

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

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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-Barré syndrome (GBS) has been documented well in adult patients—with few cases only in paediatric patients.²

GBS is an acute immune-mediated polyradiculoneuropathy 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.^{5–14}

All children required treatment with intravenous immunoglobulin with one child requiring plasma exchange,^{1 2 15} 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,¹⁶ 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 was atraumatic 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 multiorgan dysfunction.¹⁶ 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 obvious muscle wasting of his limbs and no tenderness 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 leg reflexes and just elicitable right leg reflexes. He had 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).¹⁷ 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 $5.9 \times 10^9/L$ (normal range $4.5\text{--}14.5 \times 10^9/L$), slightly decreased neutrophils $1.2 \times 10^9/L$ (normal range $1.5\text{--}8 \times 10^9/L$), platelets $414 \times 10^9/L$ (normal range $150\text{--}450 \times 10^9/L$).
- ▶ 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).



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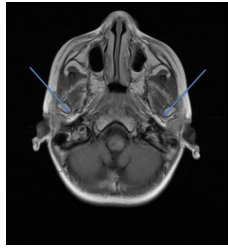


Figure 1 Brain MRI with contrast shows enhancement of the proximal mastoid segments of the facial nerves.

- ▶ Normal renal profile.
- ▶ Normal liver function tests.
- ▶ Normal serum folate and vitamin B₁₂ levels.
- ▶ Normal thyroid function.
- ▶ Normal CK.
- ▶ Serum lyme antibody, haemophilus antibody, varicella zoster PCR, Epstein-Barr virus PCR and HIV antibodies, Cytomegalovirus (CMV) PCR, enterovirus PCR, HSV1 and 2 PCR-negative.
- ▶ Normal immunoglobulin profile.
- ▶ Negative autoimmune screen—including antinuclear antibody, double stranded DNA, SS-A, SS-myeloperoxidase antibody, antismith antibody, c-ANCA, smooth muscle antibody, serum complement levels.
- ▶ Coeliac screen normal.

Routine admission nasopharyngeal swab for COVID-19 was then reported as positive.

PIMS-TS investigations (not done-not required).¹⁶

Lumbar puncture results

(Lumbar puncture was done soon after admission)

- ▶ 874/cu mm red blood cells
- ▶ <1/cu mm polymorphs.
- ▶ 2/cu mm lymphocytes.
- ▶ Glucose 3.6mmol/L (compared with 4.7mmol/L blood glucose).
- ▶ Lactate 1.71mmol/L (compared with 1.46mmol/L blood lactate).
- ▶ Protein 0.78g/L (normal range 0.15–0.40g/L)—slightly elevated and suggestive of *albumin-cytological disassociation*.
- ▶ Viral PCR for adenovirus, enterovirus, herpes simplex virus 1 and 2 and parechovirus were all negative.
- ▶ Negative culture.

Imaging studies

Plain spine X-ray was normal.



Figure 2 Spinal MRI with contrast shows enhancement of the cauda equina.

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.¹⁷

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 two times per day a 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 with good reflexes recovery. Now, he is able to walk independently. However, he still is not yet back to baseline—becoming tired more easily than usual with mild manageable backpain. He will continue to be followed up in clinic for the next year.

DISCUSSION

GBS is an immune-mediated polyradiculoneuropathy.

Symptoms usually appear 2–4 weeks after a viral infection. However, no definite resources can confirm this period after COVID-19 infection, taking into consideration that COVID-19 PCR may remain positive for several weeks.¹⁸ Therefore, our patient may have been asymptotically infected weeks before showing GBS symptoms.

Affected patients can present with limb or cranial-nerves weakness, loss of deep tendon reflexes, sensory and dysautonomic symptoms.

The main pathophysiology for the clinical presentation is demyelination and/or axonal damage to peripheral nerves or roots.

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,⁶ 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 electrodiagnostic pattern was considered demyelinating in 82.4% of the generalised variants.⁸

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 had lots 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.

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 review⁹ 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.

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Contributors SK, the author who has the right to submit in here on behalf of all authors, SK worked as a specialty doctor in paediatrics and he was involved in the clinical care of this patient. SK collected his colleagues who are the other authors of this case report, SK assigned them to different roles to prepare this report. SK reviewed the guidelines and the policies of publishing in BMJ case reports and sent them to his team to be aware of. SK was responsible to gather and bind all chapters, make the necessary amendment and to put all in the BMJ publishing frame in addition to the summary and the learning points. LW is a specialty doctor who was involved in the clinical care of this patient, and she helped in getting the patient's mother consent and in contacting their trust to get their approval and the BMJ code. LW has reviewed all references which are relevant to the case and she made the conclusion and the linkage to this case. She contributed to review and amend the final draft. SG is a paediatric specialty registrar who was involved in the clinical care of this patient as well. She made a robust conclusion of this case and gathered the radiology and laboratory reports and the images. She had an extensive review in different other references to add relevance which was mentioned in this report. KM is a foundation year2 doctor who was involved in the clinical care of this patient, she has made the initial version of the introduction, history, and physical examination and she has reviewed this report grammatically since she is genuine English tongue. In addition KM has reviewed the references and put them as per vancouver style.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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