CLINICAL PROFILE AND OUTCOME OF 6 PATIENTS WITH BIOTINIDASEDEFICIENCY: AN EXPERIENCE FROM A TERTIARY CARE HOSPITAL OF PAKISTAN

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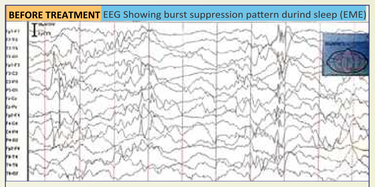
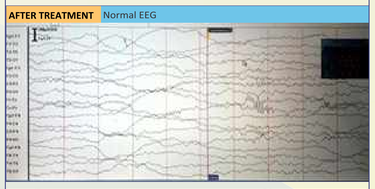
ICNC 2022 17th INTERNATIONAL CHILD NEUROLOGY CONGRESS ANTALYA, TURKEY I OCTOBER 3-7, 2022

Background

Biotinidase deficiency (OMIM 253260) is an autosomal recessive metabolic disorder disorder in which the vitamin biotin is not recycled. Its estimated global incidence of 1:60,000 newborns.[1] If untreated, affected individuals develop neurological and cutaneous symptoms. Untreated individuals with biotinidase deficiency either succumb to disease or are left with significant morbidity[2]. Most individuals with untreated biotinidase deficiency (BD) show progressive clinical features, including neurological abnormalities such as seizures, hypotonia, ataxia, developmental delay, sensorineural hearing impairment and optic atrophy.[3] In Pakistan, patients with BD are almost never diagnosed early and often remain misdiagnosed.[4]

We describe clinical course and follow-up of 6 children who presented in Paediatric Neurology department CH&ICH Faisalabad. These children were diagnosed on clinical basis and suggestive urinary organic acid profile. However Biotinidase enzyme level and BTD gene analysis could not be done due to non availability of facility in our area. All these cases responded dramatically to oral biotin within days to weeks. Biotinidase deficiency is reported in Pakistani children from different part of world, however; there are few such report from Pakistan. This highlights lack of awareness of biotinidase deficiency among physicians in Pakistan.





Specimen ID : 02032021:AO0934R
Clinical Information / Comments:
CDI
Disclaimer: "specimen brought from outside. Patient ID was not verified as the specimen was not collected by AKUH staff".

DOB / Age : 2MDD Gender : Fe
Location : FAISAL3
Attending Physician : DR IRAM JAVED
Account # : C3397251B - OSR
Requested on : 02032021 - 933
Collected on : 02032021 -9:33
Reported on : 16/03/2021 - 15:08

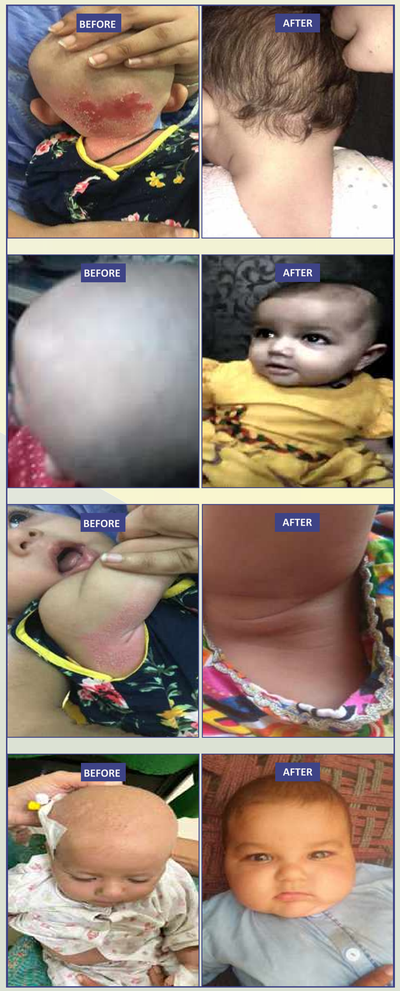
[URINE ORGANIC ACID BY GCMS] :
RESULT OF CHROMATOGRAM:
Marked excretion of 3-hydroxyisovaleric acid, moderate excretion of methylcitiric acid (double peak) are noted along with small peak of 3-hydroxypropionic acid is identified.
However, peak of 3-methylcrotonylglycine and tiglylglycine are not identified.
Furthermore, mild excretion of 4-hydroxyphenylacetic acid is noted.

INTERPRETATION:
Profile may be suggestive of biotin responsive multiple carboxylase deficiency (biotinidase or holocarboxylase synthase). Clinical correlation is indicated. Advise to consult with metabolic physician for further work-up.

Note: This case was discussed in departmental consultation conference held on 16/03/2021.

Table1: clinical presentation and outcome of 6 patients with biotinidase deficiency

No.	Age of onset	Presenting symptoms	Alopecia/ skin rash	Increased anion gap metabolic acidosis	Age at diagnosis	Follow up period	Outcome
1	1 M	Seizures, stridor Consanguinity+	+/-	No	1.5 months	6 months	Seizures controlled within 48 hours Development normal, hair grown back to normal
2	1.5 M	Seizures, epileptic encephalopathy (EME), Consanguinity +	+/-	No	2 months	6 months	Clinical and electrographic remission of seizures in 72 hours development normal, hair growth became normal.
3	1.5 M	Seizures	+/+ Seborrheic dermatitis	No	2 months	3 months	Seizures improved Development normal, rash improved, hair grown back to normal
4	2.5 M	Refractory status epilepticus, stridor	+/-	Yes	3 months	1 year	Seizures free within 48-72 hours Mild motor delay, hair growth normal
5	7 M	Developmental Regression	-/+	Yes	7.5 months	Lost Follow up	Rash improved in 2 weeks but died after discharge in home town due to poor compliance and follow up
6	3.5 M	Developmental delay, Seizures Spastic diplegia	-/-	Yes	3.6 years	1 year	Seizures controlled Spastic diplegia



Conclusion

The presently described cases also showed marked improvement following appropriate therapy except one case who expired due to poor compliance and follow up and one case with residual spastic dilplegia who was actually remained undiagnosed until 3.5 year when he presented to us.

Hence, Pakistani physicians need to be made aware of such a metabolic deficiencies which are both easily diagnosable and easily treatable to avoid long-term irreversible handicap.

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4. Afroze, B., Wasay, M. (2013). Diagnosis, treatment and follow-Up in four children with biotinidase deficiency from Pakistan. Journal of the College of Physicians and Surgeons Pakistan, 23(11), 823-825.

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