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CASE REPORT

Cerebellar syndrome as a complication of COVID-19 disease

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Abstract

COVID-19 disease is caused by the new coronavirus SARS-CoV-2. The disease first appeared in China in 2019 and quickly spread throughout the world. It primarily affects the respiratory tract, manifested by fever, cough and the development of dyspnoea, but the symptoms and complications can affect any organ system. Neurological symptoms include headaches, muscle and joint pain, taste and smell disorders. Complications include inflammatory diseases of the central nervous system, ataxia, peripheral nerve and muscle diseases, worsening of extrapyramidal diseases, and neuropsychiatric disorders. This paper presents a case report of a 62-year-old man with cerebellar syndrome, ataxia, intentional tremor and hypermetria when dealing with COVID-19 disease.

INTRODUCTION

In December 2019, many cases of serious respiratory disease, mainly affecting the lower respiratory tract and lungs, began to occur in Wuhan, Hubei, China. An epidemiological investigation in the first cases revealed a connection with the Huanan wholesale market directly in Wuhan (Bogoch *et al.* 2020). The disease subsequently spread rapidly to all permanently inhabited continents. A new ß-coronavirus, designated 2019-nCoV, was subsequently identified as the causative agent, followed by SARS-CoV-2 at short intervals. Most coronaviruses cause common non-serious respiratory diseases in humans (Cui *et al.* 2019), but highly pathogenic coronaviruses causing SARS and MERS have been known for some time. COVID-19 is most often manifested by respiratory symptoms. These include fever, cough, and dyspnoea (Huang *et al.* 2020). There is often general weakness, increased fatigue, and sometimes gastrointestinal problems. However, numerous neurological symptoms and complications are also described.

CASE REPORT

The 62-year-old man was admitted to hospital on 9 November 2020 for fever, general weakness, increased fatigue, resting tremors in all limbs, and inability to stand and walk, with COVID-19 disease established. A nasopharyngeal swab

with positive SARS-CoV-2 (PCR) was performed on 3 November 2020 at the request of the registering general practitioner. The patient had a positive epidemiological history of close contact with an infected person and, as of 25 October 2020, suffered from fever, dry cough, headache, general weakness and increased fatigue. As part of outpatient treatment, a general practitioner prescribed clarithromycin orally at a dose of 500 mg every 12 hours, recommended the use of mucolytics and expectorants, and antipyretics commonly available for fever.

Due to rapidly progressing neurological problems, the Emergency Medical Service (EMS) was called, which after a basic field assessment transported the patient to the hospital for emergency admission. At the initial examination, the patient was with spontaneous ventilation – lungs with isolated wheezing and rhonchi, without the need for oxygen therapy – and circulatory stable, conscious, fully oriented, subfebrile. The orientation neurological examination was dominated by tremor of all limbs, slightly inaccurate taxa of the left upper limb, hypermetria and standing with significant oscillations of the torso. It was not possible to examine walking due to strong tremor in the lower limbs. Meningeal syndrome was not expressed during the assessment. No neurological disease was present in the patient's history. The patient had been treated for several years for arterial hypertension, grade 2 chronic obstructive pulmonary disease, hyperlipidaemia and hyperuricemia.

Mild lymphopenia and thrombocytosis were present in the blood count. Inflammatory parameters were not significantly increased, CRP 19 mg / l, procalcitonin 0.02 ug / l, ferritin 330 ug / l. Hemocoagulation examination determined the aPTT value to be 27.6 s, the INR 1.1 and the D-dimers 0.94 mg / l FEU. Liver and renal test values were normal, and the ionogram was also without findings (Table 1). CT of the lungs showed bilateral viral pneumonia with fine infiltrates (Figure 1) as well as consolidation in the lung bases (Figure 2). Due to the anamnesis of frequent stay in the countryside in the epidemiologically important locality of the occurrence of tick-borne encephalitis and with the need to exclude other neuroinfectious diseases, lumbar puncture was performed. The cerebrospinal fluid obtained was clear, colourless and under normal pressure. The basic monitored parameters in cerebrospinal fluid were normal, only a marginally higher value of glucose 4.9 mmol / l and IgA 5.9 mg / l (Table 2). The blood-brain barrier was not broken. The presence of coronavirus SARS-CoV-2 (PCR) was not detected in cerebrospinal fluid. Examination for tick-borne encephalitis and Lyme disease was negative. Other pathogens of neuroinfection were not proven by laboratory tests.

The patient continued on oral clarithromycin. Dexamethasone was introduced into the medication intravenously at a dose of 8 mg three times a day. Symptoms of cerebellar ataxia, tremor, and hypermetria continued to dominate. Therefore, clonazepam was prescribed 0.5 mg orally three times a day. During this therapy, after a few days there was a partial remission of the symptoms, tremor occurred only on the upper limbs, the patient was able to stand independently with slight titubation in all directions and gradually was able to walk carefully with the help of another person. There were no convulsions or visual disturbances at any time. The planned MR examination of the brain showed only slight signs of cerebral atrophy.

For hypovitaminosis D, cholecalciferol was administered daily in a replacement dose. In addition to chronic medication, the patient was given low molecular weight heparin in a prophylactic dose. The patient's chronic medication was also administered. The control laboratory examination was unremarkable, without an increase in inflammatory markers. The patient was discharged to home treatment on 19 November 2020 in an overall improved condition, walking, but still having other mild symptoms of cerebellar syndrome after undergoing COVID-19 disease. He was therefore referred to an outpatient neurologist.

DISCUSSION

The clinical picture of COVID-19 disease includes a number of neurological symptoms. These are often headache or muscle and joint pain. Olfactory disorders are also reported more frequently in patients. This was observed in up to 85% of patients in a multicentre European study. In 11.8% of them, it manifested before the onset of other symptoms of the disease (Lechien *et al.* 2020). Taste disorders, including total ageusia, are often described. More frequently described neurological complications include inflammatory diseases of the central nervous system. These account for up to 6% of neurological complications (Varatharaj *et al.* 2020). Cases of Guillain-Barré syndrome in its various forms have been repeatedly reported following COVID-19 disease (Paterson *et al.* 2020, Reyes-Bueno *et al.* 2020). So far, a rarely described complication is acute meningoencephalitis with a characteristic inflammatory pattern and SARS-CoV-2 (PCR) positivity in cerebrospinal fluid (Moriguchi *et al.* 2020). In this case, the cerebrospinal fluid PCR was negative. This might be justified by taking it at an early stage of the disease. Alternatively, a non-certified laboratory method fail can be considered.

Our patient suffered from symptoms of cerebellar syndrome. The cerebellum is the part of the central nervous system involved in motor-sensitive operations. Its involvement in cognitive tasks and emotional processes is also described (Bodranghien *et al.* 2016). The picture of cerebellar syndrome includes ataxia, tremor, muscle tone disorders and sometimes cognitive impairment. Ataxia can be caused by a number of factors, including neurodegenerative or neurometabolic disease, craniotrauma, stroke, hyperthermia or

Tab. 1. Laboratory findings

	9 November 2020	19 November 2020
Blood count		
Leukocytes (x 109 / l; normal value 4.0-10.0)	6,6	9,7
Lymphocytes (proportion; normal value 0.2-0.45)	0,193	0,09
Platelets (x109 / l; normal value 150.0-400.0)	825	400
Erythrocytes (x1012 / l; normal value 3.8-5.2)	4,97	4,28
Hemoglobin (g / l; normal value 120.0-160.0)	147	137
Biochemistry		
Total bilirubin (µmol / l; normal value 0-25.0)	5	
ALT (ukat / l; normal value 0-1.0)	0,61	
AST (ukat / l; normal value 0-0.8)	0,45	
GGT (ukat / l; normal value 0-1.9)	0,99	
Urea (mmol / l; normal value 3.0-8.0)	5,4	6,6
Creatinine (µmol / l; normal value 62.0-106.0)	83	90
Sodium (mmol / l; normal 137-145)	140	140
Potassium (mmol / l; normal value 3.6-4.8)	3,9	4,2
Chlorides (mmol / l; normal value 98-109)	104	107
Calcium (mmol / l; normal 2.1-2.6)	2,51	
Magnesium (mmol / l; normal value 0.8-1.1)	0,89	
CK (ukat / l; normal value 0.1-3.2)	0,94	1,1
LDH (ukat / l; normal value 0-4.2)	3,85	3,65
TroponinT hs (ng / l; normal value <14)	4	
NTproBNP (ng / l; <125)	131	
Glucose (mmol / l; normal value 3.6-5.6)	5,4	7,0
Hemocoagulation		
APTT (s; normal value 25.9-40.0)	27,6	
Prothrombin test (s; normal value 12.0-15.0)	11,1	
Fibrinogen (g / l; normal value 1.8-4.5)	5,5	
D-dimers (mg / l FEU; normal value 0-0.5)	0,94	
Markers of inflammation		
CRP (mg / l; normal value 0-5.0)	19	1
Procalcitonin (ug / l; normal value 0-0.1)	0,02	
Ferritin (ug / l; normal value 30.0-284.0)	330	

intoxication. In the case of neurodegenerative diseases, copeptin, which is a component of pro-AVP produced by some neurons, appears to be a promising marker for early diagnosis (Baranowska, 2019). In cerebellar ataxia in laboratory rats, a decrease in IL-17 production was observed, but at the same time an increase in the number of IL-4-producing cells and CD25-expressing cells. An increased number of B lymphocytes was also observed. It is hypothesized that in humans, both cellular and humoral immune mechanisms may be involved in ataxia (Jiang *et al.* 2015). Ataxia manifested in this patient in isolation when standing. The patient stood very uncertainly, walking was impossible at first, the torso was slightly retroflexed.

Tremor is an involuntary rhythmic movement created by regular oscillations of the affected part of the body. In our patient, we observed intentional tremor accompanied by ataxia and hypermetria, which is typical for cerebellar tremor. Initially, tremor occurred on all limbs, after the introduction of corticoid and benzodiazepine treatment, it receded only to the upper limbs, and even there it was partially reduced. Benzodiazepines often improve the situation as in this case, but do not definitively resolve it. The technique of

Tab. 2. Examination of cerebrospinal fluid

Total protein (g / l; normal value 0.24-0.62)	0.35
Albumin (g / l; normal value 0.15-0.4)	0.22
Glucose (mmol / l; normal 2.9.9.8)	4.9
Lactate (mmol / l; normal value 1.4-2.6)	2.5
Beta-2-microglobulin (mg / l; normal value 1-2,2)	1.77
Elements (count / ul; normal value 0-5)	4
Erythrocytes (number / ul; normal value 0)	0
IgG (mg / l; normal value 13.9-37.5)	34.4
IgA (mg / l; normal value 0-3.9)	5.9
IgM (mg / l; normal value 0-1)	0.5

deep brain stimulation seems to be promising (Freund *et al.* 2007). The above typical hypermetria was present in the patient throughout the hospitalisation, although there was a partial correction of the conditions.

According to the laboratory findings, our patient suffered from hypovitaminosis D and its substitution was therefore necessary. Today, vitamin D is no longer one of the typical vitamins, but is referred to as a prohormone. It is crucially important, in addition to the correct bone density and fertility in both women and men, for the proper functioning of the immune system. Increasingly, studies show that its deficiency is associated with an increased risk and worse course of respiratory diseases in children and adults (Gunville, 2013). It is also used in the field of neurological diseases treatment. The incidence of multiple sclerosis has been shown to increase with increasing distance from the equator, and it is thought that vitamin D deficiency may be one of the negative factors in the development and severity of the disease (Handunnetthi *et al.* 2010, Mehta *et al.* 2011). Vitamin D deficiency negatively affects the development and course of cognitive disorders. It can also affect comorbidities such as cerebrovascular disease, muscle weakness, falls and fractures (Wilkins *et al.* 2006, Przybelski *et al.* 2007).

CONCLUSION

COVID-19 is primarily a respiratory disease, but the symptoms and complications may involve any organ system in the human body. Neurological symptoms include headaches, muscle and joint pain, taste and smell disorders. Complications include inflammatory diseases of the central nervous system, ataxia, diseases of the peripheral nerves and muscles (Guillain-Barré syndrome, myopathy, myositis), worsening of extrapyramidal diseases and neuropsychic disorders. Patients hospitalized for COVID-19 disease also have an increased risk of acute stroke. It will be necessary to map whether and by what mechanism the SARS-CoV-2 virus contributes to the described increased risks.

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