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COVID-19 Associated Dysautonomia in a Non-Critically Ill COVID-19 Patient

Dear Editor:

A wide variety of symptoms have been reported since the start of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. One of those manifestations is dysautonomia, which is autonomic nervous system (ANS) dysfunction resulting in either over-responsive or under-responsive sympathetic or parasympathetic components of the ANS. Previously, acute dysautonomia has been linked to viral infections such as mumps, herpes, human immunodeficiency virus (HIV), hepatitis C virus, Epstein-Barr virus, and Coxsackie viruses.[1]

Acute autonomic dysfunction or acute dysautonomia can manifest with a wide range of clinical manifestations, including headache, somnolence, labile blood pressure, orthostatic hypotension, tachycardia or bradycardia, impotence, bladder dysfunction, and bowel functions alterations.[2]

In response to the previously published journal article "Dysautonomia: An Overlooked Neurological Manifestation in a Critically ill COVID-19 patient" by Eshak *et al*,[2] which described dysautonomia in a critically ill patient, we report a COVID-19 case that presented initially with acute dysautonomia manifested by recurrent acute attacks of hypertension and tachycardia in the absence of respiratory symptoms in a previously healthy adult female.

A-58-year-old female patient with no previous medical history presented complaining of recurrent unexplained acute attacks of hypertension palpitations at rest, severe headache, and somnolence a few days after attending a social gathering; however, she denied any respiratory complaints or fever. Her clinical examination was unremarkable except for recurrent episodes of hypertension with blood pressure (BP) reaching 180/110 mmHg and heart rate (HR) of 130 beats/minute at rest, associated with severe headache and somnolence; nevertheless, no episodes of postural hypotension or postural tachycardia. A full laboratory and diagnostic imaging workup including complete blood count, full chemistry panel, urinary metanephrines, and computed tomography (CT) of the brain, chest and abdomen was done revealing no abnormality apart from mildly increased C-reactive protein (CRP). She tested positive for COVID-19 by reverse-transcriptase polymerase chain reaction (RT-PCR). Her condition was thought to be explained by viral infection-induced acute sympathetic dysfunction. She was managed conservatively at home with continuous BP monitoring using an ambulatory BP monitor that recorded episodes of hypertension with BP reaching 170/100 mmHg. She was commenced on short-acting calcium channel blockers (CCBs) for hypertensive episodes and instructed to maintain a euvolemic state. Two weeks later, her BP was maintained, ranging from 110/80 mmHg to 130/90 mmHg with HR ranging from 75 to 85 beats/minute at rest, without receiving any antihypertensive medications. After that she was followed-up at 2-week intervals for 3 months, at which her BP was maintained at 110/80 mmHg with a resting HR of 70 beats/minute without treatment.

Several previous reports highlighted the potential neurotropism of COVID-19 with a high binding affinity to medullary structures, due to their increased angiotensin-converting enzyme 2 (ACE2) receptor expression.[3] COVID-19 associated neurological symptoms are ranging from headache, anosmia, and dysgeusia to neuropathy, encephalitis, cerebrovascular stroke, Guillan-Barrè Syndrome (GBS) and demyelination.[3]

Eshak *et al*,[2] was the first to describe a case of acute dysautonomia causing hemodynamic instability manifested by fluctuating BP through the day, especially with postural changes, in a critically ill old age male with multiple co-morbidities admitted to intensive care unit (ICU) with COVID-19 severe pneumonia, suggesting that hemodynamic instability may be explained by afferent baroreflex failure secondary to SARS-COV-2 infection and nucleus tractus solitarius (NTS) invasion resulting in highly labile BP with hypertensive crises alternating with hypotensive episodes; orthostatic hypotension was occasionally present. Eshak *et al*,[2] recommended to maintain a euvolemic state and to avoid excessive fluid resuscitation during hypotensive episodes with gradual titration of vasopressors if needed to avoid overshooting blood pressures and short-acting anti-hypertensive medications use in hypertensive crisis.

On the contrary, our case presented only with acute dysautonomia in the form of sympathetic overactivity with recurrent attacks of elevated BP, resting tachycardia. It was neither related to posture nor associated with postural hypotension. The autonomic dysfunction improved after resolution of the acute phase of infection.

Autonomic impairment can even persist months after the acute infection. Miglis *et al*,[4] reported postural tachycardia syndrome (POTS) as a complication of COVID-19 infection in a young healthy female. Although early in the acute phase of infection she reported tachycardia as well as COVID-19 related respiratory symptoms, these symptoms resolved within 3 weeks while symptoms of autonomic dysfunction such as tachycardia persisted and augmented over the next few months after the resolution

of COVID-19 infection. Her autonomic tests revealed hyperadrenergic POTS, but her serum norepinephrine was not only normal but even lower than levels typically reported in POTS. Several mechanisms were proposed to explain the pathophysiology of post-COVID-POTS. First, SARS-CoV-2 might affect extracardiac post-ganglionic SNS neurons resulting in an increase in cardiac SNS outflow, as in neuropathic POTS. Also, it might invade the brainstem and alter medullary centers functions causing an increased central sympathetic discharge. Another possible mechanism may be autoimmune antibody production triggered by a viral infection. Finally, POTS deconditioning can be part of a vicious cycle involving low stroke volume, high SNS or SAS outflows, exercise intolerance, and fatigue.[5]

Our case highlights that even mild cases of COVID-19 can present with acute dysautonomia even in immunocompetent patients. Further close follow-up is required to detect cases of persistent autonomic dysfunction after the resolution of COVID-19 infection.

DECLARATION OF COMPETING INTEREST

All the authors declare no conflict of interest.

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