Case report: Acute transverse myelitis in COVID-19 infection with delayed onset of pulmonary manifestation

Fallbericht: Akute Myelitis transversa in COVID-19-Infektion mit verzögertem Beginn der pulmonalen Manifestation

Introduction
COVID-19 disease, caused by the novel beta-coronavirus SARS-CoV-2, has become a global pandemic, with more than 220 million confirmed cases reported to the World Health Organization (WHO) by September 2021 (WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int. Accessed 6 September 2021). The virus causes mild to moderate respiratory illness and most patients recover without requiring special treatment. However, some will become seriously ill with atypical pneumonia and acute respiratory distress syndrome (ARDS), with some cases being fatal. SARS-CoV-2 enters human cells by binding to angiotensin-converting enzyme-2 (ACE2) receptors. These receptors are expressed not only in the lung epithelium, but also in numerous other organs and tissues, such as vascular endothelial cells, heart, brain, kidney, liver, intestine, which explains the broad spectrum of extrapulmonary symptoms reported for COVID-19 disease (Machhi JS et al. J Neuroimmune Pharmacol. 2020; 15(3):385–386).

In recent publications, evidence of central nervous system involvement in COVID-19 is accumulating. In addition to mild symptoms such as dizziness, headache, ageusia, and anosmia, more severe manifestations such as acute vascular injury (ischemic stroke, venous thrombosis), demyelination (acute disseminated encephalomyelitis (ADEM), transverse myelitis), and infectious or para-infectious conditions (meningoencephalitis, Guillain-Barré-Syndrome (GBS)) have been reported. Acute transverse myelitis is a rare, acquired neuro-immune disorder that can be idiopathic or disease-associated (i.e., connective tissue disease, infections, Treponema pallidum, mycoplasma, HIV, VZV, EBV, CMV, and others), and paraneoplastic syndromes (Ellul MA. Lancet Neurol. 2020; 19(9):767–783). Based on the extent and distribution of lesions, TM is divided into partial, complete, and longitudinal extensive transverse myelitis (LETM). Symptom delay allows the distinction between acute and postinfectious TM.

43 cases of transverse myelitis associated with SARS-CoV-2 infection have been published to date, with diverging clinical presentation and outcome (Rodríguez de Antonio LA. Mult Scler Relat Disord. 2021; 49:102783). We report a case with permanent neurologic impairment after COVID-19-associated LETM, and the first case in which neurologic symptoms preceded respiratory symptoms.

Case presentation
In November 2020, an elderly man with arterial hypertension, type 2 diabetes, and paroxysmal atrial fibrillation presented at the emergency department due to lower limb weakness and unsteady gait that had begun the previous day and led to repeated falls. He denied cough, shortness of breath, anosmia, and headache. The patient’s vital parameters were within normal range. Blood results were unremarkable except for mild leukocytosis (11.72 *10^9/L). Neurological examination revealed weakness of the quadriiceps femoris, plantar flexor, and dorsiflexor muscles on both sides, but no sensory dysfunction. The man was hospitalized for analgesia and further diagnostics. A detailed timeline is shown in Fig. 1.

Conventional radiography of the pelvis excluded acute traumatic injury. Sensory deficits and urinary retention occurred on the 3rd day of hospitalization. Computed tomography (CT) of the head, lumbar spine, and pelvis was unremarkable. On day 4, the patient complained of a dry cough. A subsequent chest radiograph showed interstitial infiltrates (Fig. 2). SARS-CoV-2 infection was confirmed by pharyngeal PCR. For neurologic evaluation, CT and magnetic resonance imaging (MRI) of the spine were performed on day 6. This showed no osseous abnormalities but progressive pneumonic consolidations in both lower lobes and an increased T2 signal of the thoracic spinal cord in a trans-sectional distribution at the level of T4 to T9 (Fig. 3). Compresive spinal cord lesions were ruled out. Neurologic examination confirmed bilateral flaccid paraplegia with hyporeflexia and pallenesthesia.

Based on lesion pattern, typical symptoms, and the recent infection, the diagnosis of LETM was established. Spinal infarction was discussed as a differential diagnosis.

Due to the latency to the onset of symptoms and worsening general condition, a lumbar puncture was not performed.

The patient received a combination of high-dose corticosteroids (dexamethasone) and amoxicillin for 8 days. In addition, antiplatelet therapy was administered. Because of hypoxemia on room air (SpO2 86 %), oxygen therapy was initiated on day 11. The patient’s respiratory status improved markedly, and pharyngeal SARS-CoV-2 PCR was negative on day 30. Unfortunately, the neurological symptoms persisted, and the patient was discharged to neurological rehabilitation therapy. A follow-up examination 86 days after initial presentation showed unchanged neurologic impairment.

Discussion
We report a rare case of COVID-19-associated ATM. This is the first case in which neurological manifestation occurred before respiratory involvement. In respective case reports published to date, the respiratory symptoms manifested first with a delay of 15 hours to 6 weeks before the onset of neurological symptoms. In two cases, ATM occurred during the course of asymptomatic SARS-CoV-2 infection (Rodríguez de Antonio LA. Mult Scler Relat Disord. 2021; 49:102783).

Characteristic of ATM is an acute or subacute onset of neurological symptoms...
with progression to nadir between 4 hours and 21 days. Clinically, patients present with combined dysfunction of the motoric, sensory, and autonomic nervous system, usually in terms of symmetrical paresis and dysesthesia of the lower extremity along with bladder dysfunction (Transverse Myelitis Consortium Working Group. Neurology. 2002 Aug 27; 59(4): 499–505). All of these symptoms were present in our case. Regarding the lesion pattern, most of the previously published ATM cases were described as LETM, which is consistent with our findings. Spinal ischemia was the main differential diagnosis along with bladder dysfunction.

ATM has been described in both mild and severe respiratory courses. As in our case, no improvement or fatal outcome was noted in 17–30% of the patients. A decrease in symptoms was observed in 60–83% of the previously published cases. Corticosteroids, intravenous immunoglobulins, anti-infective therapies (antiviral, antibiotic), and plasma exchange have been the common treatment approaches, and so far, there is no uniform treatment strategy for COVID-19-associated ATM. The data suggest that the severity and progression of respiratory and neurological symptoms do not correlate. Although respiratory symptoms usually occur first, the reverse is also probable.

### Conclusion

ATM is a rare but serious complication in COVID-19 disease, with some cases resulting in permanent neurological dysfunction. Previous cases suggest that the severity and course of respiratory and neurological symptoms do not correlate. Although respiratory symptoms usually occur first, the reverse is also probable.

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Conflict of interest

E. Talakić, AK. Kaufmann-Bühler, E. Janek, P. Mrak, M. Fuchsjäger, H. Schöllnast declare that they have no competing interests.

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Bibliography

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Fig. 2 Chest radiograph shows circumscribed homogeneous opacity in projection to the left lower lung space on the a. p. view. The lateral recess is clear on both sides, there is no evidence of pleural effusion, and there is no evidence of cardiac decompensation. The hilar and mediastinal structures appear normal. The findings are consistent with COVID-19 pneumonia (arrow head).

Fig. 3 MRI of the thoracic spine shows on T2-weighted images in axial slices (T4–T5 and T8–T9 levels) hyperintensity of the thoracic cord in a transverse distribution involving spinal cord grey and white matter, predominantly posterior sensory pathways (a, b, c). Fat-saturated sagittal T1 sequence post-intravenous gadolinium contrast (d) and sagittal T2 sequence of the thoracic spine (e), demonstrating a long segment of T2 signal elevation in a central distribution from T4 to T9. No extra dural abnormalities are noted.