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Case report

Chronic demyelinating polyradiculoneuropathy presented after SARS CoV2 mild infection- a case report

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Abstract. COVID19 is an infectious disease caused by the SARS CoV-2 virus that emerged in Wuhan, China, in 2019. Common complaints are dry cough, dyspnea, fever, myalgia, headache, anosmia, and ageusia. This influenza-like virus has a nootropic potential, as seen in patients complaining of various neurological symptoms in the course of the disease or shortly after resolution. Autoimmune diseases in the nervous system can occur as a complication of viral infection. Mechanisms including molecular mimicry, bystander activation, epitope spreading can activate viral-linked autoimmunity. Therefore, we present a case of classical chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with onset one month after being diagnosed with a mild form of COVID19 in a patient with a history of diabetes and obesity. The case has been followed up for a year, being investigated thoroughly, including nerve conduction studies, spinal tap, and blood tests. The patient received periodical courses of intravenous immunoglobulin therapy.

Key Words: CIDP, SARS CoV2, demyelinating disease, nerve conduction studies, intravenous immunoglobulin

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Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired autoimmune demyelinating polyneuropathy characterized by diffuse limb weakness. CIDP was described by Dyck (1975) as a demyelinating disorder with inflammatory infiltrates and segmental demyelination in the affected fibers (peripheral nervous system). It affects large fibers both proximally and distally (patients develop gait instability and difficulties rising from a seated position) (Dyck et al 2018)

The pathological features appear as a result of the immune system affecting the myelin sheath of the peripheral nervous system. Paraclinical investigations are important in the diagnosis process; nerve conduction studies (NCS) in CIDP showed reduced motor and sensory conduction velocities or conduction blocks (Haq et al 2000), nerve biopsies describe "onion bulb" formation and endoneurial inflammatory infiltrates, nerve plexus MRI is useful for the evaluation of patients with possible CIDP and can reveal enlargement and/or increased signal intensity of nerve roots on T2 weighted sequnces, nerve ultrasound can also be performed in possible CIDP diagnosis with nerve enlargement of minimum two sites in proximal median nerve or the brachial plexus. Lumbar puncture is performed only after the criteria for CIDP has been met and it showed cerebrospinal fluid (CSF) modifications represented by increased protein levels (Mathey et al 2015). In some cases, at initial presentation, CIDP can be interpreted as AIDP or Guillain Barre syndrome (GBS)

Clinical presentation typically involves numbness, symmetrical muscle weakness and sensory ataxia (impairment of proprioceptive sensibility). Neurological examination reveals progressive or recurrent weakness with diminished/abolished osteotendinous reflexes. The respiration muscles are rarely affected at first (Dyck et al 2018, Van den Bergh et al 2021). Types of CIDP are presented in Table 1.

The multifactorial etiology, including genetic, infectious, and environmental factors, is found in all autoimmune diseases. Literature shows associations between CIDP and various organisms, including the Zika virus, Mycoplasma pneumonia, Cytomegalovirus, Epstein-Barr virus, Human immunodeficiency virus (HIV), Hepatitis B virus and *Borrelia burgdorferi* (Rodríguez et al 2019).

Treatment of CIDP includes first line therapies: corticosteroids and intravenous immunoglobulin (IVIG). Plasmapheresis (Pex) and other immunomodulatory therapies weakeley recommended (Methotrexate, Interferon beta 1a, Fingolimod) can be used in some patients. IVIG is regarded as first-line treatment revealing less severe adverse effects (Peltier et al 2012, Van den Bergh et al 2022).

COVID19 is the disease caused by the SARS CoV-2 virus that emerged at the end of 2019. Most patients present with: dry cough, dyspnea, fever, myalgia, headache, anosmia and ageusia. In some cases, it can manifest as severe viral pneumonia with acute respiratory distress syndrome (Montalvan et

Table 1 CIDP Classification (Van den Bergh et al 2021)

Typical CIDP	CIDP variants
Typical CIDP (symmetric sensorimotor)	**Distal CIDP**: "distal sensory loss and muscle weaknesspredominantly in lower limbs"
"Progressive or relapsing, symmetric, proximal and distal muscleweakness of upper and lower limbs, and sensory involvement of atleast two limbs"	**Multifocal CIDP**: "sensory loss and muscle weakness in a multifocal pattern,usually asymmetric, upper limb predominant, in more than one limb"
"Developing over at least 8 weeks"	**Motor CIDP**: "motor symptoms and signs without sensory involvement"
"Absent or reduced tendon reflexes in all limbs"	**Sensory CIDP**: "sensory symptoms and signs without motor involvement"
	Focal CIDP: "sensory loss and muscle weakness in only one limb"

al 2020). SARS CoV2 - this influenza-like virus has nootropic potential. Confusion, headache and dizziness are the most common non-specific neurological symptoms. Of great concern are neurological conditions such as ischemic or hemorrhage stroke, cerebral venous sinuses thrombosis, seizures, meningoencephalitis, Guillain-Barre, CIDP (Harapan et al 2020). SARS CoV2 virus enters CNS via the olfactory neurons or through the hematogenous spread and binds to ACE2 receptors, resulting in a cytokine storm and the damage of the blood-brain barrier (Patnaik et al 2021).

Autoimmune diseases can occur due to viral infection in the nervous system and occasionally following vaccine injections through mechanisms like molecular mimicry, bystander activation, epitope spreading (Beghi et al 2021) .

A study conducted in 2020 (Guglielmo et al.) investigated the underlying mechanisms that could elucidate the pathogenicity of SARS CoV 2 in damaging the peripheral nervous system. The results showed molecular mimicry between the virus and the human heat shock proteins 90 and 60, which are associated with autoimmune diseases(Lucchese et al 2020). The possible underlying mechanism regards the production of antibodies, which are directed to the surface glycoproteins from the pathogenic organism that resemble the protein structures of the host's PNS (peripheral nervous system) cells, leading to an autoimmune reaction (Virani et al 2020).

Case presentation

We present a case of a 59-year-old Romanian woman admitted to the Neurology department of Cluj County Emergency Hospital for muscle weakness and paresthesia in the lower limbs, predominantly distally. The symptoms started shortly after the resolution of a SARS CoV2 infection, for which no antiviral treatment was given. She had a history of diabetes mellitus type 2 treated with oral antidiabetic drugs for ten years. The patient had a mild form of COVID 19 being hospitalized in an Infectious Diseases Hospital. Two weeks after being discharged, she developed weakness in the lower limbs and paresthesia in both upper and lower limbs, presumed as a result of diabetic polyneuropathy treated with thioctic acid. The motor deficits progressed and she underwent an electrodiagnostic study. She was admitted to our clinic one month after the onset of neurological symptoms.

Neurological examination on admission revealed distal muscle weakness with a 4/5 in her right lower limb and 3/5 in the left lower limb on the muscle strength scale (MSS), global hypotonia, hypoesthesia and paresthesia located in the upper limbs, especially in the tip of the fingers. She was unable to walk without gait aid. Osteotendinous reflexes were abolished and no pathological reflexes were provoked. Cranial nerves were spared.

Electrodiagnostic studies were completed on the second day of admission showing an acute asymmetrical focal slowing both distally and proximally, with chronic axonal motor and sensory loss and absent sympathetic skin response. Those findings were supportive to the diagnosis of acute inflammatory demyelinating polyneuropathy overlapped on a chronic diabetic polyneuropathy (figure 1).

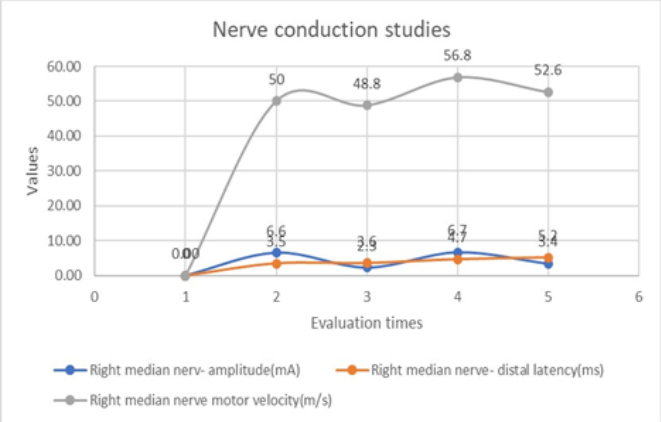

Fig. 1. Median nerve electrodiagnostic studies

We performed a lumbar puncture and the CSF analysis showed albumin-cytological dissociation (ACD), with a total protein level of 55.19 mg/dl. Cytodiagnostic examinations of CSF (cerebrospinal fluid) showed acellular specimens. Microbiological testing on serum and CSF was negative.

Other causes that can lead to demyelinating nervous system pathologies (GBS, CIDP) were excluded.We performed antibody tests to exclude possible vasculitis causes using specific antibody tests.

Cervical and lumbar MRI done before admission showed degenerative morphological condition at C5; radicular conflict at C6 more expressed in the left region and compression of the right L4 radicular root with intraforaminal disc herniation. Blood tests showed mild hepatic cytolysis and hypercholesterolemia.

At this point, the case was interpreted as Guillain Barre syndrome, and the patient received a 5-day course of IVIG - dose 2g/kg. Following the therapy, the patient reported a partial remission of paresthesia and partial improvement of the gait.

On discharge, the neurological examination objectified a motor deficit of 4/5 in the lower limbs on the MSS scale and the patient was recommended for periodical evaluation.

After three months, the patient presented with new symptoms. Neurological examination revealed the progression of symptoms to the upper limbs - poor grip strength, atrophy of the

thenar and hypothenar eminence, motor deficits in the superior limbs- 4/5 in the left superior arm and the recurrence of numbness in hands and feet.

Nerve conduction studies and needle electromyography were completed. The results were acute and chronic demyelinating and axonal, distal and proximal, motor and sensory polyneuropathy, in progression, compared to the first examination. The patient received the second course of intravenous immunoglobulin 5 g/ml-dose 2 g/kg, with a moderate recovery of motor strength, the need of assisted walking device and the attenuation of paresthesia.

We followed the case for one year including nerve conduction studies and after receiving pulse therapy with intravenous immunglobulin 5 g/ml- dose 2 g/kg, four times/year neurological examination revealed sensory impairments and inability to walk without gait aid due to motor deficits.

Discussion

It is well known that viral infections have triggered both GBS and CIDP as part of an amplified inflammatory response(Rodríguez et al 2019, Bracaglia et al 2020).

In the first presentation, regarding the onset of the areflexic paraparesis, a diagnosis of AIDP or GBS was considered on the clinical profile and NCS report. After the first and second relapse, the diagnosis of CIDP was more likely. As far as recent literature concerns (2020-2021), most of the reported cases presented as acute inflammatory demyelinating polyneuropathy were not followed up; therefore, we cannot rely solely on the cases interpreted as GBS because they could have evolved in CIDP over time.

A peculiarity in the manifestation of CIDP is that the sural nerve is spared (Peltier et al 2012) but in this case, the sural nerve is non-responsive in all the examinations and this aspect can be attributed to prior history of diabetes mellitus treated with oral antidiabetic medications and peripheral neuropathy.

One limitation of this study may be that neither antineuronal antibodies nor nerve biopsy have have been included in the investigations to better describe the pattern of peripheral nerve fiber damage.

Several studies compared the efficacy of Pex and IVIG but found no statistical differences between the two of them (Peltier et al 2012). IVIG is regarded as the first-line treatment and it may be more useful to patients having a history of diabetes or other comorbidities (Laughlin et al 2009, Hughes et al 2009). Patients respond effectively to alternating between therapies at some point in the evolution rather than following a single line of treatment in the long term (Cocito et al 2010).

Conclusions

Given the temporal dispersion of the clinical features and the response to treatment, the case met the criteria for CIDP. In the following months, the course of the disease was relapsing-remitting, both clinical and on nerve conduction studies, with partial resolution of paresthesia and without exacerbation of symptoms. Although the infection with SARS-CoV-2 is correlated with respiratory and gastrointestinal symptoms, it is still investigated for its systemic and neurological involvement. This is the first case of CIDP as a postinfectious manifestation of COVID (followed-up on a period of 1 year) in the Cluj-Napoca Neurology Department.

We described a classical case of CIDP in a patient having a history of diabetes mellitus and obesity after the clearance of SARS-CoV2 infection, adding to the already reported cases in the literature, in support of SARS-CoV-2 triggering autoimmune neurological diseases.

This article aims to bring to attention the chronic neurological manifestations of COVID-19 involving the peripheral nervous system.

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