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SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with favorable outcome

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The entire world has been experiencing the outbreak of a novel infectious agent known as severe acute respiratory syndrome corona virus 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 (36.4%) patients with COVID-19 presented with nervous system clinical findings; mainly dizziness, headache, encephalopathy, stroke, smell and taste disorders and musculoskeletal injury[4]. Zhao and collaborators 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)[5]. 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, who were studied in Geneva and Lausanne University Hospitals, Switzerland, between March and April 2020. On April

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12th, 26'144 COVID-19 cases were confirmed in Switzerland and 9360 in our catchment area.

Materials and Methods

Clinical and ancillary tests description were personally retrieved by the authors, who examined the patients. This report is conducted in compliance to Swiss Federal Act on Research involving Human Beings that wave ethic approval for case report of less 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 five days. One patient required mechanical ventilation due to respiratory failure and two underwent functional hemodynamic 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 supplementary material.

Laboratory findings showed grade 1 and 2 lymphopenia in 2/3 patients. Anti-gangliosides antibodies were negative. Cerebrospinal fluid (CSF) analysis showed classic albuminocytologic dissociation in 2/3 patients, with a white cell count < 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 2/3 patients with a negative result. Initial RT-PCR extracted from the nasopharyngeal 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.

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Magnetic resonance imaging was performed in two patients and one disclosed gadolinium enhancement of the lumbosacral roots. Nerve conduction studies (NCS) revealed a typical demyelinating pattern (3/3) and one case showed nerve conduction blocks (supplementary table), which persisted in an exam conducted one week later. Needle electromyography was recorded in one patient showing no abnormal spontaneous activity.

All patients were treated with intravenous immunoglobulins (0.4 g/kg/day for five days). Clinical outcome was favourable in one patient who was dismissed and able to walk without assistance (supplementary material, case 2), another patient was able to walk 100-200 metres with aid (case 3). The third patient remained bedbound but was able to rise from a chair with assistance (case 1).

Discussion

NCS 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 score at five weeks follow-up of 1/6, 3/6 and 4/6 respectively).

The median period between the onset of COVID-19 related-symptoms and neurological complaints was fifteen days (7-22 days); longer than the interval reported by Toscano and collaborators (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].

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

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Disclosure of potential conflict 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 supplementary material.

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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 (4^{th} test)	RT-PCR in nasopharyngeal swab (2^{nd} 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	White cell count 3 cell/µL; Protein level 60 mg/dl; Negative PCR assay for SARS-CoV-2 (day 2)	White cell count 2 cell/µL; Protein level 40 mg/dl; PCR assay for SARS-CoV-2 was not performed (day 6)	White cell count 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 45500 cells/mm^3. Normal kidney and liver function. Antibodies to	WBC 3300 cells/mm^3; Lymphocytes 800 cells/mm^3; Platelets 119000 cells/mm^3. Normal kidney function. Elevated transaminase levels	WBC 4000 cells/mm^3; Lymphocytes 600 cells/mm^3; Platelets 322000 cells/mm^3. Normal kidney and liver function. Hyponatremia (127

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	ganglioside panel* was negative	(AST 65 U/l; N<45 U/l). Antibodies to ganglioside panel* was not performed	mmol/l). Antibodies to ganglioside panel* was 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

COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; RT-PCR = reverse transcription polymerase chain reaction; WBC = white blood cell count; MRI = magnetic resonance imaging; IVIg = intravenous immunoglobulins

*Anti-ganglioside antibodies panel includes anti-GM1, GD1a and GQ1b