Infect Dis Trop Med 2022;8: e885

SARS-CoV-2 induced Guillain Barré Syndrome in a child: first case from Odisha, India

K. Muduli[1], B. Baral[2], S. Jakhmola[2], S. Elangovan[1], K.R. Jishnu[3]
N. Polakampalli[3], N.K. Mohakud[3], H.C. Jha[2]

[1]School of Biotechnology, KIIT deemed University, Odisha, India
[2]Infection Bio-Engineering Group, Department of Biosciences and Biomedical Engineering, Indian Institute of Technology Indore, Indore, India
[3]Department of Paediatrics, Kalinga Institute of Medical Sciences, KIIT deemed University, Odisha, India

Kartik Mudul and Budhadev Baral contributed equally to this work

ABSTRACT:

— ***Objective:*** Since the outbreak of coronavirus disease in 2019 (COVID-19), multiple systemic issues, including respiratory and nervous system complications, have evolved constantly.

— ***Case Report:*** We present a COVID-19 case of a 7-years old male child with Guillain Barre Syndrome (GBS) symptoms. The patient complained of cough, throat pain, and acute progressive symmetric ascending quadriparesis. Eventually, on day-12 of hospitalization, he was diagnosed with GBS. The patient's condition worsened over time; thus, he was shifted to ICU, where he had an episode of cardiac arrest and was revived through CPR. The biochemical analysis of the CSF revealed albuminocytologic dissociation. The patient was considered for regular follow-up of GBS and presently has recovered from GBS/COVID-19 induced GBS. Thus, there is a possibility of SARS-CoV-2 infection-induced GBS in children.

— ***Conclusions:*** More studies are needed to know the neurological manifestations of SARS-CoV-2 infection in the pediatric population.

— ***Keywords:*** SARS-CoV-2, COVID-19, Guillain Barré syndrome, Child.

— ***Highlights***

- The current case is a parainfectious case of COVID-19 induced GBS in children.
- He had leukocytosis and neutrophil to lymphocyte ratio > 3.5, indicating COVID-19 severity.
- Timely diagnosis, supportive measures, and intravenous immunoglobulin are essential to successful treatment.
- To the best of our knowledge, this case is the first post-COVID-19 induced GBS case in a 7-year-old boy.

INTRODUCTION

The earliest report of coronavirus disease 2019 (COVID-19) came in December 2019 from Wuhan, China.The condition is caused by a human coronavirus belonging to the *Coronaviridae* family, i.e., severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). SARS-CoV-2 infection is mainly manifested through respiratory symptoms and sometimes neurological complications[1]. Neurological alterations are broadly divided into central nervous system (CNS) (e.g., dizziness, headache, ataxia, seizure and cerebrovascular diseases), cranial and peripheral nervous system symptoms (e.g., anosmia, myalgia, ageusia, vision impairment and

Corresponding Authors: Hem Chandra Jha, Ph.D; e-mail: hemcjha@iiti.ac.in
Nirmal Kumar Mohakud, MD; e-mail: nirmal.mahakud@kims.ac.in

neuropathy, and skeletal muscle injury)[1]. According to the hypothesis, the neural invasion of the coronavirus is mainly through the hematogenous and/or retrograde axonal route[2].This may cause encephalitis by direct neuronal damage or respiratory insufficiency-induced hypoxia. Besides cytokine storms, SARS-CoV-2 may result in severe inflammation and CNS injury. Previous studies[1,3] have also reported COVID-19 induced CNS demyelination in adults.

In addition, COVID-19 associated Guillain Barré syndrome (GBS) was noted in a few children[4]. GBS is an acute monophasic demyelinating polyradiculopathy usually preceded by infections caused by Campylobacter jejuni, influenza virus, Epstein Barr Virus, Cytomegalovirus, Zika virus, and SARS-CoV[5,6].The typical clinical manifestations in GBS are ascending, symmetrical flaccid limb paralysis, progressive and hyporeflexia or areflexia. Diagnosis of GBS is primarily clinical,however analysis of cerebrospinal fluid (CSF) and peripheral nerve conduction tests support the diagnosis. Children with GBS often respond well to supportive measures and intravenous immunoglobulins, while plasmapheresis is rarely needed. Here we present a case of a 7-year male child with COVID-19 who later developed GBS most likely due to SARS-CoV-2 induced immune dysregulation.

CASE REPORT

A 7-year old male child with cough, throat pain, and weakness in the upper and lower limb was admitted to the isolation ward of the pediatrics department, KIMS hospital, Bhubaneswar, on 16th October 2020. Samples were sent for examination of SARS-CoV-2 infection and other parameters. RT-PCR test revealed that the child was SARS-CoV-2 positive, and hence the patient was shifted to Odisha COVID-19 hospital (OCH), KIMS. The child showed a progressive increase in the COVID-19 symptoms and joint pain after admission. The clinical investigation of the blood samples received on the 7th day of the admission showed decreased hemoglobin levels, hematocrit, MCH, MCV, and MCHC (***Supplementary Table 1***). The patient also had lymphocytopenia and neutrophilia throughout hospitalization and during the follow-up (Figure 1A). The platelet count was increased from 271 $X10^3$/µL on day 7 to 635 $X10^3$/µL on day 13 of hospitalization (Figure 1B). Inflammatory marker CRP 21.72 mg/L (normal; <5 mg/L) was also increased (***Supplementary Table 1***). Moreover, the X-ray chest P-A view showed non-homogenous patchy opacities in the right lower and upper lobe, indicating pneumonia (Figure 2).

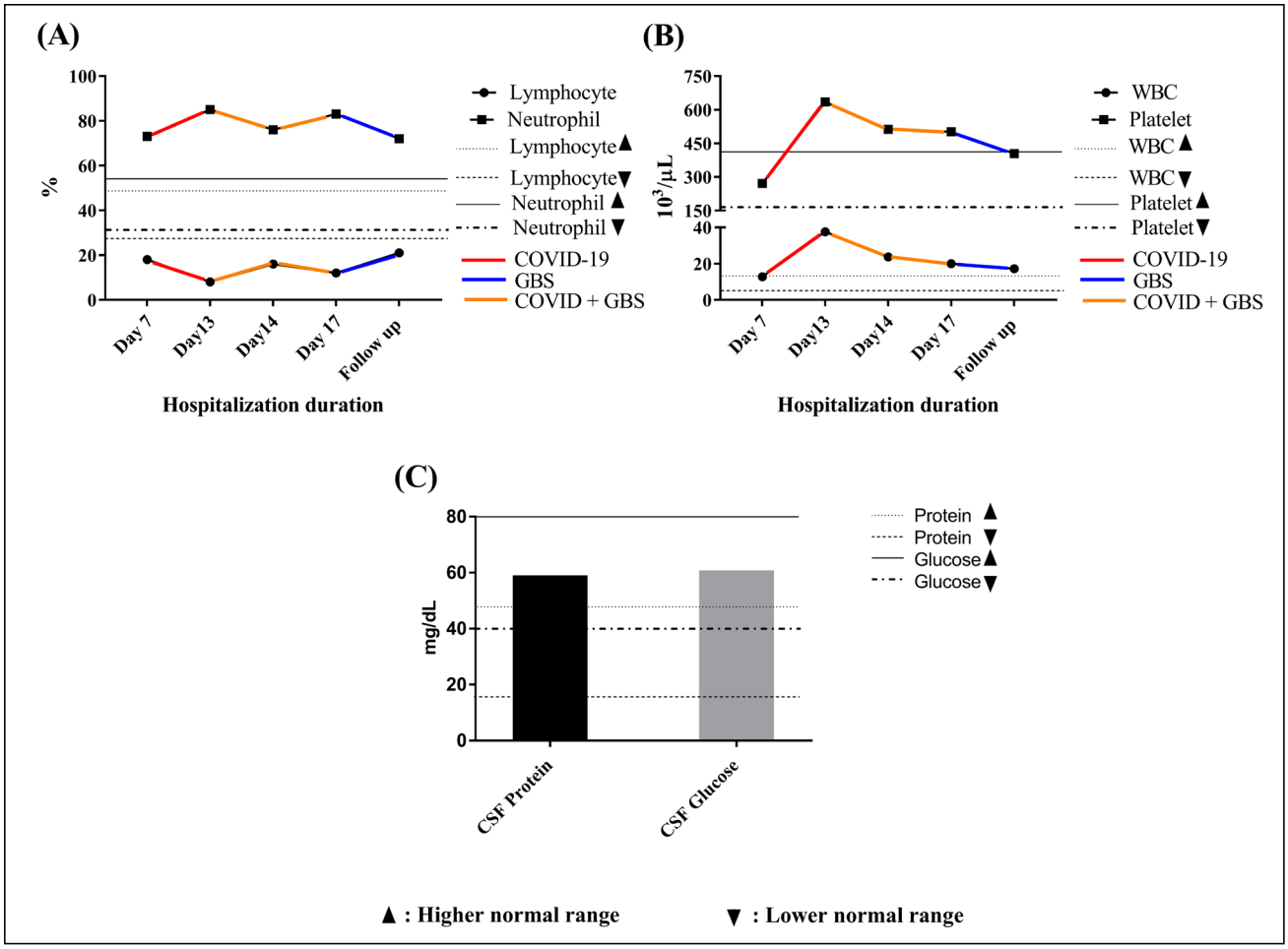

Figure 1. Graphical representation of hematological and biochemical parameters. **A**, Lymphocyte and Neutrophil levels during the period of hospitalization and follow-up. **B**, The level of WBC and platelet during the period of hospitalization and follow-up. **C**, Level of CSF protein and CSF glucose.

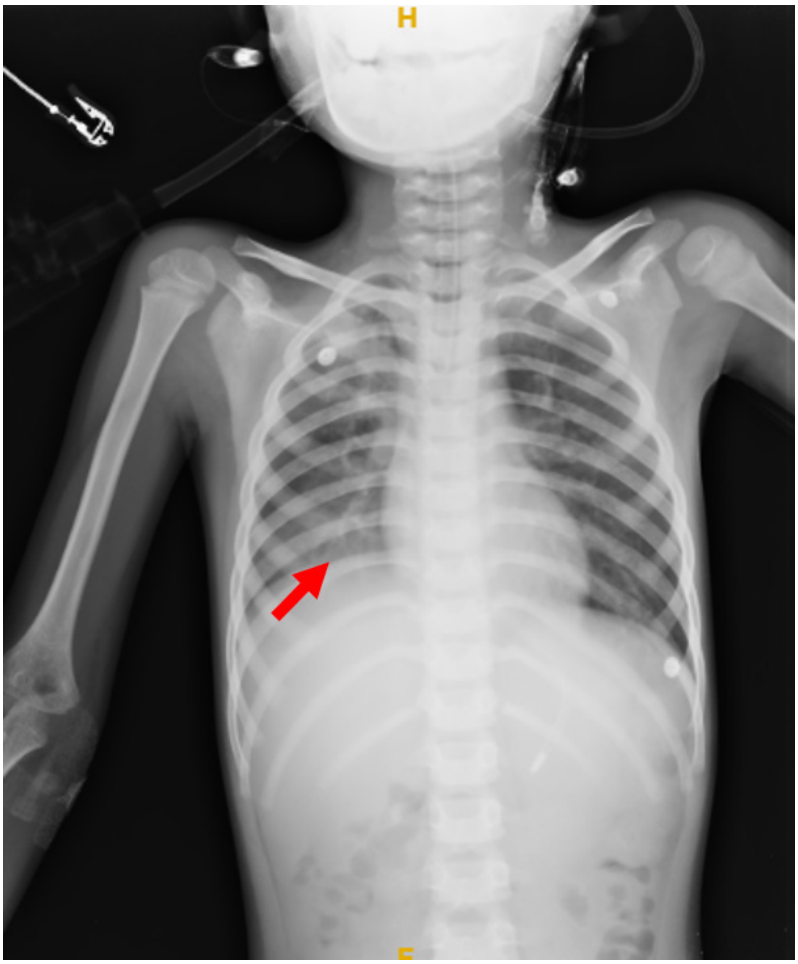

Figure 2. X-RAY of chest P-A view. Patchy opacities in the right lower lobe *(red arrow),* indicating pneumonia.

On day 12 of hospitalization, the child developed progressive weakness and could not talk, eat or walk. The muscle strength was graded 3/5 in both upper limbs and 2/5 in lower limbs. The child developed respiratory distress and was shifted to the ICU on the 12th day of hospitalization. The child was put on mechanical ventilation, and vitals were managed. The CSF analysis revealed albumin-cytological dissociation with increased CSF protein 59 mg/dl compared to normal; 15-45 mg/dl (Figure 1C) and cell count being 15/cmm (normal, 0-5/cmm). Nerve conduction studies showed slow and blocked conduction. Other hematological and biochemical investigations were presented in Figure 1A-B and ***Supplementary Table 1***.

Also, in the ICU at the COVID-19 hospital, the child had an episode of sudden cardiac arrest. However, the child was revived upon high-quality cardiopulmonary resuscitation. The treatment included multiple antibiotics, inotropes, anticonvulsants, antipyretics, ivermectin, probiotics, and supportive measures during ICU. Additionally, the child received intravenous immunoglobulin 2 g/kg over two days. After RT-PCR tested negative, the patient was extubated and shifted to the pediatric ICU of the non-COVID-19 hospital. Here, he was treated for a culture-positive *E. coli* urinary tract infection. Besides, supportive measures like physiotherapy were instituted. After a brief stay of 15 days, the child was discharged with walking support.

DISCUSSION

COVID-19 is a multisystemic disease and is known to induce immune deregulation. In COVID-19, neurological manifestations like GBS may appear prior or post SARS-CoV-2 infection[7,8]. Studies have detected antiganglioside antibodies to establish the post-infectious causes[6,9].The case presented here emphasizes the appearance of GBS after the COVID-19 diagnosis. The duration between SARS-CoV-2 infection and the manifestation of GBS in the current case was seven days. Several cases of COVID-19 patients exist that explain similar scenarios. An Italian case study consistedof five COVID-19 patients who developed GBS 5–10 days post-SARS-CoV-2 infection[10]. Though the COVID-19 manifestation was severe, marked by leukocytosis, neutrophilia, lymphocytopenia, anemia, and elevated CRP in most cases, few GBS cases with mild COVID-19 symptoms with normal hematological parameters have been reported[11]. Most children infected with SARS-CoV-2 have mild to moderate symptoms and rarely require hospitalization. Yet another investigation of an 11 years old male child with GBS and SARS-CoV-2 infection showeddecreased hemoglobin and normal CRP, WBC, neutrophil, lymphocyte, platelet, electrolytes, and liver function test while elevated CSF protein[4]. Additionally, some adult patients with GBS cases showed normal hematological parameters, while some presented elevated inflammato-

ry markers, leukocytosis, lymphocytopenia, and thrombocytopenia. The case presented here showed lymphocytopenia, neutrophilia, leukocytosis, thrombocytosis, and elevated CRP after GBS development during hospitalization. Moreover, it is worth mentioning that the hematological parameters and inflammatory markers may vary on a case-to-case basis.

Moreover, the early diagnosis of GBS is vital in managinga patient's health. The specific treatment consisted of IVIg: 0.4 g/kg for five days. Besides regular monitoring of cardiac, pulmonary, and autonomic (blood pressure, heart rate and pupil) function also needs to be done. Rarely, patients may need plasmapheresis. Respiratory insufficiency due to paralysis of diaphragmatic muscles marks the requirement of mechanical ventilation. The child under investigation was on supportive treatment and mechanical ventilation. Finally, multidisciplinary care, including psychosocial support and rehabilitation, is the key to optimal outcomes.

The study has a few limitations, like the unavailability of data pertaining to other serum inflammatory markers like ferritin, IL6, and D-dimer. Thus, a conclusion regarding the disease severity from these serum inflammatory markers could not be drawn. Also, we were unable to perform the CT-thorax of the patient due to his serious health condition. Also, it is questionable if the production of SARS-CoV-2 induced antibodies against only a particular ganglioside may lead to GBS development. However, since the diagnosis of GBS is mainly clinical, we were able to manage the case well with the existing investigation.

CONCLUSIONS

Our case reveals the possible association between SARS-CoV-2 infection and GBS development in children. Both mild and severe COVID-19 may be associated with GBS. This case report reveals various clinical presentations of SARS-CoV-2 infection and GBS-related complications. More studies are needed to know the neurological manifestations due to SARS-CoV-2 infection in the pediatric population. This is the first post-COVID-19 GBS case of a 7-year-old boy to the best of our knowledge. Early diagnosis and treatment with immunoglobulin have better outcomes for GBS with COVID-19.

Acknowledgments

We thankfully acknowledge the Kalinga Institute of Medical Sciences, Bhubaneswar, School of Biotechnology, Kalinga Institute of Industrial Technology, Bhubaneswar; and Indian Institute of Technology Indore to provide facilities support. We acknowledge the Council for scientific and industrial Research and the Department of Science and technology Govt. of India for funding. We also thankful to University Grants commission, Govt. of India for fellowship to Kartik Muduli and BudhadevBaral in the form of research stipend. We appreciate lab colleagues for insightful discussions and advice.

Funding:

The current work was supported by Council for Scientific and Industrial Research (Grant no 37 (1693) /17/EMR-II); Department of Science and Technology as Ramanujan fellowship (Grant no SB/S2/RJN-132/20/5).

Conflicts of Interest:

The Authors declare that they have no conflict of interest.

Ethics Approval:

The Ethics Committees approved the protocol for the present study of the Indian Institute of Technology, Indore, Indore (BSBE/IITI/IHEC-05/2020); School of Biotechnology, Kalinga Institute of Industrial Technology, Bhubaneswar (KIIDU/KSBT/2020/345); and Kalinga Institute of Medical Sciences, Bhubaneswar (KIIT/KIMS/IEC/372/2020). All processes were executed following the declaration of Helsinki. Written consent was obtained from the family member of the patient.

Consent to Participate:

Written consent was taken from the legal guardian of the patient.

Availability of Data and Materials:

All the data for understanding the manuscript present in the manuscript. If any other data are required by any reader, it will be obtained by mailing to the corresponding author on reasonable request.

Author's Contributions:

Kartik Muduli: conceptualization, Writing original draft, visualization, Validation. Budhadev Baral: Data curation, Conceptualization, Visualization, Validation. Shweta Jakhmola: Writing-original draft, Validation. Jishnu KR: Data curation, Visualization, validation. Nikhitha Polakampalli: Data curation, Visualization, validation. Selvakumar Elangovan: Investigation, Methodology. Nirmal Kumar Mohakud: Conceptualization, Project administration, Writing-reviewing and Editing. Hem Chandra Jha: Conceptualization, Supervision, Project administration, Writing-reviewing and Editing.

REFERENCES

1. Jakhmola S, Indari O, Chatterjee S, Jha HC. SARS-CoV-2, an Underestimated Pathogen of the Nervous System. SN Compr Clin Med 2020 Sep 28:1-10. doi: 10.1007/s42399-020-00522-7. Epub ahead of print.
2. Reza-Zaldívar EE, Hernández-Sapiéns MA, Minjarez B, Gómez-Pinedo U, Márquez-Aguirre AL, Mateos-Díaz JC, Matias-Guiu J, Canales-Aguirre AA. Infection Mechanism of SARS-COV-2 and Its Implication on the Nervous System. Front Immunol 2021; 11: 621735.
3. Ismail II, Salama S. Association of CNS demyelination and COVID-19 infection: an updated systematic review. J Neurol 2022; 269: 541-576.
4. Khalifa M, Zakaria F, Ragab Y, Saad A, Bamaga A, Emad Y, Rasker JJ. 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: 510-513.

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. Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, Narayanaswami P. COVID-19-associated Guillain-Barré syndrome: The early pandemic experience. Muscle Nerve 2020; 62: 485-491.
7. Webb S, Wallace VC, Martin-Lopez D, Yogarajah M. Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. BMJ Case Rep 2020; 13: 236182.
8. 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 Neurol 2021; 268: 1133-1170.
9. Guilmot A, Maldonado Slootjes S, Bissay V, Dubuisson N, de Broglie C, Gille M. SARS-CoV-2-associated Guillain-Barré syndrome in four patients: what do we know about pathophysiology? Acta Neurol Belg 2021 Sep 2:1–5. doi: 10.1007/s13760-021-01787-y. Epub ahead of print.
10. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, Franciotta D, Baldanti F, Daturi R, Postorino P, Cavallini A, Micieli G. Guillain-Barré Syndrome Associated with SARS-CoV-2. N Engl J Med 2020; 382: 2574-2576.
11. Padroni M, Mastrangelo V, Asioli GM, Pavolucci L, Abu-Rumeileh S, Piscaglia MG, Querzani P, Callegarini C, Foschi M. Guillain-Barré syndrome following COVID-19: new infection, old complication? J Neurol 2020; 267: 1877-1879.