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COVID-19

Guillain-Barré syndrome following BNT162b2 COVID-19 vaccine

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Dear Editor,

Guillain-Barré syndrome (GBS) is the most common and severe acute paralytic neuropathy, with about 100,000 people developing the disorder every year worldwide [1]. Up to two-thirds of patients with GBS report an antecedent infection 1–3 weeks prior to the onset of weakness [2]. Six pathogens have been associated with GBS in case–control studies: campylobacter jejuni, cytomegalovirus, hepatitis E virus, mycoplasma pneumoniae, Epstein–Barr, and Zika virus [2–4]. These infections, by either molecular mimicry or bystander activation, are thought to trigger the emblematical GBS immune response resulting in the demyelination of and damage to peripheral nerves [5]. It is possible that other pathogens are linked to GBS, but their role in the pathogenesis of GBS is still uncertain [6, 7].

Vaccines have also been associated to the pathogenesis of GBS as putative triggers [8]. The first epidemiological link between vaccines and GBS was highlighted in 1976 when was reported an increased GBS risk among individuals who received *swine* flu vaccine [9]. The attributable risk of GBS after influenza vaccination in adults is estimated to be 1–3 in 1,000,000 [10, 11]. SARS-CoV-2 is a novel infectious agent causing coronavirus disease 2019 (COVID-19), which has been declared as pandemic in March 2020 [12]. To date, FDA approved three double-dose vaccines for the prevention of COVID-19 infection [BNT162b2 (Pfizer®); mRNA-1273 (Moderna®); Ad26.COV2.S (Johnson & Johnson®)]. The safety profile of BNT162b2, the first FDA-approved nucleoside-modified messenger RNA vaccine, was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups [13]. However, COVID-19 vaccine–related GBS has been rarely reported to date [14] and some researches disavow the existence of this association [15].

We describe a case of GBS after receiving the second dose of COVID-19 vaccine [BNT162b2—Pfizer®]. A 25-year-old woman without other comorbidities presented to our department on February 26th 2021 with a history of progressive lower limbs weakness and paresthesias for 4 days. She reported difficulty in walking and climbing stairs associated to paresthesias and numbness in the anterolateral region of the right thigh. The patient had received the first dose of COVID-19 vaccine [BNT162b2—Pfizer®] on January 19th 2021 and the second dose on February 18th 2021. No infectious illness or other events were experienced in the weeks prior to the onset of symptoms. Neurological examination revealed steppage gait due by bilateral feet drop. Motor examination demonstrated normal bulk and tone in bilateral upper and lower extremities, and strength in bilateral upper extremities was noted to be 5/5 on Medical Research Council (MRC) scale in both proximal and distal muscles. Although she was able to sustain her bilateral lower extremities against gravity for over 5 s, the examination of muscle group strength testing showed an important muscle weakness of 2/5 on MRC scale in foot flexors, in particular in tibialis anterior muscle bilaterally. Her sensation to touch and pinprick was intact in bilateral upper and lower extremities but decreased in the anterolateral region of the right thigh. The patient had areflexia in lower extremities while in upper limb had normal reflexes. SARS-CoV-2 RT-PCR was negative and SARS-CoV-2 serology showed negative IgM-IgG-IgA antibodies to nucleocapsid protein and positive IgG antibodies to spike protein index: 32.41 (normal value < 1). Complete inflammatory/autoimmune/infective work-up was negative including fecal PCR test for campylobacter jejuni. Brain and spine MRI were both normal. Visual, auditory, motor, and sensory evoked potentials of the upper and lower limbs were unremarkable. Electromyography (EMG) and nerve conduction study were also performed on the day of admission: sensory studies were normal in the upper and lower limbs with the "sural sparing" pattern; motor studies demonstrated conduction block of peroneal nerve bilaterally

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across the fibular head; F waves in the upper and lower limbs were markedly prolonged in latency, suggesting a demyelinating process affecting the more proximal segments of the nerves, moreover the absence of peroneal nerves F waves confirmed the presence of proximal conduction blocks; needle EMG documented widespread spontaneous activity, subacute neurogenic restructuring of motor unit action potentials, and a reduced interference pattern in tibialis anterior muscle bilaterally. A lumbar puncture was performed and cerebrospinal fluid analysis did not show albuminocytological dissociation. The patient was diagnosed with GBS on the same day of admission and promptly started intravenous immunoglobulin (IVIg) 0.4 g/kg/day for 5 days. No complications were observed during and after the treatment and a slight clinical improvement was already appreciated after the first 4 days of intravenous IVIg. The patient received physical therapy during the hospital stay and was thereafter discharged to rehabilitation facility. At the follow-up visit, 30 days later, she reported a substantial clinical improvement. She was again able to climb stairs and difficulty in walking disappeared, and neurological examination showed muscle weakness of 4/5 on MRC scale in tibialis anterior muscle bilaterally. Follow-up NCS demonstrated normalization of F waves latency in the upper and lower limbs, including peroneal nerves F waves, and left peroneal nerve conduction block disappearance.

As far as we are aware, only one case of GBS has been associated with the COVID vaccines [14]. Thus, it might be questioned if GBS in our patient might represent a mere coincidence following SARS-CoV-2 vaccination. We believe that the clinical and laboratory findings including the lack of overt trigger are consistent with a causal association between GBS and Pfizer® anti-SARS-CoV-2 vaccine [16]. Accordingly, several surveillance studies already illustrated vaccine-related increase in GBS following modern influenza vaccines. Thus, it is possible that additional COVID-19 vaccine–associated GBS cases will be described in the near future, even though the individual risk for GBS and other rare complications is likely to be very small, and the benefit of protection against COVID-19 both for individuals and society is far greater. In this way, it might be essential to exploit the opportunity of a worldwide vaccination campaign, perhaps the largest in history, to better understand the pathogenetic mechanism that bind GBS to COVID vaccination, rather than denying such association.

Declarations

Ethical approval Ethical approval to report this case was obtained from the regional human research ethics committee of the University Magna Græcia, Catanzaro, Italy.

Informed consent Written informed consent was obtained from the patient for her anonymized information to be published in this article.

Conflict of interest The authors declare no competing interests.

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