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Guillain-Barre Syndrome associated with SARS-CoV-2 Infection in a pediatric patient: a case report from Ethiopia and review of the literature

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Abstract

Background: Guillain-Barre Syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy that is often related to previous infectious exposure. Since Corona Virus Disease 2019 (COVID-19) has been declared as a global pandemic, GBS has been reported as a possible complication of the Infection. Though severe neurological symptoms are not typical manifestations of COVID-19, there are multiple reports on cases with life-threatening neurological disorders both in adult and pediatric patients. Our patient was admitted with typical sign and symptoms of Guilain Barre Syndrome and turned positive with COVID PCR on sept 6/2021.

Objective: In this study, we reported a case of Guillain Barré Syndrome in a pediatric patient infected with COVID-19 to assess the association between COVID-19 and Gullian Barre Syndrome.

Clinical Presentation: A 9-year-old female presented with a two-day history of progressive, symmetrical, and ascending lower and upper limb weakness. . She developed these symptoms a week after she had flu-like symptoms, which resolved by itself, and she tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during the current presentation. Cerebrospinal fluid showed protein-cell dissociation. She was successfully treated with intravenous immunoglobulins (IVIGs) at St. Paul's Hospital Millennium Medical College and discharged improved..

Conclusion: In conclusion, we aimed to report a case of pediatric patient who had both SARS-CoV-2 infections and the typical neurological manifestations of Guillain-Barré Syndrome. So, it is reasonable to consider testing for COVID-19 and decide on further management particularly in children who have a history of flu-like symptoms and unexplained neurologic conditions. Further observational and controlled trials are needed to determine the association between SARSCOV2 and GBS.

Keywords: COVID-19, SARS-CoV-2, Coronavirus, Guillain–Barré syndrome, Neurology, Autoimmune

Background

The COVID-19 pandemic is our time's defining global health crisis and the greatest global challenge faced since World War Two. Since its emergence in Wuhan china 2019 and the coronavirus disease 2019 (COVID-19) declaration as a pandemic on March 11, 2020, the virus has spread to every continent except Antarctica. We have now reached the tragic milestone of more than five million deaths and over 260 million reported cases worldwide. Ethiopia's national report shows more than 6,700 deaths and over 371,000 cases (1, 2). Our patient was admitted with typical sign and symptom of Guilain Barre Syndrome and turned positive with COVID Polymerase Chain Reaction (PCR) on september 6/2021. Coronaviruses can cause multiple systemic infections.

Although respiratory complications are the most obvious symptoms, several neurological manifestations, both central and peripheral nervous systems, have been also associated with this disease. There are different reports of neurological manifestations that include headache, dizziness hyposmia, hypogeusia, in early courses, and more serious neurologic manifestations like strokes, encephalopathy, encephalitis, seizures, acute cerebral edema, acute transverse myelitis, acute myelitis, and cerebellar ataxia may appear as diseases progress in patients with Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) infection in both adult and pediatric populations. Anosmia and loss of taste sensation were also commonly reported among COVID-19 patients, especially with the alpha sub-variant. A study conducted on neurological symptoms among 214 COVID-19 hospitalized patients has shown that 36.4% had nervous system manifestations including dizziness, headache, hypogeusia, hyposmia, muscle damage, ischemic, and hemorrhage stroke (3,4).

A systematic review of 73 cases on Guillain–Barré Syndrome (GBS) spectrum association with COVID-19 suggested an association between SARS-CoV-2 Infection and the development of GBS. Guillain-Barre Syndrome is an acute immune-mediated disease of peripheral nerves and nerve roots and it is the most common cause of acute flaccid paralysis. It is usually preceded by respiratory or gastrointestinal Infection and typically presented with symmetrical progressive. For Review Only 2 ascending limb weakness, loss of deep tendon reflexes, paresthesia, sensory deficits with or without respiratory and cranial nerves involvement. Diagnosis of GBS relies on the results of clinical, electrophysiological, and cerebrospinal fluid (CSF) examinations (classically albumin cytological dissociation).The symptoms peak within 4 weeks and the patients should be monitored because 20% to 30% of them will need mechanical ventilation.

GBS is currently considered as a heterogeneous syndrome with several variant forms including acute inflammatory demyelinating polyradiculoneuropathy (AIDP), the Miller Fisher syndrome (MFS), acute motor axonal neuropathy (AMAN), and acute sensorimotor axonal neuropathy (AMSAN) (4,5,6). Zhao et al reported the first case of a 61-year-old man who presented with an Acute Inflammatory Demyelinating Polyneuropathy (AIDP) subtype of GBS, associated with SARSCov-2 Infection. After this first case, other forms of GBS were also reported (7), A review was done on 37 published cases of GBS associated with COVID-19 to summarize that GBS associated COVID-19 appears to be an uncommon condition with similar clinical and electro diagnostic patterns to GBS before the pandemic. The mean age (59 yer), gender (65% male), and the meantime from COVID-19 symptoms to GBS symptoms was 11 days. Cerebrospinal fluid, when assessed, demonstrated albuminocytologic dissociation in 76% of patients and was negative for SARS-CoV-2 in all (7,8).

Case presentation

A 9-years- old female patient who was relatively fine 2 days before admission, was admitted to the emergency department, with symptoms of acute progressive symmetric ascending quadriparesis. Neurological manifestations of the patient began with acute progressive weakness of distal lower extremities, two days before admission. At that time, the symptoms progressed from distal limbs to proximal limbs and she had quadriplegia one day before admission. There was paresthesia and pain over her lower extremity bilaterally. She had no urinary and fecal incontinence. She had a history of flu-like symptoms a week prior to her current illness which has resolved by itself. Otherwise, she has no chronic medical illness, was vaccinated according to an extended program on immunization, and has comparable growth with her peers. On physical examination, the patient was afebrile with blood pressure 98/51 mm/hg, heart rate 104 beats/minute, respiratory rate 44/minute, and oxygen saturation of 95% on room air, Body Mass Index (BMI) for Age (weight = 20 kg, length = 125cm).

BMI is 12.8, placing the BMI-for-age at the 1st percentile for 9-year-old For Review Only 3 girls which falls in category of underweight according to center of disease control (CDC) growth curve. The patient was conscious and had no dyspnea, at the time of hospitalization. There was hypotonic extremity and the muscle strength examination showed weakness in four limbs with a Medical Research Council scale power scale of 3/5 in the upper extremity, 0/5 in the lower extremities. Deep tendon reflexes were absent in all extremities. Sensation and gag reflex were intact. Initial laboratory investigations done on 9/2/2021 were as follows; white blood cells (WBCs) count of 10.0 cells per microliter (neutrophils = 71.1%; lymphocytes = 22%), RBCs of 4.44 million cells/mcL, hemoglobin 13.2 g/dL, and platelet count is 282,000 platelets/mcL, C-reactive protein was negative. Her international normalization ratio was 0.96, serum glucose 7.4 mmol/L, blood urea nitrogen 9.3 mmol/L, Cr 0.3 mg /L, alanine aminotransferase 36 U/L, potassium 4.8 mmol/L, sodium 135 mmol/L. Cerebrospinal fluid (CSF) analysis done on 9/14/2021 showed high protein; > 241 mg/L, glucose levels: 73.9 mmol/L, no white blood cell or acid fast bacilli were seen, negative culture and sensitivity, and gram stain for bacterial Infection.

On the same day at pediatric emergency OPD, gag reflex was depressed then later became absent and the patient was transferred to PICU intubated with ETT size of 5.5 and depth of 16 cm. The patient took 4 doses of intravenous immunoglobulins (IVIGs). The initial COVID RDT test done on 9/2/2021 was negative; however, for a high index of clinical suspicion for COVID, a PCR test was done and on the 5th day of PICU admission (9/6/2021). After the positive PCR test, the patient was diagnosed with COVID-19 and transferred to COVID-19 ICU at isolation in SPHMMC. The patient was treated with gabapentin, IVIG (4 doses), and morphine. During her stay, she had foul-smelling tracheal aspirate for which culture was taken on 9/22/21 and showed pseudomonas growth-sensitive for ceftazidime, cefepime, ciprofloxacin, augmentin, meropenem, and piperacillin-tazobactam. She was treated with ceftazidime for 10 days. On her 11th day of admission to COVID-19, ICU tracheostomy was done for prolonged intubation.

Discussion

In this study, we reported our case of Guillain Barré Syndrome in a pediatric patient infected with COVID-19 in Ethiopia. COVID-19 usually courses with mild symptoms in children. However, serious complications may occur during both acute Infection and multi-system inflammatory syndrome in children (9,10). Nevertheless, the full clinical spectrum of neurological symptoms in patients with COVID-19 remains to be characterized. There is an ongoing investigation into the mechanism of the neuroinvasive prospective of SARSCoV-2. There is evidence that angiotensin-converting enzyme 2 (ACE2) which usually is located on human epithelial cells of the respiratory tract, play role in central nervous system infection (10).

A broad spectrum of neurological manifestations has been reported in pediatric patients, ranging from specific to nonspecific and from self-limiting to fatal by the direct neuro- invasion of the SARS-CoV-2 and/or indirectly with the activation of the immune system. One review article on neurologic and radiologic findings in pediatric COVID-19-positive patients stated that of 27 patients, four had neurological symptoms. The most commonly reported cases were encephalopathy, headache, weakness, and brainstem signs. Subsequent disruption to normal cellular functioning, immunologically mediated cytokine storms, increased coagulation factors, and the virus affinity for angiotensin-converting enzyme 2 (ACE2) receptors are also presumed reasons for neurologic findings in pediatric and adults[10]. Three cases in one of the literature have reported autonomic complications, 2 with sphincter dysfunction and 1 with hypertension. However, in our case, and from the first case reported from Kuwait, and the 5 cases reported from Italy, there were no symptoms suggestive of autonomic system affection (11, 12, 13).

From the literature reviewed, 15 GBS patients out of 19 were treated with IVIG, and 8 were admitted to intensive care unit for ventilator support and of whom 2 have died. However, twelve other showed improvement, while 5 had residual disability at discharge (4). Our patient showed significant improvement after IVIG. Neurologic condition showed progressive improvement a week after after Intravenous Immunoglobulin (IVIG) initiation; the power changed from medical research council grade 0 to MRC grade 3. Moreover, the patient received supportive management for COVID-19. On follow-up

with the patient after 3 weeks, showed complete recovery, the patient walking without support. Summary of clinical observations, results of diagnostic tinvestigations, treatments, and outcomes for different pediatric GBS patients are shown in Table 1 along with our report.

Table 1: Summary of clinical findings, results of diagnostic investigations, treatment and outcome pediatrics GBS cases

Article	Country	Age	Sex	Onsetof weakness after respiratory symptoms/ presentation.	Management and therapy		Outcome
					GBS	COVID-19	
Frank et al. [5]	Brazil	15	M	>5days	IVIG 400 mg/kg/day (5 days)	Methylprednisolone, azithromycin, albendazole	Some improvement, weakness persisted
khalifa et al[5]	Kingdom of Saudi Arabia	11	M	20days after	IVIG 1 g/kg (2 days)	Paracetamol, azithromycin, hydroxychloroquine	Discharge to home after 15 days with clinical and electrophysiological improvement
Mozhdehipanahet al[5]	Iran	14	F	NA	Plasma exchange (5 cycles)	NA	Significant improvement of muscle weakness after 3 weeks, persistence of mild bifacial paresis
Paybast et a[5]	Iran	14	F	21 days after	5 sessions of therapeutic plasma exchange, intravenous bolus of labetalol to control sympathetic nervous system over-reactivity	Hydroxychloroquine sulphate 200 mg two times per day for a week	Persistence of generalized hyporeflexia, decreased light touch sensation in distal limbs, mild bilateral facial paresis, sympathetic over-reactivity successfully controlled with labetalol,
Hussein Karim Manji[9]	Tanzania	12	M	5 days after	400mg/kg of intravenous immune globulin [IVIG](5days)	NA	Despite significant neurologic symptom improvement the child self extubated accidentally and rapidly decompensated and died
Current Case report by Dessalegn	Ethiopia	9	F	7days after	IVIG for 4 days, gabapentin for analgesia	Supportive care	Discharged improved

Limitation

Nevertheless, the patient had typical Guillain Barre Syndrome, the patient had URTI symptoms a week prior to current presentation, and COVID-19 RDT test was only done at the initial presentation. But since there was strong clinical suspicion considering the current pandemic in any patient presented with upper respiratory tract infection (URTI), COVID-19 should be the top differential to think of. So, a clear cause and effect relationship between SARS-CoV-2 and GBS may not be identified in this patient. This case report only suggests a possible association between Guillain-Barré syndrome and SARS-CoV-2 Infection, and more cases with epidemiological data are necessary to support a causal relationship. Besides that, initially, the patient's COVID RDT test at ER was negative; however, a PCR test was done and the late result came revealed a positive result. On other hand, it is also wise to consider the alternative explanation that the patient developed Guillain-Barré Syndrome of unknown cause.

However, the initial test could also be false-negative since the sensitivity of the RDT test is only 90-93%. Hence, there is a high possibility for COVID-19 to cause GBS in this patient. Conclusion In conclusion, we aimed to report the case of the pediatric patient with typical GBS neurological manifestations and SARS-CoV-2 infections. Though severe neurological symptoms are not typical manifestations of COVID-19, there has been reports of life-threatening neurological disorders including GBS, both in adult and pediatric patients. So, it is reasonable to consider testing for COVID-19 and decide on further management, particularly in children with a history of flulike symptoms and unexplained neurologic conditions. Further observational and controlled trials are needed to determine the association between SARSCOV2 and GBS. Acknowledgements We would like to extend our gratitude to the treating team, advisors on the case, and the family of the child for giving consent to this report.

Declarations

Conflict of interest

The authors have no conflict of interest to declare.

Statement of Ethics

The patient's family gave consent to share her case

Abbreviations

Acute inflammatory demyelinating polyneuropathy, AIDP; acute motor axonal neuropathy, AMAN; acute motor-sensory axonal neuropathy, AMSAN; Body mass index, BMI; C Reactive protein, CRP; Cerebrospinal fluid, CSF; Coronavirus infectious disease-2019, COVID-19; Guillain-Barre Syndrome, GBS; intravenous immunoglobulin, IVIg; lactate dehydrogenase, LDH; Miller- Fisher syndrome, MFS; Real-time polymerase chain reaction, RTPCR; Rapid diagnostic test; RDT; Severe Acute Respiratory Distress Syndrome coronavirus 2, SARS-CoV-2

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