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Clinical Observations

# Hypoxic-Ischemic Encephalopathy Mimicking Acute Necrotizing Encephalopathy

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ABSTRACT

**BACKGROUND:** Acute necrotizing encephalopathy is a rare childhood syndrome associated with distinct and unifying neuroimaging features that are often used for the diagnosis of this entity. **PATIENT:** We describe a previously healthy 9-month-old girl who presented with upper respiratory symptoms, suspected seizures, and positive nasopharyngeal rapid antigen test for influenza A virus. Magnetic resonance imaging revealed signal abnormality in both thalami, bilateral caudate nuclei, brainstem tegmentum, subcortical white matter, and cerebellar hemispheres, suggestive of acute necrotizing encephalopathy. She subsequently had a cardiac arrest, was placed on extracorporeal membrane oxygenation, and treated with methylprednisone, intravenous immunoglobulin, and plasmapheresis without apparent clinical response. On autopsy, neuropathology showed evidence of hypoxic-ischemic injury but lacked evidence of hemorrhagic necrosis, which is typically associated with acute necrotizing encephalopathy. **CONCLUSION:** Combined clinical and neuroimaging features may be suggestive but not sufficient for the diagnosis of acute necrotizing encephalopathy.

***Keywords:*** acute necrotizing encephalopathy, pediatric, influenza, hypoxic-ischemic encephalopathy

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## Introduction

Acute necrotizing encephalopathy (ANE) is a rare childhood disease preceded by an acute febrile illness and characterized by the rapid onset of progressive symptoms including convulsions, vomiting, deteriorating consciousness, hepatic dysfunction, and ultimately resulting in coma. First reported in Japan in 1995, it has subsequently been recognized worldwide.[1] Proposed diagnostic criteria for ANE specify an acute encephalopathy after a febrile illness, deterioration of consciousness and convulsions, the absence of cerebrospinal fluid pleocytosis, a normal serum ammonia level, and imaging evidence for symmetric multifocal brain lesions of the thalami (Table 1).[2] Although there are no specific diagnostic markers, one of the most characteristic neuroimaging features include symmetric lesions affecting the bilateral thalami.[2] Additional lesions may also be found in the putamen, brainstem tegmentum, cerebellum, and deep periventricular white matter. Neuropathologically, vasogenic edema and hemorrhagic necrosis are typically located within the center of gray matter lesions.

Here we describe a child diagnosed with ANE based on a classic clinical presentation and neuroimaging findings who on postmortem lacked the neuropathologic features typically seen with this disorder. Neurohistopathology instead revealed global hypoxic-ischemic injury.

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**TABLE 1.**
Diagnostic Criteria for ANE (modified from Mizuguchi[2])

1. Acute encephalopathy following a febrile disease.
2. No CSF pleocytosis.
3. CT or MRI evidence of symmetric, multifocal brain lesions involving the thalami. Lesions also common in cerebral periventricular white matter, internal capsule, putamen, upper brainstem tegmentum, and cerebellar medulla.
4. Elevation of serum aminotransferases of variable degrees.
5. No increase in blood ammonia.
6. Exclusion of resembling diseases.

Abbreviations:
ANE = Acute necrotizing encephalopathy
CSF = Cerebrospinal fluid
CT = Computed tomography
MRI = Magnetic resonance imaging

## Patient Description

This 9-month-old African-American girl presented to the emergency department with suspected seizures after a 4-day prodromal illness with cough, rhinorrhea, and fever and a 1-day history of emesis. Two family members also had upper respiratory symptoms. Her immunizations were up to date, and she had received the seasonal influenza vaccine.

In the emergency department, a chest computed tomography (CT) suggested of pneumonia, and initial studies including a urinalysis were unremarkable. She was admitted to the general pediatric floor and given intravenous ampicillin. A respiratory rapid antigen test from a nasopharyngeal swab confirmed the presence of an influenza A infection, and oseltamivir was started.

The following morning, she developed focal seizures that included right facial droop, became unarousable, and her examination revealed miosis and decorticate posturing. She remained hemodynamically stable with no evidence of cardiac or respiratory decompensation. A head CT was unremarkable (not illustrated). Laboratory investigation showed elevated transaminase levels (aspartate aminotransferase level, 330 U/L; alanine aminostransferase level, 123 U/L), azotemia (blood urea nitrogen level, 38 mg/dL; creatinine, 0.6 mg/dL), elevated C-reactive protein (1.0 mg/dL), and thrombocytopenia (17,000 U/L). Normal studies included serum glucose, electrolytes on metabolic panel, lactate, urinalysis, and blood cultures.

Magnetic resonance imaging (MRI) performed 5 hours after head CT demonstrated numerous foci of restricted diffusion in the thalami and caudate nuclei bilaterally with associated swelling and mass effect on surrounding parenchyma (Fig 1). Additional restricted diffusion was

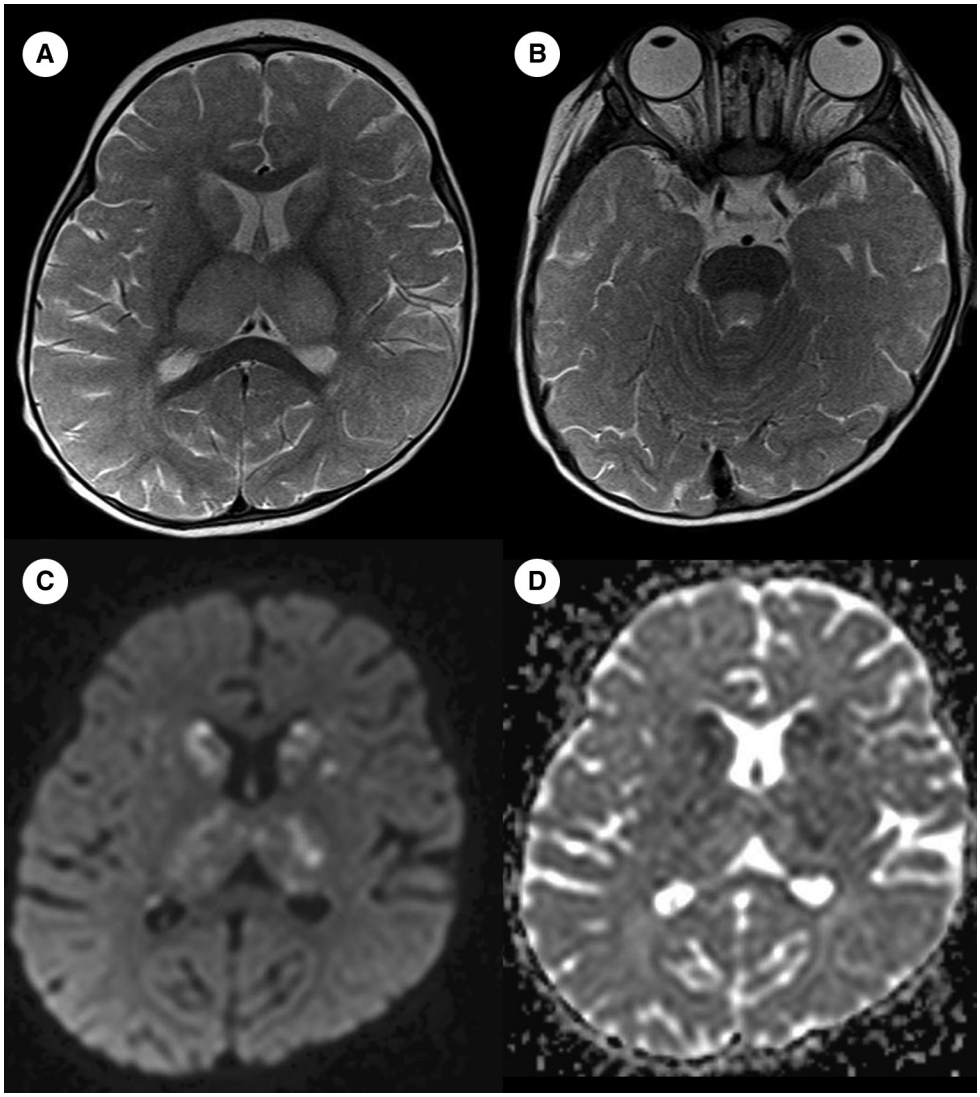


**FIGURE 1.**
$T_2$-weighted magnetic resonance imaging demonstrates increased signal intensity in the thalami, bilateral caudate nuclei, left anterior putamen (A), and brainstem tegmentum (B). Diffusion-weighted imaging (C) and apparent diffusion coefficient map (D) suggest associated regions of restricted diffusion.