Guillain-Barre syndrome (GBS) associated with COVID-19 infection that resolved without treatment in a child

Samir Kanou,¹ Lama Wardeh,¹ Sandhya Govindarajan,² Kayleigh Macnay¹

SUMMARY
A 9-year-old boy presented with unbalanced gait, back pain and lower limb weakness. His physical examination revealed almost absent lower limbs reflexes and cerebrospinal fluid (CSF) showed albuminocytologic dissociation. The brain and spine MRI with contrast illustrated abnormal enhancement—suggestive of Guillain-Barré syndrome. The case had limited distribution and it did not progress beyond the presenting clinical involvements. They did not need immunotherapy, self-recovered, managed conservatively using painkillers and gabapentin along with physiotherapy—with a wait and see approach. The child is now almost back to normal after 8–12 weeks.

BACKGROUND
COVID-19 disease is caused by SARS-CoV-2 virus infection. It has been seen symptomatically among many adults across the world. In children, the disease has been found to be more asymptomatic—with many not being aware they have even been infected.¹ However, evidence is increasing that secondary neurological disorders caused by COVID-19 could affect both adults and children. The association between COVID-19 infection and Guillain-Barre syndrome (GBS) has been documented well in adult patients—with few cases only in paediatric patients.²

GBS is an acute immune-mediated polyradiculo-neuropathy in nature that is often associated with a preceding illness (2–4 weeks earlier)—usually a respiratory tract or gastrointestinal tract infection. It usually manifests by ascending paralysis and collateral sensory impairment.³ ⁴ The paralysis may reach the whole cerebrospinal route with bulbar respiratory centre involvement in some severe cases, which can put the patient at risk of having apnoea and paralytic respiratory failure. Reported literature until present, shows eight paediatric patients who had GBS associated with COVID-19.³ ⁴

All children required treatment with intravenous immunoglobulin with one child requiring plasma exchange,³ ⁴ because they met this level of therapy criteria. Neither during admission nor for several weeks earlier, our patient did not show either the classic COVID-19 infection symptoms, like fever, cough, or taste or smell changes, or the PIMS-TS (Paediatric multisystem inflammatory syndrome Temporally associated with SARS-CoV-2) symptoms,⁶ and he had limited neurological involvement. He had reversible and self-resolving condition which didn’t require specific treatment.

CASE PRESENTATION
A 9-year-old boy presented due to worsening back pain and unsteadiness. He was accompanied by his mother who described ongoing back pain that had worsened over the last 3 weeks. This wasatraumatic with no clear cause. He had no history of blurred/double vision or any abnormal autonomic symptoms and there was no bowel or bladder incontinence. Over this time, she had noticed he had become more unsteady on his feet going from a previously fit and active 9-year-old boy to now needing assistance with basic activities of daily living like walking and dressing. He had his legs feeling weak beneath him. He did not have any of the most common symptoms of COVID-19 infection including cough, fever, smell sense or taste loss. Other systems review was unremarkable and there was no clinical evidence of any single or multigorgan dysfunction.⁷ His mother stated she thought his appetite had decreased over this time alongside some mild weight loss.

His only medical history to note was low vitamin D levels, for which he was on cholecalciferol. There was no significant family history. On examination, he was alert and orientated. Examination of the respiratory, cardiovascular and gastrointestinal system were unremarkable. On neurological examination his cranial nerves were intact, he had no tendon or fasciculations, with normal sensations (touch, pain, temperature, proprioception and pressure). He had normal tone, power, reflexes of his upper limbs. In his lower limbs, he had power 4/5 with absent left bilateral equivocal plantar reflexes. Cerebellar signs were negative. He had a wide based ataxic gait and was objectively nervous about walking. He was able to walk 10 m across an open space with help (grade 3 on GBS disability scale).⁸ He was unable to run or walk on his tip toes and could not jump with 2 ft. Based on his history and examination, he was admitted to the children’s ward and investigations were undertaken.

INVESTIGATIONS
Blood results
► Haemoglobin 126 g/L (normal range 111–147 g/L), white cell count 5.9×10⁹/L (normal range 4.5–14.5×10⁹/L), slightly decreased neutrophils 1.2×10⁹/L (normal range 1.5–8×10⁹/L), platelets 414×10⁹/L (normal range 150–450×10⁹/L).
► C reactive protein 2.4 mg/L (Normal range ≤5.0 mg/L).
► Erythrocyte sedimentation rate 10 mm/hour slightly elevated (normal range 1–7 mm/hour).
Brain and spine MRI with contrast showed symmetrical enhancement of the proximal mastoid segments of the facial nerves (figure 1) and the cauda equina (figure 2).

Nerve conduction velocity study was requested, however, the patient could not tolerate undergoing the study, therefore, we decided to postpone then we cancelled it since the child was not in need for treatment and was getting improved gradually.

DIFFERENTIAL DIAGNOSIS
Since the clinical presentation was mainly of back pain and lower limbs weakness which affected the patient's ability to stand and walk steadily, we investigated all other possibly underlying orthopaedic, muscular and neurological causes including other autoimmunological causes and all were ruled out. A significant degree of areflexia in both legs and the albuminocytological dissociation in the cerebrospinal fluid (CSF) on top of a special enhancement around some lower legs supplying nerves routes on the MRI were all suggestive of GBS.

TREATMENT
We managed the patient at the local district general with specialist paediatric neurology input from the local tertiary centre. As per our local guidelines and the paediatric neurology consultation, this patient disability grade was static (2–3) and did not worsen during admission. Conversely, he Clinically improved gradually during hospital stay, hence intravenous immunoglobulin was not given. He was managed conservatively, monitoring active symptoms as well as peak flow to ensure no respiratory involvement. His peak flows remained normal throughout admission (ranging from 210 to 240).

He had ongoing back and leg pain, for which he was successfully treated for using analgesics along with an increasing dose of gabapentin 10 mg/kg once a day on day 1, 10 mg/kg twice per day on day 2, 10 mg/kg three times per day on day 3 and then stopped.

He obtained regular physiotherapy in order to regain skills and to avoid any muscle wasting.

OUTCOME AND FOLLOW-UP
The patient has been recovering gradually without the use of any intravenous immunoglobulin or plasmapheresis and was discharged home to continue therapy in the community. He was seen in an outpatient clinic to assess his condition a few months postdischarge. Here he was found to have improved significantly. Normal power noted during the follow-up. Patient disability grade was static (2–3) and did not worsen during admission. Conversely, he Clinically improved gradually during hospital stay, hence intravenous immunoglobulin was not given.

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Other causes of muscle weakness and unsteady gait (transverse myelitis, myositis, etc) must be ruled out by a precise neurological examination along with several laboratory investigations and targeted imaging.

Neurological symptoms in COVID-19 presents as either life-threatening conditions such as GBS, encephalitis, encephalopathy, meningitis and cerebrovascular accidents, or as long-term symptoms such as chronic fatigue and myalgia termed as Long COVID-19 or Post-acute sequelae of COVID-19.7

The association of COVID-19 with GBS has been reported with incidence being more common in adult population with symptoms ranging from being mild to severe needing mechanical ventilation and mortality.

A review of published case reports8 suggests that GBS presented as cranial nerve involvement in the absence of muscle weakness in 22.9% patients: as classic sensory motor variant in 75% patients and pure motor variant in 2.1% patients.8 The electrodagnostic pattern was considered demyelinating in 82.4% of the generalised variants.9

### Learning points

- **Guillain-Barré syndrome (GBS)** is one of the neurological manifestations in COVID-19.
- The symptoms can vary from being mild to very severe including needing mechanical ventilation and death.
- Management depends on clinical severity of the disease ranging from conservative therapy to immune-mediated therapy.
- Since it is a newly reported association further studies are needed to establish the pathophysiology of GBS and COVID-19.

Another systematic review5 suggests that GBS associated with COVID-19 responded to intravenous immunoglobulins (Ig) in 78% of patients.

Literature search shows eight paediatric patients,10–15 with GBS associated with COVID-19, all patients needing intravenous Ig and 1 child needing plasma exchange.

The self-limitation, the spontaneous recovery of disease course, of GBS was explored on patients who received supportive care only during hospitalisation.19

Until present, our patient is the first presentation of GBS associated with COVID-19 which had limited disability and was self-resolving in nature.

Although nerve conduction studies could not be performed in our patient, clinical features, CSF findings and MRI were suggestive of GBS.

While immune-mediated destruction of nerve tissues is considered as the pathophysiological mechanism for GBS secondary to COVID-19, further studies are needed to establish the association of GBS and COVID-19.

### Patient’s perspective

My son has always been very active, one of the fastest running in class and the best player in his team. From the time he started to refuse to play outside and avoid chasing his baby brother and saying his legs feels different we knew something was wrong but never thought it was going to be that serious. The day when we got to the hospital my whole world collapsed, he couldn’t stand, and he was in a significant amount of pain his muscles were that weak that he even had a fall when sat on the toilet. It was surreal and scary. The Hospital paediatric team were fantastic, and I pray for them every day. The doctors involved me and my husband in every plan and they have listened to us, they put things at easy and done everything they could in time to save my son’s life even when things are not anywhere near with COVID-19. It took a lot of exams to finally get to GBS. Treatment options were discussed, and they were very honest in telling us that my son’s condition was very rare, and more research needs to be done but they assured me that he was going to overcome this. We have lot of prayers from family, colleagues, friends and that faith in God and love around us made this miracle happen. We have returned to work after 3 months caring for him and he has returned to school. His positive attitude and mental capacity to understand his condition helped him to challenge himself and be able to walk again and soon he will be the fastest running in class again. Thank you very much for the opportunity to be able to share my experience and possibly help others bypass their problems.

### REFERENCES

1 Curtis M, Bhumbra S, Felker MV, et al. Guillain-Barré syndrome in a child with COVID-19 infection. *Pediatrics* 2021;147. doi:10.1542/peds.2020-015115. [Epub ahead of print: 22 10 2020].

2 Khalifa M, Zakaria F, Ragab Y, et al. Guillain-Barré syndrome associated with severe acute respiratory syndrome coronavirus 2 detection and coronavirus disease 2019 in a child. *J Pediatric Infect Dis Soc* 2020;9:10–3.

3 Trujillo Gittermann LM, Valenzuela Feris SN, von Oetingter Giacomano A. Relation between COVID-19 and Guillain-Barré syndrome in adults. systematic review. *Neurologia* 2020;35:646–54.

4 Maramattom BV, Bhattacharjee S. Neurological complications with COVID-19: a Contemporaneous review. *Ann Indian Acad Neurol* 2020;23:468–76.

5 Goel K, Kumar A, Diwan S, et al. Neurological manifestations of COVID-19: a series of seven cases. *Indian J Crit Care Med* 2021;25:219–23.
Case report

6 Wilding T, Holt N. The neurological symptoms of COVID-19: a systematic overview of systematic reviews, comparison with other neurological conditions and implications for healthcare services. Ther Adv Chronic Dis 2021;12:20406232097697.

7 Korem S, Gandhi H, Dayag DB. Guillain-Barré syndrome associated with COVID-19 disease. BMJ Case Rep 2020;13:e237215.

8 Sansone P, Giacconi LG, Aurillo C, et al. Post-Infectious Guillain-Barré syndrome related to SARS-CoV-2 infection: a systematic review. Life 2021;11:167.

9 Khera D, Diddi S, Panda S, Tiwari S, et al. Concurrent longitudinally extensive transverse myelitis and Guillain-Barré syndrome in a child secondary to COVID-19 infection: a severe neuromuscular complication of COVID-19. Pediatr Infect Dis J 2021;40:e236.

10 Akçay N, Menentöglu ME, Bektagli G, et al. Axonal Guillain-Barré syndrome associated with SARS-CoV-2 infection in a child. J Med Virol 2021;93:5599-5602.

11 Sánchez-Morales AE, Urrutia-Osorio M, Camacho-Mendoza E. Neurological manifestations temporally associated with SARS-CoV-2 infection in paediatric patients in Mexico. Childs Nerv Syst 2021;10:1–8.

12 Curtis M, Bhumbra S, Felker MV, et al. Guillain-Barré syndrome in a child with COVID-19 infection. Pediatrics 2021;147:e2020015115.

13 Frank CHM, Almeida TRV, Marques EA, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection in a pediatric patient. J Trop Pediatr 2021;67:fmaa044.

14 Khalifa M, Zakaria F, Ragab Y, et al. Guillain-Barré syndrome associated with severe acute respiratory syndrome coronavirus 2 detection and coronavirus disease 2019 in a child. J Pediatric Infect Dis Soc 2020;9:510–3.

15 Christy A. COVID-19: a review for the pediatric neurologist. J Child Neurol 2020;35:934–9.

16 Royal College of Paediatrics and Child Health. Guidance: paediatric multisystem inflammatory syndrome temporally associated with COVID-19, 2020. Available: https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf

17 NHS England. Updated commissioning guidance for the use of therapeutic immunoglobulin (Ig) in immunology, haematology, neurology and infectious diseases in England December 2018, 2018. Available: https://www.england.nhs.uk/wp-content/uploads/2019/03/PSS9-Immunoglobulin-Commissioning-Guidance-CQUIN-1920.pdf

18 Mallett S, Allen AJ, Graziadio S, et al. At what times during infection is SARS-CoV-2 detectable and no longer detectable using RT-PCR-based tests? A systematic review of individual participant data. BMC Med 2020;18:346.

19 Wang Y. Long-Term prognosis of Guillain-Barré syndrome not determined by treatment options? Oncotarget 2017;8.