Probable fulminant subacute sclerosing panencephalitis in a vaccinated 8-year-old girl: Clinical, radiological features and response to treatment

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Sri Lanka Journal of Child Health, 2022; **51**(4): 617-620
DOI: http://dx.doi.org/10.4038/sljch.v51i4.10383
(Key words: Subacute sclerosing panencephalitis, SSPE, Fulminant SSPE, Measles vaccination, Anti-viral treatment)

Introduction

Subacute Sclerosing Panencephalitis (SSPE) is a destructive cerebral disease due to persistent measles virus infection, usually following a latent period of 7-10 years. It usually has a four-stage, slow progressive deteriorating course[1]. In contrast, fulminant SSPE presents with progressive encephalopathy with a rapidly descending course leading to death within 6 months[2]. Measles vaccination in Sri Lanka has made SSPE an almost non-existent neurological sequela. However, rare cases have been reported in fully vaccinated children without a history of measles[3]. We report a case of fulminant SSPE with rapid progression in an 8-year-old girl who had been fully vaccinated for measles, with no previous measles infection, in whom treatment with ribavirin and interferon-alpha prevented a fatal outcome.

Case report

An 8-year-old girl, vaccinated with measles, mumps and rubella (MMR) vaccine at 1 and 3 years of age, with no history of measles, was admitted with complex partial seizures on the left side. She gave a one-month history of behavioural change and myoclonic jerks in the left upper limb for a week before admission. Controlling her seizures was difficult, and she rapidly became encephalopathic with a deteriorating Glasgow Coma Scale (GCS) score, requiring intubation and ventilation.

Cerebrospinal fluid (CSF) analysis revealed no abnormality (1 lymphocyte and no significant sugar difference) except a mildly elevated protein level of 57mg/dL (normal up to 40mg/dL). Tests for Japanese encephalitis, herpes simplex virus, and anti–N-methyl- d-aspartate receptor antibodies were negative. Blood and CSF cultures yielded no growth but she had very high anti-measles IgG antibodies >5000 IU/l. Electroencephalography (EEG) showed periodic waves characteristic of 'Radermecker complexes' with symmetrical high voltage polymorphic delta waves occurring at 4-6 seconds in a background of generalized slowing (Figure 1).

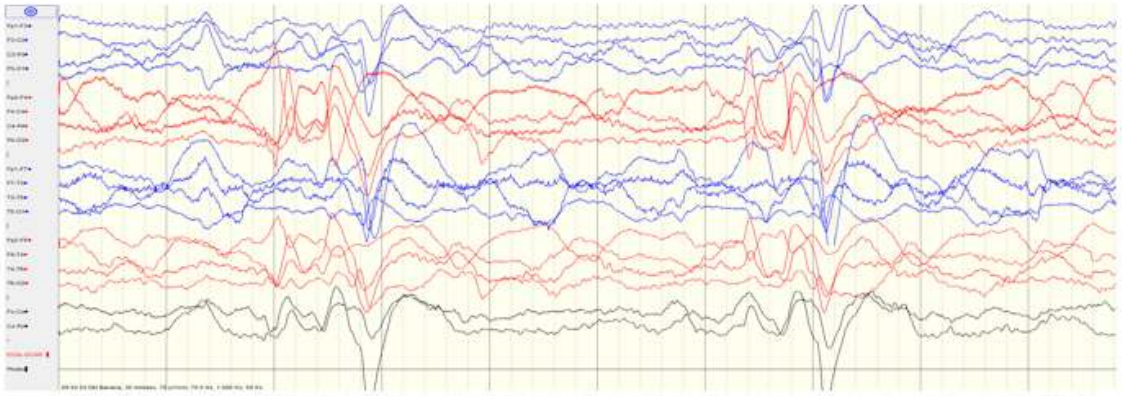

Figure1: ***Electroencephalogram in longitudinal bipolar montage showing characteristic "Radermecker" complexes***

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(Received on 13 December 2021: Accepted after revision on 21 January 2022)
The authors declare that there are no conflicts of interest
Personal funding was used for the project.

Brain magnetic resonance imaging (MRI) showed asymmetric confluent areas of transverse relaxation time-2 weighted (T2W) and fluid-attenuated inversion recovery (FLAIR) hyperintensities in periventricular and subcortical white matter mainly in the frontal and parietal lobes. Lesions were hypointense in the transverse relaxation time-1 weighted (T1W) sequences and did not show diffusion restriction or enhancement after contrast. The genu and anterior part of the body of the corpus callosum also showed abnormal signal intensities. The basal ganglia, thalami, and brain stem demonstrated normal signal intensities (Figure 2, A and B). Multi-voxal Magnetic Resonance Spectroscopy (MRS) obtained from lesions of the left frontal lobe revealed a prominent decrease in the N-acetyl aspartate (NAA)/creatine ratio with increased choline and lactate (Figure 2C).

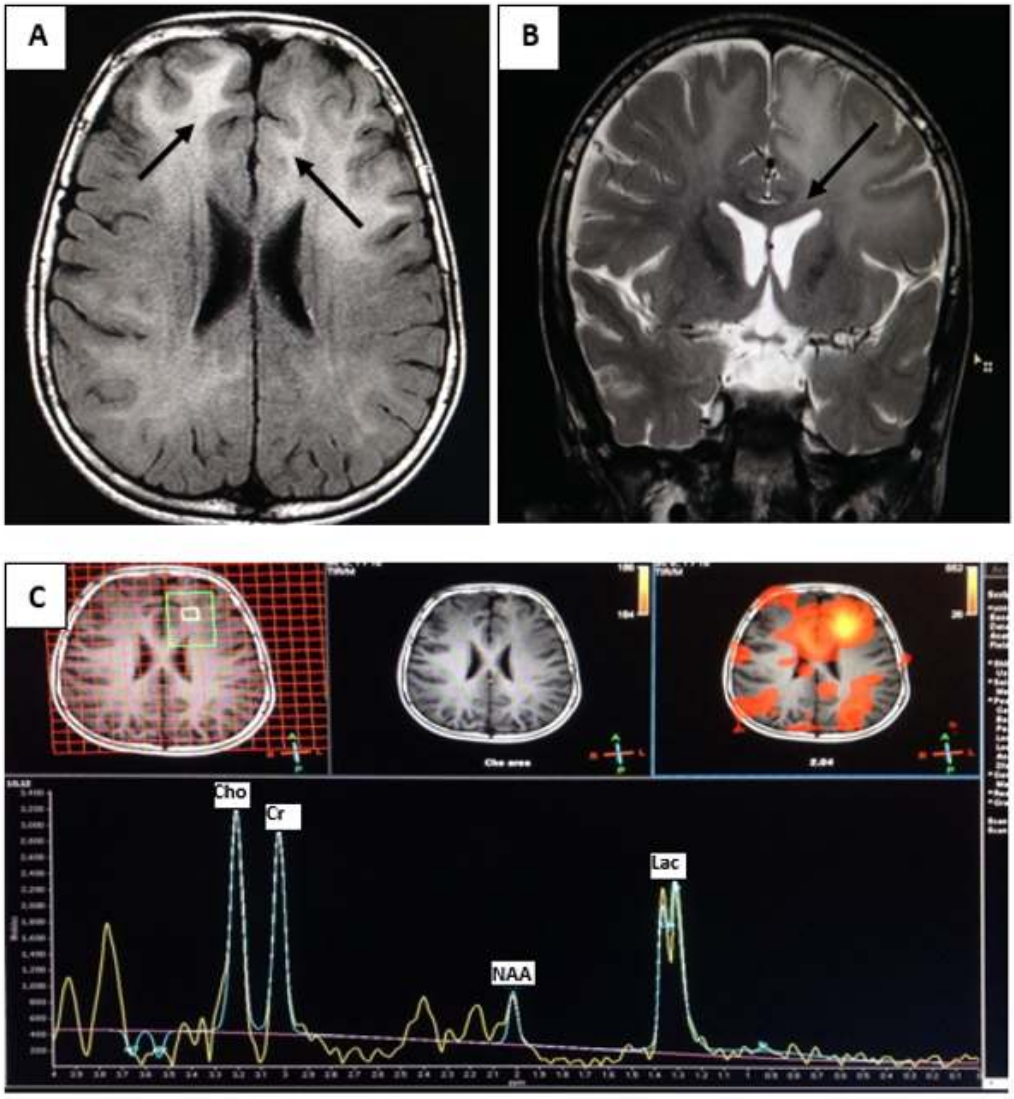

Figure 2: ***Magnetic resonance imaging of brain and magnetic resonance spectroscopy (MRS)***

A- Fluid-attenuated inversion recovery (FLAIR) axial image with white matter hyperintensities in bilateral frontal and parietal lobes

B- Time-2 weighted (T2W) coronal image hyperintensities in frontal lobes and corpus callosum.

C- MRS showing elevated choline (Cho) and lactate (Lac) peaks with decreased N-acetyl aspartate (NAA)

After starting on oral ribavirin and intrathecal interferon-alpha through an ommaya reservoir, there was a marked improvement and she became seizure-free and was extubated two weeks later with improvement in the GCS score. Three months later, with continuous treatment with ribavirin and monthly interferon injections, she was stable. Myoclonic jerks were absent, she was seizure-free and she was responsive to mother with vocalization.

This case was reported to the epidemiology unit due to its public health importance.

Discussion

SSPE is diagnosed using Dyken criteria[5] (requires two major criteria and one minor criterion) and fulminant SSPE is present when there is a progressive neurological deficit of more than 66% in three months or death within 6 months of onset[2]. In this case, there was one major criterion with a rapidly progressive history and one minor criterion (EEG findings characteristic of 'Radermecker' complexes). It was difficult to appreciate the other major criterion which requires CSF anti-measles antibodies to be elevated greater than or equal to 1:256 in serum as there were very high anti-measles antibody titres in both blood and CSF. However, an acute infection with measles was unlikely. MRI changes matched reported findings from other case series. MRS findings of reduced NAA/ creatine ratio with increased choline, myo-inositol, and lactate are commonly demonstrated and have aided early diagnosis of SSPE[6].

This case was further subclassified as a case of acute fulminant SSPE due to the brief duration of early stages and rapid progression to encephalopathy. Acute fulminant SSPE is a diagnostic challenge due to the rarity of cases, atypical presentations, misleading clinical findings and not fulfilling Dyken criteria all the time; hence a high index of suspicion is needed, especially in patients presenting with features of acute encephalitis. Most reported cases have succumbed to the illness within a very short duration[2].

The index case had been fully vaccinated for measles and did not have a history of measles. Thus it was a dilemma why she developed SSPE. Strong evidence from epidemiological and genetic studies indicates that the measles vaccine strain does not cause SSPE and is attributed to the strain of wild-type virus prevalent in that geographical region[4]. In our case, a subclinical infection cannot be ruled out, due to a variant of mutant measles virus, poor seroconversion, or vaccine failure. However, a more likely event would be an asymptomatic infection before vaccination, and Sri Lanka faced a large outbreak of measles infections in 2013-2014[7] during this child's first year of life. This needs further investigation as this may have implications for our immunization schedule.

Without initiation of treatment with ribavirin and interferon, our child's condition would have rapidly progressed and would have been fatal. Recent trials of treatment with ribavirin, isoprenosine and interferon have shown promise in combating this fatal disease[8].

In conclusion, this case illustrates a rare presentation of an acute fulminant SSPE responding to ribavirin and interferon in a fully vaccinated child, which needs further discussion and study in the backdrop of measles being declared eradicated in Sri Lanka.

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