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Relation between Guillain-Barré syndrome and Covid-19: Case-Series

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ABSTRACT

Approximately two-thirds of the Guillain-Barré syndrome (GBS) cases are preceded by upper respiratory tract infection or enteritis. There has been previous documentation of a clear association between Covid-19 and GBS. Covid-19 can affect the nervous tissue either through direct damage or through triggering a host immune response with subsequent development of autoimmune diseases such as GBS. Covid-19 can affect the host`s immune system through the activation and interaction of the T-and B-lymphocytes with subsequent production of antibodies that cross-react with the gangliosides. Depending on the nature of the neuronal autoimmune destruction, the affected individual may have either a demyelinating or axonal subtype of GBS. These subtypes differ not only in symptoms but also in the likelihood of recovery. This report presents two cases of GBS that developed after the respiratory symptoms of Covid-19. Their neurological features indicated demyelination, axonal damage, irritation of spinal nerve roots, and impaired sensory and motor transmission with additional facial nerve palsy in the second-studied case. This case report highlights the relationship between GBS and Covid-19 infection.

KEYWORDS: Covid-19, GBS, Guillain-Barré syndrome

ABBREVIATIONS: Covid-19: Corona-virus disease-19; CSF: Cerebro-spinal fluid; CT: Computerized tomography; GBS: Guillain-Barré syndrome; ICU: Intensive care unit; MFS: Miller-Fisher syndrome; MRC: Medical Research Council; PCR: Polymerase chain reaction; SARS: Severe acute respiratory syndrome; TR: Tendon reflexes; UTI: Urinary tract infection; WKMU: West Kazakhstan Medical University

INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute or subacute, rapidly progressing autoimmune disease of the peripheral nervous system (monophasic immune-mediated neuropathy) manifested by limb paraesthesia, muscle weakness, and/or flaccid paralysis [1]. It may also present as defective facial, oculomotor, and bulbar nerves, known as the Miller-Fisher syndrome (MFS) [1, 2]. About two-thirds of the GBS cases present with nerve root pain before the onset of muscle weakness [3]. In most cases of GBS, there are decreased tendon reflexes (TR) in the affected limbs. However, the tendon reflexes may be unchanged in the early stages of the disease [4]. The incidence of GBS is 1.2-2.3 cases per 100,000 individuals [5]. In contrast, for people over the age of 50 years, it can reach 3.3 per 100,000 individuals [6]. For this population, GBS can lead to residual functional disability [7]. Recent reports discovered that severe acute respiratory syndrome (SARS)-Cov-2 (Covid-19) was associated with neurological complications including febrile seizures, headache, dizziness, myalgia, encephalopathy, stroke, and peripheral nerve diseases [8]. About two-thirds of the GBS cases are preceded by upper respiratory infection or enteritis [9]. Covid-19 can affect the nervous tissue either through direct damage or through triggering the host`s immune response [10, 11] with subsequent development of autoimmune diseases such as GBS [12]. This report highlights the relationship between GBS and the COVID-19 infection.

CASE PRESENTATION

Case-1

A 23-year-old woman, primipara, pregnant at 30 weeks gestation, was admitted to the infectious diseases hospital of West Kazakhstan Medical University (WKMU) with acute weakness of the lower limbs, nasal voice, cough, shortness of breath, dizziness, and headache. She gave a history of hospital admission, due to a urinary tract infection (UTI) with pregnancy, treated with intravenous antibiotics 3 weeks before the current admission. On admission, the patient presented with a temperature of 37.5°C, blood pressure of 110/65 mmHg, pulse rate of 82 beats/min., and respiratory rate of 22/min, as well as with a positive nasopharyngeal swab polymerase chain reaction (PCR) test for Covid-19. The blood panel showed leukocytosis, lymphocytopenia, and increased lactate dehydrogenase (LDH), while the chest computerized tomography (CT) showed bilateral lower lobe pneumonia. The neurological examination showed decreased right pharyngeal reflex, lower limbs flaccid symmetrical paraparesis [Medical Research Council (MRC) scale 4/5 proximal, and 2/5 distal], lost lower limb reflexes (knee and ankle reflexes), legs tingling, and no signs of meningeal irritation. The electroneurography showed acute motor demyelinating neuropathy (delay in the distal nerve latency, decreased conduction velocity, and decreased amplitude of the action potential). The patient clinically improved after receiving combined antimicrobial medication (azithromycin 500 mg/once daily for 5 days and amoxicillin/clavulanic acid 1 gm/twice daily for 7 days) and intravenous immunoglobulins 0.4 g/kg/day for 5 days (after obstetrics consultation).

Case-2

A 59-year-old woman was admitted to the intensive care unit (ICU) of WKMU with general weakness associated with chest pain, coughing, and shortness of breath. On admission, she presented with a temperature of 38.5°C, blood pressure of 140/80 mmHg, pulse rate of 86 beats/min., and a respiratory rate was 25/min. The patient had a positive nasopharyngeal swab PCR test for COVID-19, bilateral lower lobe pneumonia, and interstitial pneumonitis (ground glass opacities) on chest CT. The blood panel showed lymphopenia with increased C-reactive proteins and increased LDH. The neurological examination showed bilateral facial paresis, bilateral ptosis, dysphonia, dysphagia, and quadriplegia [Medical Research Council (MRC) scale 1/5 proximal and 0/5 distal in the lower limbs], diffuse muscle hypotonia, tingling with absent hand and feet reflexes with positive tension symptoms of the nerve roots, and positive right Babinski sign. The electroneurography showed acute demyelinating polyneuropathy (sensory and motor with delay in the distal nerve latency, decreased conduction velocity, and decreased amplitude of the action potential). The brain magnetic resonance imaging (MRI) was completely normal and the cerebrospinal fluid (CSF) examination following the lumbar puncture showed an increased immunoglobulin (IgG)/albumin ratio. The COVID-19 PCR test was negative. The patient was diagnosed with classic Miller-Fisher syndrome with cerebrospinal fluid protein-cell dissociation and received intravenous immunoglobulins in a dose of 0.4 g/kg/day for 5 days. Despite all treatment efforts, she developed severe respiratory distress which progressed to respiratory failure, and died. The diagnosis of the COVID-19 infection in the studied cases was based on the nasopharyngeal swab PCR test, blood picture (lymphopenia, increased inflammatory markers such as C-reactive proteins and LDH), and chest CT. The GBS was diagnosed using the World Health Organisation (WHO) international criteria [13] and Brighton Collaboration diagnostic criteria [14].

DISCUSSION

Roughly two-thirds of the GBS cases are preceded by an upper respiratory infection or enteritis [9]. Gigli *et al* [15], reported an increased incidence of GBS (5.41 times) in 2019-2020. A definite association between Covid-19 and GBS was present in many reports [16-18]. GBS-related polyneuropathy has been reported to occur at the onset Covid-19 symptoms as well as before or after the appearance of Covid-19 symptoms [19-22]. Sedaghat *et al.* [23] reported instances of GBS occurring after the onset of Covid-19 symptoms, while Ottaviani *et al.* [24] reported GBS after the Covid-19 symptoms. Alberti *et al.* [25] reported GBS occurring before the onset of Covid-19 respiratory symptoms in a 71-year-old male. Additionally, Zhao *et al.* [26], presented cases of acute progressive weakness in both legs 8 days before the Covid-19 symptoms. Covid-19 can affect the nervous tissue through direct damage or triggering the host`s immune response [10, 11] with subsequent development of autoimmune diseases such as GBS [12]. Moreover, GBS can occur after vaccination, pregnancy, or a surgical procedure [27]. The SARS-CoV-2 infection may trigger the host`s immune response through the activation and interaction of the T-and B-lymphocytes with subsequent production of antibodies against SARS-CoV-2 [28]. These antibodies cross-react with the gangliosides (sialic acid-containing glycosphingolipids, located on the neuronal cells surface) leading to either autoimmune destruction of myelin sheaths or axons [29-30]. Fantini *et al.* [31] reported a cross-reaction between the SARS-CoV-2 spike saccharides and myelin sheaths or axon gangliosides. A review suggests that SARS-CoV-2 can directly destroy the gangliosides [32]. Depending on the level of neuronal autoimmune destruction, the affected individual may have either a demyelinating or axonal GBS subtype which can differ in symptoms and the probability of recovery [33]. Moreover, some viruses, such as the cytomegalovirus and the chickenpox virus, can cause peripheral neuropathy through direct nerve damage [34]. This report presents two cases of GBS developed after the respiratory symptoms of Covid-19 and their neurological features indicated demyelination, axon damage, irritation of spinal nerve roots, and impaired sensory and motor transmission with additional facial nerve palsy in the second case studied, similar to findings reported by literature. Myckatyn *et al.* [35] also reported facial nerve palsy in 27-50% of the GBS cases.

CONCLUSION

SARS-CoV-2 is a newly diagnosed virus that affects the nervous system through a para-infectious phenomenon. It is important to consider Covid-19 screening in patients with GBS, as the disease can develop concurrently with the onset of COVID-19 symptoms, after the appearance of the symptoms, or even in the lack of symptoms. Further research is required to confirm the increased incidence of GBS during the Covid-19 pandemic and the definite relation between GBS and Covid-19.

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Conflict of interest

The authors declare no conflict of interest.

Consent to publish

Written consent was obtained from the two patients to publish their data as a case-series.

Data availability

Further data are available from the corresponding author upon reasonable request.

Authorship

MBJ, DNA, and NMT are responsible for the manuscript design, neurological examination, collection and review of the participants' data, and final revision before submission for publication. IAA, SSS, and YJK are responsible for editing and final revision.

REFERENCES

1. Leonhard SE, Mandarakas MR, Gondim FAA, Bateman K, *et al.* Diagnosis and management of Guillain-Barré syndrome in ten steps. Nat Rev Neurol. 2019; 15(11): 671-683. doi: 10.1038/s41582-019-0250-9.
2. Wong AH, Umapathi T, Nishimoto Y, Wang YZ,*et al.* Cytoalbuminologic dissociation in Asian patients with Guillain-Barré and Miller Fisher syndromes. J Peripher Nerv Syst. 2015; 20(1): 47-51. doi: 10.1111/jns.12104.
3. Ruts L, Drenthen J, Jongen JL, Hop WC, *et al.* Dutch GBS Study Group. Pain in Guillain-Barre syndrome: a long-term follow-up study. Neurology. 2010; 75(16): 1439-47. doi: 10.1212/WNL.0b013e3181f88345.
4. Yuki N, Kokubun N, Kuwabara S, Sekiguchi Y, *et al.* Guillain-Barré syndrome associated with normal or exaggerated tendon reflexes. J Neurol. 2012; 259(6): 1181-90. doi: 10.1007/s00415-011-6330-4.
5. van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome. Lancet Neurol. 2008; 7(10): 939-50. doi: 10.1016/S1474-4422(08)70215-1.
6. McGrogan A, Madle GC, Seaman HE, de Vries CS. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. Neuroepidemiology. 2009; 32(2): 150-63. doi: 10.1159/000184748.
7. Amatya B, Khan F, Whishaw M, Pallant JF. Guillain-Barré syndrome: prevalence and long-term factors impacting bladder function in an Australian community cohort. J Clin Neurol. 2013; 9(3): 144-50. doi: 10.3988/jcn.2013.9.3.144.
8. Helms J, Kremer S, Merdji H, Clere-Jehl R, *et al.* Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020; 382(23): 2268-2270. doi: 10.1056/NEJMc2008597.
9. Kim JE, Heo JH, Kim HO, Song SH, *et al.* Neurological Complications during Treatment of Middle East Respiratory Syndrome. J Clin Neurol. 2017; 13(3): 227-233. doi: 10.3988/jcn.2017.13.3.227.
10. Wu Y, Xu X, Chen Z, Duan J, *et al.* Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun. 2020; 87: 18-22. doi: 10.1016/j.bbi.2020.03.031.
11. Troyer EA, Kohn JN, Hong S. Are we facing a crashing wave of neuropsychiatric sequelae of COVID-19? Neuropsychiatric symptoms and potential immunologic mechanisms. Brain Behav Immun. 2020; 87: 34-39. doi: 10.1016/j.bbi.2020.04.027.
12. Desforges M, Le Coupanec A, Stodola JK, Meessen-Pinard M, Talbot PJ. Human coronaviruses: viral and cellular factors involved in neuroinvasiveness and neuropathogenesis. Virus Res. 2014; 194: 145-58. doi: 10.1016/j.virusres.2014.09.011.
13. Piradov MA, Suponeva NA. Autoimmune Diseases of the Nervous System: Problem Statement and Prospects. Vestnik Rossiiskoi Akademii Meditsinskikh auk = Annals of the Russian Academy of Medical Sciences. 2015; 70 (2): 183-187. doi: 10.15690/vramn. v70i2.1311.
14. Fokke C, van den Berg B, Drenthen J, Walgaard C, *et al.* Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014; 137(Pt 1):33-43. doi: 10.1093/brain/awt285.
15. Gigli GL, Bax F, Marini A, Pellitteri G, *et al.* Guillain-Barré syndrome in the COVID-19 era: just an occasional cluster? J Neurol. 2021; 268(4): 1195-1197. doi: 10.1007/s00415-020-09911-3.
16. Assini A, Benedetti L, Di Maio S, Schirinzi E, Del Sette M. New clinical manifestation of COVID-19 related Guillain-Barrè syndrome highly responsive to intravenous immunoglobulins: two Italian cases. Neurol Sci. 2020; 41(7): 1657-1658. doi: 10.1007/s10072-020-04484-5.
17. Lascano AM, Epiney JB, Coen M, Serratrice J, *et al.* SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with a favourable outcome. Eur J Neurol. 2020; 27(9): 1751-1753. doi: 10.1111/ene.14368.
18. Padroni M, Mastrangelo V, Asioli GM, Pavolucci L, *et al.* Guillain-Barré syndrome following COVID-19: new infection, old complication? J Neurol. 2020; 267(7): 1877-1879. doi: 10.1007/s00415-020-09849-6.
19. Rana S, Lima AA, Chandra R, Valeriano J, *et al.* Novel Coronavirus (COVID-19)-Associated Guillain-Barré Syndrome: Case Report. J Clin Neuromuscul Dis. 2020; 21(4): 240-242. doi: 10.1097/CND.0000000000000309.
20. Scheidl E, Canseco DD, Hadji-Naumov A, Bereznai B. Guillain-Barré syndrome during SARS-CoV-2 pandemic: A case report and review of recent literature. J Peripher Nerv Syst. 2020; 25(2): 204-207. doi: 10.1111/jns.12382.
21. Oguz-Akarsu E, Ozpar R, Mirzayev H, Acet-Ozturk NA, *et al.* Pandemic Study Team. Guillain-Barré Syndrome in a Patient With Minimal Symptoms of COVID-19 Infection. Muscle Nerve. 2020; 62(3): E54-E57. doi: 10.1002/mus.26992.
22. Helbok R, Beer R, Löscher W, Boesch S, *et al.* Guillain-Barré syndrome in a patient with antibodies against SARS-COV-2. Eur J Neurol. 2020; 27(9): 1754-1756. doi: 10.1111/ene.14388.
23. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. J Clin Neurosci. 2020; 76:233-235. doi: 10.1016/j.jocn.2020.04.062.
24. Ottaviani D, Boso F, Tranquillini E, Gapeni I, *et al.* Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. Neurol Sci. 2020; 41(6): 1351-1354. doi: 10.1007/s10072-020-04449-8.
25. Alberti P, Beretta S, Piatti M, Karantzoulis A, *et al.* Guillain-Barré syndrome related to COVID-19 infection. Neurol Neuroimmunol Neuroinflamm. 2020; 7(4): e741. doi: 10.1212/NXI.0000000000000741.
26. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol. 2020; 19(5): 383-384. doi: 10.1016/S1474-4422(20)30109-5.
27. Stoian A, Motataianu A, Bajko Z, Balasa A. Guillain-Barré and Acute Transverse Myelitis Overlap Syndrome Following Obstetric Surgery. J Crit Care Med (Targu Mures). 2020; 6(1): 74-79. doi: 10.2478/jccm-2020-0008.
28. Wen W, Su W, Tang H, Le W, *et al.* Immune cell profiling of COVID-19 patients in the recovery stage by single-cell sequencing. Cell Discov. 2020; 6: 31. doi: 10.1038/s41421-020-0168-9.
29. Furukawa K, Ohmi Y, Yesmin F, Tajima O, *et al.* Novel Molecular Mechanisms of Gangliosides in the Nervous System Elucidated by Genetic Engineering. Int J Mol Sci. 2020; 21(6): 1906. doi: 10.3390/ijms21061906.
30. Cutillo G, Saariaho AH, Meri S. Physiology of gangliosides and the role of antiganglioside antibodies in human diseases. Cell Mol Immunol. 2020; 17(4): 313-322. doi: 10.1038/s41423-020-0388-9.
31. Fantini J, Di Scala C, Chahinian H, Yahi N. Structural and molecular modelling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection. Int J Antimicrob Agents. 2020; 55(5): 105960. doi: 10.1016/j.ijantimicag.2020.
32. van den Berg B, Walgaard C, Drenthen J, Fokke C, *et al.* Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol. 2014; 10(8): 469-82. doi: 10.1038/nrneurol.2014.121.
33. Yu RK, Usuki S, Ariga T. Ganglioside molecular mimicry and its pathological roles in Guillain-Barré syndrome and related diseases. Infect Immun. 2006; 74(12): 6517-27. doi: 10.1128/IAI.00967-06.
34. Sung EJ, Kim DY, Chang MC, Ko EJ. Prediction of Functional Outcome in Axonal Guillain-Barre Syndrome. Ann Rehabil Med. 2016; 40(3): 481-8. doi: 10.5535/arm.2016.40.3.481.
35. Myckatyn TM, Susan E, Mackinnon SE. A Review of Facial Nerve Anatomy. Semin Plast Surg 2004; 18(1): 5-11. doi: 10.1055/s-2004-823118.