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CASE REPORT

Post-COVID-19 Guillain-Barré Syndrome

A case report from Oman

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abstract: Guillain-Barré syndrome (GBS) has been reported as one of the neurological manifestations linked to COVID-19, a severe acute respiratory syndrome caused by coronavirus 2. We present the case of a 72-year-old male patient attending a tertiary care hospital in Muscat, Oman, in 2020 with a history of progressive bilateral limb weakness and numbness. The current diagnosis was in line with a rare complication of COVID-19. After exclusion of other possible causes, a diagnosis of GBS induced by COVID-19 was made. The patient received 0.4g/kg of intravenous immunoglobulin (IVIG) per day for five days. This case report highlights the characteristics and course of GBS following COVID-19 infection. Further studies are needed to characterize the manifestations and course of various neuromuscular disorders in relation to COVID-19 infection.

Keywords: COVID-19; Guillain-Barré syndrome; IVIG; Oman.

Severe acute respiratory syndrome coronavirus 2 (COVID-19) was announced as a pandemic in March 2020 by the world health organization (WHO).[1] The neurological manifestations and complications of COVID-19 have been reported since then.[2] Chinese and Spanish studies reported the prevalence of neurological manifestations in admitted patients with COVID-19 as 36.4% and 57.4%, respectively.[3,4]

Guillain-Barré syndrome (GBS) is an immune-mediated inflammatory polyradiculoneuropathy with acute ascending symmetrical weakness along with areflexia.[1,4,5] It is one of the demyelinating disorders affecting the peripheral nerves in the body.[4] Few case reports and series of post-COVID-19 GBS cases have been published.[1,4] These case reports have suggested a relationship between the occurrence of GBS and recent COVID-19 infection that preceded the onset of GBS by a few weeks. Thus, a post-infectious dysregulation of the immune system that is triggered by COVID-19 appears to be the main cause.[2,4] To the best of the authors' knowledge, no case report of post-COVID-19 GBS has been published in Oman, at the time of writing.

Case Report

A 72-year-old male patient known to have hypertension and ischemic heart disease had mild COVID-19 infection confirmed in August 2020. The patient did not require hospitalisation as he only suffered from mild fever, runny nose and myalgia for a few days after which the symptoms resolved.

The patient presented to a tertiary care hospital in Muscat, Oman, in 2020 with a one-day history of bilateral lower limb weakness and numbness. The symptoms evolved over few hours with numbness starting at his feet followed by heaviness in his legs and the inability to walk. The patient noted weakness and numbness in his upper limbs and also reported mild dysphagia starting a few days prior to the symptoms. He denied any difficulty in breathing, had normal bowel motions and showed no new urinary symptoms. There was no past medical history of any neurological symptoms. The patient also denied any history of smoking or alcohol consumption.

On admission, the patient was alert, oriented and was in no pain or distress. He had a heart rate of 56 beats/minute, blood pressure of 162/96 mmHg, respiratory rate of 18 breaths/minute and oxygen saturation of 100% on room air. His random blood sugar was 6.3 mmol/L. The neurological examination showed normal cranial nerves. Motor exam in the upper limbs was normal except for diminished reflexes. The tone in the lower limb was reduced and the patient's strength, measured by Medical Research Council scale, revealed hip flexion of 2/5, knee flexion of 3/5, knee extension of -4/5, plantar and dorsiflexion (of the ankles) of -4/5. The reflexes in his lower limbs were diminished and plantars were down-going. The sensory examination was normal apart from a decrease in the joint-position sense in the toes and coordination of the upper limbs was normal and not examined in lower limbs in view of the weakness.

The laboratory investigations included normal complete blood count, urea and electrolyte, coagulation profile, liver function test, thyroid function test (TFT) and serum folate. The C-reactive protein level was <1 mg/L (reference range: 0–5 mg/L), creatine kinase

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Table 1: Motor nerve conduction study and F-Wave values of a 72-year-old male patient with COVID-19 admitted to a tertiary care centre in Muscat, Oman

Site	Nerve	DML in ms	AMP* in mV	CV in m/s	Duration† in ms	TDR	F wave Latency in ms
Right	Median	5.8	5.5/6.8	46	8.6/8.1	1.060	35.9
	Ulnar	4.3	5.6/6.5	51	9.5/8.8	1.070	39.7
Left	Median	5.7	5.5/6.0	41	9.9/9.8	1.125	34.8
	Ulnar	4.2	5.3/6.0	58	7.9/9.4	0.840	37.9
Right	Tibial	7.6	1.7/3.5	32	16.2/11.2	1.450	53.3
	Peroneal	8.3	0.3/0.4	30	14.6/13.1	1.110	67.9
Left	Tibial	8.2	0.6/0.9	32	20.4/15.5	1.300	NR
	Peroneal	10.3	1.6/3.1	36	13.2/10.2	1.290	63.5

DML = distal motor latency; ms = milliseconds; AMP = amplitude; mV = millivolt; m/s = metres/second; CV = conduction velocity; TDR = temporal dispersion ratio; NR = not recordable.

**The amplitudes for each nerve are presented as proximal/distal amplitude. †The durations for each nerve are presented as proximal/distal compound muscle action potential duration.*

Table 2: Sensory nerve conduction values of a 72-year-old male patient with COVID-19 admitted to a tertiary care centre in Muscat, Oman

Site	Nerve	Onset Latency in ms	Peak Latency in ms	AMP in µV	CV in m/s
Right	Median	3.9	4.7	8	36
	Ulnar	3.0	4.4	8	37
Left	Median	3.7	4.8	11	38
	Ulnar	3.2	4.1	8	35
Right	Sural	2.6	3.7	10	46
Left	Sural	2.3	3.3	15	52

ms = milliseconds; AMP = amplitude; µv = microvolt; CV = conduction velocity; m/s = metres/second.

stood at 340 U/L (reference range: 39–308 U/L) and vitamin B12 at 128 pmol/L (reference range: 138–652 pmol/L). Nasopharyngeal polymerase chain reaction (PCR) testing for COVID-19, done during admission, confirmed COVID-19. The results from the chronic hepatitis screen, HIV-1 and 2 antigen/antibody test, syphilis screen, blood culture and urine microscopy, culture and sensitivity were all negative. The patient's cerebrospinal fluid analysis showed proteins of 2.7 g/L (reference range 0.15–0.45 g/L) with no leucocytes; however, PCR and autoantibodies were not tested again during admission.

On the third day of admission, a detailed nerve conduction study (NCS) was performed [Table 1]. The following motor nerves of the upper and lower limbs on both sides were stimulated: the median nerve on the wrist and elbow, the ulnar nerve on the wrist and below the elbow, the tibial nerve on the ankle and popliteal fossa and the peroneal nerve on the ankle and fibula head. The motor NCS showed a decrease in compound muscle action potential amplitude from multiple nerves in the upper and lower limbs with prolonged distal motor latencies and mildly reduced velocities. F-waves were present in most of the nerves tested but were in the upper range. There was no conduction block or temporal dispersion. The sensory NCS revealed borderline reduced sensory nerve action potential amplitude from the upper limbs nerves with mildly reduced velocities. However, results from the sural nerve tests were normal [Table 2]. These findings suggested diffuse motor and sensory neuropathy with a predominance of demyelinating changes. Magnetic resonance imaging scans of the brain and spinal cord showed no acute changes.

During admission, the patient's upper limb weakness worsened with a shoulder abduction of 2/5 bilaterally, elbow extension of 3/5, elbow flexion of -4/5 and intrinsic hand muscle flexion and extension were 4/5. The patient was diagnosed with post-COVID-19 GBS. Therefore, he was given one course of intravenous immunoglobulin (IVIG) at 0.4 g/kg/day for five days. Additionally, the patient received a 10 mg hydrocortisone tablet (once, daily), 3 mL injection of vitamin B complex (daily, for four days) and extensive physiotherapy during admission. He showed slow but progressive improvement in his symptoms during admission. The patient's neurological examination was normal apart from the minimal weakness of his limbs on the day of discharge.

Consent has been obtained from the patient for the publication of this case report.

Discussion

The immune-mediated nature of GBS is mostly based on observational studies of *Campylobacter jejuni*-induced GBS and the fact that immunotherapy has

a central role in the management of GBS.[6–12] GBS is well-documented to be seen following a number of infections such as those caused by *Campylobacter jejuni*, *mycoplasma*, Epstein-Barr virus, cytomegalovirus and recently the Zika virus.[7,13–15] The most common variant of GBS is acute inflammatory demyelinating polyneuropathy (AIDP).[6,16,17] The development of polyneuropathies due to any viral infection suggests molecular mimicry leading to a neural inflammatory reaction, even presenting as an inflammatory response syndrome.[18,19] However, these mechanisms of COVID-19 related neuropathy need to be studied more deeply.

Existing literature shows that the predominant clinical presentation of GBS induced by COVID-19 is the classical sensorimotor GBS. In addition, a majority of the cases fulfilled the electrophysiological criteria for a diagnosis of AIDP. There is a male predominance in the reported cases and it appears across a wide age range: patients from 11–94 years of age.[19] However, the mean age of patients was approximately 55 years, with the majority of cases being reported among those above 40 years of age. While few cases reported para-infectious onset of GBS, most patients had a post-infectious onset of GBS. Hence, GBS induced by COVID-19 generally seems to follow similar trends to the classical post-infectious GBS that is induced by other infective organisms.[19]

The present case of GBS seems to be a post-infectious phenomenon as it manifested after the resolution of the initial COVID-19 infection. His mild course of COVID-19 is in keeping with some of the cases already reported in the literature.[20] However, GBS has been reported to occur even after a severe form of COVID-19.[1,4] This might be interpreted to be an AIDP variant.[18]

In comparison to the current patient's significant improvement following the IVIG course, a patient in the United Kingdom with a case of para-infectious GBS due to COVID-19 failed to respond to IVIG with weakness progression, a drop in respiratory vital capacity and he required intubation with ICU admission.[1] Worsening of such cases could be due to direct invasion of toxins from the COVID-19 virus or related to the severity of pneumonia. However, there was no difference in response to IVIG or plasma exchange between para-infectious and post-infectious GBS in COVID-19 cases as per the few cases reported in the existing literature.[4]

Although ribonucleic acid was detected in the nasopharyngeal swab, it is unclear evidence of an active infection as it only represents the shedding of viral RNA.[21,22] Moreover, seroconversion to immunoglobulin G antibodies was detected in our patient. Given that the current patient responded to the IVIG course, it favours the conclusion that GBS, in this case, is a post-infectious immune-mediated phenomenon.

Conclusion

As post-COVID-19 GBS is becoming increasingly apparent, larger studies are needed to better characterise the illness, including its clinical presentation. In particular, the effectiveness of IVIG or plasma exchange in para-infectious and post-infectious cases remains to be studies more extensively. Therefore, it is important to report cases of GBS induced by COVID-19 to help build the cumulative, worldwide evidence-base needed for the best approach to the management of similar cases. Moreover, reports of GBS induced by COVID-19 in the Middle East are limited. Such reports need to be published so any possible differences in the presentation or management of future cases between different populations can be detected. It is also vital to recognise that GBS could be an important comorbidity in critically ill COVID-19 patients and should be considered in patients not improving despite improvement of other clinical parameters, especially when chest imaging is inconsistent with the poor respiratory status of the patient.

AUTHORS' CONTRIBUTION

MMAZ drafted the manuscript after extensive follow-up of patient records. EAS and MAM were involved in case report writing and extensive review of the manuscript before submission. ARG was responsible for reviewing and re-writing the manuscript following the work that was done by the first three authors and answering all the reviewers' questions that could not be answered by the first three authors. AAA was responsible for reviewing the entire manuscript before submission. All authors approved the final version of the manuscript.

References

1. Webb S, Wallace VCJ, Martin-Lopez D, Yogarajah M. Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. BMJ Case Rep 2020; 13:1–4. https://doi.org/10.1136/bcr-2020-236182.

2. Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, et al. The emerging spectrum of COVID-19 neurology: Clinical, radiological and laboratory findings. Brain 2020; 143:3104–20. https://doi.org/10.1093/brain/awaa240.

3. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, Sánchez-Larsen Á, Layos-Romero A, García-García J, et al. Neurologic manifestations in hospitalized patients with COVID-19: The ALBACOVID registry. Neurology 2020; 95:e1060–70. https://doi.org/10.1212/WNL.0000000000009937.

4. Zito A, Alfonsi E, Franciotta D, Todisco M, Gastaldi M, Cotta Ramusino M, et al. COVID-19 and Guillain–Barré Syndrome: A Case Report and Review of Literature. Front Neurol 2020; 11:1–7. https://doi.org/10.3389/fneur.2020.00909.

5. Aljaafari D, Ishaque N. Paraparetic variant of guillain-barré syndrome in first 24 hours of postpartum period: A case report. Sultan Qaboos Univ Med J 2020; 20:227–30. https://doi.org/10.18295/squmj.2020.20.02.015.

6. Ogawara K, Kuwabara S, Mori M, Hattori T, Koga M, Yuki N. Axonal Guillain-Barré syndrome: relation to anti-ganglioside antibodies and Campylobacter jejuni infection in Japan. Ann Neurol 2000; 48:624–31. https://doi.org/10.1002/1531-8249(200010)48:4<624::AID-ANA9>3.0.CO;2-O.

7. Rees JH, Soudain SE, Gregson NA, Hughes RA. Campylobacter jejuni infection and Guillain-Barré syndrome. N Engl J Med 1995; 333:1374–9. https://doi.org/10.1056/NEJM199511233332102.

8. Visser LH, Van der Meché FG, Van Doorn PA, Meulstee J, Jacobs BC, Oomes PG, et al. Guillain-Barré syndrome without sensory loss (acute motor neuropathy): A subgroup with specific clinical, electrodiagnostic and laboratory features. Brain 1995; 118:841–7. https://doi.org/10.1093/brain/118.4.841.

9. Yuki N, Yoshino H, Sato S, Miyatake T. Acute axonal polyneuropathy associated with anti-GM1 antibodies following Campylobacter enteritis. Neurology 1990; 40:1900–2. https://doi.org/10.1212/wnl.40.12.1900.

10. Aspinall GO, Fujimoto S, McDonald AG, Pang H, Kurjanczyk LA, Penner JL. Lipopolysaccharides from Campylobacter jejuni associated with Guillain- Barre syndrome patients mimic human gangliosides in structure. Infection and Immunity 1994; 62:2122–5. https://doi.org/10.1128/iai.62.5.2122-2125.1994.

11. Osterman PO, Fagius J, Lundemo G, Pihlstedt P, Pirskanen R, Sidén A, et al. Beneficial effects of plasma exchange in acute inflammatory polyradiculoneuropathy. Lancet 1984; 2:1296-9. https://doi.org/10.1016/s0140-6736(84)90819-5.

12. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. Cochrane Database Syst Rev 2014; 2014:CD002063. https://doi.org/10.1002/14651858.CD002063.pub6.

13. Winer JB, Hughes RA, Anderson MJ, Jones DM, Kangro H, Watkins RP. A prospective study of acute idiopathic neuropathy. II. Antecedent events. J Neurol Neurosurg Psychiatry 1988; 51:613–8. https://doi.org/10.1136/jnnp.51.5.613.

14. Orlikowski D, Porcher R, Sivadon-Tardy V, Quincampoix JC, Raphaël JC, Durand MC, et al. Guillain-Barré syndrome following primary cytomegalovirus infection: a prospective cohort study. Clin Infect Dis 2011; 52:837–44. https://doi.org/10.1093/cid/cir074.

15. Parra B, Lizarazo J, Jiménez-Arango JA, Zea-Vera AF, González-Manrique G, Vargas J, et al. Guillain-Barré Syndrome Associated with Zika Virus Infection in Colombia. N Engl J Med 2016; 375:1513–23. https://doi.org/10.1056/NEJMoa1605564.

16. Doets AY, Verboon C, van den Berg B, Harbo T, Cornblath DR, Willison HJ, et al. Regional variation of Guillain-Barré syndrome. Brain 2018; 141:2866–77. https://doi.org/10.1093/brain/awy232.

17. Ye Y, Wang K, Deng F, Xing Y. Electrophysiological subtypes and prognosis of Guillain-Barré syndrome in northeastern China. Muscle Nerve 2013; 47:68–71. https://doi.org/10.1002/mus.23477.

18. Sriwastava S, Kataria S, Tandon M, Patel J, Patel R, Jowkar A, et al. Guillain Barré Syndrome and its variants as a manifestation of COVID-19: A systematic review of case reports and case series. J Neurol Sci 2021; 420:117263. https://doi.org/10.1016/j.jns.2020.117263.

19. Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. J Neuro 2021; 268:1133–70. https://doi.org/10.1007/s00415-020-10124-x.

20. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia: An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med 2019; 200:e45–67. https://doi.org/10.1164/rccm.201908-1581ST.

21. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. Clin Infect Dis 2020; 71:2663–6. https://doi.org/10.1093/cid/ciaa638.

22. Liu WD, Chang SY, Wang JT, Tsai MJ, Hung CC, Hsu CL, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. J Infect 2020; 81:318–56. https://doi.org/10.1016/j.jinf.2020.03.063.