Antianglioside antibodies in Guillain-Barré syndrome associated with SARS-CoV-2 infection

The pandemic SARS-CoV-2 is dramatically spreading around the world. Patients with COVID-19 typically present with viral pneumonia and resultant life-threatening respiratory complications. Although little information is available regarding the neurological manifestations of COVID-19, there are a few reports that describe Guillain-Barré syndrome (GBS) as an acute presentation of SARS-CoV-2. Here, we report a new case of COVID-19 initially presenting with acute GBS. On 24 March 2020, a 72-year-old woman arrived at the emergency department of our hospital presenting with lumbar pain, lower limb weakness and paresthesia, which started abruptly and progressed within 2 days (table 1). In the previous 10 days she had fever (Tmax 38.5°C, 101.3°F), anosmia, hypogeusia, dry cough and sore throat lasting for 3 days. Neurological examination disclosed symmetric weakness Medical Research Council (MRC) grade 3/5 in both legs and MRC grade 4/5 in both arms and hands, with generalised areflexia. Laboratory results on admission were unremarkable except for an increase of fibrinogen (634 mg/dL; normal: 200–400 mg/dL), normal glucose level (65% of blood glucose level); RT-PCR assay for SARS-CoV-2 on CSF was negative. Screening tests for Epstein–Barr virus, Campylobacter jejuni, cytomegalovirus, herpes simplex virus, varicella zoster virus, influenza A virus, Haemophilus influenzae, HIV and culture examinations were negative. The findings were generally consistent with GBS. The antangioglioside antibodies ELISA test (Bühlmann GanglioCombi) was positive for IgG, anti-GM1, anti-GD1a and anti-GD1b. On this day, an intravenous immunoglobulin standard protocol was started. On the third day, after admission, muscle weakness rapidly evolved to a flaccid areflexic tetraparesis and facial diplegia. She developed respiratory failure with neuromuscular features and for this reason was admitted to the intensive care unit (ICU). During her ICU stay, she was also treated with hydroxychloroquine for 15 days and doxycycline hydrochloride. At day 25, she was negative to RT-PCR for nasopharyngeal swab SARS-CoV-2. At this point, although still partially respiratorily supported, we observed a significant clinical improvement: MRC superior limb 4/5 and 3/4 inferior limb.

Until now, six other cases of SARS-CoV-2 infection associated with GBS have been reported. As in other patients, ours showed a classic post-infectious profile as reported in GBS, while until now antangioglioside antibody detection for different gangliosides (anti-GM1, anti-GD1a and anti-GD1b) represents a novelty in GBS associated with SARS-CoV-2 infection. Antangioglioside autoantibodies of the IgG type are detected in a half of patients with GBS and their detection strongly supports the diagnosis. Antangioglioside antibodies are strongly associated with acute motor axonal neuropathy subtype more than acute inflammatory demyelinating polyneuropathy. Complexes of gangliosides may also be targeted by autoantibodies in GBS and its variants, the GD1a/GD1b is one of the more frequent especially when cranial nerves are involved. These results suggest a broad antangioglioside antibody response as observed in Zika virus-associated patients with GBS. Antianglioside antibodies could be responsible for acute ascendent polyneuropathy but could also explain other neurological symptoms such as anosmia, as GD1a gangliosides are strongly expressed in the olfactory bulb. This new description gives new information about GBS as an acute presentation of SARS-CoV-2. Antianglioside antibody evaluations could also be useful to understand other and more frequent neurological symptoms related to SARS-CoV-2.

Table 1

<table>
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<tr>
<th>Onset of neurological syndrome</th>
<th>Neurological signs and symptoms</th>
<th>CSF findings*</th>
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| 10 days after fever, cough, sore throat and anosmia | Flaccid paraplegia; global areflexia; lower limb paresis (day 2) | Day 2; protein level, 198 mg/dL; white cell count, 18/mm³; negative PCR assay for SARS-CoV-2 | Positive: Anti-GM1 (1:70); Anti-GD1a (1:72); Anti-GD1b (1:54) | Not tested | Received one cycle of IVIg, still partially respiratorily supported | **Correspondence to Dr Carlo Civardi, Department of Neurology, ASL TO4, Ivrea, Piedmont, Italy c_civardi@yahoo.com

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Day 2: protein level, 198 mg/dL; white cell count, 18/mm³; negative PCR assay for SARS-CoV-2 |

* On CSF analysis, all the patients had a normal glucose level and IgG index and a polyclonal pattern on electrophoresis. The normal range for the protein level is <55 mg/dL.

1Antianglioside antibody ELISA test (Bühlmann GanglioCombi) was used to test for antibodies to GM1, GD1b, GD1a and GD1b. Normal value <50.

CSF, cerebrospinal fluid; ICU, intensive care unit; IVIg, intravenous immunoglobulin; MRC, Medical Research Council.
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