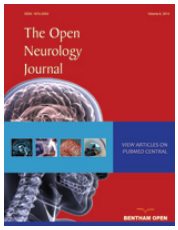
1874-205X/22



The Open Neurology Journal

Content list available at: https://openneurologyjournal.com

CASE REPORT

Guillain-Barré Syndrome with Lethal Outcome Following COVID-19 Vaccination - Case Report Supported by Autopsy Examination

Kristina Mosna[1,2,*], Peter Vadkerti[3], Ladislav Papp[4], Michal Palkovic[1,2], Pavol Janega[1,2] and Pavel Babal[1,2]

[1]*Institute of Pathological Anatomy, Faculty of Medicine, Comenius University and University Hospital, Sasinkova 4, 811 08, Bratislava, Slovakia*
[2]*Health Care Surveillance Authority, Žellova 2, 829 24, Bratislava, Slovakia*
[3]*Department of Neurology, ProCare a.s., Velkoblahovska 23, 929 01, Dunajska Streda, Slovakia*
[4]*Department of Anaesthesiology and Intensive Care, ProCare a.s., Velkoblahovska 23, 929 01, Dunajska Streda, Slovakia*

Abstract:

Objective:

After the outbreak of the global pandemic caused by SARS-CoV-2 infection at the end of the year 2019, it took one year to start vaccination against this infection with products from various manufacturers. As of November 2021, more than 8 billion vaccine doses against COVID-19 have been administered, which is essentially linked to a spike in adverse events reports following these vaccinations, including a number of neurological adverse events.

Case Report:

We report a case of a 71-year-old patient with lethal fulminant onset of Guillain-Barré syndrome after the second dose of mRNA vaccine tozinameran. This is, to our best knowledge, the first case report of this adverse event supported by autopsy and histological examination. The patient presented with progressive ascending weakness and paresthesia, with typical cytoalbuminologic dissociation in cerebrospinal fluid and severe motoric and sensitive axonal-demyelinating polyneuropathy on electromyography. The patient's history and complex diagnostic workup did not reveal any other possible causative factors. The patient did not respond to the treatment with intravenous immunoglobulins and died 10 days later due to aspiration bronchopneumonia as a complication of respiratory muscles paralysis.

Conclusion:

Most of the reported adverse reactions following COVID-19 vaccination include mild or moderate events noticed in the post-vaccination period; however, reports of possible lethal outcomes are no exception. Still, the overall incidence of GBS after vaccination does not significantly exceed its incidence in the general population. Each such report should be carefully examined by a team of specialists to prevent overestimation of lethal adverse events linked to vaccinations, especially in fatalities that happen in the post-vaccination period.

Keywords: Guillain-Barré syndrome, COVID-19, Vaccination, mRNA vaccine, Adverse event, Autopsy, Case report.

Article History	Received: January 13, 2022	Revised: March 16, 2022	Accepted: April 19, 2022

1. INTRODUCTION

Guillain-Barré syndrome (GBS) is a potentially life-threatening autoimmune disorder presenting with a spectrum of neurological symptoms. A typical clinical picture of GBS includes acute onset of sensory-motor ascending neuropathy [1]. Currently recognized different subtypes result from the immune attack on different components of the peripheral nervous system, including myelin sheets, Schwan cells, or axolemma [2]. The incidence of GBS is estimated to be between 0.62 – 2.66, which increases with age, more commonly affecting males [3]. Although GBS is relatively rare, it is recognized as the most common cause of acute postinfectious flaccid paralysis, so early detection and timely management of patients are of great importance.

Pathogens associated with the development of GBS include various bacteria and viruses; most recently, the development of GBS was noticed following COVID-19 infection [4, 5]. *Campylobacter jejuni* is so far considered the most common causative agent, with an estimation of 30 – 40% of GBS patients suffering from this infection shortly before the

* Address correspondence to this author at the Institute of Pathological Anatomy, Faculty of Medicine, Comenius University, Sasinkova 4, 811 08 Bratislava, Slovakia, Tel: 00421290119256; Fax: 00421290119592;
E-mail: giertlova2@uniba.sk

onset of first symptoms [6, 7]. Less commonly, GBS has been reported in association with non-infectious factors, such as surgical interventions [8 - 10], intake of certain drugs [11 - 13], or vaccinations.

The association of GBS with vaccination has been an ongoing discussion. A causative link has been so far established only with strain A/NewJersey/76 influenza vaccine [14] and rabies vaccine cultured in neural tissues [15]. Sporadic case studies following different vaccines continue to emerge, including vaccinations against seasonal influenza [16], H1N1 [17], hepatitis B [18], human papillomavirus (HPV) [19], and meningococcal vaccine [20].

With the COVID-19 pandemic, new vaccines have been introduced to the general population. As of October 2021, WHO approved several vector-based vaccines, inactivated virus vaccines, and mRNA-based vaccines [21]. Although rare, several severe nervous system disorders following these vaccines have been reported, including Bell's palsy, stroke, acute disseminated encephalomyelitis, transverse myelitis, as well as Guillain-Barré syndrome [22, 23]. Here, we present a case of an acute onset of GBS following mRNA vaccination against COVID-19 with a lethal outcome. The diagnosis was confirmed by a post-mortal examination conducted by Slovak Health Care Surveillance Authority and evaluated by Slovak State Institute for Drug Control as a probable adverse event following vaccination, based on WHO-UMC (Uppsala Monitoring Center) system for standardized case causality assessment.

2. CASE PRESENTATION

A 71-year-old male patient with a history of chronic obstructive lung disease (GOLD A) and lung emphysema was vaccinated with the second dose of mRNA-based vaccine against COVID-19 (tozinameran). The next day, the patient observed increased temperature (38.1 °C), followed by a progressive tingling sensation, first mainly affecting the lower extremities and shortly moving to the upper extremities as well. He experienced a problematic and insecure gait, with a reduced sensation of soles while walking as well as decreased perception of grasped objects. At admission, the patient was COVID-19 negative (PCR test), normothermic (36.5 °C), and normotensive (125/85 mmHg) with 105 beats per minute. The patient was lucid, well oriented, without meningeal symptomatology, with isocoric pupils, correct optokinetics, and pupillary reflexes, without nystagmus. Facial expressions were symmetrical, without pathological axial reflexes, without signs of bulbar palsy, and the tactile perception of the face was symmetrically well preserved. Upper and lower extremities showed bilaterally symmetrical muscle tonus and muscle strength, and myotatic reflexes were symmetrically lowered, without signs of pyramidal tract and cerebellar involvement. Examination of tactile perception showed hypesthesia on all four extremities. Standing pose of the patient was independent but uncertain, with a positive Romberg's sign. The gait was independent but only at short distances and uncertain. Phatic functions were normal; however, severe dysphonia and moderate dysphagia were detected. The patient did not report any similar symptoms in the past, nor has he suffered from any neurological condition prior to this. He was on chronic treatment with a combination of inhaler sympathomimetics and anticholinergics for chronic obstructive lung disease (GOLD A), and on a replacement therapy with levothyroxine (100 µg/day) due to thyroidectomy that the patients underwent in the past following subacute thyreoiditis with non-toxic diffuse goiter.

Laboratory workup at admission showed mildly elevated CRP (39.29 mg/l), D-dimer (0.92 mg/l FEU), and fibrinogen (7.54 g/l), with normal kidney and liver function. Examination of the cerebrospinal fluid showed protein-cytological dissociation with normal levels of glucose, lactate, chloride content, and increased levels of albumin (35.0 mg/l), total protein (0.54 g/l), and IgG (71.5 mg/l), without increased erythrocytes and leukocytes (< 2/ul).

Results of electromyography conducted on the second admission day indicated severe motoric and sensitive axonal demyelinating polyneuropathy of the lower extremities (with bilaterally markedly reduced CMAP (compound muscle action potential) and markedly prolonged H reflex). On the right leg, the segment of abductor hallucis-ankle showed a latency difference of 7.3 ms, the ankle-popliteal fossa segment had a latency difference of 22.3 ms, distance of 410 mm and conduction velocity of 18 m/s. On the left leg, the segment of abductor hallucis-ankle showed a latency difference of 6.4 ms, and ankle-popliteral fossa segment showed a latency difference of 18.8. ms, distance 420 mm and conduction velocity 22/ms. The activity in the neurogram of fibular nerve was absent. Left tibial nerve M-wave showed a latency of 8.2 ms and amplitude of 0.8 mV, and the H-reflex had a latency of 50.2 ms. Subsequent brain CT revealed leukoaraiosis without fresh and expansile lesions; without midline shift, the ventricular system was without dilation, and the subarachnoid space was normodense without signs of obstruction.

The diagnosis of Guillain-Barré syndrome was established as the most probable cause of patient's deterioration based on the test results and clinical symptoms. The treatment with intravenous human immunoglobulins (IVIg) was started (30 g per day) on the third admission day, together with symptomatic treatment. Muscle weakness progressed, also affecting the respiratory muscles and leading to respiration insufficiency. The patient had to be analgosedated, intubated, and was started on mechanical ventilation. The inflammatory markers started to rise (CRP 75.22 mg/l). Chest X-ray showed diffuse ground-glass opacity over the right lung, and cultivation of bronchoalveolar lavage fluid detected multiresistant *Pseudomonas aeruginosa* (interpreted by clinicians as consistent with nosocomial infection in the setting of ventilated ICU patients). In spite of the treatment, the respiration insufficiency progressed to the development of acute respiratory distress syndrome, followed by hemodynamic instability and death 6 days after hospitalization and 10 days after the second dose of mRNA vaccine against COVID-19.

Subsequently, a full-body autopsy was conducted. The pleural cavity revealed firm adhesion between the visceral and parietal pleura on the right side. The lungs were bilaterally increased in size and weight (right 1260 g, left 950 g), of tough elastic consistency, with a large amount of turbid beige fluid

coming out from the cut surface, with round areas of grey-pink merging consolidations in the lower lobes with multiple abscesses measuring 3 – 5 mm, filled with creamy beige-green substance. Histological examination indicated post-aspiration absceding bronchopneumonia as the immediate cause of death of the patient.

Gross and microscopic examination of the brain tissue and meninges did not reveal any pathological changes apart from slight edema. Histological examination of the spinal cord did not show any substantial changes in motoric neurons of the ventral roots nor in the captured spinal nerve roots. A thorough examination of the peripheral nerves of the lumbar plexus showed areas of focal demyelination (Fig. **1**), prevalently perivascular infiltration by T-lymphocytes with a slight prevalence of T-cytotoxic over T-helper phenotype and the presence of numerous macrophages (Fig. **2**). No significant penetration by polymorphonuclear leukocytes was observed. Described histological changes supported the clinical diagnosis of Guillain-Barré syndrome, an acute inflammatory demyelinating polyradiculoneuropathy (AIDP) subtype.

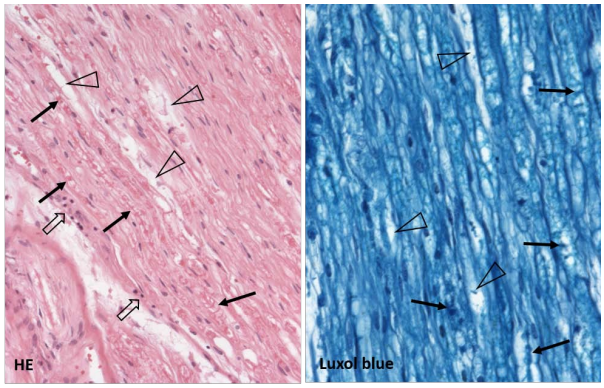


Fig. (1). Ischiadic nerve histology in Guillain-Barré syndrome. Left: granular clumping (arrow) with extinction (arowhead) of myelin; Hematoxylin and eosin (HE), 100x. Right: focal lympho-histiocytic infiltrates in the nerve tissue (open arrow); Luxol blue, 200x.

3. DISCUSSION

Guillain-Barré syndrome represents a group of potentially life-threatening neurological disorders developing typically after certain infections and less commonly following surgical procedures, selected drug intake as well as vaccinations [2]. GBS encloses several variants with variable clinical presentation, prognosis, as well as electrophysiological findings, including acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), Miller-Fisher syndrome (MFS), and Pharyngeal-cervical-brachial variant. These subtypes present with different geographical distributions, with AIDP being the most common variant in North America and Europe [24].

GBS development is attributed to an autoimmune reaction aimed against constituents of the peripheral nervous system. The pathogenesis is not fully understood yet; however, a subset of GBS is considered to be driven by molecular mimicry, which is supported by the finding of serum antibodies that cross-react with gangliosides of peripheral nerves in a subset of susceptible GBS patients, mainly suffering from an axonal subtype of GBS resulting in nerve conduction failure and axonal degeneration [25, 26]. In the AIDP subtype, the targeting of the myelin sheets' antigens leads to myelin degeneration by macrophages and T-lymphocytes [27, 28].

The symptoms of the AIDP variant include symmetrical and progressive neurological symptomatology, starting typically with paresthesias of the hands and feet and continuing as numbness, limb weakness, and areflexia, usually involving the lower extremities first [1, 25]. In other variants, the symptoms can affect different regions of the body, and vary from purely sensory to purely motor symptoms with their various combinations [25]. The progression of symptoms is usually rapid, with maximum muscle weakness within 5 – 12 days. Our patient reached the nadir on the 5th day after the initial symptoms occurred, the time when he needed mechanical ventilation. Generally, the duration of the disease plateau varies from 2 days to 6 months, followed by slow improvement, with the possibility of residual symptomatology in a subset of patients [2, 29].

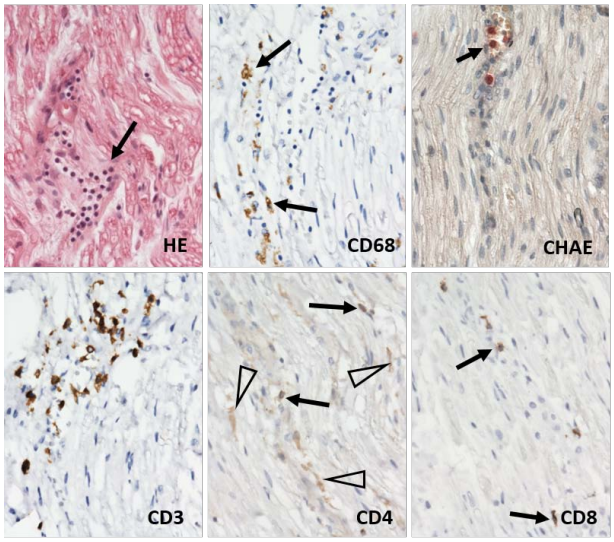


Fig. (2). Histological picture of peripheral nerve tissue in Guillain-Barré syndrome. Top and Left: perivascular infiltrate of lymphocytes (arrow); Hematoxylin and eosin (HE), 200x. Top and Middle: diffuse infiltration with macrophages; CD68, 200x. Top and Right: polymorphonuclear leukocytes located in the blood vessels; chloracetate esterase (CHAE), 200x. Bottom Left to Right: perivascular lymphocytic infiltration with the T-cell phenotype (CD3) and slight prevalence of T-suppressor (CD8) over T-helper (CD4) phenotype, also showing macrophages (arrowhead), 200x.

The diagnosis of GBS relies on typical progressive clinical symptomatology and the elimination of other possible causes with similar neurological symptoms. The examination of cerebrospinal fluid is important; however, in a subset of patients, the parameters of CSF might show normal levels within the first week of symptom onset [29]. The diagnosis is further supported by nerve conduction studies; however, it might take up to two weeks for the electrophysiological abnormalities to be fully expressed [2, 29].

Histologic examination of the nerves is not a usual part of the diagnostic process; however, in disputed cases, it can aid the correct diagnosis. The typical histological presentation of the AIDP subtype includes patchily dispersed foci of demyelination, so it does not have to be necessarily captured during the sural nerve biopsy. There is typically irregular mononuclear infiltration, predominantly by T-lymphocytes and macrophages within the myelin sheaths. Histological findings in the peripheral nerve tissue of the presented case supported the clinical diagnosis of GBS, the AIDP subtype. AMAN and AMSAN subtypes show axonal degeneration, which is most prominent in the ventral spinal roots and paucity of lymphocytic infiltrate when compared to AIDP. There is typically central chromatolysis noted in the anterior horn cells of the spinal cord [30], which was not found in our autopsied patient.

Treatment of GBS that has proven to be effective consists of intravenous immunoglobulin (IVIg) or plasma exchange [2]. Early treatment together with continuous careful monitoring, prophylaxis of possible complications, timely rehabilitation, and psychological support represent important aspects of successful management of GBS patients.

Due to the involvement of respiratory muscles, patients can develop neuromuscular respiratory failure with the need of mechanical ventilation, followed in the majority of cases either by nosocomial or aspiration pneumonia, as in our case [31, 32]. Other complications include involvement of the autonomous nervous system, which can lead to instability of blood pressure and cardiac arrhythmias. The overall mortality of GBS patients is estimated to be around 3% [33, 34].

As of November 2021, there were 517 reports within the United States of America to VAERS (The Vaccine Adverse Event Reporting System) of Guillain-Barré syndrome possibly associated with COVID-19 vaccination by mRNA vaccine with 9 fatal cases. The reports represented less than 0.1% of all adverse event reports. The European database of suspected adverse drug reactions (EduraVigilance) recorded so far 1127 cases of GBS possibly associated with COVID-19 mRNA vaccine, with 19 fatal cases. GBS represented less than 0.2% of the reported adverse events associated with vaccination [35, 36].

At the time of writing this paper, the GBS cases reported in European Union and European Economic Area countries as a possible adverse effect after COVID-19 vaccination, regardless of the type of vaccination, represented 2605 cases, which stand for 0.0003% cases of all vaccine doses, which is less than expected in the general population regardless of vaccination status [36]. A case series study examining GBS admissions up to 28 days after the first dose of SARS-CoV-2 vaccine and COVID-19 infection in England showed an increased risk of GBS connected to AZD-1222 vaccine (incidence rate ratio 2.90); however, the risk of development of neurological complications, including GBS, is far greater after COVID-19 infection than vaccination [37].

With the progression of COVID-19 vaccination, reports of possible adverse events will rise. In cases of deaths associated with vaccinations, the reporting, as well as investigation of these, differs throughout countries. In Slovakia, all deaths reported as suspected after COVID-19 vaccination are investigated by full-body autopsy performed by professionals working for the Slovak Health Care Surveillance Authority in cooperation with the State Institute of Drug Control. As of November 2021, there were 1121 reports of possible serious side effects out of 5,117,618 doses of COVID-19 vaccinations. Out of these, there were 7 deaths interpreted to have a causal connection with vaccination, 4 deaths were categorized according to the WHO-UMC system as a possible adverse event following COVID-19 vaccination, and 3 deaths as a probable adverse event, including this described case and two cases leading to intracranial bleeding [38]. In any case, the reported cases of GBS are low, and even if some of the reported cases can be causally connected to vaccination, the overall risk of possible serious side effects remains very low.

CONCLUSION

The rollout of new vaccinations ensuing COVID-19 pandemic is naturally followed by a spike in adverse event reports, including a number of neurological conditions. A slightly increased risk of GBS development was associated with vector-based vaccines against COVID-19. In the case of mRNA vaccines, the rate of these so far does not seem to be higher than the incidence in the general population; however, the causality between some GBS cases and mRNA vaccination cannot be ruled out with certainty. Thus, doctors have to be vigilant about GBS symptomatology in the post-vaccination period to start timely management of these patients, and potentially reduce the fatal outcome of this diagnosis.

LIST OF ABBREVIATIONS

AIDP	=	Acute Inflammatory Demyelinating Polyradiculoneuropathy
AMAN	=	Acute Motor Axonal Neuropathy
AMSAN	=	Acute Motor And Sensory Axonal Neuropathy
CMAP	=	Compound Muscle Action Potential
CRP	=	C-Reactive Protein
CSF	=	Cerebrospinal Fluid
CT	=	Computed Tomography
GBS	=	Guillian-Barré syndrome
GOLD	=	Global Initiative for Chronic Obstructive Lung Disease
MFS	=	Miller-Fisher Syndrome
PCR	=	Polymerase Chain Reaction
UPC	=	Uppsala Monitoring Center
VAERS	=	The Vaccine Adverse Event Reporting System
WHO	=	World Health Organization

AUTHORS' CONTRIBUTIONS

PV and LP collected and interpreted the patient's clinical data. KM, MV, PJ, and PB analyzed and interpreted the patient's clinical data in association with autopsy data. KM, PB, and PV were major contributors to writing the article. MP provided data on adverse post-vaccination events. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

The spouse of the deceased patient provided a written consent for publication of the case.

STANDARDS OF REPORTING

CARE guidelines have been followed in the preparation of this case report.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

This research was funded by Slovak Research and Development Agency (Grant number PP-COVID-20-051).

CONFLICTS OF INTEREST

The authors declare no conflicts of interest in preparing this case report.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Head VA, Wakerley BR. Guillain–Barré syndrome in general practice: clinical features suggestive of early diagnosis. Br J Gen Pract 2016; 66(645): 218-9. [http://dx.doi.org/10.3399/bjgp16X684733] [PMID: 27033501]

[2] Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016; 388(10045): 717-27. [http://dx.doi.org/10.1016/S0140-6736(16)00339-1] [PMID: 26948435]

[3] Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology 2011; 36(2): 123-33. [http://dx.doi.org/10.1159/000324710] [PMID: 21422765]

[4] Jacobs BC, Rothbarth PH, van der Meché FGA, *et al.* The spectrum of antecedent infections in Guillain-Barré syndrome. Neurology 1998; 51(4): 1110-5. [http://dx.doi.org/10.1212/WNL.51.4.1110] [PMID: 9781538]

[5] Hadden RDM, Karch H, Hartung HP, *et al.* Preceding infections, immune factors, and outcome in Guillain-Barre syndrome. Neurology 2001; 56(6): 758-65. [http://dx.doi.org/10.1212/WNL.56.6.758] [PMID: 11274311]

[6] McCarthy N, Giesecke J. Incidence of Guillain-Barré syndrome following infection with Campylobacter jejuni. Am J Epidemiol 2001; 153(6): 610-4. [http://dx.doi.org/10.1093/aje/153.6.610] [PMID: 11257070]

[7] Nyati KK, Nyati R. Role of Campylobacter jejuni infection in the pathogenesis of Guillain-Barré syndrome: an update. BioMed Res Int 2013; 2013(Aug): 852195. [PMID: 24000328]

[8] Gong Q, Liu S, Liu Y, *et al.* Guillain-Barré syndrome triggered by surgery in a Chinese population: a multicenter retrospective study. BMC Neurol 2021; 21(1): 40. [http://dx.doi.org/10.1186/s12883-021-02067-1] [PMID: 33509120]

[9] Bao L, Chen X, Li Q, Zhang R, Shi H, Cui G. Surgery and guillain-barré syndrome: A single-center retrospective study focused on clinical and electrophysiological subtypes. Neuropsychiatr Dis Treat 2020; 16: 969-74. [http://dx.doi.org/10.2147/NDT.S241128] [PMID: 32346291]

[10] Rudant J, Dupont A, Mikaeloff Y, Bolgert F, Coste J, Weill A. Surgery and risk of Guillain-Barré syndrome: A French nationwide epidemiologic study 2018; 91(13): e1220-7. [http://dx.doi.org/10.1212/WNL.0000000000006246]

[11] Ali AK. Peripheral neuropathy and Guillain-Barré syndrome risks associated with exposure to systemic fluoroquinolones: a pharmacovigilance analysis 2014; 24(4): 279-85. [http://dx.doi.org/10.1016/j.annepidem.2013.12.009]

[12] Shin ISJ, Baer AN, Kwon HJ, Papadopoulos EJ, Siegel JN. Guillain-Barré and Miller Fisher syndromes occurring with tumor necrosis factor α antagonist therapy. Arthritis Rheum 2006; 54(5): 1429-34. [http://dx.doi.org/10.1002/art.21814] [PMID: 16645971]

[13] Rizawati RI, Shamila K, Shafira MS, Ruslinda M. Guillain-Barre Syndrome Associated with Cyclosporine A. J Clin Nephrol Ren Care 2016; 2(1)

[14] Schonberger LB, Hurwitz ES, Katona P, Holman RC, Bregman DJ. Guillain-Barr syndrome: Its epidemiology and associations with influenza vaccination. Ann Neurol 1981; 9(S1)(Suppl.): 31-8. [http://dx.doi.org/10.1002/ana.410090707] [PMID: 7224614]

[15] Hemachudha T, Griffin DE, Chen WW, Johnson RT. Immunologic studies of rabies vaccination-induced Guillain-Barre syndrome. Neurology 1988; 38(3): 375-8. [http://dx.doi.org/10.1212/WNL.38.3.375] [PMID: 2450302]

[16] Martín Arias LH, Sanz R, Sáinz M, Treceño C, Carvajal A. Guillain-Barré syndrome and influenza vaccines: A meta-analysis. Vaccine 2015; 33(31): 3773-8. [http://dx.doi.org/10.1016/j.vaccine.2015.05.013] [PMID: 25999283]

[17] Souayah N, Yacoub HA, Khan HMR, *et al.* Guillain-Barré syndrome after H1N1 vaccination in the United States: a report using the CDC/FDA Vaccine Adverse Event Reporting System (2009). Neuroepidemiology 2012; 38(4): 227-32. [http://dx.doi.org/10.1159/000336113] [PMID: 22555646]

[18] Khamaisi M, Shoenfeld Y, Orbach H. Guillain-Barré syndrome following hepatitis B vaccination. Clin Exp Rheumatol 2004; 22(6): 767-70. [PMID: 15638054]

[19] Miranda S, Chaignot C, Collin C, Dray-Spira R, Weill A, Zureik M. Human papillomavirus vaccination and risk of autoimmune diseases: A large cohort study of over 2 million young girls in France. Vaccine 2017; 35(36): 4761-8. [http://dx.doi.org/10.1016/j.vaccine.2017.06.030] [PMID: 28750853]

[20] Velentgas P, Amato AA, Bohn RL, *et al.* Risk of Guillain-Barré syndrome after meningococcal conjugate vaccination. Pharmacoepidemiol Drug Saf 2012; 21(12): 1350-8. [http://dx.doi.org/10.1002/pds.3321] [PMID: 22807266]

[21] WHO. Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process whoint 2021. Available from: https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_20Oct2021.pdf

[22] Kim DD, Kung CS, Perez DL. Helping the Public Understand Adverse Events Associated With COVID-19 Vaccinations. JAMA Neurol 2021; 78(7): 789-90. [http://dx.doi.org/10.1001/jamaneurol.2021.1042] [PMID: 33835153]

[23] Finsterer J, Scorza FA. SARS-CoV-2 vaccines are not free of neurological side effects. Acta Neurol Scand 2021; 144(1): 109-10. [http://dx.doi.org/10.1111/ane.13451] [PMID: 34002379]

[24] van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol 2014; 10(8): 469-82. [http://dx.doi.org/10.1038/nrneurol.2014.121] [PMID: 25023340]

[25] Leonhard SE, Mandarakas MR, Gondim FAA, *et al.* Diagnosis and management of Guillain–Barré syndrome in ten steps. Nat Rev Neurol 2019; 15(11): 671-83. [http://dx.doi.org/10.1038/s41582-019-0250-9] [PMID: 31541214]

[26] Sinha S, Prasad KN, Jain D, Pandey CM, Jha S, Pradhan S. Preceding infections and anti-ganglioside antibodies in patients with Guillain–Barré syndrome: a single centre prospective case-control study. Clin Microbiol Infect 2007; 13(3): 334-7. [http://dx.doi.org/10.1111/j.1469-0691.2006.01636.x] [PMID: 17391394]

[27] van den Berg B, van der Eijk AA, Pas SD, *et al.* Guillain-Barre syndrome associated with preceding hepatitis E virus infection. Neurology 2014; 82(6): 491-7.

[http://dx.doi.org/10.1212/WNL.0000000000000111] [PMID: 24415572]

[28] Kuwabara S, Yuki N. Axonal Guillain-Barré syndrome: concepts and controversies. Lancet Neurol 2013; 12(12): 1180-8. [http://dx.doi.org/10.1016/S1474-4422(13)70215-1] [PMID: 24229616]

[29] Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barre syndrome and validation of Brighton criteria. Brain 2014; 137(1): 33-43. [http://dx.doi.org/10.1093/brain/awt285] [PMID: 24163275]

[30] Nakano Y, Kanda T. Pathology of Guillain-Barré syndrome. Clin Exp Neuroimmunol 2016; 7(4): 312-9. [http://dx.doi.org/10.1111/cen3.12342]

[31] Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EFM. Anticipating mechanical ventilation in Guillain-Barré syndrome. Arch Neurol 2001; 58(6): 893-8. [http://dx.doi.org/10.1001/archneur.58.6.893] [PMID: 11405803]

[32] Orlikowski D, Sharshar T, Porcher R, Annane D, Raphael JC, Clair B. Prognosis and risk factors of early onset pneumonia in ventilated patients with Guillain–Barré syndrome. Intensive Care Med 2006; 32(12): 1962-9. [http://dx.doi.org/10.1007/s00134-006-0332-1] [PMID: 17019557]

[33] van den Berg B, Bunschoten C, van Doorn PA, Jacobs BC. Mortality in Guillain-Barre syndrome. Neurology 2013; 80(18): 1650-4. [http://dx.doi.org/10.1212/WNL.0b013e3182904fcc] [PMID: 23576619]

[34] Kulkarni GB, Rao S, Netto AB, Taly AB, Umamaheswara Rao GS. Mortality in mechanically ventilated patients of Guillain Barré Syndrome. Ann Indian Acad Neurol 2011; 14(4): 262-6. [http://dx.doi.org/10.4103/0972-2327.91942] [PMID: 22346014]

[35] United States Department of Health and Human Services (DHHS), Public Health Service (PHS), Centers for Disease Control (CDC), Food and Drug Administration (FDA). Vaccine Adverse Event Reporting System (VAERS) 1990. Availiable from: http://wonder.cdc.gov/vaers.html

[36] (EMA), European Medicines Agency. EduraVigilance - European Database of Suspected Adverse Drug Reaction Reports. Availiable from: https://www.adrreports.eu/en/index.html

[37] Patone M, Handunnetthi L, Saatci D, *et al.* Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. Nat Med 2021; (Oct): 1-10. Online ahead of print

[38] Slovak State Institue of Drug Control (ŠÚKL). Weekly statistics of reports of suspected side efefcts of COVID-19 vaccination (18112021) 2021. Availiable from: https://www.sukl.sk/hlavna-stranka/slovenska-verzia/media/tlacove-spravy/tyzdenna-statistika-hlaseni-podozreni-na-neziaduce-ucinky-vakcin-na-prevenciu-covid-19-18.-11.-2021?page_id=5729