

# Transverse myelitis in COVID-19 patients: Report of two cases

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## **Case Report**

**Keywords:** Transverse myelitis, COVID-19, Paraparesis, LETM

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# Abstract

**Background:** COVID-19 has been associated with several neurological complications. One of these complications is transverse myelitis. Several cases of acute transverse myelitis are reported in association with this disease among the world. As there is lack of knowledge about the association of COVID-19 and myelitis and the clinical features of this complication are still ambiguous, we report two patients with transverse myelitis following COVID-19 infection.

**Patients:** This study was performed in a referral center of COVID-19 in Iran(Shohada Tajrish hospital) and two patients with paraparesis and diagnosis of transverse myelitis were enrolled. Both patients had longitudinally extensive transverse myelitis that resulted in paraparesis. One of the patients had favorable outcome after treatment with plasma exchange but the other had no improvement following treatment.

**Conclusion:** Transverse myelitis could be a complication of COVID-19 and infarction and inflammation could be suggested as probable mechanisms for this condition.

## Background

The novel 2019 coronavirus epidemic first started in Wuhan, China and spread to almost all countries around the world, most of them currently struggling with the consequences of the disease.(1) Common clinical manifestations of coronavirus disease 2019(COVID-19) are fever and cough but the disease can progress to a fatal respiratory distress.(2) In addition, COVID-19 has been associated with several neurological manifestations including febrile seizures, headache, myalgia, encephalopathy, encephalitis, stroke, and acute polyneuropathy.(3)

It has been suggested that COVID-19 enters cells via angiotensin-converting enzyme 2 (ACE2). (4) The ACE2 receptors are expressed on brain and spine vascular cells as well as alveolar epithelial cells, intestinal enterocytes and arterial and venous endothelial cells and this is suggested as a pathway of virus entry to central nervous system.(5)

As the pandemic is evolving, new complications are attributed to COVID-19. One of these complications is transverse myelitis. Several cases of acute transverse myelitis are reported in association with this disease among the world. (6–10) In this article we report two cases of transverse myelitis following COVID-19 infection that were hospitalized in Shohada-Tajrish hospital, affiliated with Shahid-Beheshti university of medical sciences.

## Patient 1

A 47 year old man was admitted to the emergency room with paraplegia since 6 hours ago. His earliest symptoms was urinary retention that started 12 hours before lower limbs weakness. The paraplegia occurred abruptly and was accompanied with a dull pain in the flanks and abdomen that subsided 1-2 hours later. The patient also reported decreased sensation of lower limbs and torso. He denied any

symptoms in upper limbs. 10 days before the onset of paraplegia, the patient had fever, cough and diarrhea. He was diagnosed with COVID-19 and was quarantined at home. He had no past medical history.

On physical examination the patient was afebrile with respiratory rate of 15/minute, and oxygen saturation of 98% on room air. Initial neurological examination revealed intact cranial nerves, and lower limbs weakness with medical research council(MRC) score of 0/5 in proximal and distal. Lower limbs were flaccid and had absent deep tendon reflexes. Sensory examination showed decreased sensation of all modalities in lower limbs with a sensory level at T10. Plantar reflexes were neutral and abdominal reflex was also absent. Motor and sensory and cerebellar examination of upper limbs was normal.

Nasopharyngeal swab test for severe acute respiratory syndrome coronavirus 2(SARS-COV-2) polymerase chain reaction(PCR) was positive, SARS-COV-2 serology was as follows: IgM:11.72 IU/ml(>1.1 positive), IgG:18.31 IU/ml(>1.1 positive). Whole spinal magnetic resonance imaging(MRI) was performed that revealed a longitudinal extensive myelitis(LETM) involving second cervical to second thoracic segment of spine.(figure 1) The lesion had gadolinium enhancement. Lumbar puncture was performed with glucose:60 mg/dl, protein:110 mg/dl and white blood cell: 650(80% polymorphonuclear cells and 20% mononuclear cells). Gram stain, culture, herpes zoster, varicella zoster and Epstein-Barr virus (EBV) serology of cerebrospinal fluid(CSF) returned negative. Patient's serum Aquaporin-4 antibody was also negative. Autoimmune immunological screening including Lupus anticoagulant, Protein S and C levels, Anti-Neutrophil Cytoplasmic antibodies, Rheumatoid factor, Anti Cardiolipin, and Anti Beta 2 Glycoprotein were all negative. The patient was diagnosed with COVID-19 associated transverse myelitis but infectious etiology was still kept in mind due to patient's CSF analysis.

Treatment was started with parenteral antibiotics(ceftriaxone and vancomycin), acyclovir and 5 sessions of plasma exchange. Unfortunately the patient had no response to treatment and was discharged to a rehabilitation center.

The patient was disappointed with the treatment we provided. He felt no improvement and wanted us to further treat him with plasma exchange. Although he was cooperative in his rehabilitation session, at the end of his hospital stay, he felt hopeless.

## Patient 2

A 67 year old woman was referred from neurology clinic for a 1 month history of paraparesis. Her symptoms started with a sensory level and paresthesia at chest and urinary frequency that progressed to paraparesis that resulted in frequent falling. She declared that her symptoms had a worsening nature at the time of visit. She didn't have any symptoms in upper limbs. She denied having fever, cough, dyspnea or gastrointestinal symptoms in weeks prior to her symptoms but she had decreased appetite since 3 weeks ago. None of her close relatives had these symptoms or COVID-19 that she knew of. Her past medical history was unremarkable.

On physical examination she was afebrile, had no respiratory distress and her oxygen saturation was 99%. Her general examination was unremarkable. Initial neurologic examination revealed an increased tone in lower limbs and symmetric lower limbs weakness with 4-/5 MRC score in proximal and distal. Deep tendon reflexes were increased symmetrically in lower limbs. She had no sensory level and plantar reflexes were downward. Abdominal reflexes were not reliable due to previous pregnancies. Cranial nerves, sensory and cerebellar examination was unremarkable.

Nasopharyngeal swab test for SARS-COV-2 PCR was negative, SARS-COV-2 serology revealed a positive IgG test(3.58 IU/ml with >1.1 considered as positive) and negative IgM(0.7 IU/ml with >1.1 considered as positive). This was interpreted as a chronic infection. Her chest computed tomography was also suspicious for COVID-19.(figure 2) Whole spinal MRI was performed that revealed a LETM involving third cervical to sixth cervical segment of spine. The lesion had gadolinium enhancement.(figure 3) Lumbar puncture was performed with glucose:80 mg/dl, protein:40 mg/dl and no cells. Gram stain, culture, varicella zoster and EBV serology of CSF returned negative. Patient's serum Aquaporin-4 antibody was also negative. Autoimmune immunological screening including Lupus anticoagulant, Protein S and C levels, Anti-Neutrophil Cytoplasmic antibodies, Rheumatoid factor, Anti Cardiolipin, and Anti Beta 2 Glycoprotein were all negative. CSF was tested for oligoclonal bands(OCB) that came positive(many bands) and IgG index was 0.9(positive>0.7)

The patient was diagnosed with transverse myelitis and after ruling out infectious causes, she was treated with a 5-day course of parenteral methylprednisolone(1gram for each session) that did not result in any recovery. She was started on plasma exchange. After 5 sessions of plasma exchanged the patient experienced significant recovery. She was fully ambulatory with lower limbs muscle power of 4+/5 at the time of discharge.

The patient was very pleased with the course of her hospital stay and treatment. She was happy that she was free of paresthesia and her gait improved significantly. She declared that she was going to finish her rehabilitation sessions and was very hopeful to get full recovery.

## Discussion

Transverse myelitis is caused by inflammation of spinal cord. There are various possible etiologies for this neurologic condition that include viral or bacterial infections, multiple sclerosis, neuromyelitis optica, systemic autoimmune diseases and infarction.(11) When transverse myelitis is a result of viral or bacterial infection, it is usually considered as an immune mediated response.

In our study, two cases of transverse myelitis following COVID-19 were distinct in many aspects. These aspects include the latency of disease onset from acute infection, mode of onset, severity of symptoms and respond to immunomodulation therapy. The symptoms of our first case happened abruptly 7 days after acute symptoms of COVID-19 and were severe in nature and the patient had poor treatment outcome. These symptoms were very similar to previous cases of COVID-19 related transverse myelitis reported by Kang Zhao et al, Abdelhady et al and Alketbi et al. (12–14) The abrupt onset of symptoms in

these cases was similar to spinal cord infarction. Furthermore neck or back pain is another symptom of cord infarction and this symptom was declared by our patient.(15) A cohort study showed that more than 95% of COVID-19 patients had elevated D-dimer and fibrinogen levels(16) and there are reports of acute ischemic stroke and abdominal visceral infarction in COVID-19 patients. (17,18) These could point to the possibility of ischemic nature of our patient's condition.

In our second case the symptoms evolved rather insidiously, were milder and responded well to treatment. There were similarities between our case and Sarma et al and Zachariadis et al reported cases.(9,19) The milder symptoms and response to immunomodulatory treatment can point to inflammatory nature of the condition but lack of CSF reactions like lymphocytosis or increase in protein were against this deduction.

Aside from differences, the location of transverse myelitis was somewhat similar in our cases. The most common site of spinal involvement in previous reports were cervicothoracic and this was also seen in both of our patients.(cervicothoracic in the first and cervical in the second case)

## **Conclusion**

Transverse myelitis could be a complication of COVID-19 and although the data is very limited to have certain deductions, infarction and inflammation could be suggested as probable mechanisms for this condition.

## **List Of Abbreviations**

COVID-19: corona virus disease 2019, ACE2: angiotensin-converting enzyme 2, MRC: medical research council, PCR: polymerase chain reaction SARS-COV-2: severe acute respiratory syndrome coronavirus 2, MRI: magnetic resonance imaging, CSF: cerebrospinal fluid, EBV: Epstein-Barr virus , LETM: longitudinal extensive myelitis, OCB: oligoclonal bands

## **Declarations**

Acknowledgements: Not applicable

Ethics approval and consent to participate: Both patients were provided with information about the report and written informed consent was obtained.

Consent for publication was obtained from both patients and is available from the corresponding author.

Availability of data and materials: The datasets used during the current study are available from the corresponding author on reasonable request.

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Contribution of authors: SA drafted the article and was in charge of patient care. FA propose the subject of the study, drafted the article and is the corresponding author. AZ did scientific revision, and drafted the article. DO did English revision and drafted the article. AF drafted the article and was in charge of patient care. RJ did scientific revision and drafted the article.

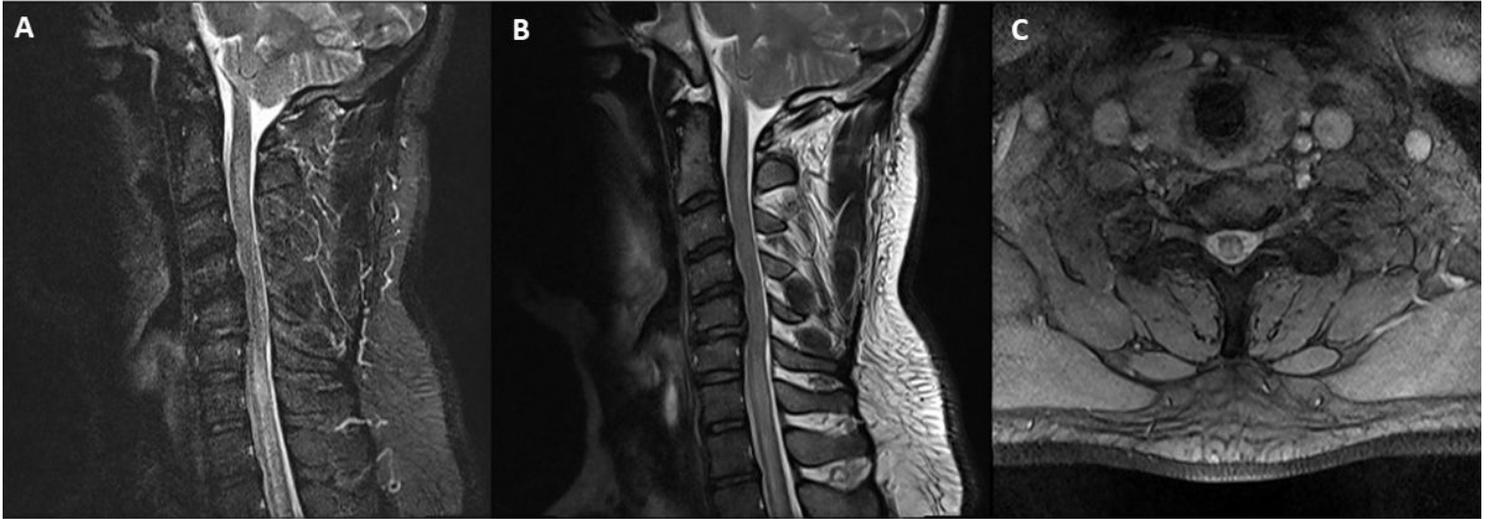
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## Figures



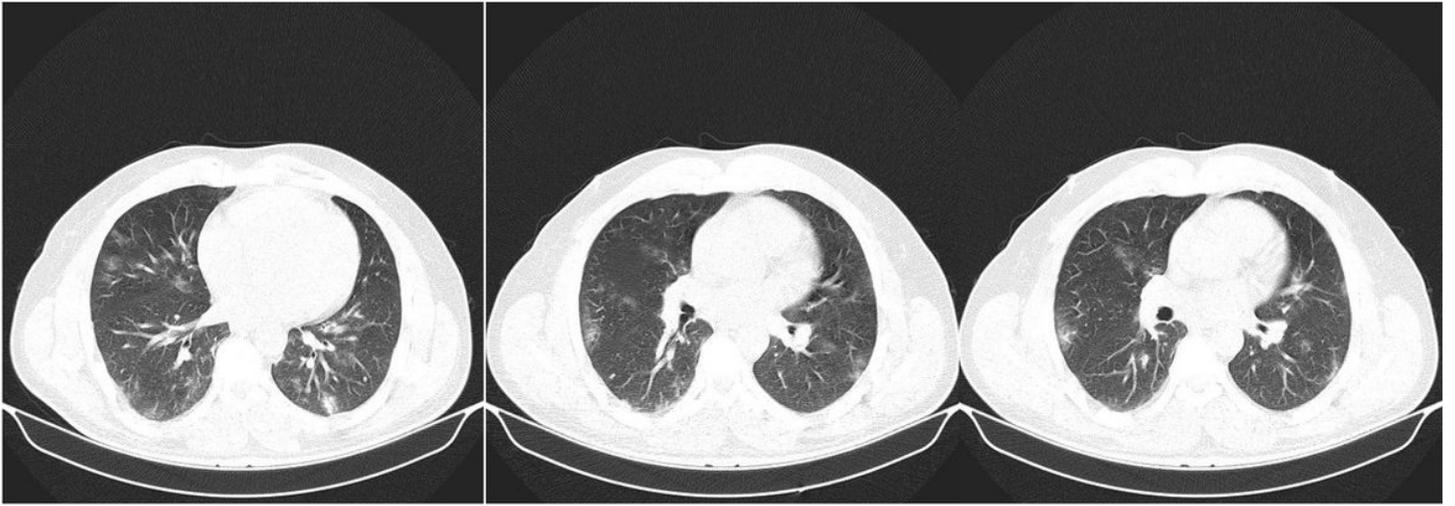
**Figure 1**

Cervical magnetic resonance imaging of first patient: longitudinally extensive transverse myelitis involving second cervical segment to second thoracic segment of spinal cord. A: Sagittal section, Short-T1 Inversion Recovery sequence. B: Sagittal section, T2 sequence. C: Axial section, T2 sequence: hyperintensity involving more than 2/3 of axial section.



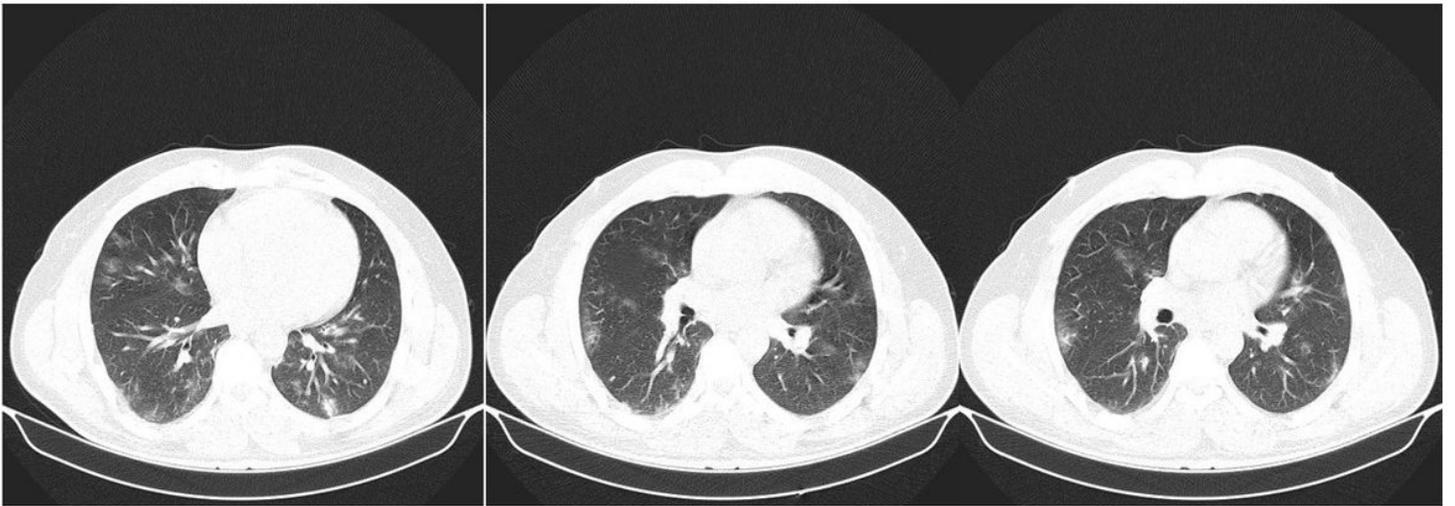
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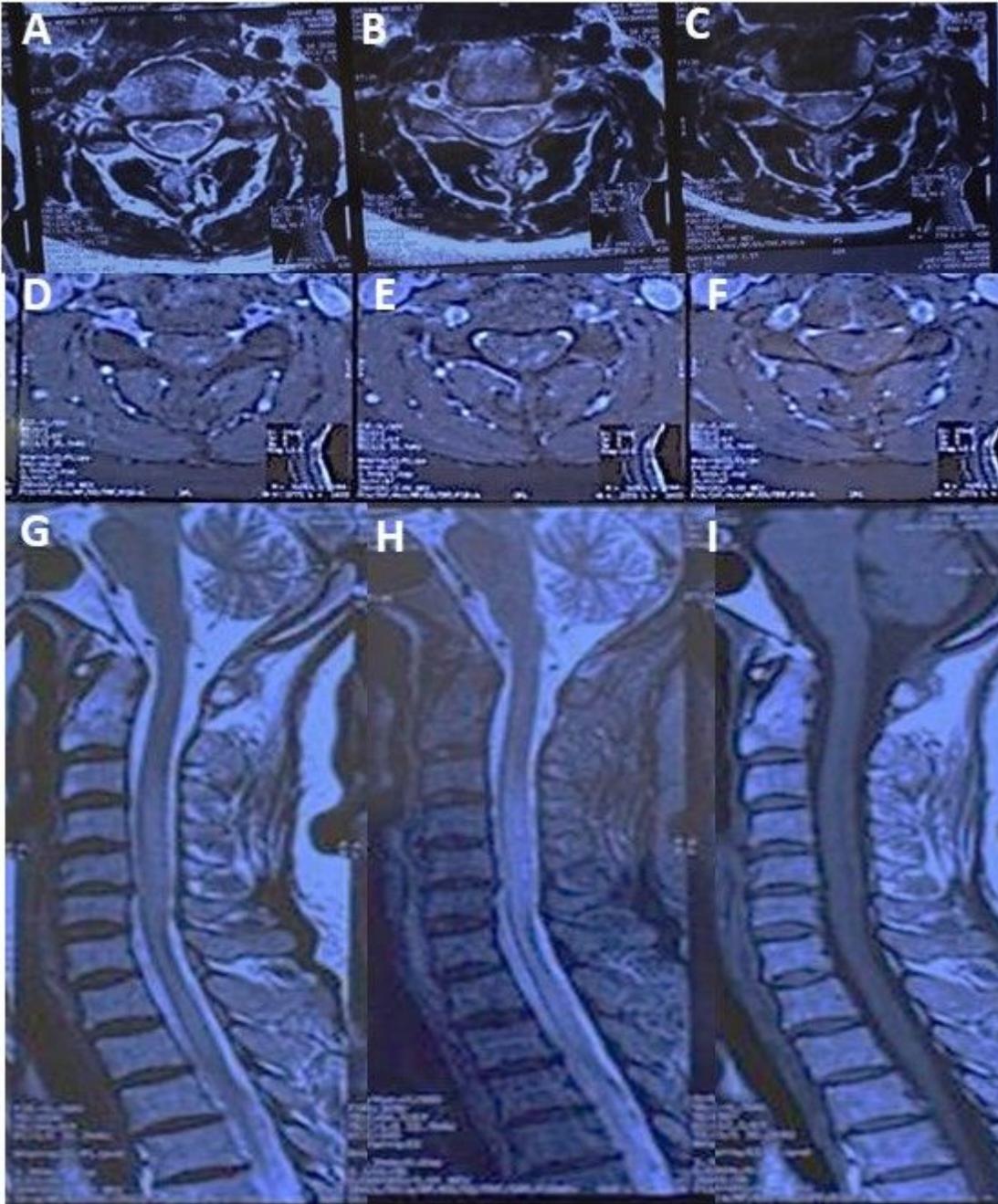
**Figure 2**

Chest computed tomography with diffuse ground glass hyperdensities involving both lungs. Some non-significant mediastinal lymph nodes are also detected. These findings are suspicious for COVID-19.



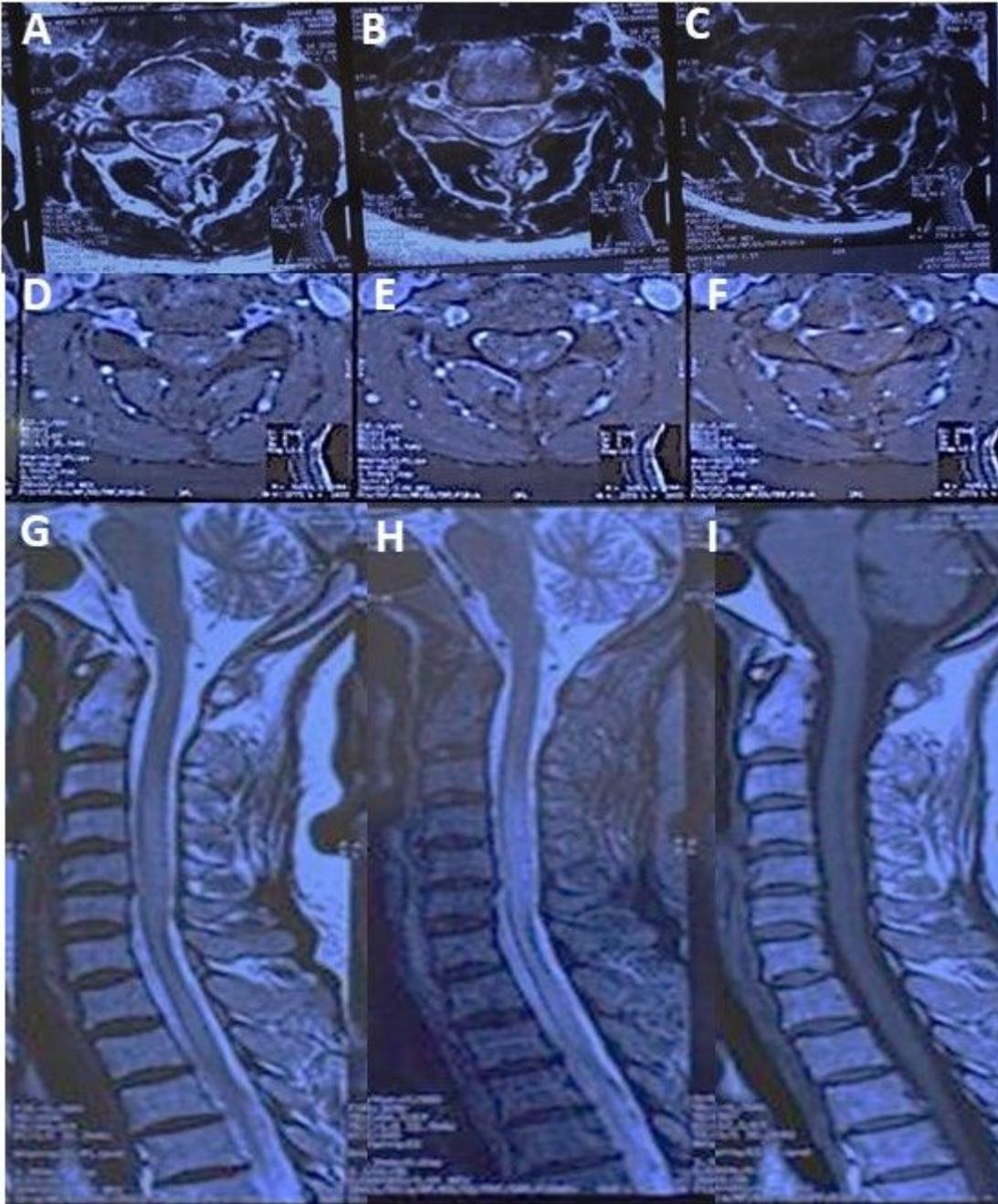
**Figure 2**

Chest computed tomography with diffuse ground glass hyperdensities involving both lungs. Some non-significant mediastinal lymph nodes are also detected. These findings are suspicious for COVID-19.



**Figure 3**

Cervical magnetic resonance imaging of second patient: longitudinally extensive transverse myelitis involving third to sixth cervical segment of spinal cord. A-C: Axial section, T2 sequence: hyperintensity involving more than 2/3 of axial section. D-F: Axial section, T1 with gadolinium sequence: faint enhancement of aforementioned lesion. G: Sagittal section, T2 sequence. H: Sagittal section, Short-T1 Inversion Recovery sequence. I: Sagittal section, T2 sequence shows hypointense lesion from C3 to C6.



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Cervical magnetic resonance imaging of second patient: longitudinally extensive transverse myelitis involving third to sixth cervical segment of spinal cord. A-C: Axial section, T2 sequence: hyperintensity involving more than 2/3 of axial section. D-F: Axial section, T1 with gadolinium sequence: faint enhancement of aforementioned lesion. G: Sagittal section, T2 sequence. H: Sagittal section, Short-T1 Inversion Recovery sequence. I: Sagittal section, T2 sequence shows hypointense lesion from C3 to C6.