

LETTERS

Antiganglioside 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.^{1,2} 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 (T_{max} 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 feet 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) and C reactive protein test (2.94 mg/dL; normal 0.1–0.75 mg/dL). Due to the pandemic situation, RT-PCR for nasopharyngeal swab SARS-CoV-2 was performed routinely and it displayed positivity. Nerve conduction studies (day 2) showed prolonged distal latencies, absent F waves, conduction blocks for the tibial nerves at the popliteal fossa and spare of sural nerve, supporting demyelinating neuropathy (online supplementary table e-1). Cerebrospinal fluid (CSF) testing showed a slight increase of cell counts (0.02 $\times 10^9/L$, normal 0–0.01 $\times 10^9/L$ all monocytes), and a significant increased protein level (198 mg/

dL, normal: <55 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.³ The antiganglioside 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 hyclate. 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.^{1,2} As in other patients,¹ ours showed a classic postinfectious profile as reported in GBS, while until now antiganglioside antibody detection for different gangliosides (anti-GM1, anti-GD1a and anti-GD1b) represents a novelty in GBS associated with SARS-CoV-2 infection. Antiganglioside autoantibodies of the IgG type are detected in a half of patients with GBS and their detection strongly supports the diagnosis.⁴ Antiganglioside antibodies are strongly associated with acute motor axonal neuropathy subtype more than acute inflammatory demyelinating polyneuropathy.⁴ 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.⁴ These results suggest a broad antiganglioside antibody response as observed in Zika

virus-associated patients with GBS.⁵ Antiganglioside antibodies could be responsible for acute ascending polyneuropathy but could also explain other neurological symptoms such as anosmia, as GD1a gangliosides are strongly expressed in the olfactory bulb.⁴ This new description gives new information about GBS as an acute presentation of SARS-CoV-2. Antiganglioside antibody evaluations could also be useful to understand other and more frequent neurological symptoms related to SARS-CoV-2.

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Table 1 Patient characteristics

Onset of neurological syndrome	Neurological signs and symptoms	CSF findings*	Antiganglioside antibodies	MRI results	Treatment and outcomes
10 days after fever, cough, sore throat and anosmia	Flaccid paraplegia; global areflexia; lower limb paresthesia (day 2). Muscle weakness rapidly evolved to a flaccid areflexic tetraparesis, facial diplegia and respiratory failure admitted to the ICU (day 3)	Day 2: protein level, 198 mg/dL; white cell count, 18/mm ³ ; negative PCR assay for SARS-CoV-2	Positive: Anti-GM1 (1:70) Anti-GD1a (1:72) Anti-GD1b (1:64)	Not tested	Received one cycle of IVIg; still partially respiratory supported. Significant clinical improvement: MRC superior limb 4/5 and 3/4 inferior limb (day 33)

*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.

†Antiganglioside antibody ELISA test (Bühlmann GanglioCombi) was used to test for antibodies to GM1, GQ1b, GD1a and GD1b. Normal value ≤ 50 .

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

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