

Autoimmune Encephalitis Following Herpes Simplex Virus Encephalitis in an Infant

A 6-month-old developmentally normal boy presented to us with fever, recurrent right focal seizures and altered sensorium for two days. He was unconscious with poor respiratory effort requiring mechanical ventilation. Cerebrospinal fluid (CSF) analysis showed high protein (96 mg/dL), normal glucose (60 mg/dL), and lymphocytic pleocytosis (90 lymphocytes and 250 RBC's/HPF). Polymerase Chain Reaction for Herpes Simplex Virus type 1 DNA (HSV-1 DNA PCR) in CSF was positive. Magnetic Resonance Imaging (MRI) of brain showed multiple infarcts in bilateral temporal, frontal regions and left insular cortex. Electroencephalography (EEG) showed focal slowing over left hemisphere. Seizures were controlled with levetiracetam and fosphenytoin. The infant was treated with parenteral acyclovir for 3 weeks. At discharge, he was well without neurological deficit.

Ten days after discharge, he was re-admitted with involuntary movements, loss of social smile, and not recognizing parents. He was hypotonic with poor visual fixation. Perioral dyskinesia and marked choreoathetotic movements was present. Repeat CSF analysis showed high protein (83 mg/dL), and lymphocytic pleocytosis (96% lymphocytes). Repeat CSF HSV PCR was negative. CSF NMDAR antibody was positive. Infant was initially treated with Intravenous immunoglobulin and Pulse methylprednisolone. As there was no response, he was subsequently treated with 750 mg/m² of

Rituximab followed by monthly 750 mg/m² cyclophosphamide. There was good response; choreoathetoid movements settled and encephalopathy improved.

Herpes Simplex Encephalitis triggers NMDAR antibodies and potentially other brain autoimmunity [1]. These patients can present with relapsing neurologic symptoms or choreoathetosis after Herpes Simplex infection [2]. Prompt diagnosis and early immunotherapy has been shown to improve clinical outcome in these children [3]. In any child who presents with relapsing symptoms or choreoathetosis after HSV encephalitis, the possibility of autoimmune encephalitis should be considered.

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Evaluation of Asthma Control in Children Using Questionnaires

Somashekar, *et al.* [1] published their study on evaluation of asthma control in children Using Childhood-Asthma Control Test (C-ACT) and Asthma Therapy Assessment Questionnaire (ATAQ) in a recent issue of *Indian Pediatrics* [1]. I seek following clarifications:

1. Spirometry is an important objective measure of airflow limitation, but valid measurements depend on patient's ability to perform full, forceful and prolonged expiratory efforts, which are generally feasible in children aged >6 years. At ages <6 years, its valid measurement is exception rather than rule, and highlights effort-dependence of valid spirometric testing [2].

Peak expiratory flow rate monitoring devices are less sensitive and less reliable as compared to spirometry. If

used over a period of several weeks, they enable to find out personal best and diurnal variation.

2. Study was done over a period of 6 months (It should be from April 2014 to September 2014).
3. Although authors' acknowledge language barrier being one of the limitations of the study, I would like to know if C-ACT Questionnaire was translated in Hindi/ Kannada or English version was used? Getting it translated and answering in regional/ local language would have better validated results.
4. Whether clinicians taking patient history and performing clinical evaluation to assess asthma control were blinded to patient responses on the questionnaires to reduce the subjective nature of the questionnaire [3]?

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AUTHOR'S REPLY

1. Due to the limitations of FEV1 in the age group of below 6 years, both FEV1 and PEFR were used in this study, and their values were clinically interpreted and analyzed with GINA criteria (as GINA criteria allows the use of either).
2. We regret a typographical error in mentioning the duration of the study. The study was conducted from April 2014 to September 2014.
3. Indeed, the questionnaires were verbally translated by the person administering the questionnaire. Photographic representation of the responses provided as a feature in the questionnaire, aided in helping the children understand the questions and to optimally answer it. A written translated version was not used because the study sample was heterogeneous with respect to education level and the language spoken at home (varying from Hindi, Bengali, Tamil, Telugu and Kannada). Hence, to maintain uniformity, a standard English questionnaire was used, and was verbally translated appropriately according to the participant's needs. Further, translated versions would itself need a validation process before being used for the study.
4. One author was solely responsible for clinical evaluation and the other author was involved in administering the questionnaire.

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Two Novel Missense Mutations in Very Long Chain Acyl-CoA Dehydrogenase Deficiency

Very long chain Acyl-CoA dehydrogenase deficiency (VLCADD) is an inherited metabolic disease caused by deleterious mutations in the *ACADVL* gene [1]. In this communication, we describe two novel mutations in a patient with VLCADD and his parents, and suggest a phenotype-genotype correlation.

The full term male infant had uneventful antenatal and perinatal history. His newborn screening was performed at 7 days of age in our facility. Analysis of blood acylcarnitine profile indicated markedly increased

levels of long chain acylcarnitines, with significantly elevated C14:1 level of 2.17 μM . Blood samples from the infant and his parents were collected for genetic studies and mutation analysis, after informed consent. Genetic analysis of the infant's sample showed two heterozygous mutations in the *ACADVL* gene. Two novel missense mutations *ACADVL* NW_001270447: c.1768C>T (p.Arg590Trp) and *ACADVL* NW_001270447: c.1865A>G (p.Glu622Gly) were detected. The father was heterozygous for c.1768C>T (p.Arg590Trp) and the mother was heterozygous for c.1865A>G (p.Glu622Gly). Blood glucose, creatine kinase and alanine aminotransferase levels in the infant were normal, and the baby had no symptom or sign associated with VLCADD. As recommended [1], the parents were instructed to feed the baby boy every 3 h, to avoid fasting,