Case Report

A Rare Case of Acute Encephalopathy with Biphasic Seizures and Late Diffusion Restriction

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DOI: http://dx.doi.org/10.21276/ijcmsr.2021.6.3.5

How to cite this article: Vihag Raman, Nipun Gumber. A rare case of acute encephalopathy with biphasic seizures and late diffusion restriction. International Journal of Contemporary Medicine Surgery and Radiology. 2021;6(3):C20-C22.

A B S T R A C T

Introduction: Acute encephalopathy with biphasic seizure and late diffusion restriction (AESD) is a rare encephalopathy mostly reported in Japan, but has recently been reported in Asian pediatric age group. It is characterized by prolonged febrile seizure lasting for > 30 minutes in the acute stage (day 1) and followed by cluster of complex partial seizures in subacute phase (4-6 days). Affected children show variable neurological outcome. The exact pathogenesis is uncertain. However, etiology has been attributed to viral infections, mainly Influenza A and Human Herpes Virus 6. It is during the subacute phase that MR findings of diffusion restriction in bilateral cerebral hemispheres are evident.

Case Report: A 10 month old child with complaints of seizure and high grade fever was evaluated with MRI study of brain and short interval follow up scan. On basis of clinico-radiological correlation, diagnosis of AESD was made.

Conclusion: We highlight this case report for its rarity. This identity should be considered as a differential diagnosis for acute encephalopathy in pediatric age group. Clinico-radiological approach is required for establishing a diagnosis.

Keywords: Acute Encephalopathy, Biphasic Seizure, Late Diffusion Restriction, Magnetic Resonance Imaging and AESD.

INTRODUCTION

A 10 month old child presented with clinical history of seizure and high grade fever. MR imaging of the brain during subacute phase revealed symmetrical areas of diffusion restriction involving the bilateral cerebral subcortical white matter with sparing of perirolandic region and basal ganglia. Follow up MRI after 6 weeks showed resolution of diffusion abnormalities with mild generalized cerebral atrophy.

The etiology for AESD has been attributed to viral infections, mostly Influenza A and Human Herpes Virus 6 (HHV-6).[1] The exact pathogenesis of AESD in unknown. The proposed hypothesis behind this is excitotoxic injury with delayed neuronal death.[2]

CASE REPORT

A previous healthy, full term born 10 month old child presented to department of radiodiagnosis with clinical history of generalized tonic clonic seizure lasting for around 20-30 minutes and consistent high grade fever for first 2-3 days. On day 5, child presented with multiple episodes of complex partial seizures. CT scan of the brain done on day 2 of symptoms was unremarkable. Patient was clinically drowsy and in post ictal state. Blood and CSF examination did not reveal any infectious etiology. CRP was negative (2.84). Liver function test showed mild increase in SGOT, SGPT and ALP levels.

MR imaging of brain done on 6th day, showed extensive bilateral symmetrical areas of diffusion restriction with low ADC (Fig. 3 and 4) involving the bilateral cerebral subcortical white matter with sparing of perirolandic region and basal ganglia. Similar signal changes were also seen in splenium of corpus callosum. Corresponding T1 (Fig. 1) and T2 weighted images revealed no abnormal signal intensity changes. Infratentorial brain parenchyma was unremarkable. Patient was put on steroid therapy and showed clinical improvement, but did not return to complete normal mental status. Follow-up MRI was done after 6 weeks which revealed complete resolution of diffusion restriction with mild generalized atrophy.

Based on clinic-radiological approach, diagnosis of acute encephalopathy with biphasic seizure and late diffusion restriction was made. Other close differentials were ruled out. Possibility of hypoxic ischemic injury was ruled out by sparing of basal ganglia, thalamus and perirolandic region. Metabolic disorders like metachromatic leukodystrophy was ruled out on clinical history of no milestone regression. Toxic leukoecephalopathy (drug induced) was also ruled out.

DISCUSSION

Acute encephalopathy with biphasic seizures and late diffusion restriction (AESD) is a well known clinic-radiological syndrome to pediatrician and pediatric neurologists. This entity is characterized by prolonged seizure with fever for 1-2 days (acute stage) followed by worsening of clinical state

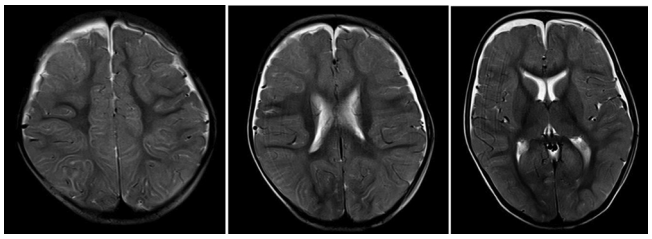

Figure-1: T2 weighted images do not reveal any significant signal intensity changes.

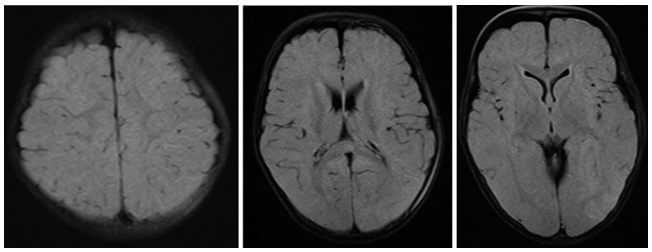

Figure-2: FLAIR images show mild hyperintensities in the subcortical white matter.

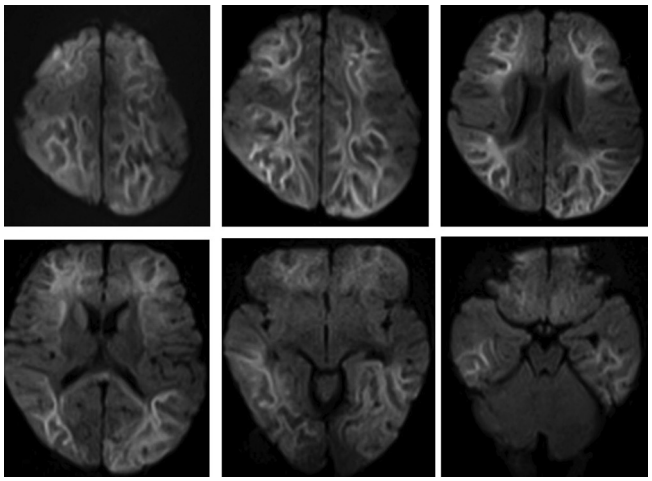

Figure-3: Diffusion weighted images show diffuse areas of symmetrical hyperintensities in the bilateral subcortical white matter with sparing of basal ganglia and perirolandic region.

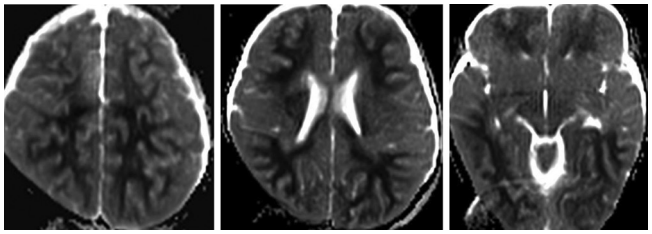

Figure-4: Corresponding ADC (apparent diffusion coefficient) maps show hypointensity in the areas of true diffusion restriction (bilateral subcortical white matter with spared basal ganglia and perirolandic region).

with cluster of seizures and altered sensorium for 3-9 days later.[1,3] This subacute phase is identified by areas of restricted diffusion on MR imaging.

Etiology has mostly been attributed to viral infections namely Influenza A and Human Herpes Virus- 6. Exact pathogenesis is uncertain. However, the proposed

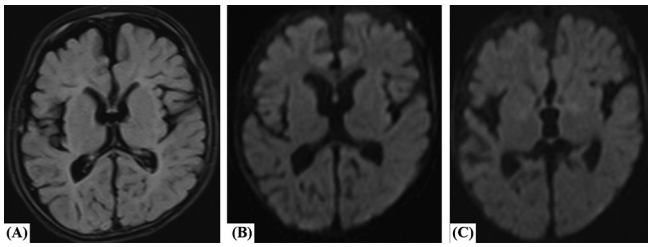

Figure-5: FLAIR (A) and diffusion weighted images (B,C) of the brain done after 6 weeks shows resolution of diffusion abnormalities with mild generalized cerebral atrophy.

pathogenesis is excitotoxic injury with delayed neuronal death, which may be supported by cytokine profile of CSF. CSF cytokine analysis in AESD shows elevated interleukin (IL) - 6 without elevated IL - 10 (an anti-inflammatory cytokine). This profile is different from a cytokine storm seen in inflammatory cases which shows elevated IL-6, IL-10 and sTNFR1 (soluble tumor necrosis factor receptor 1).[4] Few cases of bacterial etiology (streptococcus pneumonia) have also been reported.[5]

MR imaging findings in initial presentation and before secondary cluster seizures is generally normal.[6] In subacute phase (after cluster seizures), MRI shows restricted diffusion with hypointensity on ADC in the bilateral subcortical white matter, predominantly in the fronto-parietal region. T2 WI / FLAIR images show mild hyperintensities in the cortex and white matter. Follow up MR imaging after 3-4 weeks shows resolution of diffusion restriction with development of cerebral atrophy.[6]

Recently Okumura[6] has described two distinct patterns of AESD on MR imaging: Central sparing lesions and diffuse lesions. Diffuse lesions / AESD are characterized by reduced diffusion in the cortex and/or subcortical white matter of bilateral cerebral hemispheres. Central sparing lesions / AESD are defined by lack of diffusion restriction in the perirolandic region and sylvian fissures. Patients with central sparing type show less severe phenotype of acute encephalopathy with mild laboratory abnormalities. In both types, no diffusion restriction is seen in basal ganglia and thalami.

On MR spectroscopy, Glx (glutamine/glutamate complex) appears elevated in subacute stage and normalized in later stage. Elevated Glx causes excitotoxic neuronal damage.[7] Separation of Glu from Gln is impossible at 1.5 T MRI. NAA (N-acetylaspartate) appears low in end of first week and may remain low in lateral stages as well suggesting permanent neuronal damage, which is likely related to neurological sequelae and atrophy on follow up MRI. Elevated Cho (choline) peak is a marker for demyelination or cell membrane disruption.[8] In patients with mild AESD, Cho peak may normalize by day 14 reflecting minimal damage to myelin. It is therefore suggested that MR spectroscopy might be predictive of neurological outcome.

Reduced diffusion in bilateral hemispheres can also be seen in other causes, such as hypoxic ischemic encephalopathy and metabolic causes. Toxic encephalopathy may also show similar imaging abnormalities. It is therefore suggested that a diagnosis of AESD show be made only after considering

ISSN (Online): 2565-4810; (Print): 2565-4802 | ICV 2019: 98.48 |

clinical symptoms, examination and laboratory findings along with MR imaging abnormalities.

CONCLUSION

AESD should be kept in mind as a differential diagnosis of acute encephalopathy in pediatric age group. Definite diagnosis can be made by clinico-radiological correlation with MRI imaging and MR spectroscopy during the subacute phase of the disease. MR spectroscopy can prove beneficial in predicting neurological outcome.

REFERENCES

1. Takanashi J, Oba H, Barkovich AJ, Tada H, Tanabe Y, Yamanouchi H, et al. Diffusion MRI abnormalities after prolonged febrile seizures with encephalopathy. Neurology. 2006; 66(1):1304–9.
2. Mizuguchi M, Yamanouchi H, Ichiyama T, et al. Acute encephalopathy associated with influenza and other viral infections. Acta Neurol Scand 2007; 115(5):45–56.
3. Takanashi J, Tsuji M, Amemiya K, et al. Mild influenza encephalopathy with biphasic seizures and late reduced diffusion. J Neurol Sci 2007; 256(1):86 –89.
4. Ichiyama T, Suenaga N, Kajimoto M, et al. Serum and CSF levels of cytokines in acute encephalopathy following prolonged febrile seizures. Brain Dev 2008; 30(3):47–52.
5. Kuwata S, Senzaki H, Urushibara Y, Toriyama M, Kobayashi S, Hoshino K, et al. A case of acute encephalopathy with biphasic seizures and late reduced diffusion associated with Streptococcus pneumonia meningoencephalitis. Brain Dev. 2012; 34(2):529–32.
6. Okumura A, Kidokoro H, Tsuji T, Suzuki M, Kubota T, Kato T, et al. Differences of clinical manifestations according to the patterns of brain lesions in acute encephalopathy with reduced diffusion in the bilateral hemispheres. AJNR Am J Neuroradiol. 2009;30(6):825–30.
7. Takanashi J, Tada H, Terada H, Barkovich AJ. Excitotoxicity in acute encephalopathy with biphasic seizures and late reduced diffusion. AJNR Am J Neuroradiol. 2009;30(5):132–5.
8. Takanashi J, Inoue K, Tomita M, et al. Brain N-acetylaspartate is elevated in Pelizaeus-Merzbacher disease with PLP1 duplication. Neurology 2002;58(6):237–41.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 15-06-2021; **Accepted:** 09-07-2021; **Published online**: 11-08-2021