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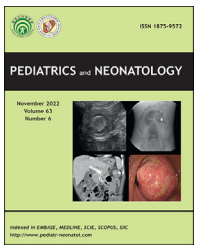

Short Communication

Acute necrotizing encephalopathy caused by SARS-CoV-2 in a child

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1. Introduction

Neurological manifestations in patients with coronavirus disease 2019 (COVID-19) including anosmia, ageusia, meningoencephalitis, encephalopathy, cerebrovascular disease, Guillain-Barré syndrome, acute disseminated encephalomyelitis, and seizures, have been reported.[1] Acute necrotizing encephalopathy (ANE) is a rare brain disease characterized by multiple necrotic lesions with a symmetric distribution. ANE has been reported in adults and children with COVID-19.[2–4] The Omicron variant surged in Taiwan in April 2022, and fatal neurological diseases emerged in children. ANE caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has not been reported in Taiwan. Herein, we report a child with COVID-19 who presented with high fever and seizure and was diagnosed with ANE.

2. Case presentation

A 2-year-and-10-month-old girl, who had no previous comorbidity and reached normal developmental milestones for her age, was admitted to our emergency department (ED) for fever up to 40°C for one week. She also experienced productive cough, vomiting, decreased appetite, and decreased urine output. On arrival to the ED, she had a generalized tonic-clonic seizure lasting 10 min with an eardrum temperature of 42.1°C. The seizures stopped after the administration of intravenous lorazepam. The patient remained drowsy after the seizures. SARS-CoV-2 RNA polymerase chain reaction (PCR) performed on a nasopharyngeal swab was positive, with a cycle threshold value of 22.57 (Roche cobas Liat system, Rotkreuz, Switzerland). A non-contrast computed tomography of the head revealed no intracranial lesions, hemorrhage, edema, or hydrocephalus. Subsequently, she was admitted to our intensive care unit. On admission, the Glasgow Coma Scale (GCS) score was E2V2M4. Her respiratory pattern was smooth. Lumbar puncture was performed, and the open and close pressure were 20.5 and 23 cmH2O, respectively. Cerebrospinal fluid (CSF) study showed normal glucose and no pleocytosis; protein level was elevated (99.4 mg/dL) and the PCR for SARS-Cov-2 and 14 pathogens in CSF were negative. Electroencephalogram revealed excessive slow waves at her age. Laboratory workup revealed elevated ferritin (1557 ng/mL), D-dimer (4214 ng/mL), and lactate dehydrogenase (760 U/L) levels. Serological examinations for herpes simplex virus, Epstein–Barr virus, and cytomegalovirus were negative. Mycoplasma DNA PCR was negative. Remdesivir and intravenous immunoglobulin (1 g/day) were administered for five and two days, respectively. Mannitol and dexamethasone were used for

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the relatively high intracranial pressure. Syndrome of inappropriate antidiuretic hormone secretion developed on day 2 of admission. Fluid restriction and 3 percent saline were then administered. No fever was detected on day 2; elevation of alanine aminotransferase level (559 U/L) was observed on day 3. Her consciousness level improved to GCS E4V2M6 on day 4 but fluctuated afterwards. Tocilizumab was administered once on day 5 immediately after serum interleukin-6 level was checked, which turned out to be $<$1.5 pg/mL. Follow-up laboratory data revealed leukopenia (white blood cell count, 1780/μL) and decreased ferritin, D-dimer, alanine aminotransferase, and lactate dehydrogenase levels. Magnetic resonance imaging (MRI) of the brain with and without contrast on day 7 showed peripheral diffusion restriction in the bilateral thalami and pons (Fig. 1). The bilateral thalami lesions showed a high T1 rim. Edema was observed in bilateral thalami, pons, and posterior limb of the bilateral internal capsule and external capsule. The imaging findings were compatible with ANE of childhood. Thus, methylprednisolone 30 mg/kg was administered on day 8—10. She could obey simple orders sometimes and sit for 4 min after methylprednisolone pulse therapy; however, no verbal output was noted. The patient was transferred to the general ward on day 9 and underwent rehabilitation.

3. Discussion

The neurological consequences associated with SARS-CoV-2 infection are diverse, ranging from anosmia and ageusia to fatal cerebral edema and encephalopathy. ANE is a rare and severe encephalopathy commonly triggered by viral infection. Seizures and a rapid deterioration of consciousness are common presentations. Symmetric lesions in the bilateral gray matter involving thalami are characteristic MRI findings.[5] Dysregulation of cytokine production, especially interleukin-6, rather than direct viral invasion, is believed to be a potential mechanism of ANE.[6] Treatment with corticosteroids and interleukin-6 receptor antagonist have been described.[6] Many pathogens have been reported to precede the development of ANE, such as influenza and HHV-6.[6] SARS-CoV-2 has been reported in adults and two pediatric cases in the pre-Omicron period.[2—4] To the best of our knowledge, no ANE of childhood due to SARS-CoV-2 infection has been reported during the Omicron wave. Our case presented with typical clinical,

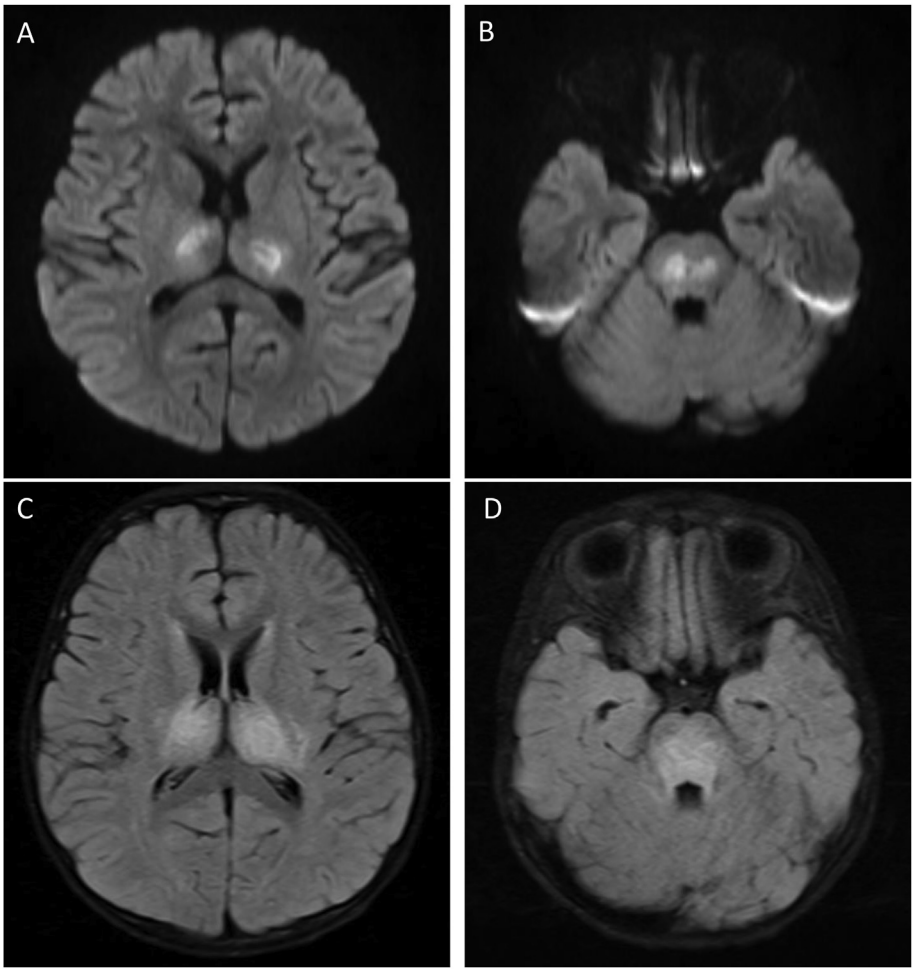

Figure 1 Brain magnetic resonance imaging. Diffusion-weighted images reveal peripheral diffusion restriction in bilateral thalami (A) and pons (B). T2-weighted-fluid-attenuated inversion recovery images of the same cuts as diffusion-weighted images shows edema in bilateral thalami (C) and pons (D).

laboratory, and imaging findings of ANE during the omicron surge period. MRI provides crucial information for diagnosis, and our report highlights prompt management specific to ANE to improve neurological outcomes in children.

Declaration of competing interest

None.

References

1. Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, et al. The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. *Brain* 2020;**143**:3104—20.
2. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated acute hemorrhagic necrotizing encephalopathy: Imaging features. *Radiology* 2020;**296**:E119—20.
3. Lazarte-Rantes C, Guevara-Castañón J, Romero L, Guillén-Pinto D. Acute necrotizing encephalopathy associated with SARS-CoV-2 exposure in a pediatric patient. *Cureus* 2021;**13**:e15018.
4. Khan M, Bhattarai S, Boyce TG, Hayek RA, Zhadanov SI, Hooper EE, et al. Acute necrotizing encephalopathy associated with coronavirus disease 2019 in an infant. *J Pediatr* 2022;**247**:160—2.
5. Mizuguchi M, Abe J, Mikkaichi K, Noma S, Yoshida K, Yamanaka T, et al. Acute necrotising encephalopathy of childhood: a new syndrome presenting with multifocal, symmetric brain lesions. *J Neurol Neurosurg Psychiatry* 1995;**58**:555—61.
6. Shukla P, Mandalla A, Elrick MJ, Venkatesan A. Clinical manifestations and pathogenesis of acute necrotizing encephalopathy: The interface between systemic infection and neurologic injury. *Front Neurol* 2022;**12**:628811.