Case Report

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Hypoglycaemic Encephalopathy following Coronavirus Disease in a Six-month-old Infant: A Rare Case Report

Radiology Section

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ABSTRACT

Hypoglycaemia refers to a state when the blood sugar level drops below the normal range of 70-110 mg/dL. Blood sugar level, or glucose in the blood, is responsible for various vital functions. A decrease in blood glucose levels causes a wide range of clinical presentations, from tremors to coma and even death. Long-term hypoglycaemia can lead to extensive neuronal damage due to apoptosis and energy failure. Additionally, authors discuss a rare case of a six-month-old male neonate who presented with fever, diarrhoea, and two episodes of convulsions over the last two days. The movements started with an ictal cry and were followed by micturition and defecation. Nasal and throat swabs were positive for SARS-CoV-2 viral antigen. A plane Magnetic Resonance Imaging (MRI) of the brain was performed, which revealed evidence of altered signal intensity in the cortical and subcortical areas of the right frontal-temporal-parietal-occipital region, suggesting hypoglycaemic encephalopathy. The patient was given a breastfeeding trial and managed with 25% dextrose initially at a rate of 0.2 g/kg for 48 hours, as the patient was symptomatic, followed by an infusion of dextrose normal saline. After ruling out all possibilities of hypoglycaemic encephalopathy, the diagnosis of hypoglycaemic encephalopathy secondary to Coronavirus Disease (COVID-19) was made.

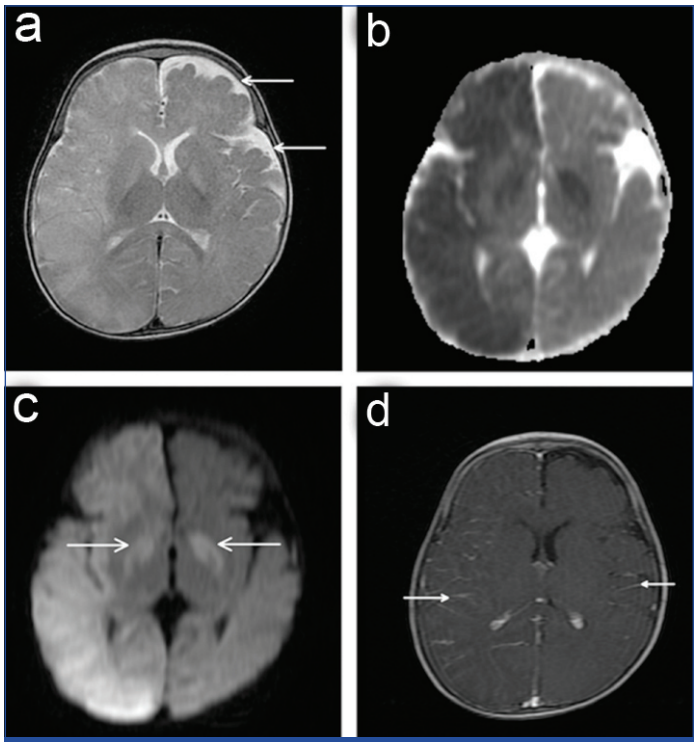
Keywords: Apoptosis, Neuronal damage, Paediatric, Radiology, Viral antigen

CASE REPORT

A six-month-old male neonate patient was brought to the paediatric outpatient department with chief complaints of decreased activity, fever, vomiting, diarrhoea, and two episodes of generalised tonic-clonic seizures that occurred over the last two days, with the mother as the informant. The patient had a normal peripartum period. The patient was vaccinated, up-to-date, and had normally achieved developmental milestones as per age. The fever had an insidious onset, was continuous in nature, high-grade in severity with no aggravating factors, but relieved with medication, and showed no diurnal variation. The patient also experienced four episodes of non bilious and non projectile vomiting over two days. Loose stools were also reported, which were watery in consistency. The patient had two episodes of uncontrolled movements, starting with an ictal cry and followed by micturition and defecation. Nasal and throat swabs were positive for SARS-CoV-2 viral antigen. The patient was admitted to an isolation ward for further evaluation and management. The SpO_2 percentage on admission was 92 on the right arm. On routine examination, the patient had a haemoglobin level of 11.5 g/dL, a total leukocyte count of 339,000/cumm, and a serum bilirubin level of 0.6 µmol/L. A lumbar puncture was performed, and cerebrospinal fluid examination revealed a glucose level of 206 mg/dL and a protein level of 41 mg/dL. No pathogenic organisms were seen on culture of the cerebrospinal fluid.

A plane MRI of the brain was conducted, which showed evidence of altered signal intensity in the cortical and subcortical areas of the right frontal-temporal-parietal-occipital region. The bilateral head of the caudate nucleus, genu and posterior limb of the internal capsule, and globus pallidus appeared hyperintense on T2, showing restriction on Diffusion-Weighted Imaging (DWI) with corresponding areas of dark signals on Apparent Diffusion Coefficient (ADC), leading to effacement of adjacent sulci-gyri spaces. This finding was suggestive of hypoglycaemic encephalopathy [Table/Fig-1].

The patient was given a breastfeeding trial and managed with 25% dextrose initially at a rate of 0.2 g/kg for 48 hours, as the patient was symptomatic. This was followed by an infusion of dextrose normal saline. Potassium chloride infusion was started to increase the serum potassium, as hypokalaemia is often seen in cases of hypoglycaemia. The patient was also started on injections of levetiracetam, remdesivir, dexamethasone, fluconazole, phenytoin, meropenem, vancomycin, calcium gluconate, emeset, and paracetamol. All medications were given in the recommended paediatric doses.



[Table/Fig-1]: a) T2WI axial section of the brain shows hyperintensity in the right fronto-parietal-temporal lobe and bilateral head of caudate nucleus and globus pallidus; b) ADC axial image shows low signal intensity in the right fronto-pareito-temporal lobe and bilateral head of caudate nucleus and globus pallidus; c) DWI axial image shows restriction in the right fronto-pareito-temporal lobe and bilateral head of caudate nucleus and globus pallidus; d) Contrast-enhanced T1WI image shows effacement of sulcal spaces with linear enhancement along sulcogyral spaces of bilateral cerebral hemispheres suggestive of COVID-19-induced encephalitis leading to hypoglycaemic encephalopathy.

The patient's activity improved, they started tolerating feeds, and there were no episodes of vomiting and seizures. As a result, the injections of levetiracetam, vancomycin, dextrose, and calcium gluconate were discontinued. Later, the patient was started on syrup levetiracetam and deocal. The patient was kept under observation before discharge for the next seven days. The patient was advised to continue syrup levetiracetam for the next two years and to follow-up every month for the next six months. They were also instructed to visit the emergency department if symptoms reappeared.

During the one-month follow-up, the patient had no active complaints, and they were compliant with syrup levetiracetam, remaining seizure-free for the month. On examination, the patient had delayed motor developmental milestones, for which developmental therapy, special education, and speech therapy were advised.

DISCUSSION

Hypoglycaemic encephalopathy is broadly used to describe symptoms of altered sensorium when blood glucose levels fall below critical levels [1,2]. It is widely described as a blood glucose level below 50 mg/dL and a state of stupor or coma persisting for 24 hours without any secondary factors. Hypoglycaemia has widespread clinical manifestations like sweating, gnawing hunger, and other sympathetic symptoms like tremors, palpitations, and anxiety. Focal deficits such as hemiplegia, aphasia, hemianopia, and cortical blindness can also be seen [3]. Generalised seizures and myoclonic jerks are two different types of seizures that can be seen in hypoglycaemia. Severe cases can result in decerebrate posture, sluggishness, vegetative states, and coma [4].

In present case, arriving at the diagnosis was challenging, but the recent pandemic provided some clues. The diagnosis was difficult as the patient presented with symptoms of fever, convulsions, vomiting, and diarrhoea. The patient's fever had an insidious onset, was continuous in nature, and was high-grade, which was consistent with COVID-19 infection. The positive nasal and throat swab for SARS-CoV-2 viral antigen further supports this diagnosis. The patient's normal developmental milestones do not rule out COVID-19 infection. The vomiting and loose stools were also consistent with COVID-19 disease, as gastrointestinal symptoms such as nausea, vomiting, and diarrhoea have been reported in some COVID-19 cases. The two episodes of convulsions could be attributed to the neurological effects of COVID-19. However, it is important to note that other underlying conditions that can cause convulsions were also considered, such as meningitis and septicaemia, which were ruled out through diagnostic tests such as complete blood count, blood culture, and imaging studies. The patient was closely monitored for any complications of COVID-19 infection and received supportive care, including intravenous fluids and antipyretics.

The exact mechanism of damage is unknown, but some hypotheses suggest that hypoglycaemia leads to the failure of the Krebs cycle, decreased Adenosine Triphosphate (ATP) production, and apoptosis of brain cells [5]. These effects mainly affect the cerebral cortex, caudate nucleus, and hippocampus. MRI brain imaging was employed for the final diagnosis of hypoglycaemic encephalopathy. Two out of three MRI studies suggested that the typical areas affected were the posterior limb of the internal capsule, the cerebral cortex (particularly the parieto-occipital and insula), the hippocampus, and the basal ganglia. These areas are usually affected bilaterally. In adults, the cerebellum, brainstem, and thalami are typically spared, but newborns can be affected. Damage to the corpus callosum can also be seen, referred to as the 'boomerang sign' [6].

Various prognostic factors include the degree of hypoglycaemia, co-morbidities, and duration of hypoglycaemia. Between 25% to 240% of patients with hypoglycaemic encephalopathy die over the long-term, mainly due to acute medical issues [5]. There are few indicators for long-term consequences. The prognosis has been shown to be influenced by both the initial blood glucose level and the duration of hypoglycaemia. Research has shown negative outcomes for hypoglycaemia lasting beyond eight hours [6]. The occurrence of seizures has also been associated with a poorer prognosis. Hypoglycaemia related to diabetes has a worse prognosis than hypoglycaemia from other causes. The extended duration of hypoglycaemia in index patient was a negative prognostic indicator.

The management of hypoglycaemic encephalopathy in COVID-19 patients was primarily supportive and symptomatic. Close monitoring of glucose levels is necessary, and intravenous glucose should be administered to maintain euglycaemia. Treatment of the underlying infection or inflammatory response is also essential. This case report does not explicitly establish a cause-and-effect relationship between hypoglycaemic encephalopathy and COVID-19. Further research should be conducted to understand the pathophysiology behind the occurrence of hypoglycaemic encephalopathy.

CONCLUSION(S)

Among the various presentations of COVID-19, ranging from minor cold symptoms to multisystem involvement syndrome, this case report highlights the occurrence of hypoglycaemic encephalopathy as a rare complication of COVID-19 in a paediatric patient. Delayed diagnosis and treatment of hypoglycaemic encephalopathy in COVID-19 can have significant long-term consequences. However, due to the rarity of this presentation, it is often misdiagnosed or undiagnosed, leading to delayed treatment. Early recognition and management are crucial to prevent permanent neurological damage, highlighting the need for increased awareness and understanding among healthcare professionals. Diagnostic modalities like MRI should be employed for accurate diagnosis. Moreover, studies are required on this topic to clarify the aetiology and the variables affecting the results, especially in the paediatric population.

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