

Autoimmunity complicating SARS-CoV-2 infection in selective IgA-deficiency

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Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 can result in severe disease and become critically challenging to hospitals via high demand for intensive care and mechanical ventilation.

Guillain-Barré syndrome (GBS) and its variants have been described as neurologic complications of COVID-19, and fatal cases were reported.¹ The mechanisms by which COVID-19 predisposes to autoimmunity are unclear, and potential biomarkers or risk factors remain unknown.

Case report

A 35-year-old, healthy Caucasian woman initially presented with fever and coughing over 1 week (days 0–7, figure, A for timeline) at her family doctor and was subsequently tested positive for SARS-CoV-2 via PCR. The patient had experienced no other infections in previous weeks and had not received any vaccinations.

On day 8, she developed severe diabetic ketoacidosis (DKA) as the first manifestation of type 1 diabetes (T1D; pH: 6.7; base excess: –27 mmol/L; blood glucose: 25.1 mmol/L, HbA1c: 6.4%), and antibodies against islet cell antigen 2 and glutamate decarboxylase (GAD65) were positive. There was no history of polyuria or polydipsia. She was admitted to intensive care unit and transiently recovered after fluid resuscitation and insulin treatment.

However, because of rapidly developing respiratory insufficiency, intubation became necessary on day 10. Chest x-ray and CT scan showed signs suggestive of COVID-19.

During ICU treatment, the patient recovered from COVID-19, and nasopharyngeal swabs for SARS-CoV-2 were repeatedly negative (first on day 15). The patient was weaned from ventilatory support, and extubation was performed on day 17. Blood glucose levels remained well controlled throughout after IV insulin substitution.

However, restrictive lung disorder resulting from diaphragmatic paralysis rapidly evolved, and poor management of pharyngeal secretions forced reintubation within 24 hours. A rapidly progressive proximal tetraparesis and dysautonomia with tachycardia and absent heart rate variability were first noticed on day 19 and repeatedly let to self-limiting, symptomatic bradycardia on day 20.

MRI scans of the brain and cervical cord were unremarkable. CSF analysis showed albuminocytologic dissociation (CSF total protein: 1421 mg/L, CSF cell count: 2/μL, and CSF oligoclonal bands were negative). SARS-CoV-2 was not detectable in the CSF. Nerve conduction studies revealed widespread axonal damage as indicated by reduced compound motor action

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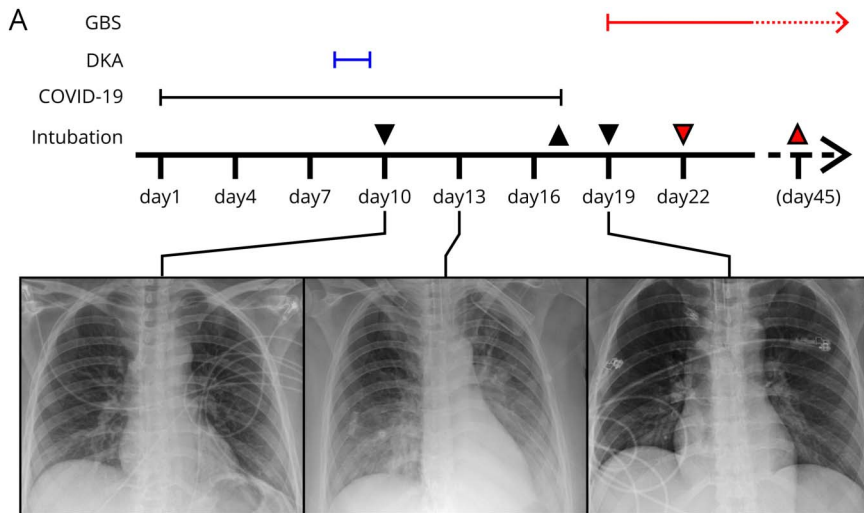
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Figure Clinical course of our patient with COVID-19



B

Sensory recordings	SAP amplitude (µV)	Velocity (m/s)	
Ulnar	26.5/18.2	57.6/52.1	
Sural	8.0/7.8	51.9/50.5	
Motor recordings	Distal latency (ms)	CMAP amplitude (mV)	Velocity (m/s)
Peroneal	5.8/4.8	0.8/1.1	46.3/48.1
Tibial	4.8/4.6	3.7/4.2	45.6/44.4
Ulnar	2.3/3.0	3.2/3.1	64.5/51.9

(A) Clinical course of our patient. Downward arrows indicate intubation, upward arrow indicates extubation, colored arrows indicate tracheostomy and decannulation. Chest x-ray images refer to the respective dates. (B) Data from nerve conduction studies on day 20. *Abnormal. Reference for CMAP is >5 mV in all examined nerves. EMG was not performed. COVID-19 = coronavirus disease 2019; CMAP = compound muscle action potential; DKA = diabetic ketoacidosis; GBS = Guillain-Barré syndrome; SAP = sensory action potential.

potentials (figure, B). Antibodies against Gd1B were positive, whereas antibodies against other gangliosides were negative.

Laboratory analysis revealed selective immunoglobulin A deficiency (sIgAD; serum IgA <0.05g/L) but was otherwise unremarkable for autoimmune or hematologic disorders. Virologic and serologic testing was negative for hepatitis, HIV, herpes viruses, other respiratory viruses, and Campylobacter.

We performed 5 courses of plasma exchange. After this, we observed early recovery with increasing muscle strength and reemerging muscle reflexes. However, bulbar palsy persisted and prompted early tracheostomy on day 22. Decannulation was performed on day 45. Currently, symptoms mostly resolved but mild neurogenic dysphagia persists. C-peptide levels remain below thresholds, and insulin treatment is continued.

Discussion

We believe that our patient suffered from sIgAD since childhood but remained undiagnosed in the absence of symptoms until autoimmunity was finally induced by COVID-19.

SARS-CoV-2 has been identified as a potential trigger for GBS because its spike viral protein interacts with ganglioside antigens on human cells and thereby paves the way for an antiganglioside immune reaction.¹ Such association has not been shown yet for T1D, but previous reports on the development of DKA within already 1 week after nivolumab treatment² indicate that a single trigger can result in rapid-onset T1D in susceptible patients and normal HbA1c levels render preexisting yet undiscovered T1D unlikely here. In addition, sIgAD is a known risk factor for T1D.³

Moreover, previous cases on GBS after COVID-19 mostly showed an onset within 5–10 days supporting that COVID-19 is a sufficient trigger of rapid-onset autoimmunity.¹ However in GBS, the role of sIgAD is less clear, although asymptomatic ganglioside antibodies are more common in patients with sIgAD compared with the general population.⁴

Clinically, our case here shares many features with previously published reports. Our patients suffered from a predominantly axonal variant of GBS, which has been observed

before. Previous patients also developed GBS already within 7–10 days after the onset of COVID-19.¹ Furthermore, bulbar involvement has been described in previous cases.^{5,6} Especially, it was present in a case of Miller-Fisher syndrome that also presented with Gd1b antibodies.⁵ We have not observed ophthalmoplegia, yet dysphagia subsequent to bulbar palsy resulted in necessity for tracheostomy in our patient as described before.⁷

Finally, our findings expand the spectrum of autoimmunity after COVID-19. Although COVID-19 was repeatedly demonstrated as an inducer of GBS alone, we believe that the preexisting sIgAD significantly contributed to the development of 2 different autoimmune disorders after COVID-19.

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Disclosure

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Appendix Authors

Name	Location	Contribution
Steffen Pfeuffer, MD	University Hospital Münster	Study concept and design, acquisition and interpretation of data, and drafted the manuscript
Matthias Pawlowski, MD, PhD	University Hospital Münster	Acquisition and interpretation of data and critical revision of the manuscript for intellectual content
Gunter Joos	University Hospital Münster	Acquisition of data and critical revision of the manuscript for intellectual content
Jens Minnerup, MD	University Hospital Münster	Critical revision of the manuscript for intellectual content
Sven G. Meuth, MD, PhD	University Hospital Münster	Critical revision of the manuscript for intellectual content
Rainer Dziewas, MD	University Hospital Münster	Study concept and design and critical revision of the manuscript for intellectual content
Heinz Wiendl, MD	University Hospital Münster	Study concept and design and critical revision of manuscript for intellectual content

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