

COVID-19 and restless leg syndrome

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Abstract

The deadly COVID-19 pandemic has affected more than 200 million people and has killed more than 4 million people worldwide. A number of neurological manifestations of COVID-19 infection have been described, though sleep related problems are less reported. We describe a case of restless leg syndrome related to COVID-19 infection, which improved after treatment with dopaminergic therapy. We discuss the possible pathophysiological mechanisms underlying sleep disturbances and RLS in a patient with COVID-19. The sleep related problems could be another important manifestation of the deadly virus and need to be actively looked for.

Keywords: Restless legs; COVID-19, sleep disorders, movement disorders

INTRODUCTION

The Coronavirus 19 pandemic is nearing its second anniversary and has affected close to 200 million people worldwide with more than four million deaths. Effects of the viral infection, host inflammatory response and post-infectious sequelae have been reported to involve almost all organ systems of the human body. It is well known that nervous system involvement in form of anosmia or ageusia herald disease onset.¹ Central nervous system involvement, peripheral neuropathies and neuropsychiatric manifestations have been reported, both concurrent with COVID-19 as well as after a bout of viral illness. Sleep disturbances in form of insomnia and restless leg syndrome (RLS) have been reported in limited number of cases previously.^{2,3} Here we report another patient presenting with restless leg syndrome due to COVID-19.

CASE REPORT

A 65-year-old man, previously diagnosed to have diabetes mellitus, presented to us with fever, dry cough, generalized body weakness and malaise. He complained of an uncomfortable sensation in his thighs and legs. Because of this, he could not lie down or sit at one place and felt an urge to move around the room, after which the sensations were partially relieved. These symptoms were more prominent in the evening hours than during the day or when the patient had prolonged sitting.

The patient did not have similar complaints or any sleep disturbances in the past. On examination, pulse oximeter saturation was 92% on room air. He did not have any lateralizing neurological deficits. Lower limb motor power, sensory examination and deep tendon reflexes were normal. Chest radiograph revealed bilateral opacities. Computed tomography of chest showed ground glass opacities in both lung fields, predominantly in the lower lobes and sub-pleural location with a CT severity index 15/25. (Figure 1) On basis of these findings, a possibility of atypical (viral) pneumonia was considered. Nasopharyngeal swab was positive for COVID-19. Laboratory testing revealed mild anemia (Hb = 10.5gm%) with low leucocyte count, high ESR (54mm) and C-reactive protein (35 mg/L). Glycated hemoglobin level was 6.8%. Other parameters, including liver and kidney function tests, serum ferritin levels (220 ng/mL), d-dimer and coagulation profile were normal. In view of positive COVID-19 swab, he was treated with oxygen supplementation, azithromycin, favipiravir, ivermectin and other supportive therapy, as per the local guidelines. Nerve conduction study of all four limbs was normal. The patient continued to complain of unpleasant, aching and uncomfortable sensation in his legs because of which he did not sit at one place. A possibility of restless leg syndrome (RLS) was considered and he was started on gabapentin 600 mg/ day and clonazepam 1.5 mg/day. The severity of RLS based on the International RLS

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study group (IRLSSG) scale was “severe” – a score of 27/40. Polysomnography could not be done due to COVID-19 positivity. The patient recovered from his viral illness over the next 5 days. However, the symptoms of RLS could not be controlled even after 10 days of escalating drug doses and hence, ropinirole was added in doses of 0.5 mg at night. After 2-3 days of starting ropinirole, patient reported improvement in his symptoms. The dose of ropinirole was increased to 1mg/day after 1 week and was continued at that dose.

DISCUSSION

Neurological involvement due to COVID-19 has been extensively reported, both in the central and the peripheral nervous system. But, the relationship of sleep disturbances and COVID-19 has not been studied in detail. Any acute illness or hospital admission is known to cause some amount of sleep problems, mainly in form of insomnia and frequent awakenings. RLS is a very specific sleep related phenomenon which is generally due to a neurotransmitter imbalance in the brain. Though there is no definite cause; iron deficiency, pregnancy, uraemia, peripheral neuropathy and hypoxia are suggested to trigger RLS like symptoms.⁴

The possible link between RLS and COVID-19 can be attributed to different factors which were seen in our patient. Firstly, the patient was

mildly anemic. This in association with systemic iron deficiency due to widespread inflammation and cytokine storm can trigger RLS. Secondly the patient had diabetes, which itself has been previously linked to RLS by causing diabetic peripheral neuropathy. However, the patient had a good control of diabetes and did not have any signs or symptoms suggestive of peripheral neuropathy. Thirdly, our patient had low oxygen saturation. Hypoxia itself can lead to a number of hormonal and neuro-transmitter changes, triggering RLS. Finally, any acute illness and hospitalization is known to disturb sleep. The anxiety caused by a diagnosis of COVID-19 along with isolation in a single room can further exacerbate sleep disturbances.

Another possible link between COVID-19 and RLS may be through the renin-angiotensin-aldosterone system (RAAS). It is well established that the novel coronavirus-19 utilizes the angiotensin-converting enzyme-2 (ACE2) for cell entry and therefore has a direct effect on the RAAS.⁵ Involvement of the RAAS has been suggested in genesis of sleep related problems including RLS in patients with uraemia.⁶ In experimental models, angiotensin (via type I receptors) has been shown to amplify dopaminergic degeneration and neuroinflammation leading to dopamine deficiency in brain.⁷ Stimulation and over-reaction of RAAS may be responsible for the myriad manifestations of COVID-19, including RLS.

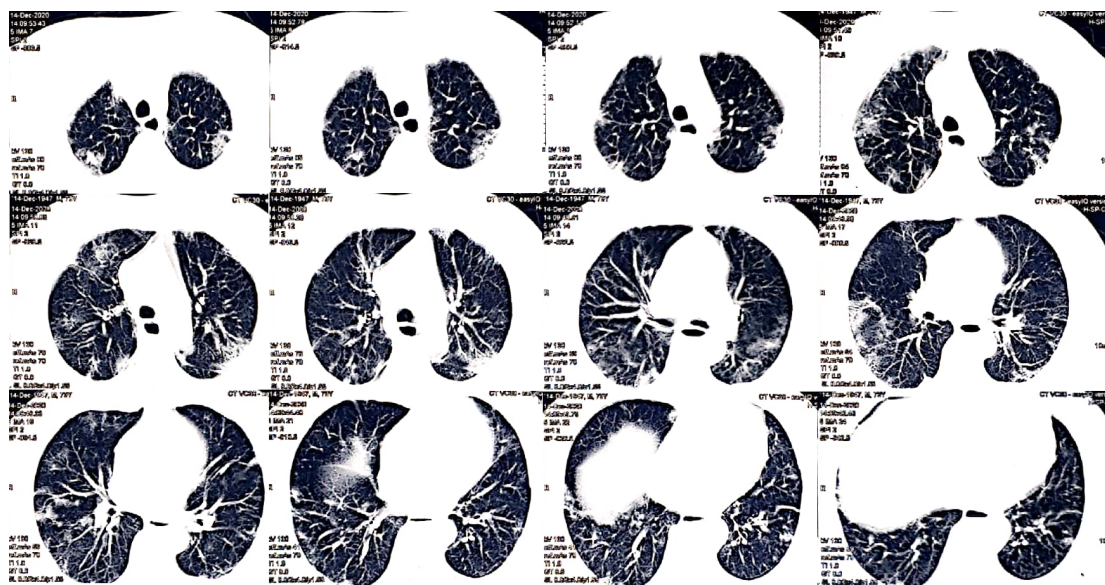


Figure 1. CT scan of the chest: Ground glass opacities in bilateral lung fields, predominantly in the lower lobes and sub-plural location. CT severity index 15/25.

Our patient was treated with dopaminergic drugs, ropinirole and gabapentin. The patient remained symptomatic for almost 2 weeks, before reporting mild improvement after dose adjustment of these drugs. Significant improvement after adding ropinirole points to a possible role of dopaminergic imbalance in the pathophysiology of RLS. The patient is doing well and is asymptomatic at 3 months follow up.

DISCLOSURE

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