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Post SARS-CoV-2 vaccination Guillain-Barre syndrome in 19 patients

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SARS-CoV-2 vaccinations are not free from side effects. Usually, they are mild or moderate but occasionally severe. One of these severe side effects is Guillain-Barre syndrome (GBS). This review summarizes and discusses GBS as a side effect of SARS-CoV-2 vaccinations (SCoVaG) based on recent research reports. Altogether, nine articles reporting 18 patients with SCoVaG were identified and one more report on another patient is under review. The age for the studies ranged between 20-86y. Nine patients were male, and ten were female. In all 19 patients, SCoVaG developed after the first dose of the vaccine. The Astra Zeneca vaccine was used in fourteen patients, the Pfizer vaccine in four patients, and the Johnson & Johnson vaccine was applied in one patient. The latency between vaccination and onset of GBS ranged from 3h to 39d. The treatment of SCoVaG included IVIGs (n=13), steroids (n=3), or no therapy (n=3). Six patients required mechanical ventilation. Only a single patient recovered completely and partial recovery was achieved in nine patients. In conclusion, GBS may develop time-linked to the first dose of a SARS-CoV-2 vaccination. Though a causal relationship between SARS-CoV-2 vaccinations and SCoVaG remains speculative, more evidence is in favour than against it.

KEYWORDS: SARS-CoV-2; COVID-19; Neuro-COVID; Complications; Vaccination; Polyradiculitis.
and the outcome was not reported in nine patients (Table 1).

All four patients reported from the study of Allen et al. (3) experienced bifacial muscle weakness with paresthesias within three weeks after administering vector-based SARS-CoV-2 vaccine being classified as polynuertitis cranialis (PNC) variant of GBS (3). Three patients benefited from intravenous immunoglobulins (IVIGs) or steroids, and one recovered without treatment (3). None of the four patients required mechanical ventilation.

The fifth patient with SCoVaG was a 32y old male who developed GBS, subtype acute, inflammatory, demyelinating polyneuropathy (AIDP), eight days after the first dose of a vector-based SARS-CoV-2 vaccine (Table 1) (4). This patient had a previous history of AIDP 14 years earlier, from which he recovered completely and benefited from two IVIG cycles and plasmapheresis but is still handicapped and currently undergoing immune-adsorption (4).

The sixth patient with SCoVaG was a 69y old female who developed AIDP 39d after the first dose of a vector-based SARS-CoV-2 vaccine and after 15d was tested positive for SARS-CoV-2 (Table 1). The case has not been published yet but is under review.

The seventh patient with SCoVaG is an 86y old female who developed back pain 14d after the first dose, which progressed to facial diplegia, quadriparesis, and muscular respiratory insufficiency and required mechanical ventilation. The second patient was a 67y old female who developed limb paresthesias 14d after the first dose, which progressed to facial diplegia, abducens palsy, quadriparesis and respiratory insufficiency and required mechanical ventilation. The third patient was a 53y old female who developed lower limb paresthesias and weakness 12d after the first dose, which progressed to facial diplegia, quadriparesis and respiratory insufficiency and required mechanical ventilation. The fourth patient was a 68y old female who developed upper and lower limb paresthesias and muscle weakness that progressed to facial diplegia, dysphagia, and respiratory insufficiency and was treated with mechanical ventilation (Table 1). The fifth patient was a 70y old male who developed facial diplegia, bulbar palsy, and bilateral distal upper and lower limb numbness 11d after the first dose, which progressed to quadriparesis and respiratory insufficiency and required artificial ventilation (7). The sixth patient was a 60y old female who developed facial diplegia, bulbar palsy, ophthalmoplegia, quadriparesis, and distal upper and lower limb numbness 12d after the first dose (7). She did not develop affection of the respiratory muscles. The seventh patient was a 69y old female who developed facial diplegia, bulbar palsy, and quadriparesis with upper and lower limb numbness 13d after the first dose. She developed respiratory muscle involvement and required artificial ventilation (7).

The 60y old female reported by Marquez-Loza et al. (8) developed back and leg pain followed by headache, nausea, vomiting, double vision, facial diplegia, and paraparesis of lower legs. She benefited from IVIG and recovered partially (8). NCSEs revealed the absence of late responses, being interpreted as early signs of GBS.

The patient reported by Narasimhalu et al. (9) is a 32y old female who developed back pain 10d after the first dose, which progressed to facial diplegia, quadriparesis, and muscular respiratory insufficiency and required mechanical ventilation.
revealed perineural sheath enhancement V/3. No cerebrospinal fluid (CSF) investigations or NCSs were carried out (9).

Concerning the case reported by Aomar-Milian et al. (10), it remains unclear if acute, motor, and sensory axonal neuropathy (AMSAN) was due to SARS-CoV-2 infection or vaccination that he received before the onset of GBS. The second patient reported by these authors experienced GBS most likely due to SARS-CoV-2 infection and not due to vaccination he received before the infection (10).

The 37y old male reported by Patel et al. (11) presented with progressive quadriparesis and distal sensory disturbances without involving respiratory muscles. He responded only partially to IVIGs (11).

The patient with SCoVaG, as reported by Sadoff et al. (12), was not included in the present review as no details were provided.

According to the Medicines and Healthcare products Regulatory Agency (MHRA), six patients with SCoVaG were further registered, but no details about these patients were reported and hence not included in this review (13).

The Vaccine Adverse Event Reporting System (VAERS) does not list GBS as an adverse reaction to SARS-CoV-2 vaccination (14). However, in the 13th July 2021 update from FDA News Release, it was mentioned that 100 patients developed preliminary SCoVaG after receiving the Johnson & Johnson vaccine (15). In 95 of these patients, GBS was severe, requiring hospitalization. Furthermore, the European Medicines Agency’s (EMA) COVID-19 vaccine safety update indicates that as of 27th June 2021, 227 patients with SCoVaG after receiving the AZV have been reported (16). However, these cases were collected by passive surveillance and were not revised cases. According to the WHO Global Advisory Committee on Vaccine Safety (GACVS) COVID-19 subcommittee on the reports of GBS following adenovirus vector COVID-19 vaccines, only rare cases of SCoVaG have been reported (17). The committee indicates that more rigorous studies using alternative data sources and robust study designs and comparison of vaccinated and unvaccinated populations are warranted (17).

**DISCUSSION**

This narrative review shows that since the introduction of the SARS-CoV-2 vaccination in December 2020, at least 19 patients have been reported to experience SCoVaG time-linked to the first dose of a SARS-CoV-2 vaccination. Additionally, more than 300 SCoVaG patients were reported by the FDA and the EMA. In the majority of the 19 cases, SCoVaG developed after the application of a vector-based SARS-CoV-2 vaccine. The latency between vaccination and onset of SCoVaG was highly variable. The severity of the complications ranged from mild to severe and required mechanical ventilation in six patients. In most cases, the outcome was favourable, but only partial recovery was achieved on the reporting date.

The presence of a causal relationship between vaccination and the occurrence of SCoVaG remains speculative, but several arguments can be raised in favour and against a causal relationship. Arguments favouring a causal relationship are that SARS-CoV-2 infections are associated with GBS development (1); GBS occurred time-linked to the first dose of a SARS-CoV-2 vaccination that he received before the infection (10).

The presence of a causal relationship between vaccination and the occurrence of SCoVaG remains speculative, but several arguments can be raised in favour and against a causal relationship. Arguments favouring a causal relationship are that SARS-CoV-2 infections are associated with GBS development (1); GBS occurred time-linked to the first dose of a SARS-CoV-2 vaccination. Whether there is a causal relationship between vaccination and GBS remains speculative. Still, more arguments in favour than against a causal relationship can be raised, suggesting that GBS can complicate SARS-CoV-2 vaccination in single cases. Despite adequate treatment, some patients may not recover completely. Those involved in the management of SARS-CoV-2 vaccination should remain vigilant for severe side effects in single patients. Early recognition and treatment of GBS may improve the outcome.

**AUTHOR CONTRIBUTIONS**

Finsterer J was responsible for the design, literature search, discussion, manuscript first draft and critical comments. Scorza FA and Scorza CA were responsible for the literature search, discussion, manuscript critical comments and final approval.

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