**Title:** Emergence of seizures despite presymptomatic treatment in a sibship with Biotinidase deficiency

Olla Amer Alkhoja[1], Waseem Mahmoud Fathalla[2]

[1] Department of Pediatrics, sheikh shakhbout medical city , Abu Dhabi , united Arab emirates

[2] Department of Pediatrics, Division of Pediatrics Neurology, sheikh shakhbout medical city , Abu Dhabi , united Arab emirates

**Abstract Text:**

1. **Introduction or background:**
   Biotinidase Deficiency is an autosomal recessive metabolic disorder that is readily responsive to early presymptomatic treatment with standard dose Biotin.

2. **Objectives:** To report on 2 sibships who were appropriately treated pre-symptomatically but had emergence of seizures that were responsive to conventional anti-seizure drug therapy.

3. **Clinical Case:**
   We report an interesting case of a 7-week old female with biochemically confirmed Biotinidase deficiency that was detected on newborn screening. This newborn was started on Biotin from day 1 of life based on a family history of a confirmed proband. Despite compliance with standard Biotin daily therapy, she developed seizures that were initially managed by doubling then tripling the dose of biotin, despite the fact that standard dose of 5-10 mg daily prevents the emergence of neurological manifestations of Biotinidase deficiency when started presymptomatically. Her seizures then responded to levetiracetam. Of interest, her older male sibling, the proband, has also suffered from emergence of seizures while on Biotin therapy, and required levetiracetam for seizure control. He is now 7 years old and has normal neurodevelopment. There is a history of 2 sibling death before 6 months of age due to metabolic crisis before the confirmed diagnosis of Biotinidase deficiency.

4. **Conclusions**: Our case series demonstrates several learning points; (1) Early presymptomatic biotin replacement prevents death and poor neurodevelopmental outcome, (2) emergences of seizures on biotin replacement should raise concern for a comorbid independent epileptic disorder and warrant initiation of appropriate antiepileptic drug therapy.

## 5. References:


1. Wolf B, Heard GS. Disorders of biotin metabolism. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The metabolic basis of inherited disease. New York: McGraw-Hill, 1989:2083–103.

2. Wolf B. The neurology of biotinidase deficiency. *Molecular Genetics and Metabolism* 2011; 104(1-2):27-34.http://dx.doi.org/10.1016/j.ymgme.2011.06.001PMid: 21696988

3. Wolf B. Biotinidase Deficiency. GeneReviews 2016 Jun 9

4.Outcomes of individuals with profound and partial biotinidase deficiency ascertained by newborn screening in Michigan over 25 years Allison M Jay [1], Robert L Conway [1], Gerald L Feldman [2], Fatimah Nahhas [3], Linda Spencer [1],Barry Wolf. 2015 Mar;17(3):205-9.doi: 10.1038/gim.2014.104. Epub 2014 Aug 21.