Electroclinical Response to a Vitamin: Simple Remedy for a Profound Deficiency

Chandana Bhagwat, Pradip Paria, Gunjan Didwal[1], Arushi Gahlot Saini

Department of Pediatrics, Pediatric Neurology Unit, Post Graduate Institute of Medical Education and Research, [1]Department of Pediatrics, Pediatric Biochemistry Division, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Case

A 3-month-old, developmentally normal infant presented with worsening irritability and flexor spasms over the past 15 days. There was no fever, respiratory problems, loose stools, or failure to thrive. Examination showed normal head size, pallor, scalp alopecia, and seborrhea. Syndromic diagnosis of infantile-onset epileptic encephalopathy was considered. Possibility of metabolic epilepsy due to biotinidase deficiency, holocarboxylase synthetase deficiency, and phenylketonuria was thought. An electroencephalograph (EEG) showed burst attenuation pattern, confirming epileptic encephalopathy [Figure 1a]. Plasma ammonia, arterial lactate, pH, blood glucose, electrolytes, and reducing substances in the urine were normal. Mass spectroscopy showed normal acyl carnitine and amino acids in blood and normal organic acid excretion in the urine. Biotinidase enzyme level was 0.5 nmol/min/ml (normal 5–9), suggesting profound deficiency. Initiation of oral biotin (10 mg/day) resulted in remission of clinical seizures within the first 24 h. By the end of the first week, irritability and skin changes improved. The serial EEGs showed gradual normalization by the end of 4 weeks of biotin supplementation [Figure 1a–d]. Magnetic resonance imaging of the brain showed delayed myelination. Genetic studies confirmed the presence of homozygous mutation in exon 2 of the *BTD* gene [c.133C>T (p.H447Y)].

Discussion

Biotinidase deficiency (BD) is an inborn error of biotin metabolism secondary to absent or markedly reduced activity of biotinidase enzyme. Affected children usually present early in life with neurocutaneous manifestations such as epilepsy, developmental delay, alopecia [Figure 2], and skin rash on the flexural surfaces.[1] They can also present later in life with spastic paraplegia and subacute myelopathy that mimics neuromyelitis optica.[2] It is important to remember biotinidase deficiency as an important differential diagnosis of recurrent seizures in infants, especially when associated with skin manifestations as it is a treatable inborn error of metabolism and the diagnosis can easily be established by a simple enzyme assay.[3]

Epilepsy in BD occurs in two scenarios, one as a presenting feature of an untreated deficiency and the other as a neurological sequela with abnormal EEG even on biotin replacement. A distinctive feature of epilepsy in BD is the brisk clinical response to initiation of biotin supplementation within the first 24–48 h in nearly three-fourth children with drug refractory epilepsy.[4] The cutaneous abnormalities start improving by the end of the first

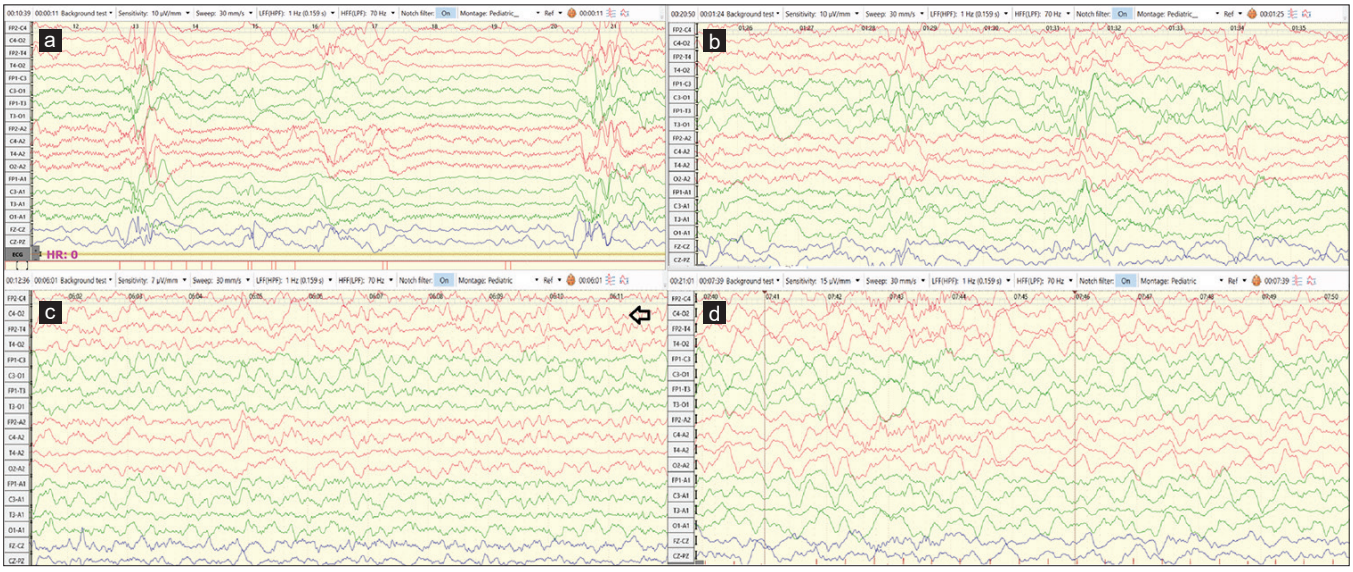

Figure 1: a–d: Interictal electroencephalographs (a) bursts consisting of multifocal spike slow waves (duration 1 sec) with variable periods of attenuation, (b) multifocal spikes with an improvement in burst attenuation by day 8, (c) disappearance of burst attenuation and mild occipital slowing by 1 m, (d) organized background with sleep spindles by 2 m of biotin supplementation

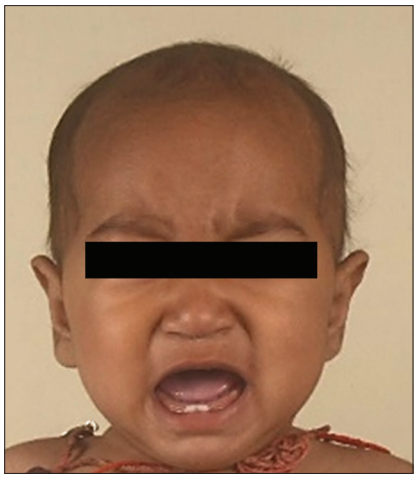

Figure 2: Scalp alopecia and seborrheic dermatitis characteristically seen in biotinidase deficiency

week of therapy. However, despite clinical response, interictal EEG takes a longer time (~6 weeks to 6 m) to resolve.[5] In routine outpatient practice, the serial EEG changes are not analyzed in detail due to the more evident clinical response. As the serial EEG in children with BD is scarcely described, our case adds to the spectrum of electroencephalographic changes and response to treatment in BD. Oral biotin should be initiated in every patient with unexplained epilepsy, especially as the absence of newborn screening misses these treatable inborn errors at birth.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Dhawan SR, Sharawat IK, Saini AG, Suthar R, Attri SV. Diaper rash in an infant with seizures. J Pediatr 2019;206:296.
2. Kasinathan A, Suthar R, Vyas S, Saini AG, Sankhyan N, Attri S. Subacute myelopathy: Think beyond neuromyelitis optica spectrum disorder. Ann Indian Acad Neurol 2019;22:541-2.
3. Reddy C, Saini AG. Metabolic epilepsy. Indian J Pediatr 2021;88:1025-32.
4. Salbert BA, Pellock JM, Wolf B. Characterization of seizures associated with biotinidase deficiency. Neurology 1993;43:1351-5.
5. Guliyeva U, Okur I, Dulac O, Khalilov O, Guliyeva S. Epilepsy in biotinidase deficiency is distinct from early myoclonic encephalopathy. Neuropediatrics 2018;49:417-8.

Address for correspondence: Dr. Arushi Gahlot Saini, Department of Pediatrics, Pediatric Neurology Unit, Advanced Pediatric Centre, Postgraduate Institute of Medical, Education and Research, Chandigarh - 160 012, India.
E-mail: doc.arushi@gmail.com

Submitted: 14-Dec-2021 **Revised:** 09-Jan-2022 **Accepted:** 22-Jan-2022
Published: 06-Apr-2022

DOI: 10.4103/aian.aian_1071_21