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Acute Motor Axonal Neuropathy Related to COVID-19 Infection: A New Diagnostic Overview

To the Editor:

Currently, several cases of Guillain–Barré syndrome (GBS) resulting from COVID-19 infection have been reported.[1,2] Among GBS types, acute motor axonal neuropathy (AMAN) diagnosis is based on decreased compound muscle action potentials and absence of demyelination.[3] Here, we present a singular case of AMAN after COVID-19 infection with some clinical, electromyoneurography, and laboratory features that have not been reported so far.

A 57-year-old man was admitted to the Emergency Department of Macerata Hospital, Italy, due to the onset, 2/3 days before, of hyposthenia, mainly at the proximal level in the upper limbs, first on the left side, with loss of mobility. The patient previously had a SARS-CoV-2 infection, ascertained by a naso-oropharyngeal swab subjected to transcription-polymerase chain reaction. The patient's initial symptoms included a high fever (poorly responsive to antipyretics), coughing, and dyspnea, treated at home. About 2 days after the second (and last) negative naso-oropharyngeal swab, performed 15 days after, neurological symptoms arose. An urgent brain computed tomography (CT) was performed, showing a normal finding. The conclusions of the neurological examination were as follows: right facial neuropathy outcomes, upper limb flaccid paraparesis [proximal 0/5, distal 3/5, according to the Medical Research Council [MRC] scale], and absent biceps and triceps reflexes. In the lower limbs, hyposthenia was found in the dorsal flexion of the right foot and toes (3/5 according to the MRC scale). There were no sensory deficits. Patellar and Achilles tendon reflexes were present on the left side and absent on the right side. Plantar skin flexion reflex was present bilaterally. On the first day of hospitalization, diagnostic rachicentesis was performed, with chemical-physical, virological (with the exclusion of SARS-CoV-2 testing), and cytological analyses of the cerebral fluid. Standard laboratory tests and special blood tests (*Campylobacter jejuni* serology, HbA1c, ANA, ENA, anti-DNA, c-ANCA, p-ANCA, HIV, HBV, HCV, serum vitamin B12-level, and serum protein electrophoresis) were also within the normal range. To complete the diagnostic framework, antiganglioside antibodies tests, total body CT, cervical magnetic resonance imaging, and electromyoneurography were performed. Our patient received 0.4 g/kg/day intravenous immunoglobulin and desametasone at a age of 500 mg/day, both for 5 consecutive days. Cerebrospinal fluid analysis was performed and confirmed an albumin/cytological dissociation (0.62 g of protein vs. 2 cells). Electroneurography results (performed on the third day of hospitalization and after a week) showed axonal-only motor neuropathy, with decreased amplitude at compound muscle action potential, sensitive responses preserved, and the absence of demyelinations. Electromyography showed decreased recruitment to the analysis of voluntary muscle activity, with appearance of spontaneous activity in the second electromyography compared with the first.

Antiganglioside antibodies, in particular GM1 Immunoglobulin G (IgG) and GD1a IgG, were positive. After therapy with intravenous immunoglobulin, the patient presented a slight improvement in strength in the distal upper limbs (according to the MRC scale 0/5 in the abduction of the arm and in the rotation of the arm outward, while the actions of the biceps, triceps, and hand movements were quantified as 4/5). In the lower limbs, there was a deficit of strength in the dorsiflexion of the right foot 3/5, whereas a slight deficit of strength also appeared in the contralateral foot quantified as 4/5. Deep tendon reflexes were absent generally. Our case had an axonal and nondemyelinating neuropathy with a double positivity to antiganglioside antibodies, GM1 and GD1a; all sensitive responses were preserved, and no

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sensory disturbances were presented during the course of hospitalization.

Antiganglioside antibodies are principally associated with autoimmune peripheral neuropathies. In these disorders, immune attack is inadvertently directed at peripheral nerve by autoantibodies that target glycan structures borne by glycolipids, particularly gangliosides concentrated in nerve myelin and axons. The most thoroughly studied disorder, in which IgG autoantibodies against gangliosides arise following acute infections, notably *C. jejuni* enteritis, is the acute paralytic disease, GBS. Two GBS variants, AMAN and Miller Fisher syndrome, are consistently and highly associated antiglycolipid autoantibodies. In AMAN, the primary target is the motor axolemmal membrane[4] rather than the myelin sheath, and antiganglioside antibodies are directed to sialylated epitopes on GM1a, GM1b, GD1a, and GalNAc-GD1a.[5]

In light of our clinical, electromyoneurography, and laboratory findings, it is conceivable that COVID-19, similarly to *C. jejuni* enteritis, triggers the production of specific subclasses of antiganglioside antibodies causing acute motor neuropathy. It is now widely confirmed that GBS should be considered as neurological complications of COVID-19 infection, but further studies are needed to better define the pathogenesis and therefore the clinical and prognostic characteristics of all possible GBS variants.

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Painless Diabetic Lumbosacral Radiculoplexus Neuropathy: A Manifestation of Treatment-Induced Neuropathy of Diabetes

To the Editor:

A 58-year-old White woman presented with a 2-month history of bilateral leg weakness. Three months ago, she was diagnosed with type 2 diabetes mellitus with a hemoglobin A1C (HbA1C) of 17.2% and was treated with insulin. One month after the treatment, she noticed progressive weakness in both legs with left foot drop, numbness in feet, and 40-kg weight loss. She is a vegetarian and takes daily multivitamins. She denied any pain and alcohol intake history.

On examination, she had an asymmetric leg weakness, worse distally with a left foot drop. Muscle strength by the Medical Research Council scale was 3 of 5 for bilateral proximal legs, 2 of 5 for right ankle eversion, inversion, dorsiflexion and plantar flexion, and no movement of the left ankle in any directions. Diminished all sensations below ankles and areflexia in legs were noted. She could not stand or walk. The rest of the examination was normal.

Complete blood counts, renal and liver function tests were normal. HbA1C significantly dropped from 17.2% to 8.1%. Electrodiagnostic studies of the left extremity showed severe left L4 and L5 lumbosacral