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CASE REPORT

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Case report of brain death in a child due to COVID-19 and literature review

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Abstract

Purpose Although COVID-19 typically presents with respiratory symptoms, it can also lead to severe neurological manifestations in children. While case reports of COVID-19–associated encephalopathy (including acute necrotizing encephalopathy) have increasingly appeared, gaps remain regarding optimal management strategies and outcome predictors for children with rapid-onset neurological decline. This report aims to underscore the critical need for standardized clinical approaches to severe pediatric COVID-19–related encephalopathy.

Methods In this case report, We detail the case of an 8-year-old girl who presented with fever, rash, headache, and recurrent seizures. Her diagnostic workup included polymerase chain reaction (PCR) testing for SARS-CoV-2 and a range of neurological assessments: contrast-enhanced computed tomography (CT) to evaluate structural changes, transcranial Doppler ultrasound to assess intracranial hemodynamics, and electroencephalography (EEG) to monitor electrical activity. Intensive therapeutic measures—encompassing mechanical ventilation, hemodynamic support, antimicrobial agents, and corticosteroids—were initiated. In addition, a targeted narrative literature review of pediatric COVID-19–associated neurological complications was conducted to contextualize this presentation.

Results The patient tested positive for COVID-19;imaging revealed brain edem, and EEG suggested brain death. Despite aggressive critical care interventions, her condition did not improve, ultimately resulting in brain death. Our review of current literature revealed several reported instances of acute necrotizing encephalopathy in pediatric COVID-19, highlighting a growing body of evidence on the potential for severe central nervous system sequelae.

Conclusion This case highlights the importance of early recognition and close neurological surveillance in pediatric patients with COVID-19. Although accumulating evidence describes COVID-19–related neurological complications such as acute necrotizing encephalopathy, uncertainties persist regarding definitive treatment protocols and long-term outcomes. Greater understanding of the underlying mechanisms and standardized management pathways is imperative to improve prognosis in this vulnerable population.

Clinical trial Not applicable.

Keywords COVID-19, Encephalitis, Immune response, Children, Case report

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Introduction

Acute necrotizing encephalopathy of childhood (ANEC) is an infection-triggered disorder characterized by focal blood-brain barrier breakdown, affecting young children and infants, and leading to symmetrical lesions in key brain regions [1]. Acute brain dysfunction in children can manifest through a variety of symptoms, including altered consciousness, seizures, and neurological deficits [2, 3]. This condition is often associated with severe underlying pathologies such as infections, metabolic disturbances, or traumatic injuries. The diagnostic criteria for childhood brain dysfunction typically encompass a thorough neurological evaluation, neuroimaging (e.g., magnetic resonance imaging or computed tomography), electroencephalographic (EEG) recording, and laboratory investigations to identify or exclude potential etiological factors. Current literature [4] emphasizes the importance of early recognition and intervention, as prognosis can be significantly influenced by prompt diagnosis and management of pediatric patients with severe neurological impairments.

Since the discovery of the novel coronavirus (SARS-CoV-2) in 2019, it has posed a significant threat to global public health [5–10]. Although most infected individuals exhibit only mild symptoms or are asymptomatic, an increasing number of studies suggest that children may have severe COVID-19, particularly in terms of the nervous system [6, 8]. COVID-19-related encephalopathy in children ANE is a rare but severe complication, with clinical manifestations including altered consciousness, seizures, and movement disorders [11]. Currently, research on ANE is still in its early stages, and the related pathogenesis, clinical features, and diagnostic criteria are not yet fully understood. Therefore, exploring the relationship between COVID-19 infection and childhood encephalopathy is of significant clinical importance.

Case presentation

We present the case of an 8-year-old girl who developed acute necrotizing encephalopathy (ANE) due to infection with the novel coronavirus, which ultimately progressed to brain death.

Initial presentation and prior history

The patient developed a fever (peak 38.6 °C) frontal headache, pruritic dark-red maculopapular rash (limbs to trunk), and non-projectile vomiting on the first day of illness (approximately 2 days prior to admission), with no identifiable trigger. The local health clinic administered oral medication (specifics unclear), but there was no relief. On day 2, the child experienced the first episode of generalized tonic-clonic seizures: limbs stiffened and shook, with right eye blinking, upward gaze, and frothing at the mouth, lasting for 5 min and resolving spontaneously, with a return to a relatively good mental state. On the same day, the child was transferred to a hospital in Guangzhou, where they were alert and responsive upon admission. At 20:00, a similar seizure occurred again but lasted for 1 min; at this time, the temperature was 36.3℃, accompanied by three episodes of non-projectile vomiting. Blood gas analysis revealed metabolic acidosis (pH 7.23, BE -9, Lac 5.4 mmol/L), prompting the initiation of sodium bicarbonate to correct acidosis, combined with ceftriaxone and azithromycin for infection control.

At midnight that night, the child became drowsy. On the morning of the third day at 7:00, a third seizure (with limb stiffness) occurred, which was alleviated by intravenous diazepam after 1 min; the temperature had risen again to 39℃. After the seizure, the child quickly entered a comatose state, and by 7:30, there was unequal pupil size, indicating increased intracranial pressure, prompting immediate treatment with mannitol for dehydration. At 8:00, respiratory failure occurred (with cyanosis and inability to maintain blood oxygen levels), necessitating emergency intubation and mechanical ventilation. Following fluid resuscitation with saline and dopamine (15 μg/kg·min) for blood pressure support, circulation improved, but the child remained in a deep comatose state. The child was then transferred to our hospital for continued treatment (on September (Sep) 9).

Past medical history

Hospitalized for 5 days due to pneumonia at age 4. Denies history of infectious diseases (e.g., hepatitis, tuberculosis). History of cow's milk protein allergy. Denies drug allergies, glucose-6-phosphate dehydrogenase (G6PD) deficiency, trauma, or prior surgeries. History of blood transfusion.

Laboratory and ancillary test results

Relevant laboratory tests during the patient's hospitalization are as in Table 1. Plasma ammonia measurement: 20.9 umol/L. Serum ferritin was 95.39 ng/mL. Serum immunoglobulin E (IgE) 414.00 IU/ml. Creatine kinase B (CK-MB) 36.4 ng/ml. Apolipoprotein E 71.0 mg/ml.B-type natriuretic peptide precursor (PRO-BNP) 10093.20 pg/ml (Sep.13), 13730.09 pg/ml (Sep.17), PRO-BNP 16390.98 pg/ml (Sep.18).

Cerebrospinal fluid (CSF) was obtained via lumbar puncture in An Ding Town (Sep. 9). The child was positioned on their left side, with their back arched and knees flexed, while sedation and analgesia were administered. After disinfecting the surgical area, the puncture procedure was performed. There were no adverse reactions after sedation, and the vital signs remained stable during and after the procedure. The cerebrospinal fluid is clear and colorless.The opening pressure was 90mmH2O. Cell

Table 1 Laboratory parameters of the patient

Examination Item	Test Result	Reference/Normal Range
Serological Testing(2024.9.09-2024.9.18)		
2024.09.09 IgE	414.00 IU/mL	0–200 IU/mL (depends on age)
2024.09.10 PRO-BNP	10093.20 pg/mL	< 125 pg/mL
Creatine Kinase-MB (CK-MB)	36.4 ng/mL	0.0–5.0 ng/mL
2024.09.12 Apolipoprotein E	71.0 mg/mL	35–80 mg/mL
2024.09.13 PRO-BNP	10093.20 pg/mL	< 125 pg/mL
2024.09.15 PRO-BNP	6107.69 pg/mL	< 125 pg/mL
2024.09.17 PRO-BNP	13730.09 pg/mL	< 125 pg/mL
2024.09.18 PRO-BNP	16390.98 pg/mL	< 125 pg/mL
CSF Routine Check (2024.09.09)		
Traits	Colorless, clear, transparency clear	Clear, Colorless
Protein qualitative	2+	Protein < 0.45 g/L typical
WBC	0.0 × 10^6/L	0–5 × 10^6/L
RBC	2000.0 × 10^6/L	RBC normally 0 in CSF
LDH	358 U/L	< 40 U/L
Pathogen Detection(2024.09.11–15)		
Stool rotavirus test	Weak positive	Negative
Respiratory infection pathogens 9 items	Negative	Negative
Respiratory pathogens class III (PIV1、PIV3 、RHV、hMPV、hBOV) nucleic acid detection	Negative	Negative
Herpes simplex virus	Negative	Negative
Cerebrospinal fluid full-process pathogen metagenomic detection	Below detection limit	Below detection limit
Cytomegalovirus DNA quantification	Negative	Negative
Sputum tNGS(COVID-19)	Sequence count: 22,057	Negative
COVID-19 virus(Throat swab)	Positive	Negative
Blood Full Process Pathogen Metagenomic Detection	Negative	Negative
Imaging(2024.09.09)		
X-ray(Lung)	Bilateral lung exudation, right upper lung consolidation	The lung fields are uniformly transparent, with no abnormal shadows or increased density
X-ray(Abdominal)	No clear abnormalities	No significant abnormalities, such as masses, foreign bodies, or other pathological changes
CT(Cranial CT scan + enhancement)	Diffuse cerebral edema in bilateral cerebral hemispheres and brainstem; cerebellar tonsils unclear, to rule out brain herniation; enhanced scan showed reduced surface vascular shadows	No significant abnormalities
Pediatric Ultrasound (2024.09.11)		
Gallbladder Ultrasound	Abnormal ultrasound of the gallbladder, consider bile sludge	No significant abnormalities
Liver Ultrasound	No significant abnormalities	No significant abnormalities
Spleen Ultrasound	No significant abnormalities	No significant abnormalities
Pancreas Ultrasound	No significant abnormalities	No significant abnormalities
Kidney Ultrasound	Bilateral kidney ultrasound showed no significant abnormalities	No significant abnormalities
Gastrointestinal Ultrasound	Abnormal gastrointestinal gas accumulation, several mesenteric lymph nodes, largest 14 × 4 mm	No significant abnormalities
Intestinal Findings	No signs of intestinal intussusception, no signs of intestinal obstruction, no significant abscesses	No significant abnormalities
Bedside Transcranial Doppler Ultrasound (2024.09.12)		
Transcranial Doppler (TCD)	Bilateral middle cerebral arteries show oscillatory wave spectrum	No significant abnormalities

Table 1 (continued)

Examination Item	Test Result	Reference/Normal Range
Serological Testing(2024.9.09-2024.9.18)		
Basilar Artery	Nail wave blood flow	No significant abnormalities
Clinical Interpretation	Indicates intracranial anterior and posterior blood flow circulation failure, increased intracranial pressure	No significant abnormalities
Diagnostic Conclusion	Meets TCD brain death determination criteria	No significant abnormalities
Video EEG Monitoring (2024.09.15)		
Long-term EEG	Electrical resting state, meets brain death determination criteria	No significant abnormalities

count revealed: RBC 2000×10^6/L, WBC 0.0×10^6/L. CSF protein was qualitatively positive at 2+ (no quantitative value available), lactate dehydrogenase was 358 U/L, and CSF glucose was 5.53 mmol/L with a CSF-to-blood glucose (12mmol/L) ratio of 0.46.

Metagenomic next-generation sequencing (mNGS) of the CSF was negative for bacterial and viral pathogens. Nine-panel respiratory pathogen testing on nasopharyngeal swabs was also negative, as was herpes simplex virus testing. Cytomegalovirus DNA was below the detectable limit. Stool screening indicated a weakly positive result for rotavirus. In contrast, high-throughput sequencing of a sputum sample returned 22,057 reads matching COVID-19, a finding consistent with positive COVID-19 nucleic acid tests in both throat swabs and sputum. Metagenomic testing of blood and CSF samples was negative. A blood culture was done on Sep.18, and returned result Gram-positive cocci reported.

Imaging findings

The key radiologic findings are shown in Fig. 1A bedside chest and abdominal X-ray was performed on Sep.9 (Day 1 of admission) to evaluate for possible respiratory or abdominal etiologies of her fever and deteriorating condition. The chest film revealed bilateral pulmonary infiltrates (sometimes described as "exudation") and notable consolidation in the right upper lung field, raising suspicion of pneumonia (Fig. 1A). Abdominal X-ray showed no obvious abnormalities.

A contrast-enhanced cranial CT (Fig. 1B & C) demonstrated diffuse cerebral edema involving both hemispheres and the brainstem. Although no overt midline shift was specifically noted, the degree of edema suggested high intracranial pressure. Radiologically, there was concern for impending brainstem herniation; however, a definitive brain shift was not documented. The enhanced images showed decreased visualization of surface vessels (part of the formal radiology report), which may reflect diminished cerebral perfusion in the context of severe edema. A more detailed assessment with Magnetic Resonance Imaging (MRI) was recommended, but due to the child's critical status and subsequent confirmation of brain death, an MRI was not performed. In our center, CT is often the initial modality for critically ill patients because it is faster and more widely accessible than MRI for unstable cases.

An abnormal gallbladder ultrasound suggested possible bile sludge. Liver, spleen, and pancreas ultrasounds showed no significant lesions, while bilateral kidney ultrasound was unremarkable. Several enlarged mesenteric lymph nodes were noted, the largest measuring 14×4 mm, with no signs of intussusception or bowel obstruction.

Transcranial Doppler Ultrasound (TCD) findings (Fig. 1.D) demonstrate oscillatory wave spectra in the bilateral middle cerebral arteries and spike-like waveforms in the basilar artery, indicating failure of intracranial anterior-posterior circulatory blood flow and elevated intracranial pressure. These findings meet the TCD diagnostic criteria for brain death.

A prolonged EEG recording showed an "electrical resting state," implying complete cessation of cortical activity. This finding aligns with one of the ancillary study criteria for confirming pediatric brain death [12]. Clinical brainstem reflex examinations (e.g., fixed pupils, absent corneal, cough reflexes) corroborated these EEG findings prior to official declaration of brain death.

Hospital course and management

After admission (Sep 9), the patient received mechanical ventilatory support and hemodynamic stabilization measures in a pediatric intensive care setting. Saline and albumin were administered for volume expansion, and vasopressor/inotropic agents—including dopamine (Sep.9), dobutamine (Sep 9–16), norepinephrine (Sep 9–10), and milrinone (Sep9–16)—were employed to maintain adequate blood pressure and cardiac output. Hydrocortisone (Sep.9) and methylprednisolone (Sep10–14 at 4 mg/kg/day, then Sep 15–16 at 2 mg/kg/day), along with levothyroxine (Sep 9–16), aminocaproic acid (Sep 9–14), and posterior pituitary hormone (Sep 9–13), provided hormone replacement or metabolic support as indicated by the child's evolving clinical state. Hypertonic sodium solutions were administered to manage suspected elevated intracranial pressure. Additional treatments included omeprazole for stress-ulcer prophylaxis

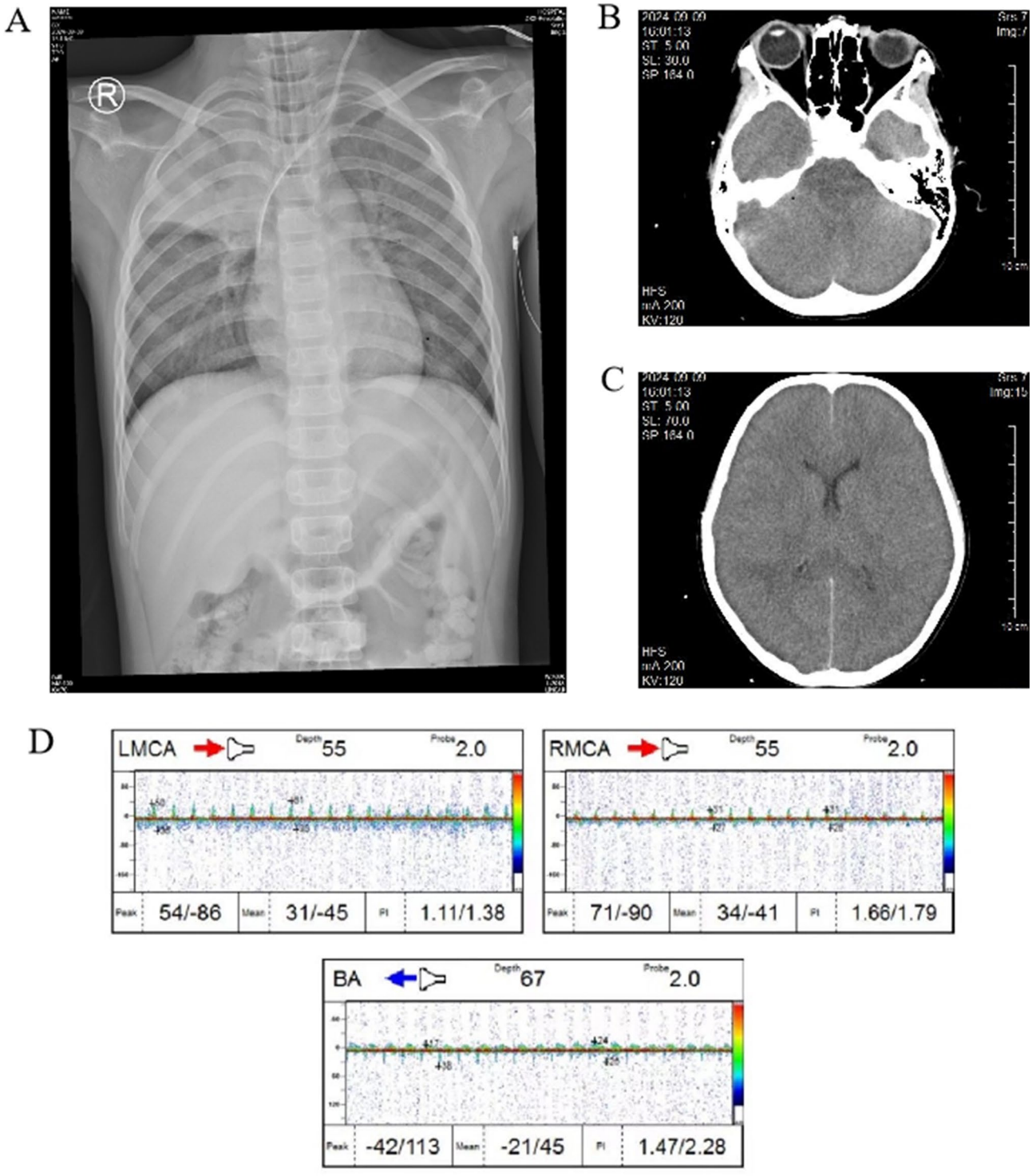

Fig. 1 Imaging findings findings in Patient. **A** X-ray examination, Bilateral pulmonary exudates, consolidation of the right upper lobe. **B**&**C** cranial computed tomography examination, The boundary between the gray and white matter of both cerebral hemispheres is unclear, with a generally reduced density. The brainstem is diffusely swollen, with decreased density. **D** Transcranial Doppler (TCD), Bilateral middle cerebral arteries show oscillating wave spectra, and the basilar artery shows nail-like blood flow

Table 2 Case reports reviewed in literature

Reference	Age (year)	Gender	Clinical manifestations	Lab & Imaging findings	Outcome
Shian and Chi [14], n = l	0.8	M	Ofdrowsiness, high fever and vomiting, Respiratory failure	1 Lab findings: EBV 2 Imaging finding: CT showed hypodensity of the brainstem Ultrasonography showed hyperechogenicity of the brainstem	Death
Ismael Gomes et al. [8], *n* = 1.	1.2	F	vomiting, hypotonia, episodic seizures and respiratory failure.	1 Lab findings: SARS-CoV-2 2 Imaging finding: CT shows abnormal enlargement of the third and lateral ventricles, with loss of gray-white matter differentiation.	Death
Pager C, et al. [19], *n* = 1.	0.1	M	Vomiting, unwilling to suck, disseminated intravascular coagulation.	1 Lab findings: Rotavirus	Death
Wang PYal, et al. [15], *n* = 2.	3.3, 8	F(*n* = 2)	High fever, vomiting, and diarrhea, convulsions, and consciousness disorders; Persistent high fever, convulsions, and consciousness disorders.	1 Lab findings: H3N2 2 Imaging finding: No specific imaging findings mentioned due to rapid disease progression	Death
Ku, Young-Su et al. [16], *n* = 1	7	F	High fever, altered mental status	1 Lab findings: SARS-CoV-2 2 Imaging finding: MRI revealed hyperintense areas in bilateral thalamus, posterior basal ganglia, internal capsule posterior limb, and upper midbrain, in FLAIR images	Residual deficits
Zhang, Jianzhao et al. [17], *n* = 4	1.9,1.1,2.1,6	M(*n* = 2) F(*n* = 2)	prodromal symptoms of virus infection altered consciousness, seizures andcognitive/language disturbances	1 Lab findings: SARS-CoV-2 2 Imaging finding: MRI scans revealed damage to the thalamus, basal ganglia and brainstem	Death(*n* = 1) Residual deficits(*n* = 3)
Choi, Yoon Yeong et al. [18], *n* = 2	7,6	F(*n* = 2)	Fever and mental, generalized seizures	1 Lab findings: SARS-CoV-2 2 Imaging finding: MRI revealed symmetrical edematous lesions in the bilateral thalamus	Recovered(*n* = 1), Residual deficits(*n* = 1)
This study, *n* = 1	8	F	Fever, headache, convulsions	1 Lab findings: SARS-CoV-2,Mildly positive for rotavirus in fecal matter. 2 Imaging finding: CT showed Bilateral cerebral hemispheres and brainstem diffuse cerebral edema, Enhanced scan shows reduced vascular shadows on the brain surface. 3.EEG was characterized by generalized slow activity.	Death

CT,Computed Tomography; **EEG**,Electroencephalogram; **F**, Female; **M**, Male; **MRI**, Magnetic Resonance Imaging; **EBV**, Epstein-Barr virus; **H3N2**, influenza A virus,

and intravenous sodium creatine phosphate for myocardial support. Initial empiric anti-infective therapy included ceftriaxone (Sep9–10), escalated to meropenem (Sep 10–16) for broader coverage. Nirmatrelvir/ritonavir (Sep15–16) was given to lower SARS-CoV-2 viral load after confirmation of COVID-19.

Outcome and brain death determination

Despite aggressive therapy, the patient remained in profound coma without sedation or analgesia, with absent brainstem reflexes (pupillary light, corneal, cough, and pain reflexes), no spontaneous respirations, and a Glasgow Coma Scale (GCS) of 2T. Two consecutive pediatric brain death evaluations were performed on Sep 11and Sep 12, each meeting the criteria stipulated in National/Institutional Pediatric Brain Death Guidelines [13]. As a result, the patient was declared brain-dead on Sep 18. The parents declined an autopsy.

Note on literature review

A literature search methodology was performed using the PUBMED, SPRING, SCOPUS, and EMBASE databases identified 10 published pediatric cases of brain death associated with infectious etiologies. Table 2 in the Results section summarizes 16 previously reported cases plus our case (total of 17). Most of these children had fever, seizures, and reduced consciousness, with confirmatory imaging and EEG changes supporting a diagnosis of brain death. Although these data illustrate that multiple pathogens (e.g., EBV ([14], influenza ([15], SARS-CoV-2 [8, 13–15], rotavirus ([19] can precipitate fatal encephalopathies in children, systematic gaps remain in understanding why certain infected children progress to irreversible brain damage while others recover.

By highlighting the rapid clinical evolution of severe pediatric COVID-19 encephalopathy, this case underscores the importance of vigilant neurological monitoring

in infected children and calls for further research into the mechanisms driving acute brain injury in COVID-19. Ultimately, improved evidence-based protocols may offer hope for better outcomes in these critically ill pediatric populations.

Discussion

Acute necrotizing encephalopathy (ANE) is often associated with infections, classically viral but also including other pathogens Despite multiple case reports and small series on ANE in pediatric populations, its pathogenesis and optimal management—especially in the context of SARS-CoV-2 infection—are still not fully defined. Uncertainties remain regarding the interplay of immune-mediated injury, direct viral effects on the central nervous system, and co-infections. Further research is needed to (1) clarify the pathophysiological mechanisms that lead to ANE in pediatric COVID-19, (2) refine diagnostic criteria that integrate imaging, CSF analysis, and EEG findings, and (3) establish evidence-based management protocols to improve outcomes. Thus, investigating the relationship between SARS-CoV-2 infection and severe encephalopathic processes is clinically crucial.

The child in our case rapidly progressed toward deep coma and ultimately fulfilled the criteria for pediatric brain death. While the initial onset of fever was documented approximately 48 h prior to admission, her most significant neurological deterioration (from the first generalized seizure to coma) occurred over a very short timeframe (<72 h from the initial convulsion). This rapid decline is broadly compatible with ANE, which is characterized by sudden onset and rapid progression.

The child's elevated immunoglobulin E (IgE) level—an immunoglobulin class typically linked to parasitic infections or allergic reactions—may suggest an immune dysregulation triggered by SARS-CoV-2 [20, 21]. In some brain injury cohorts, elevated serum IgE has been proposed as a marker of robust or aberrant immune activation. Although we did not assay additional immunological biomarkers (e.g., cytokine profiles), the high IgE level may reflect the heightened inflammatory milieu, potentially contributing to the pathophysiology of acute encephalopathy. Future prospective studies should examine whether IgE correlates with disease severity or risk of encephalopathy in pediatric COVID-19.

Elevated B-type natriuretic peptide precursor (pro-BNP) in this child may signify cardiac strain in response to systemic inflammation [22]. Although overt cardiac dysfunction (e.g., arrhythmias or cardiogenic shock) was not clearly documented, increased pro-BNP suggests myocardial stress or subclinical dysfunction, which can worsen cerebral hypoperfusion. Given that adequate cerebral blood flow is paramount in preventing neurological damage, any cardiac compromise could exacerbate an already inflamed or edematous brain.

The patient's cerebrospinal fluid (CSF) analysis showed elevated lactate dehydrogenase (LDH) and protein, which may indicate neuronal or glial cell damage, inflammation, or infection [23]. While conventional pathogens were not identified by metagenomic sequencing, SARS-CoV-2 was detected in sputum and nasopharyngeal samples. This finding underscores the possibility of an indirect or para-infectious inflammatory mechanism in the central nervous system, even if the virus is not isolated from CSF.

Rotavirus was weakly positive in the stool sample, and it too can precipitate various neurological complications, including seizures and encephalitis [24] However, based on the child's clinical presentation and the high SARS-CoV-2 sequence reads (22,057) found in her sputum, COVID-19 is the more likely dominant factor in this severe encephalopathy—though a co-infection scenario cannot be fully excluded. Without autopsy or direct pathogen detection in the brain tissue, the definitive culprit remains uncertain. Clinically, however, the robust respiratory findings (bilateral pulmonary infiltrates) and marked inflammatory response suggest that SARS-CoV-2 was a key driver of her acute and fulminant neurological decline.

In contrast to reports indicating that children and neonates often have milder courses of COVID-19 [7, 9], our case and other published reports demonstrate that some pediatric patients can develop catastrophic neurological outcomes [9, 25]. Notably, Wang et al. [25] described a case of ANE in a child with COVID-19 where initial CT imaging appeared normal but MRI confirmed characteristic lesions. Our patient's CT, in contrast, showed diffuse cerebral edema, underscoring that COVID-19–related encephalopathy can present variably on neuroimaging—from subtle or atypical changes to extensive edema or necrosis. Furthermore, whereas Stafstrom et al. [9] reported primarily fever and seizures in COVID-19 children, our patient manifested rapid progression to coma, absent brainstem reflexes, and eventual declaration of brain death according to the Chinese pediatric brain death standards [13]. This emphasizes the heterogeneity in clinical courses and the necessity for high vigilance, particularly in children with severe comorbidities or rapidly worsening neurological signs.

Our case cannot definitively prove causation between SARS-CoV-2 and ANE in the absence of direct viral detection in brain tissue. Moreover, the concurrent weakly positive rotavirus test raises the question of co-infection. An autopsy might have shed light on the pathological underpinnings, but it was declined by the family. Consequently, clinicians treating pediatric patients with complex or rapidly deteriorating neurologic symptoms during a COVID-19 infection should consider broad

pathogen evaluation—especially for viruses like rotavirus, influenza, or enterovirus—and maintain a low threshold for advanced imaging and intensive supportive management. Prospective multicenter studies and registry data on pediatric COVID-19 encephalopathy are essential to clarify pathophysiology, refine diagnostic criteria, and optimize therapy.

Research reflection and conclusion

Discussion of limitations

The limitations of this report is that it describes only a single case from a single center, resulting in a small sample size; The child's family did not consent to autopsy, to enable clinical-pathological correlation.

Conclusion

This case highlights the urgent need for early recognition of neurological complications in children with COVID-19, emphasizing actionable strategies such as proactive tracking of evolving neurological symptoms (e.g., seizures, altered consciousness) and evaluation of biomarkers like IgE/PRO-BNP for risk stratification. Clinicians should maintain heightened vigilance for atypical presentations, including rapid neurological deterioration post-infection. These findings advance our understanding of COVID-19-associated encephalopathy in children and highlight urgent research priorities: (1) elucidating viral neuroinvasion mechanisms, (2) optimizing acute-phase interventions (e.g., seizure control, intracranial pressure management), and (3) validating predictive biomarkers. We advocate for multidisciplinary collaboration across pediatrics, neurology, and virology to establish evidence-based protocols. Joint clinical trials and international data-sharing initiatives are imperative to refine diagnostic criteria, therapeutic approaches, and long-term neuroprotective strategies, ultimately improving outcomes for this vulnerable population.

Abbreviations

ANEC	Acute necrotizing encephalopathy of childhood
ANE	Acute Necrotizing Encephalopathy
CK-MB	Creatine kinase B
CSF	Cerebrospinal fluid
CT	Computed Tomography
EEG	Electroencephalogram
GCS	Glasgow Coma Scale
IgE	Serum immunoglobulin E
LDH	Lactate dehydrogenase
MRI	Magnetic Resonance Imaging
PRO-BNP	B-type natriuretic peptide precursor

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Author contributions

XTT and ZB design of the work; LT, YYQ and LLW revised and provided guidance on the manuscript's table and figures. WCB, XMS, CY and ZJM acquisition of data, KL has drafted the work. All authors discussed the results and commented on the manuscript.

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Data availability

All data supporting the findings of this study are available within the paper and its Supplementary Information.

Declarations

Ethics approval and consent to participate

This project was approved by the Ethics Committee of Guangzhou Women and Children's Medical Center, and the informed consent of the participants' parents or guardians was obtained.

Consent for publication

We have obtained written informed consent from the patients' parents to publish clinical details and images.

Competing interests

The authors declare no competing interests.

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