directly on neurons due to the affinity of the virus's S1 spike protein to ACE2 receptors expressed on neurons. Damage to brain tissue could be due to COVID-19-related hypercoagulation, hypoxia, electrolyte imbalances, inflammation, and the immune response (cytokine storm). [13]

The association of Parkinson's with viral infections was found during the Spanish influenza pandemic (influenza A H1N1 virus) in 1918 when most patients who also developed encephalitis during infection with the influenza virus also presented symptoms of Parkinson's. Data from the literature support the relationship between Parkinson's disease and some viral infections such as influenza virus infections, herpes simplex virus, hepatitis B virus, and hepatitis C virus. [15]

The primary encounter with the virus occurs in mononuclear phagocytic cells, such as monocytes, macrophages, and dendritic cells. The stimulation of the innate and adaptive immune system in response to viral infections leads to the destruction of infected cells and the release of cytokines (one of the first synthesized is the tumor necrosis factor-alpha TNF) with the induction of inflammation that has severe pathological consequences for the host. Inflammation is caused by the excessive release of antibodies, interferons, proinflammatory cytokines, activation of the complement system, or cytotoxic T-cell hyperactivity. [16]

Detection of viral RNA and specific characteristic proteins in brain specimens examined post-mortem from patients diagnosed with COVID-19 suggests SARS-CoV-2 neurotropism. [13] The N protein of SARS-CoV-2 accelerates alpha-synuclein aggregation in vitro, leading to an accumulation of alpha-synuclein in the nigrostriatal dopaminergic system and results in neurodegeneration, clinically visible in symptoms typical of Parkinson's disease. [17]

The SARS-CoV-2 virus uses transmembrane ACE2 receptors as the intracellular pathway of entry. They can be found both in the olfactory tract and at the intestinal level, common primary locations of alpha-synuclein aggregates in both Parkinson's disease and COVID-19. The renin-angiotensin system was found to be involved in initiating the proinflammatory cytokine cascade because patients with Parkinson's disease treated with ACE inhibitors had a better response to treatment. [8]

Conclusion

Establishing a cause-and-effect relationship between the onset of Parkinson's disease and infection with the SARS-COV2 virus is possible.[19] As a result, regular monitoring of people diagnosed with COVID-19 is essential. The presented case emphasizes that the emergence of a degenerative neurological pathology, in the context of the COVID-19 pandemic, by affecting the functional status and work capacity, has a negative impact on professional activity. Adapting the patient's work schedule, temporarily removing from night shifts, and regulating the circadian rhythm improved symptomatology and quality of life.

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