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Case Report

Case Report of Acute Necrotizing Encephalopathy of Childhood Challenge of Diagnostic and Treatment

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Abstract

Acute Necrotizing Encephalopathy of Childhood (ANEC) is a rare disease with a higher prevalence in East Asia. It is characterized by symmetrical and multifocal involvement of areas including the thalamus, brainstem, cerebellum, and white matter. ANEC is associated with death as well as long-term neurological disabilities (sequelae) in individuals who survive. In this report, we describe a case of a child with acute neurological symptoms resulting from a possible infection and explain his brain MRI, and paraclinical symptoms.

Introduction: Acute necrotizing encephalopathy of childhood (ANEC) is a progressive encephalopathy. The aim of this study was to report a rare case of ANEC in an eleven-year-old child with bilateral thalamic necrosis. ***Case Presentation:*** An 11-year-old child presented four days before admission with an infectious episode characterized by fever (not quantified) and flu-like symptoms. This was further complicated by functional impotence of both lower limbs. MRI showed multiple cerebral lesions above and below the tentorial level, involving the brainstem, cerebellum, thalamus, and bilateral white matter. The patient received intravenous methylprednisolone 30 mg/kg/day and 2 mg/kg for 6 weeks. ***Discussion:*** Acute necrotizing encephalopathy of childhood (ANEC) is a rapidly progressing encephalopathy characterized by fever and a depressed level of consciousness. Diagnosis depends on clinical presentation and characteristic neuroimaging findings of abnormal signal flair T2 of the thalami and supratentorial region, followed by treatment with steroids and immunoglobulin, as well as supportive care. Patients with ANEC have a variable prognosis, but mortality is very high. ***Conclusion:*** ANEC is a rare neurological entity in children, and its treatment is challenging. Early interventions, including emergency intravenous methylprednisolone or immunoglobulin, or plasma exchange, or a combination of these treatments, are crucial. However, further studies are needed to establish consensus guidelines.

Keywords: ***ANEC, Encephalopathy, Thalamus, Brainstem, Multifocal brain lesions, Children, MRI, Case report.***

Introduction

Acute necrotizing encephalopathy (ANE) is a rare neurological condition originally observed in populations in Southeast Asia, particularly in Japan and Taiwan. While an increasing number of cases have been reported in Caucasian populations, assessing its true incidence remains challenging. ANE primarily affects infants under 1 year old and often follows a viral infection or vaccination, presenting with nonspecific clinical signs. It manifests as a rapid neurological deterioration within 3 to 5 days of a common viral infection, carrying a high mortality rate (30%) and frequent neurological sequelae in survivors. Diagnosis typically relies on brain magnetic resonance imaging (MRI), revealing characteristic symmetrical and focal necrotic lesions in the thalamus.

Case Presentation

An 11-year-old child, the third of four siblings, weight 25 kg, with a history of generalized febrile tonic-clonic seizures between ages 4 and 6, without documents, presented four days prior to admission with fever, flu-like symptoms, functional impairment of both lower members, headaches without neck stiffness, and altered consciousness (Glasgow Coma Scale score of 10). Upon admission to the intensive care unit, the child exhibited symmetrical and reactive pupils, no neck stiffness, a negative Kernig sign, 2/5 muscle strength in upper and lower members, absent reflexes, sphincter atony, and sensory disturbances. A cerebral CT scan showed hippocampal hypodensity; lumbar puncture revealed no abnormalities, and neuromeningeal PCR type panel filmarray was negative. Laboratory findings included a hemoglobin concentration

of 12.9 g/dL, white blood cell concentration of 15.150 g/L, platelet count of 249 G/L, lymphocytes of 2.15 G/L, urea concentration of 0.32 g/L, creatinine concentration of 4.26 mg/L, and C-reactive protein concentration of 86 mg/L, with negative immunoassay results. Brain MRI revealed multiple lesions involving the brainstem, cerebellum, corpus callosum, thalamus, and bilateral white matter (Figure1). The patient received a three-day intravenous bolus of methylprednisolone, followed by oral form at a dosage of 2 mg/kg per day associated to a alongside adjuvant therapy. The neurological status improved to a Glasgow Coma Scale score of 13 within three days, with slight improvement in reflexes and muscle strength. The patient was then transferred to pediatric department where he stayed for a week before discharge with muscle strength in all four limbs at 3/5 and improuved coughing and feeding reflexes.

The patient was satisfied with the treatment.

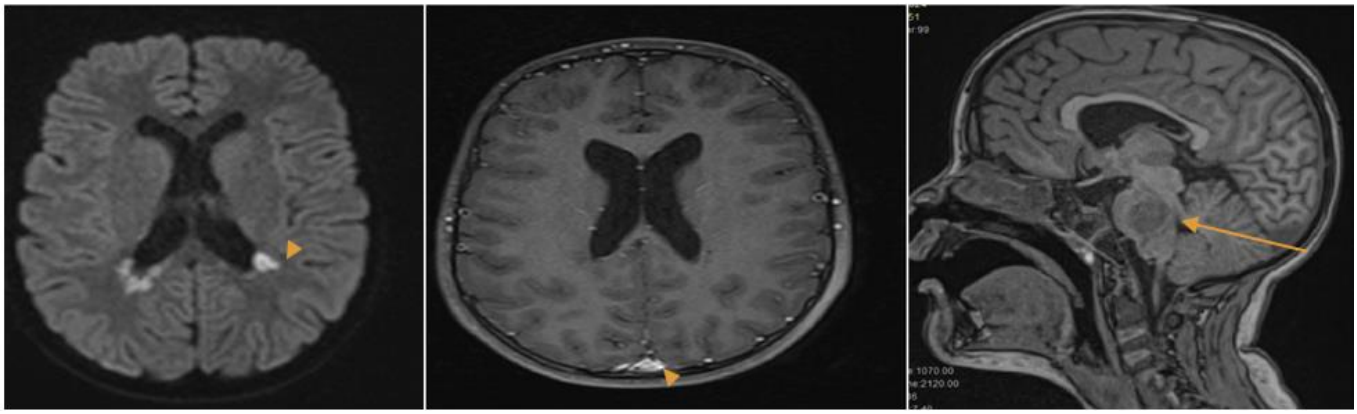

Figure 1: Hypersignal T1 with widened aspect of the brainstem, Hyperintense flair T2 signal in the semi-oval centers, and periventricular parietal regions, right temporal region, and right splenium.

Discussion

The initial descriptions of ANE primarily focused on children from Southeast Asia, but an increasing number of cases have been reported in European and American populations. In our observation, the patient had no particular medical history. ANE presents as an acute neurological syndrome characterized by rapid deterioration of consciousness, sometimes accompanied by seizures, 3 to 5 days after a viral infection. At present, the etiology and pathogenesis of ANE remain incompletely clear. Both environmental factors, which may contribute to the antecedent infections, and host factors such as individual susceptibility or genetic alterations might be involved [16]. Usually, ANE develops secondary to viral infections, including influenza A and B, novel influenza A (H1N1), parainfluenza, varicella, human herpesvirus 6 and 7 (HHV-6 and HHV-7), enterovirus, novel reovirus strain (MRV2Tou05), rotavirus, herpes simplex virus, rubella, coxsackie A9 [4,5-7,9]. Prodromal viral infections appear to play a critical role in the initiation of ANE. Despite the various antecedent infections, ANE is not considered to be an inflammatory encephalitis. These cells produce a high level of cytokines, suggesting that NK cells might be associated with the pathogenesis of ANE. Additionally, several lines of evidence show that levels of cytokines are elevated in the serum and/or CSF in different virus-associated ANE cases, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), soluble TNF receptor (sTNFR), and interferon-gamma (IFN-γ) [10-13]. IL-6 and TNF-α are critical among these cytokines because the former is neurotoxic at high concentrations, whereas the latter can damage the endothelium of the central nervous system. Hypercytokinemia engenders proteolytic destruction of the blood-brain barrier (BBB), which subsequently increases vascular permeability and causes brain oedema, petechial hemorrhage, and necrosis [16]. The diagnosis of ANE includes prodromal symptoms due to different viral infections, which include fever, signs of upper respiratory tract infections, gastroenteritis, and erythema. Patients with ANE often have signs of systemic inflammatory response syndrome like shock, multiple organ failure, and disseminated intravascular coagulation [9,11]. With the development of ANE, brain dysfunctions may present as seizures, disturbances of consciousness, and focal neurological deficits [3,9,11]. Gadolinium-contrast MRI has been reported useful in identifying lesions at the very early stage of ANE when conventional CT is less effective. The center of thalamic lesions is perivascular hemorrhage and necrosis of neurons and glial cells corresponding to slightly high signals, while the periphery of the center portion reveals congestion of arteries, veins, and capillaries, and acute swelling of oligodendrocytes corresponding to low signals in the surrounding areas, with extravasations at the edge of the thalamic lesions corresponding to high signals in the outermost regions. There have been no recommended therapies for ANE thus far. Intensive care, symptomatic treatment, empirical antiviral therapy, and immunomodulatory agents were tested in a majority of cases [2,10]. However, despite the severity of presentation and the late administration of steroids, good outcomes were still found in some patients, and some researchers suggested that a trial of steroids should be given to all patients with ANE [6,9,10]. Conversely, another study reported that ANE patients treated with steroids had poor outcomes [13]. The prognosis of ANE varies from complete recovery to death. It is estimated that the mortality rate is about 30%, and less than 10% of patients recover completely, while neurological sequelae are frequent in survivors.

Conclusion

ANE is an immune-mediated disease with an incompletely recognized pathogenesis. It is underdiagnosed partially due to insufficient awareness. The diagnosis of ANE is mainly based on the clinical and radiologic features. Immunomodulatory and ant-cytokine therapies are promising in dealing with ANE, whereas more studies are still needed. The prognosis of ANE is variable; however, it is still a potentially disease leading to death and severe neurological sequelae.

Abbreviations

ANEC: Acute Necrotizing Encephalopathy of Childhood
CT SCAN: Computed Tomography Scanner
MRI: Magnetic Resonance Imaging
GCS: Glasgow Coma Scale
IG: Immunoglobulin

Conflict of interest statement

None

Sources of funding

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Ethical approval

The article type (case report), the ethical approval was not necessary.

Consent

Obtained from the patient.

Registration of research studies

This is not an original research project involving human participants in an interventional or an observational study but a case report. This registration is was not required.

Provenance and peer review

Not commissioned, externally peer reviewed.

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