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CLINICAL BRIEF

Acute Infantile Encephalopathy Predominantly Affecting the Frontal Lobes (AIEF)

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Abstract Acute Infantile Encephalopathy Predominantly Affecting the Frontal Lobes (AIEF) is a relatively recent described entity. This article includes case reports of two patients who had bifrontal involvement during acute febrile encephalopathy. Case 1 describes a 1-y-old boy who presented with hyperpyrexia and dialeptic seizures. Imaging revealed significant bilateral frontal lobe involvement while serology proved presence of Influenza B infection. Over a period of one wk, he recovered with significant cognitive decline and perseveratory behavior. Another 6-y-old boy presented with language and behavioral problems suggestive of frontal dysfunction after recovering from prolonged impairment of consciousness following a convulsive status epilepticus. Bilateral superior frontal lesions with gyral swelling was evident on neuroimaging. These cases are among the very few cases of AIEF described in recent literature and the article also reviews this unique subtype of acute encephalopathy.

Keywords Acute encephalopathy · Predominantly affecting frontal lobes

Introduction

Encephalitides in childhood presents as impairment of consciousness in the context of fever [1]. The organisms causing encephalitides are often viral but lately there is a growing list of clinico-radiological syndromes that are thought to be viral associated encephalopathies. Acute Infantile Encephalopathy predominantly affecting the Frontal lobes (AIEF) is one of them.

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Case Reports

Case 1

A 1-y-old boy presented with complaints of high grade fever, cluster of prolonged generalized seizures and frequent brief episodes of behavioral arrest. His birth, past medical and developmental history was normal. He was fully vaccinated.

Investigations revealed normal hemogram, smear for malarial parasites, Chest radiograph, electrolytes, glucose, ammonia, liver and renal function tests. CSF (cerebrospinal fluid) analysis was normal and HSV (herpes simplex virus) was not detected. Plasma lactate was high once (25.1 mg/dl against normal range of 5.0 to 22.0).

Cranial MRI (Magnetic Resonance Imaging) revealed symmetrical signal abnormality of both frontal lobes involving cortex and white matter along with restricted diffusion in bilateral frontal white matter (Fig. 1a).

Video EEG (Electroencephalogram) confirmed absence seizures with frontally dominant generalized ictal activity (Fig 2).

Treatment included parenteral antiepileptics and Ceftriaxone, which was given till cultures became sterile.

On recovery he had regressed in his verbal/nonverbal communication, had developed obsessive traits and hand/mouth stereotypies. Serology by immunofluorescence demonstrated recent infection with Influenza B virus.

Three wk from the onset of illness, behavioral observation by a clinical psychologist confirmed his autistic

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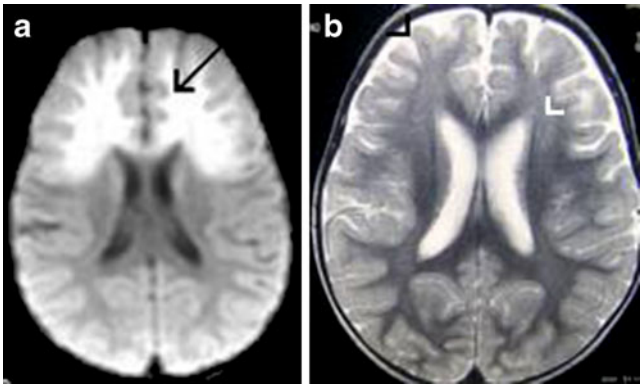

Fig. 1 **a** MRI (Magnetic Resonance imaging) done at day 5 of illness in a 1-y-old boy with Acute Infantile Encephalopathy predominantly affecting the frontal lobes (AIEF) shows restriction of diffusion in bilateral frontal lobes (*black arrow*) in Diffusion weighted Imaging (DWI). **b** A repeat Magnetic resonance imaging (MRI) performed 6 mo from the illness shows gyral thinning (*black arrow head*) at the frontal cortical convexity and signal changes in adjacent white matter (*white arrow head*). T2 weighted image

features. Childhood autism rating scale showed a score of 25; Childhood autism checklist (CHAT) scores were 65%; both suggestive of mild autism with loss of communication skills. A repeat imaging, 6 mo later showed bifrontal gyral thinning and signal changes in adjacent white matter (Fig. 1b). At 1 y follow up the child had only mild language delay.

Case 2

A 6-y-old boy presented with abnormal behaviour, reduced speech output and new onset left hand use. About a month prior the child had an upper respiratory tract infection with high grade fever. On day 3 of illness he developed generalized tonic–clonic status epilepticus lasting 2 h. He remained in altered sensorium for a few days, while hemodynamically stable and was given parenteral antiepileptic drugs. Investigations for viral and bacterial causes of encephalopathy were negative and metabolic workup was not performed.

Neuroimaging revealed bilateral superior frontal cortical lesions extending into parasagittal cortex with significant gyral swelling (Fig. 3).

He had a mild right hemiparesis; his cognitive skills were relatively intact. Neuropsychological assessment revealed—He was partially cooperative for assessment; his comprehension was adequate for simple small direct questions; he had echolalia, echopraxia and compulsive behavior suggestive of frontal lobe dysfunction.

The child attained a verbal Intelligence quotient (IQ) of 94 (normal range) but performance IQ could not be completed as he had significant perseveration. Color cancellation task indicated moderate impairment of sustained attention. Motor coordination was found to be inadequate. He had adequate ability for expressive, repetitive, nominative speech and inadequate narrative speech. A repeat testing done 10 mo from onset of illness showed complete recovery.

Discussion

Mizuguchi and Yamanouchi et al. first described Acute Infantile Encephalopathy predominantly affecting the frontal lobes (AIEF) in 2006 [1, 2].

Their proposed diagnostic criteria include 1) Acute encephalopathy in infancy and early childhood following a

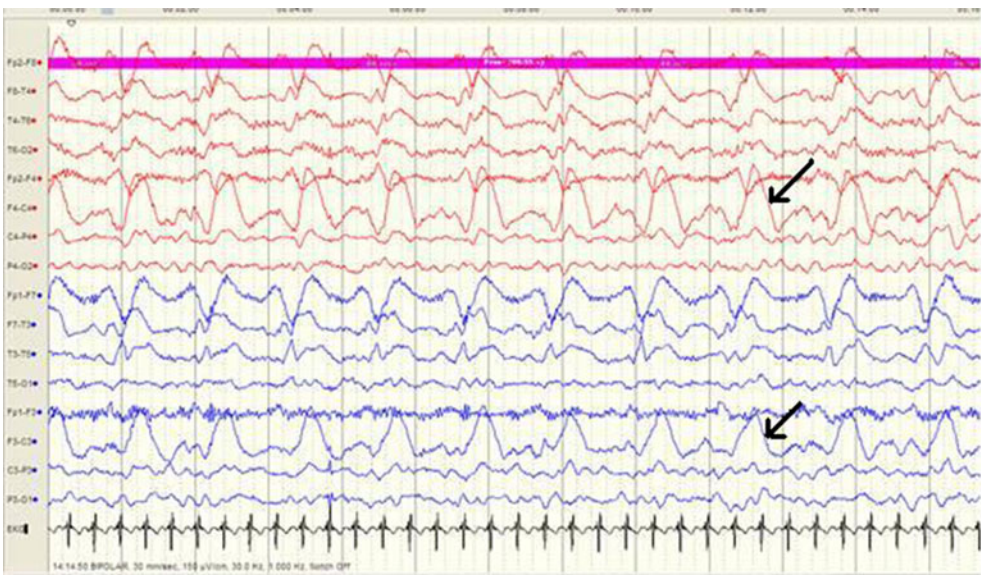

Fig. 2 Video EEG (Electroencephalogram) recorded absence-like seizures with presence of frontally dominant generalized ictal activity in a 1-y-old boy with Acute Infantile Encephalopathy predominantly affecting the frontal lobes (AIEF)

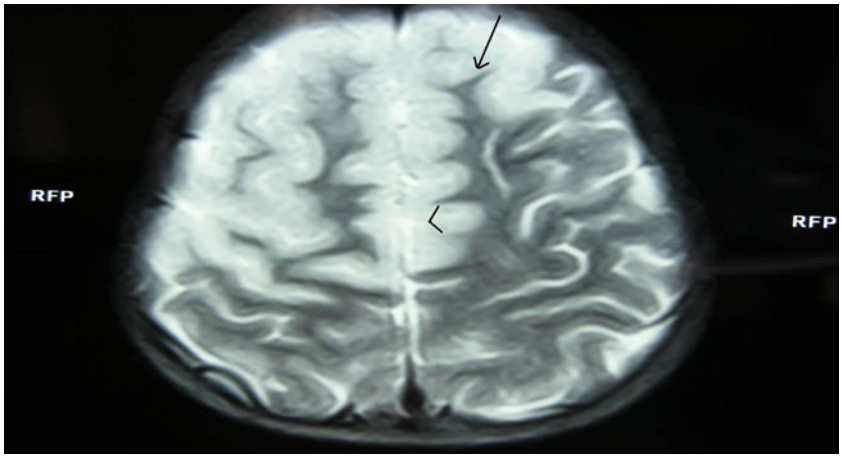

Fig. 3 Magnetic resonance imaging (MRI) performed in a 6-y-old boy 15 d from the onset of illness shows bilateral superior frontal cortical lesions (*arrow*) extending into parasagittal cortex (*arrow head*) with significant gyral swelling suggestive of Acute Infantile Encephalopathy predominantly affecting the frontal lobes (AIEF)

febrile illness due to viral infection. 2) Neurological manifestations suggesting frontal lobe dysfunction. 3) Radiological features showing selective involvement of the cortex in the frontal lobes. 4) Absence of laboratory and radiological findings for infections, inflammatory disease of the brain and systemic metabolic disorder [2].

Both of the present patients had acute febrile encephalopathy followed by frontal lobe dysfunction in form of regression of verbal functions, stereotypies or perseveratory behavior; MRI revealed selective frontal lobe involvement and there was absence of any other infection, inflammation or metabolic derangement. Moreover Case 1 had evidence of Influenza B infection. Mild lactatemia once noted in Case 1 could be secondary to seizures during the acute illness.

One patient was 6-y-old, unlike those described by Yamanouchi et al. wherein the oldest child was a 3-y-old [1]. This may suggest that late childhood presentation of AIEF is possible; but since majority of affected children are infants, the term AIEF is appropriately coined.

Among the patients described by Yamanouchi et al., 7 out of 9 had retardation of language development 12 mo after follow up; both of the present patients recovered almost completely, 12 and 10 mo after the acute event [1].

Virus associated encephalopathies are not due to direct viral invasion or due to conventional immune dysfunction like Acute disseminated encephalomyelitis. The various subtypes include Acute Necrotising Encephalopathy (ANE), Hemorrhagic Shock Encephalopathy Syndrome (HSE), Reye like Syndrome, Hemiconvulsion Hemiplegia Epilepsy syndrome (HHE) and Acute Infantile Encephalopathy predominantly affecting Frontal lobes (AIEF).

The clinical syndrome of AIEF has been found to be associated with either influenza or HHV-6 (human herpes virus 6) [2–4]. Sato et al. described a similar syndrome with influenza A infection with normal MRI but decreased function in bilateral frontal lobes in single photon emission computed tomography (SPECT) [5]. Yamanouchi et al. found an association with Influenza A and HHV 6 infection in 6 out of 10 patients [2]. A study of influenza associated encephalopathy from Canada showed dual infection with Influenza and M. Pneumoniae in five children [6].

The pathologic event is excitotoxic delayed neuronal death [3]. In a study done in patients of influenza associated encephalopathy, serum tumor necrosis factor-á (TNF á) and cytochrome *c* values were high [7]. Very high levels of TNF á and Interleukin 6(IL 6) are associated with ANE or HSE; in AIEF some increase in serum and CSF IL-6 has been detected [3, 8]. In Japan, methylprednisolone and Immunoglobulin have been used in these patients to suppress cytokine activity.

AIEF does exist beyond Japan; and possibly has a more favorable outcome. Influenza vaccine now being available, further studies to prove definite association may be of significance.

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Conflict of Interest None.

Role of Funding Source None.

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