Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion following SARS-CoV-2 Infection—A Rare Case Report

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Abstract

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a clinicoradiological syndrome first recognized during the influenza pandemic in Japanese population in the late twentieth century.[1]

In this article, we presented a rare case report of AESD in a young child due to severe acute respiratory syndrome coronavirus 2 infection (SARS-CoV-2) who presented with febrile status epilepticus, persistent encephalopathy, and had recurrence of seizures on day 4 of illness with characteristic magnetic resonance imaging findings and a relatively fair outcome

Keywords

- biphasic seizures
- bright tree appearance
- encephalopathy
- febrile status epilepticus
- late reduced diffusion
- SARS-CoV-2 infection

Introduction

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a syndrome characterized by febrile seizures and encephalopathy in the acute stage followed by recurrence of seizures and restricted diffusion in the subcortical white matter on magnetic resonance imaging (MRI) in the subacute stage.[1] It occurs most commonly due to infections with human herpes virus 6 and influenza viruses.[2,3]

The likely pathogenesis of AESD is excitotoxic neuronal injury followed by delayed neuronal death, vasospasm, and mitochondrial dysfunction.[3]

It is predominantly reported from Asia; it may mimic other causes of acute encephalitis syndromes (AES).[1–3] Neurological morbidity is high in AESD, although mortality is infrequent.[1] This diagnosis needs consideration in a child with prolonged febrile seizures with persistent encephalopathy. Characteristic MRI findings help clinch the diagnosis.

Methods

Patient details were retrieved using a retrospective chart review. Informed consent was obtained from the child's parents.

Case Report

A 1.10-year-old male child patient with premorbid normal development presented to our hospital with febrile status epilepticus (SE) requiring ventilator support.

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He tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcription polymerase chain reaction (RT-PCR). Initial computed tomography and MRI brain were normal (►**Fig. 1**). The cerebrospinal fluid analysis including multiplex PCR was normal.

Child remained encephalopathic with intermittent stereotypic movements.

On day 4 of admission, child had recurrence of seizures in clusters. Repeat MRI brain showed restricted diffusion of white matter and corpus callosum including bilateral perirolandic areas and subcortical U fibers characteristic of "bright tree appearance" (BTA) suggestive of AESD (►**Fig. 2**). Electroencephalogram showed diffuse slowing with intermixed polyspike wave discharges in bilateral posterior head regions (►**Fig. 3**).

Laboratory investigations showed elevated transaminase levels: serum glutamic oxaloacetic transaminase -max. at 135 U/L and thrombocytosis. Workup for demyelination and autoimmune panel came negative.

He was treated with antiseizure medications (ASM), intravenous immunoglobulin (IVIG 2 g/kg), pulse methylprednisolone, vitamins (B1, B6, and carnitine), and standard supportive care.

Beyond the acute phase, he developed neurological sequelae in the form of developmental regression, hypertonia, bruxism, cortical visual impairment (CVI), and sleep disturbances. Subsequently, child was discharged with nasogastric feeds, multiple ASMs, physiotherapy, and visual stimulation exercises.

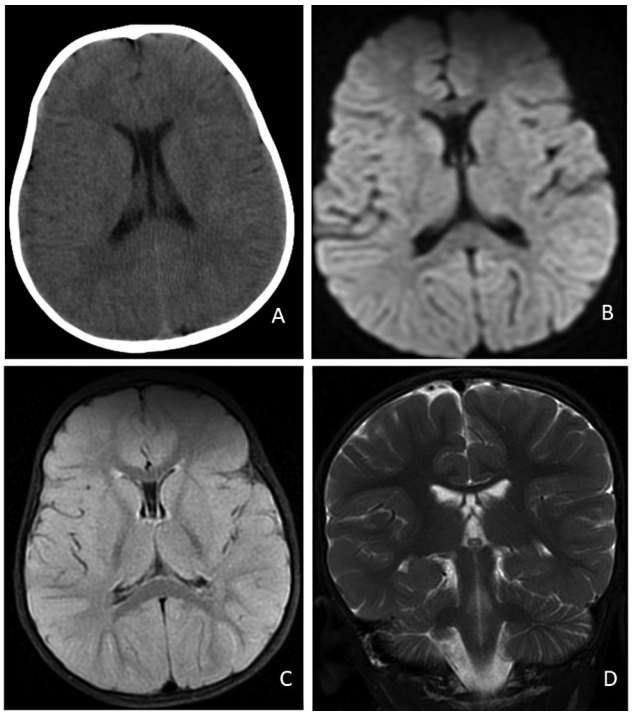

Fig. 1 (**A**) Computed tomography scan of the brain on day 1 of illness—axial view appears normal. (**B**, **C**) Magnetic resonance imaging brain—axial diffusion-weighted image and fluid-attenuated inversion recovery sequence showing no areas of restricted diffusion or abnormal signal changes, respectively. (**D**) Coronal T2-weighted sequence showing no abnormality.

He had a gradual recovery, following intense neurorehabilitation.

At 1-year follow-up, he had independent ambulation, speech comprehension, and minimal vocabulary; however, his residual CVI remained.

Discussion

AESD is a distinct clinical–radiological syndrome with fever-associated biphasic seizures and characteristic MRI findings on days 3 to 14 of illness.[1] It most commonly follows SE but is also infrequently seen after short seizures.[3] Infants are commonly susceptible probably due to the immaturity of their brain.

AESD is infrequently reported from the Indian subcontinent secondary to viral infections like dengue and influenza.[2,4] To the best of our knowledge, this is the first report of AESD from India secondary to SARS-CoV-2 infection.

Okumura et al[5] divided AESD into two types based on the pattern of brain lesions, that is, diffuse type—involving the cortical and subcortical white matter of bilateral hemispheres giving the BTA like in our case, and central sparing type—with lack of reduced diffusion in the perirolandic areas.

BTA on MRI brain has also been described in other conditions like infantile traumatic brain injury where it is termed as infantile traumatic brain injury with a biphasic clinical course and late reduced diffusion,[6] septic encephalopathy,[7] and neonatal rotaviral encephalitis.[8] Transient BTA has been reported in the acute phase in an anecdotal report of *CLCN2*-related leukoencephalopathy.[9]

Neuromorbidity is generally severe not only in patients with diffuse involvement of the brain compared with the central sparing type but also in those patients with prolonged seizures than those with shorter seizure duration[3]

There is no specific therapy for AESD. Apart from standard supportive care, mitochondrial rescue and dextromethorphan (N-methyl-D-aspartate receptor antagonist) have been used anecdotally with some success.[10,11] IVIG, pulse methylprednisolone, and mitochondrial rescue with vitamin cocktail were used in our patient.

AESD mimics other acute encephalopathies or febrile SE initially. One should suspect AESD in a child with initial febrile seizure, with persistent encephalopathy or high transaminase levels, especially if biphasic seizures with distinctive MRI brain pattern are seen around day 4. Biomarkers for prompt diagnosis like glutamate levels on proton magnetic resonance spectroscopy need to be established. Intensive care and neurorehabilitation to harness the neuroplasticity of the brain may improve prognosis.

Conflict of Interest
None declared.

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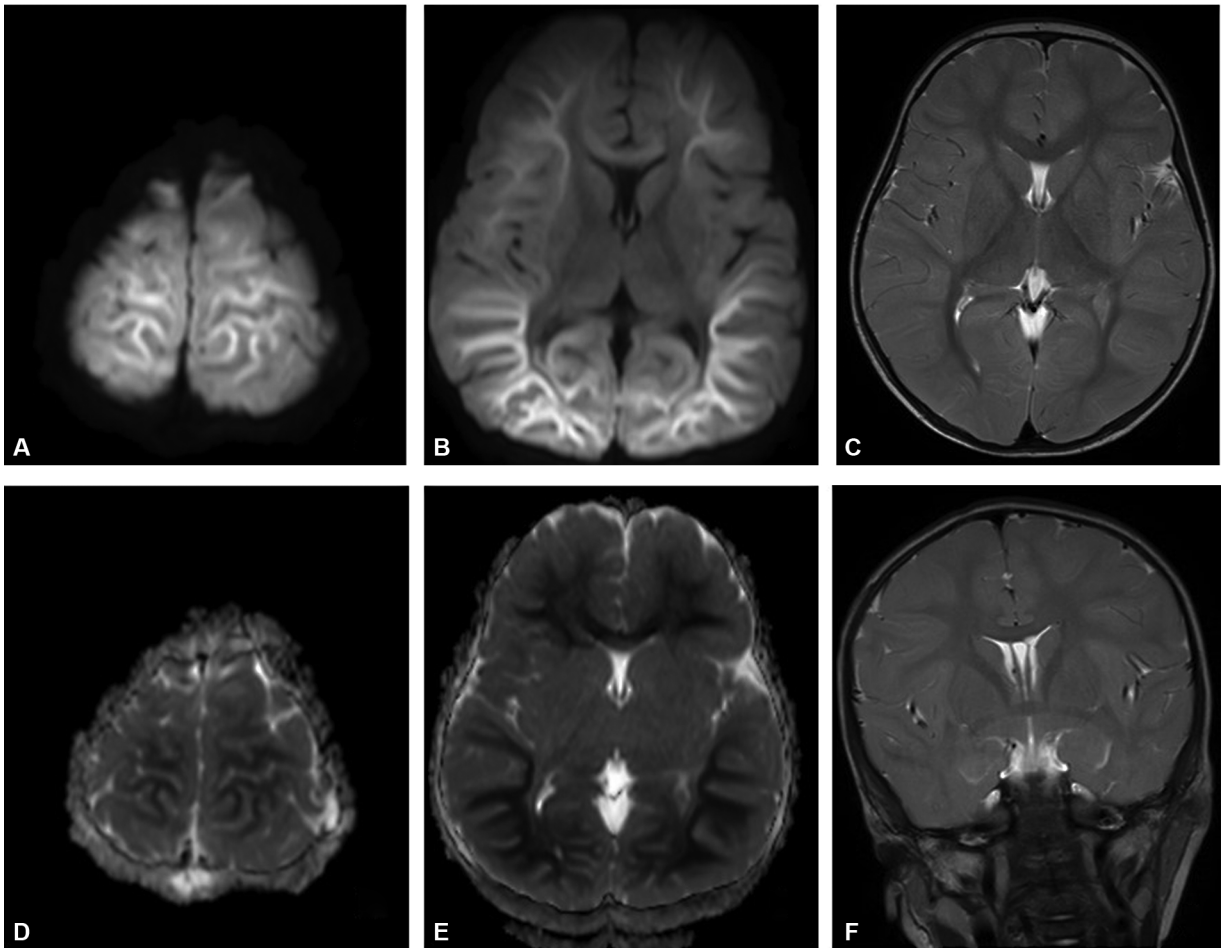

Fig. 2 Magnetic resonance imaging brain done on day 4 of illness. Axial diffusion-weighted imaging (**A**, **B**) and corresponding apparent diffusion coefficient maps (**C**, **D**) showing diffuse restricted diffusion of subcortical white matter including U fibers and perirolandic areas with "Bright tree appearance." (**E** and **F**) Axial and coronal T2-weighted images showing sparing of basal ganglia.

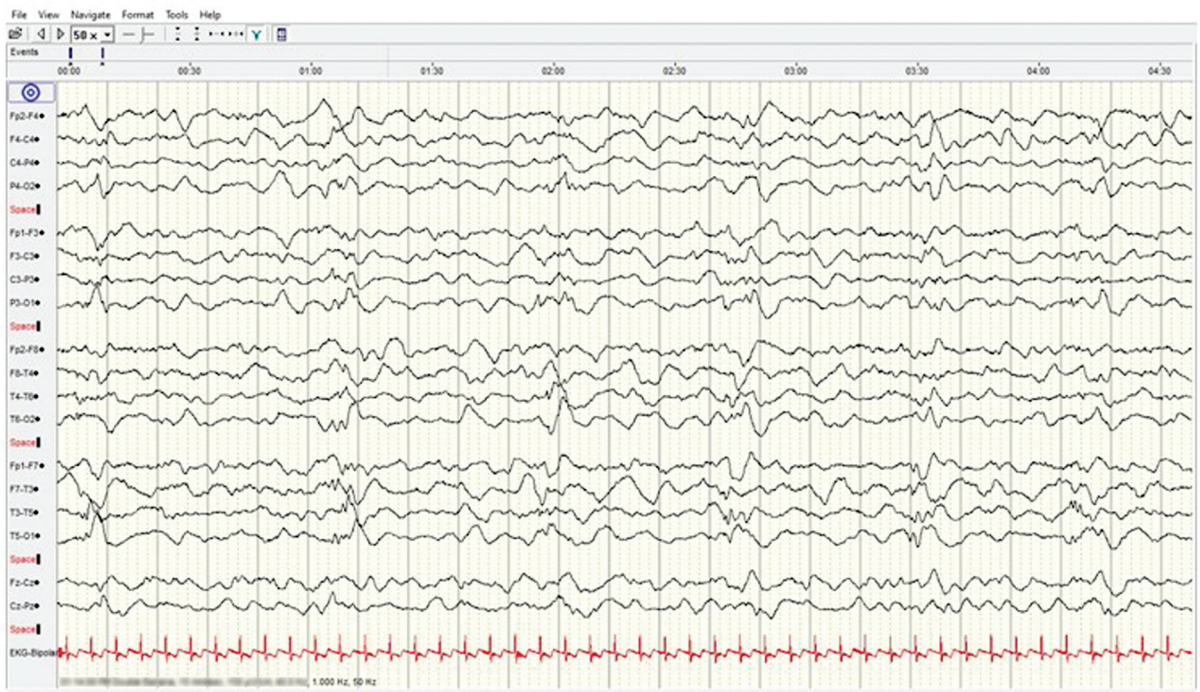

Fig. 3 Electroencephalography done on day 4 showing diffuse slowing with intermixed polyspike wave discharges in bilateral posterior head regions.

Dr. Pramod Krishnan, Consultant Neurologist, and Mr. Mohan Dass, Pediatric Physiotherapist, Manipal Hospital, in the acute treatment and rehabilitation of the patient discussed in this article.

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