Guillain–Barré syndrome after an asymptomatic COVID-19 Infection: a case report

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Abstract

Background: Guillain–Barré syndrome (GBS) is an acute, immune-mediated generalized polyradiculoneuropathy often preceded by several infections. In most cases of GBS linked to SARS-CoV-2 worldwide, the infected individuals developed COVID-19 symptoms. This case report aims to present a case of a GBS post asymptomatic COVID-19 infection discovered in the emergency department of the regional hospital of Ksar Hellal.

Case Presentation: A 55-year-old man consulted the emergency department complaining of lumbar pain treated as a lumbar discal hernia. After 2 days, he developed acute weakness in the lower limbs. Neurological examination revealed a sensory-motor deficit in the lower limbs. The evolution was: absent deep tendon reflexes in the lower limbs, ascending flaccid symmetrical limb paralysis with tetraplegia, swallowing disorder, urinary incontinence, and central respiratory depression. A clinical diagnosis of GBS was made. The patient was transferred to the intensive care unit. He required invasive mechanical ventilation. Cerebrospinal fluid analysis revealed albumin cytologic dissociation. The serology was in favor of a recent COVID-19 infection. The patient was treated with intravenous immunoglobulin at 0.4 g/kg/day for 5 days. His clinical condition improved gradually. He was transitioned out of the intensive care unit after one month.

Conclusion: During the pandemic, all patients with suspected GBS should have SARS-CoV-2 tests to allow eventual rapid isolation. We expect an increase in the rate of GBS without an obvious cause, as long as one can have GBS after an asymptomatic COVID-19 infection. The doctor should be standing by to provide rapid, adequate assistance if required.

Keywords: Guillain-Barré syndrome; COVID-19; Tunisia; Case Report

INTRODUCTION

In December 2019, the novel coronavirus (SARS-CoV-2) was detected in China and has spread worldwide, causing a pandemic: the coronavirus disease-2019 (COVID-19) (1). After an incubation period of 5 days, the respiratory symptoms are the most frequent. Acute renal failure, gastrointestinal, and cardiac damage have also been reported (2). Several neurological symptoms have been related to COVID-19: loss of taste and smell, headache, myalgia, dizziness, and confusion (3).

Neurological complications such as encephalitis and stroke have occurred after COVID-19 infection (4).

Guillain–Barré syndrome (GBS) is an acute, immune-mediated generalized polyradiculoneuropathy often preceded by several infections: mainly Campylobacter Jejuni, Epstein–Barr virus, Cytomegalovirus, Influenza, Zika, Human Herpes virus, less frequently H1N1, HIV and Hepatitis-E (5). Around 100 cases of a confirmed or suspected GBS have been linked to SARS-CoV-2 worldwide (6, 7). Only a few cases were reported in Tunisia (8, 9). We report a case of a GBS diagnosed in a patient initially presenting without symptoms of COVID-19 in a regional hospital.

CASE REPORT

A 55-year-old man, a retired teacher with no medical condition, presented to the emergency department complaining of acute lumbar pain, tingling, and numbness in the right leg progressing within one day. He was treated for a lumbar discal hernia. After two days, he developed acute weakness in both legs and returned. He denied having respiratory or digestive symptoms. On examination, the patient was afebrile; vital parameters and lung auscultation were all normal. Neurological examination showed a sensory-motor deficit in the distal lower extremities. As his wife was tested positive for SARS-CoV-2 five days previously, the patient was admitted to the COVID ward where he was treated symptomatically with paracetamols. He had a negative PCR test for SARS-CoV-2. Laboratory testing revealed no significant abnormalities. Brain computed tomography revealed the presence of a hypodense area of the left semi-ovale centrum, which could be in line with a lacunar cerebral infarct.

The next day, a physical examination found that the lower extremities' deep tendon reflexes were absent, and their strength was significantly lower than that of the upper extremities. His symptoms progressed, and he developed ascending flaccid symmetrical limb paralysis. On day 6 of admission, the patient manifested tetraplegia, peripheral facial paralysis, swallowing disorder, urinary incontinence, and central respiratory depression with a respiratory rate of 35 cycles per minute and an oxygen saturation of 90 % under 15 L of oxygen. A clinical diagnosis of GBS was made. At biology control, there was an appearance of cytolysis, aspartate aminotransferase (ASAT) at 107 UI/L and alanine aminotransferase (ALAT) at 152 UI/L, at three times normal and biological inflammatory syndrome, CRP at 129 mg/L. The patient was immediately transferred to the intensive care unit, where he required invasive mechanical ventilation. Cerebrospinal fluid analysis revealed albumin cytologic dissociation: Glucose at 4.4 mmol/L, proteins at 1.21 g/L, and chlorides at 123 mmol/L with normal levels of red and white cells at 2 elements /mm^3 in the cytological formula. The diagnosis of GBS was confirmed. A serology test, in favor of a recent COVID-19 infection, explained the etiology of

the GBS. The patient was treated with intravenous immunoglobulin (IV Ig) at 0.4 g/kg/day for 5 days.

His clinical condition improved gradually. On day 27, the patient was extubated and was discharged from the intensive care unit to a rehabilitation facility.

DISCUSSION

We report a case of GBS with a serology suggesting a recent COVID-19 infection. GBS is a rare, serious, post-infectious, immune-mediated disease of the peripheral nervous system. Previous studies have suggested that GBS was not associated with COVID-19 (10). However, the incidence of GBS has significantly increased since the onset of the COVID-19 pandemic. Many reports have described the association between SARS-CoV-2 infection and GBS, which is supported by the chronology of the GBS cases following the same propagation pattern of COVID-19 worldwide (11). Numerous hypotheses have been proposed to explain the association pathogenesis, including immune dysregulation and systemic inflammation (12). Following infection, there is the generation of antibodies against surface glycoproteins or epitopes (spike) of SARS-CoV-2. These antibodies bind the gangliosides present in peripheral neurons due to the structural resemblance of the SARS-CoV-2's epitopes with gangliosides (molecular mimicry) (13). The systematic inflammation theory is explained by the massive cytokine release in infected patients, which may also contribute to amplifying the dysimmune process underlying GBS (14). A mean age of 50 years and male predominance were noticed among patients with the association of both diseases (7, 11).

Inconsistent with most literature data, which reported that respiratory symptoms typically precede the onset of neurologic symptoms (6, 7, 11), our patient was asymptomatic but had evidence of a COVID-19 infection. The median latency period between the COVID-19 infection and GBS was 14 days for most reported cases, supporting the post-infectious immunopathogenesis mechanism.

This duration could be longer than reported, as COVID-19 can initially be asymptomatic (6, 7). Few GBS reported cases had a para-infectious profile[17] as reported with the Zika virus (15 – 18). Nevertheless, the chronology of GBS preceding COVID-19 symptoms, described with few cases, has not been previously reported with other viral agents (6). A systematic review of 73 GBS cases associated with COVID-19 published from January 2020 to July 2020 (11) revealed that only two cases never developed COVID-19 respiratory or systemic symptoms but tested positive for SARS-CoV-2 (19, 20). Our findings were consistent with those of the literature concerning common symptoms of GBS and their mean time to nadir, which was equal to 5 days (range, 1.5–10 days), according to JB. Caress *et al*. (7) and the results of cerebrospinal fluid analysis as albumin cytologic dissociation being the most frequent finding (6,7,11). Like our patient, most reported cases received intravenous immunoglobulin therapy (6). In

terms of clinical outcomes, the admission to the intensive care unit and the requirement of mechanical ventilation were reported respectively in 40 and 33 of 109 cases by M. Aladawi *et al*. (6) JB. Caress *et al*. have reported the response to therapy in 33 of 37 (89%) patients (7).

CONCLUSION

This case report raises several concerns about the few cases of GBS following an asymptomatic COVID-19 infection and brings more attention to the possible atypical association between them. However, the main clinical, radiological, and CFS features of our case report are found to be similar to GBS cases associated with other infectious diseases. Therefore, during the pandemic, all patients with suspected GBS should have SARS-CoV-2 tests to allow eventual rapid isolation. We expect an increase in the rate of GBS without an obvious cause, as long as one can have GBS after an asymptomatic COVID-19 infection. The doctor should be standing by to provide early adequate assistance if required to prevent worse outcomes. Further studies to explore the immunogenicity of COVID-19 in the development of GBS are necessary and should consider the variations between different populations.

Consent

Written informed consent for publication of their clinical details and/or images was obtained from the patient.

Data availability statement

All data underlying the results are available as part of the article and no additional source data are required.

Competing interests

No competing interests were disclosed.

Grant information

No grants were involved in supporting this work.

REFERENCES

1. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol. 2020;92:401-402.

2. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China | Critical Care Medicine | JAMA | JAMA Network. Accessed October 4, 2022. https://jamanetwork.com/journals/jama/fullarticle/2761044

3. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China | Global Health | JAMA Neurology | JAMA Network. Accessed October 4, 2022. https://jamanetwork.com/journals/jamaneurology/fullarticle/2764549

4. Oxley TJ, Mocco J, Majidi S, et al. Large-Vessel Stroke as a Presenting Feature of Covid-19 in the Young. N Engl J Med. 2020;382:e60.

5. 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;10:469-482.

6. Aladawi M, Elfil M, Abu-Esheh B, et al. Guillain Barre Syndrome as a Complication of

COVID-19: A Systematic Review. Can J Neurol Sci.:1-11.

7. Caress JB, Castoro RJ, Simmons Z, et al. COVID-19-associated Guillain-Barré syndrome: The early pandemic experience. Muscle Nerve. 2020;62(4):485-491.

8. Ameny A, Bouguila H, Ghachem I, Syrine B, Samia Y. Syndrome de Guillain– Barré post-COVID-19 : à propos de 3 cas. Revue Neurologique. 2022;178:S77.

9. Khemekhem A. Syndrome de Guillain-Barré post-COVID-19 traité par échanges plasmatiques. Transfusion Clinique et Biologique. Published online 2021:S114-S115.

10. Keddie S, Pakpoor J, Mousele C, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. Brain. 2021;144:682-693.

11. Guillain–Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases - PMC. At: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7445716/

12. Khan F, Sharma P, Pandey S, et al. COVID-19-associated Guillain-Barre syndrome: Postinfectious alone or neuroinvasive too? J Med Virol. 2021;93:6045- 6049.

13. Kajumba MM, Kolls BJ, Koltai DC, Kaddumukasa M, Kaddumukasa M, Laskowitz DT. COVID-19-Associated Guillain-Barre Syndrome: Atypical Para-infectious Profile, Symptom Overlap, and Increased Risk of Severe Neurological Complications. SN Compr Clin Med. 2020;2:2702-2714. doi:10.1007/s42399-020-00646-w

14. Teuwen LA, Geldhof V, Pasut A, Carmeliet P. COVID-19: the vasculature unleashed. Nat Rev Immunol. 2020;20:389-391.

15. Ottaviani D, Boso F, Tranquillini E, et al. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. Neurol Sci. 2020;41:1351-1354.

16. Paterson RW, Brown RL, Benjamin L, et al. The emerging spectrum of COVID- 19 neurology: clinical, radiological and laboratory findings. Brain. 2020;143:3104- 3120.

17. Oguz-Akarsu E, Ozpar R, Mirzayev H, et al. Guillain-Barré Syndrome in a Patient With Minimal Symptoms of COVID-19 Infection. Muscle Nerve. 2020;62:E54-E57.

18. Parra B, Lizarazo J, Jiménez-Arango JA, et al. Guillain-Barré Syndrome Associated with Zika Virus Infection in Colombia. N Engl J Med. 2016;375(16):1513-1523.

19. *Bracaglia M, Naldi I, Govoni A, Brillanti Ventura D, De Massis P. Acute inflammatory demyelinating polyneuritis in association with an asymptomatic infection* by SARS-CoV-2. *J Neurol*. Published online June 25, 2020:1-3. doi:10.1007/s00415- 020-10014-2

20. Chan JL, Ebadi H, Sarna JR. Guillain-Barré Syndrome with Facial Diplegia Related to SARS-CoV-2 Infection. *Can J Neurol Sci*.:1-3. doi:10.1017/cjn.2020.106