SARS-CoV-2 and Guillain–Barré syndrome: AIDP variant with a favourable outcome

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Background and purpose: The spectrum of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 infection (SARS-CoV-2), includes different neurologic manifestations of the central and peripheral nervous system.
Methods: From March through April 2020, in two university hospitals located in western Switzerland, we examined three patients with Guillain–Barré syndrome (GBS) following SARS-CoV-2.
Results: These cases were characterized by a primary demyelinating electrophysiological pattern (Acute inflammatory demyelinating polyneuropathy or AIDP) and a less severe disease course compared to recently published case series. Clinical improvement was observed in all patients at week five. One patient was discharged from hospital after full recovery with persistence of minor neurological signs (areflexia). Two of the three patients remained hospitalized: one was able to walk and the other could stand up with assistance.
Conclusions: We report three cases of typical GBS (AIDP) occurring after SARS-CoV-2 infection and presenting with a favourable clinical course. Given the interval between COVID-19-related symptoms and neurological manifestations (mean of 15 days) we postulate a secondary immune-mediated mechanism rather than direct viral damage.

The world has been experiencing the outbreak of a novel infectious agent known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is responsible for the coronavirus disease 19 (COVID-19) [1]. Life-threatening complications described in SARS-CoV-2-infected patients include acute respiratory distress syndrome, acute kidney failure and cardiac injury [2]. Nonetheless, only few neurological complications have been described so far [3].

A recent retrospective study performed in the city of Wuhan, China, reported that 78/214 patients (36.4%) with COVID-19 presented with nervous system clinical findings: mainly dizziness, headache, encephalopathy, stroke, smell and taste disorders, and musculoskeletal injury [4]. Zhao *et al.* [5] published the first case of a 61-year-old patient presenting with a rapidly evolving ascending weakness and mild distal sensory complaints, followed by COVID-19-related symptoms, leading to the diagnosis of Guillain–Barré syndrome (GBS). The authors concluded that SARS-CoV-2 might have triggered GBS in this case, following a para-infectious pattern, as described with Zika virus (ZIKV) infection [6]. A recent series of five GBS cases from northern Italy describes a severe disease course with predominant axonal involvement [7].

We report a series of three cases of typical GBS, preceded by classic signs and symptoms of biologically confirmed COVID-19, which were studied in Geneva and Lausanne University Hospitals, Switzerland, between March and April 2020. On April 12 2020, 26

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144 COVID-19 cases were confirmed in Switzerland and 9,360 in our catchment area.

Materials and methods

Clinical and ancillary test descriptions were personally retrieved by the authors, who examined the patients. This report was conducted in compliance with the Swiss Federal Act on Research involving Human Beings that waive ethic approval for case reports of fewer than five patients.

Case reports

All patients presented with distal paresthesias and rapidly progressive limb weakness, evolving to either moderate tetraparesis (2/3) or tetraplegia (1/3) and areflexia (3/3) within the first 5 days. One patient required mechanical ventilation due to respiratory failure and two underwent functional haemodynamic monitoring of dysautonomic signs. Additionally, two patients presented with pain and only one with bulbar signs and facial biplegia. Neurological symptoms appeared within the first 22 days (7, 15 and 22 days) after the appearance of typical COVID-19-related symptoms. For clinical details see Appendix S1.

Laboratory findings showed grade 1 and 2 lymphopenia in two out of three patients. Anti-ganglioside antibodies were negative. Cerebrospinal fluid (CSF) analysis showed classic albuminocytological dissociation in two out of three patients, with a white cell count of < 4 cell/μl (additional results are detailed in Table 1). Reverse-transcription polymerase-chain-reaction (RT-PCR) assay for SARS-CoV-2 of the CSF was tested in two out of three patients with a negative result. Initial RT-PCR extracted from the nasopharyngeal

Table 1 Clinical characteristics and laboratory findings of three patients with Guillain–Barré syndrome after COVID-19

	Case 1	Case 2	Case 3
Age/Gender	52/Female	63/Female	61/Female
Comorbidities	None	Type 2 diabetes	None
Symptoms of COVID-19	Dry cough, fever, odynophagia, arthralgia, diarrhoea	Dry cough, shivering, odynophagia, breathing difficulties, chest pain	Productive cough, fever, myalgia, vasovagal syncope, diarrhoea, nausea and vomiting
Method for COVID-19 diagnosis	Antibodies for SARS-CoV-2 IgM/IgG, followed by RT-PCR positive in nasopharyngeal swab (4th test)	RT-PCR in nasopharyngeal swab (2nd test)	RT-PCR in nasopharyngeal swab
Neurological signs and symptoms	Back pain, limb weakness, ataxia, distal paresthesia, dysgeusia, cacosmia. Developed respiratory failure, dysautonomia and tetraplegia with areflexia (day 4)	Lower limb pain, mild weakness and normal deep tendon reflexes. Developed tetraparesis, distal paresthesia and areflexia (day 5)	Lower limb weakness and distal paresthesia, dizziness, dysphagia, dysautonomia, areflexia. Presented worsening of bulbar symptoms and bilateral facial palsy (day 4)
Time of neurological symptom onset (days)	15	7	22
Cerebrospinal fluid findings	WBC 3 cell/μl; Protein level 60 mg/dl; Negative PCR assay for SARS-CoV-2 (day 2)	WBC 2 cell/μl; Protein level 40 mg/dl; PCR assay for SARS-CoV-2 was not performed (day 6)	WBC 4 cell/μl; Protein level 140 mg/dl; Negative PCR assay for SARS-CoV-2 (day 1)
Serum studies	WBC 8900 cells/mm^3; Lymphocytes 1200 cells/mm^3; Platelets 45 500 cells/mm^3. Normal kidney and liver function. Antibodies to ganglioside panel[a] were negative	WBC 3300 cells/mm^3; Lymphocytes 800 cells/mm^3; Platelets 119 000 cells/mm^3. Normal kidney function. Elevated transaminase levels (AST 65 U/l; N < 45 U/l). Antibodies to ganglioside panel[a] were not performed	WBC 4000 cells/mm^3; Lymphocytes 600 cells/mm^3; Platelets 322 000 cells/mm^3. Normal kidney and liver function. Hyponatremia (127 mmol/l). Antibodies to ganglioside panel[a] were not performed
MRI results	Spinal cord: no nerve root gadolinium enhancement	Not performed	Spinal cord: lumbosacral nerve root enhancement. Normal brain imaging
Treatment	1 cycle of IVIg (day 2)	1 cycle of IVIg (day 10)	1 cycle of IVIg (day 2)
Clinical outcome at 5 weeks	Improvement of tetraparesis. Able to stand up with assistance. GBS disability clinical score 4/6	Dismissal with full motor recovery. Persistence of lower limb areflexia and distal paresthesia. GBS disability clinical score 1/6	Improvement of tetraparesis and ability to walk with assistance. Persistence of neuropathic pain and distal paresthesia. GBS disability clinical score 3/6

AST, aspartate transaminase; COVID-19, coronavirus disease 2019; GBS, Guillain–Barré syndrome; IVIg, intravenous immunoglobulins; MRI, magnetic resonance imaging; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WBC, white blood cell count. [a]Anti-ganglioside antibodies panel includes anti-GM1, GD1a and GQ1b.

swab was positive in two cases. The third case showed a SARS-CoV-2 seroconversion in the serum and the fourth nasopharyngeal swab was positive. Magnetic resonance imaging was performed in two patients, and one disclosed gadolinium enhancement of the lumbosacral roots. Nerve conduction studies revealed a typical demyelinating pattern (3/3) and one case showed nerve conduction blocks (Table S1), which persisted in an examination conducted one week later. Needle electromyography was recorded in one patient showing no abnormal spontaneous activity.

All patients were treated with intravenous immunoglobulin (0.4 g/kg/day for 5 days). The clinical outcome was favourable in one patient who was discharged and able to walk without assistance (Appendix S1, case 2); another patient was able to walk 100–200 m with aid (case 3). The third patient remained bedbound, but was able to rise from a chair with assistance (case 1).

Discussion

Nerve conduction studies showed a classic demyelinating pattern (AIDP) in the three patients. This observation contrasts with previous publications, which reported axonal loss correlating with a more severe disease course and greater disability at one month [7]. In our cohort, full recovery was observed in one patient, another one was able to walk with assistance and the last remained bedridden but was able to rise to standing up (GBS disability scores at five weeks follow-up of 1/6, 3/6 and 4/6, respectively).

The median (range) period between the onset of COVID-19-related symptoms and neurological complaints was 15 (7–22) days, which was longer than the interval reported by Toscano *et al*. (5–10 days) [7]. In addition, PCR SARS-CoV-2 was not detected in the CSF of our patients nor in the Italian cohort [7].

These observations support the hypothesis that SARS-CoV-2 triggers GBS via a secondary immune-mediated mechanism rather than via direct viral neuropathic damage, as described after ZIKV infection [6]. Additional clinical data are needed to further elucidate the exact mechanism underlying SARS-CoV-2-associated GBS.

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Disclosure of conflicts of interest

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and/or its Appendix S1 and Table S1.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Clinical history of patients with Guillain-Barré syndrome.

Table S1. Nerve conduction studies in three patients with Guillain-Barré syndrome and COVID-19.

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