A Death for Guillain-Barrè Syndrome After Receiving a COVID-19 Vaccine: A Case Report

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ABSTRACT: The virus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) causes COVID-19, a potentially fatal disease. The COVID-19 vaccine is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2. We reported the case of a 66-year-old woman with a medical history of hypertension and anxious-depressive syndrome who developed Guillain Barré Syndrome (GBS) 4 weeks after receiving the COVID-19 vaccine. During the patient's hospital stay, they received cycles of high-dose intravenous immunoglobulin (IVIG) and plasmapheresis treatments.. Despite the treatment, a deterioration of respiratory function led the patient to premature mortality.

KEYWORDS: Guillan Barré syndrome, GBS, COVID-19, SARS-CoV-2, neurology

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Introduction

The virus SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)[1] can cause COVID-19, a potentially deadly illness.[2] This virus has an incubation period of 2 days to 2 week.[3]

The onset of the disease is usually accompanied by symptoms such as fever, cough, throatache, headache, myalgia, rhinorrhea, and loss of smell or taste. SARS-COV-2 seems to have a particular affinity with the nervous system; nervous-system-related symptoms are headache, impaired consciousness, delirium, and less frequent seizures, strokes, encephalo-myelitis, and peripheral nervous manifestations such as bell's palsy and GBS. Manifestations like new hyposmia and hypogeusia are pathognomonic.[4] In instances of more severe manifestations of the condition, individuals may require hospitalization and admission into an intensive care unit due to the possibility of unexpected complications, such as Acute Respiratory Distress Syndrome (ARDS), that can result in death in a relatively short period of time.[5]

One of the most effective ways of preventing an infectious disease is vaccination. The nucleic acid-genetic approach is a novel method of creating vaccines. Prior to the COVID-19 pandemic, no such vaccines had been approved for human use. However, due to the outbreak, research in this field has progressed rapidly, resulting in emergency use authorization for some mRNA vaccines for COVID-19.[6]

COVID-19 can result in a variety of side effects, most of which are mild or moderate, and vanish within a few days. Common side effects include injection site pain, feverish state, tiredness, headache, muscular pains, shivers, and diarrhea, even though.

COVID-19 has been linked to immune-mediated neurological complications such as Guillain-Barré syndrome (GBS). It is known that infections can lead to neurological problems and previous viral outbreaks have shown that immune-mediated mechanisms can cause damage to the nervous system, including GBS. There is a theory that molecular mimicry between SARS-CoV-2 and various human organs may trigger multi-organ autoimmunity in COVID-19.[7,8]

Our case report aims to present a rare post-vaccine side effect like Guillain-Barré Syndrome (GBS) with premature mortality.

Case Presentation

In May 2021 a 66-year-old Caucasian woman with a medical background of hypertension and anxious depressive syndrome in treatment with bupropion, pregabalin, and lorazepam was accepted to the emergency unit exhibiting symptoms of acute progressive weakness of distal extremities, especially to the right leg, she had related symptoms like cephalalgia, nausea, and vomiting, no urinary and fecal incontinence, and no rigor. No previous neurologic history was reported from the patient. The patient reports that the onset of neurological symptoms occurred almost 4 weeks after she received COVID-19 vaccination with Comirnaty (mRNA COVID-19 Vaccine from Pfizer-BioNTech).

The patient was oriented in space and time, and hemodynamically stable. She was apiretic and her vitals sign were as follows: SpO2 98% in ambient air, pressure level 130/80 mmHg, breathing frequency 18 breaths/minute, and heart frequency 72 beats per minute. The patient was arrived to Neurology unit where the neurological examination revealed a Bell's palsy with facial asymmetry. Except for the seventh, no other cranial nerve was involved. During the upper limbs examination, it was observed that there were no signs of muscle

Diagnostic criteria	Level of diagnostic certainty			
	1	2	3	4
Bilateral and flaccid weakness of limbs	+	+	+	+/–
Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/–
Monophasic course and time between onset-nadir 12 h to 28 days	+	+	+	+/–
CSF cell count <50/μl	+	+*	-	+/–
CSF protein concentration > normal value	+	+/–*	-	+/–
NCS findings consistent with one of the subtypes of GBS	+	+/–	-	+/–
Absence of alternative diagnosis for weakness	+	+	+	+

+, present; –, absent; +/–, present or absent; GBS, Guillain–Barré syndrome; NCS, nerve conduction studies. *If CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis of Guillain-Barré syndrome. Level 1 is the highest level of diagnostic certainty, level 4 is the lowest level of diagnostic certainty. Reproduced with permission from Oxford University Press © Fokke, C. *et al.*

Figure 1. Key diagnostic criteria and Brighton case definitions for Guillain-Barre´ syndrome.

atrophy or abnormal muscle tone in the upper limbs (Medical Research Council's scale of muscle power was 3).[9] The patient showed progressive failure during Mingazzini I test (A test for subtle hemiparesis, where the participant holds their arms out in front of them with fingers spread),[10] without evident lateral deficit. The upper limbs' examination also revealed a weakness of the interosseous muscles of the hands, and tendon reflexes were absent. Lower limbs examination revealed normal muscle tone (Medical Research Council's scale of muscle power was 3) but with reduced trophism. The right leg was in a posture of external rotation. The patient could not assume the Mingazzini II position (a supine position, to bend the knees bringing the tips of the feet toward the face),[10] the iliopsoas muscles were plegic, and all limb' reflexes were absent.

Brain, cervical, and lumbosacral Computed Tomography (CT) revealed regular findings except for mild herniation of lumbar intervertebral discs (L3-L4 and L4-L5) and widespread osteoarthritis. Laboratory investigation revealed high white blood cells (WBC) with neutrophil and electrolyte imbalance. A lumbar puncture for cerebrospinal fluid examination (CSF) was performed urgently. It revealed clear fluid, normal opening pressure, and high protein with normal glucose and cell counts (albuminocytological dissociation).

Based on physical examination, laboratory investigations, instrumental examinations, and CSF findings, a provisional diagnosis of acute, rapidly progressive, inflammatory polyneuropathy like Guillain-Barrè syndrome was done. The following conditions were ruled out: sarcoidosis, Sjogren syndrome, acute transverse myelitis, brainstem stroke, vitamin deficiencies, and acute flaccid myelitis. Additionally, metabolic or electrolyte disorders, some infections (such as Lyme disease, cytomegalovirus, HIV, Epstein-Barr virus, or varicella-zoster virus), and neuromuscular junction diseases (like myasthenia gravis and Lambert-Eaton myasthenic syndrome) were also excluded.

Electrophysiological studies have shown that the patient has a type of Guillain-Barrè syndrome that causes a demyelinating polyneuropathy. This type of GBS is different from other subtypes such as acute inflammatory demyelinating polyradiculoneuropathy (AIDP), which is characterized by a progressive areflexic weakness and mild sensory changes. In AIDP, sensory symptoms often occur before motor weakness sets in. Another subtype is acute motor axonal neuropathy (AMAN), which is a paralytic disorder that causes abrupt onset and is characterized by motor nerve fiber degeneration of varying severity and sparing of sensory fibers. Acute motor sensory axonal neuropathy (AMSAN) is another subtype, which causes acute onset of distal weakness, loss of deep tendon reflexes and sensory symptoms. Finally, Miller Fisher syndrome (MFS) usually presents with at least two of the following features: ataxia, areflexia, and ophthalmoplegia.

The patient met the diagnostic criteria for Guillain-Barré syndrome (GBS) level 1 certainty according to Brighton criteria.[11] Figure 1 displays the Brighton diagnostic criteria for GBS.

Nevertheless, limb weakness got worse, and severe respiratory failure developed almost 11 days after admission so he was moved to the Intensive Care Unit (ICU) and required mechanical ventilation. According to the clinical and arterial blood gases (ABG) parameters, the patient started a cycle of non-invasive ventilation (NIV) with helmet interface in assisted pressure-controlled ventilation (APCV) mode (Pressure Support 10 mmHg, Positive end-expiratory pressure 7 mmHg, Fraction of inspired O2 60%) with good response. She also started intravenous continuous infusion of dexmedetomidine (0.8 γ/kg/h) with a Glasgow coma scale (GCS) 15. After 9 days, considering the patient's clinical and hemodynamic stability (heart rate 58 bpm, SpO2 98%, Blood Pressure 110/60 mmHg), the good respiratory mechanics, and the invariability of the neurological clinical picture, the patient ended the NIV cycle and a Venturi mask at FiO2 60% was applied. Therefore, the patient was moved from the ICU to the Neurology department. During the hospitalization, the patient started presenting problems of psycho-motor agitation treated with the administration of antipsychotic drugs such as an aliphatic

phenothiazine neuroleptic. The hyposthenia of the lower limbs was raised. Simultaneously, a deterioration of respiratory function arised, and the patient was treated once again with the application of oxygen therapy (FiO2 50%). Based on the results of the ABG (pH 7.45, pO2 51 mmHg, pCO2 30 mmHg) and considering the vital signs (heartbeat 120 bpm, SpO2 80%, blood pressure 170/80 mmHg), the patient was once again transferred to ICU where she started a new cycle of NIV with helmet interface in pressure support ventilation (PSV) mode (PS 12 cmH2O; PEEP 10; FiO2 100%) and intravenous continuous infusion of dexmedetomidine (0,6 γ/kg/h) considering the psychomotor agitation.

High-dose intravenous immunoglobulin (IVIG) (2 gr/kg) over 5 days and heat therapy were started 24 hours after the hospitalization. The patient started a plasmapheresis cycle of 5 sessions, 48 hours after the first hospitalization in the intensive care unit. At the end of the plasmapheresis cycle, a new neurological assessment revealed a mild improvement in the nervous system. At the end of the plasmapheresis cycle, a new neurological assessment revealed a mild improvement in the neurological system. A second plasmapheresis cycle was started when the patient returned to ICU.

Almost 14 hours after the last admission to the Intensive Care Unit (ICU) the control ABG revealed a serious deterioration of respiratory gas exchange. The patient was intubated and connected to Mechanical Artificial Ventilation (VAM). One hour after intubation the electrocardiogram heart tracing revealed ST segment depression, and severe bradycardia (FC 20 bpm) followed by cardiac arrest. Cardiopulmonary resuscitation maneuvers with the use of an automatic external defibrillator were performed according to Advanced Cardiovascular Life Support (ACLS).[12] After 30 minutes there was no evidence of cardiac response so the patient's death was declared.

Discussion

Guillain–Barré Syndrome is a serious health disorder, triggered by an infection or immune stimulus, in which a person's immune system damages his/her peripheral nerve cells due to molecular mimicry, causing muscle weakness, sometimes paralysis, and infrequently death.[13,14] Various diagnostic criteria have been proposed for Guillain-Barré Syndrome, including one recently established by the Brighton Collaboration.[11]

The time between the start of a viral illness and the first symptoms of Guillain-Barré syndrome is comparable to the time seen with Guillain-Barré syndrome that happens during or after other infections. There have been accounts linking Guillain-Barré syndrome with coronavirus infections.[15] It is difficult to determine whether severe deficits and axonal involvement are common characteristics of Covid-19-associated Guillain-Barré syndrome based on this observation. It is important to differentiate Guillain-Barré syndrome with Covid-19 from critical illness neuropathy and myopathy, which usually occur later in the course of critical illness than Guillain-Barré syndrome.[16,17] Vaccine-associated Guillain-Barre syndrome (GBS) occurs when GBS symptoms appear within 6 weeks of receiving a vaccine, as reported by VAERS.[18]

Abara et al suggest that there is an increased risk of Guillain-Barré Syndrome (GBS) associated with Ad26.COV2.S vaccination. The study found that GBS reporting after Ad26.COV2.S vaccination was around 9 to 12 times more common than after BNT162b2 or mRNA-1273 vaccination within 21- and 42-day post-vaccination intervals. Similarly, observed GBS cases after Ad26.COV2.S vaccination were 2 to 3 times greater than expected based on background rates within 21- and 42-day post-vaccination intervals. According to an EudraVigilance analysis, GBS cases were slightly more frequent after adenovirus vaccination than after mRNA vaccination.[19]

Among individuals aged 57 through 88 years, 10 deaths were reported, and GBS was the documented cause of death after medical records and death certificate review for 7 individuals. It is worth noting that increasing age is associated with a poorer GBS prognosis and an increased mortality risk. Of these deaths, 8 occurred after mRNA COVID-19 vaccination, but there was no epidemiologic evidence to suggest an association between either mRNA vaccine and GBS. There were 2 deaths reported after Ad26.COV2.S vaccination. In one of the deaths, the individual had onset of GBS symptoms at 70 days after vaccination, which is outside an epidemiologically accepted risk interval to assume an association between vaccination and GBS. In the other death, the individual had symptom onset 5 days after Ad26.COV2.S vaccination, and GBS was documented as the cause of death.[20] Mass immunization is crucial for individual protection, but vaccine surveillance is necessary to identify any potential associated risks. In addition it is important to consider the possibility of temporal bias before concluding the causal relationship between the vaccine and an adverse effect that is attributable to it.[21] Another large study study conducted on nearly 900 patients who developed Guillain-Barré syndrome (GBS) after receiving COVID-19 vaccination revealed that the first dose of ChAdOx1 nCoV-19 vaccine is linked with an increased risk of GBS. The analysis of the linked NID/NIMS dataset suggested that there is an excess GBS risk of 0.576 (with a 95% confidence interval of 0.481-0.691) cases per 100 000 doses for the first dose of the said vaccine.[22] In a study conducted by Maramattom et al, approximately 1.5 million people in India have been vaccinated against COVID-19. Of these, more than 80% (1.2 million) received the ChAdOx1-S/nCoV-19 vaccine. During a period of 4 weeks, 7 cases of Guillain-Barre syndrome (GBS) were observed in this population. All 7 patients developed severe GBS within 2 weeks of receiving the first dose of the vaccine.[23] According to Allen et al, SARS-CoV-2 vaccines are generally safe, but they have reported 4 cases of Guillain-Barré syndrome (GBS) with bifacial weakness and paresthesias variant. These cases occurred within 3 weeks of receiving the Oxford-AstraZeneca SARS-CoV-2 vaccine. It is worth mentioning that this rare neurological syndrome has been previously associated with SARS-CoV-2 infection itself.[24]

COVID-19 infection creates a systemic response through the immune system characterized by cytokine storm.[25,26] It is still unclear whether GBS linked to COVID-19 is caused by antibodies against gangliosides, T-cell action, or direct neuroinvasive events.[27,28] The potential link between COVID-19 vaccination and the development of Guillain-Barré Syndrome (GBS) is still being debated. While GBS cases have been reported following various vaccines, including meningococcal, poliovirus, flu, and rabies vaccines, an explicit connection to COVID-19 vaccination is not yet clear.[29]

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In principle, a single observation is not appropriate to establish a link between an adverse reaction and the triggering agent, especially since specific markers for characterizing the effect of the mRNA vaccine and possible interactions with the co-medication were not investigated. The cardiac symptoms leading to cardiac arrest do not speak against the causal involvement of the Covid-19 vaccine.

Author Contributions

Antonio Coviello: conceptualization of the content; reviewing final manuscript before submission. Carmine Iacovazzo: conceptualization of the content; reviewing final manuscript before submission. Antonio Coviello and Carmine Iacovazzo are 2 first co-authors because they did the same work and put the same effort. Maria Vargas: conceptualization of the academic content related to topic; choice of journal to which the article will be submitted. editing the final version and approving it before submission. Concetta Posillipo: data curation; writing the preliminary version of the manuscript. Francesco Sagnelli: acquisition data; co-writing the preliminary version of the manuscript. Pasquale Diglio: analysis and/or interpretation of data; methodology; co-writing the preliminary version of the manuscript. Dario Cirillo: study design; reviewing and approving final manuscript. Giuseppe Servillo: supervising the work; editing the final version and approving it before submission.

Availability of Data and Materials

The authors confirm that the data supporting the findings of this case report are available within the article.

Informed Consent

The patient's family provided written informed consent for the publication of this case.

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