Case Report

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Biotinidase Deficiency: Detection through Organicaciduria on TLC

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Abstract

Biotinidase is responsible for cleaving Biotin from Biocytin. Deficiency of biotinidase affects carboxylase enzymes causing dermatological, neurological, immunological or Ophthalmological complications. Biotinidase deficiency is known inborn error of metabolism having a prevalence of 1: 60,000 live births. We are presenting a case of biotinidase deficiency detected and diagnosed at our center.

Keywords: Biotinidase; Biotin; Biocytin; TLC; Organicaciduria.

Introduction

Vitamin B_7, Biotin, acts as coenzyme for multiple carboxylase enzymes in human. A dietary deficiency of biotin is very rare as requirement is only 5-35mcg/ day [1], but deficiency may result from partial or complete absence of enzyme Biotinidase. Biotin is usually conjugated with lysine of carboxylase apoenzyme for its coenzymatic role; the complex is referred to as Biocytin. Enzyme biotinidase is responsible for the cleavage of biotin from Biocytin. Thus a partial or complete absence of biotinidase can cause deficiency of free available biotin. Unavailability of this coenzyme affects the activity of a number of carboxylases viz, Pyruvate carboxylase, Acetyl CoA carboxylase, Propionyl CoA carboxylase, β methyl crotonyl CoA carboxylase, causing dermatological, neurological, immunological or Ophthalmological complications [2] .

Deficiency of biotinidase is known metabolic disorder as common as other inborn errors. The incidence of biotinidase deficiency reported from USA is 1:60,000 to 1:75,000 live births [3]. Very few cases have been reported from India.

We are presenting a rare case of biotinidase deficiency detected by simple Thin Layer Chromatography (TLC) [4] and treated successfully at our center.

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Initial History of Patient's Illness

A second male child of 3 years age was admitted at the Government Hospital in Hubali having a brief history of two days fever with seizure. Two to three incidences of epileptic seizures occurred in the past three months. Parent complaint of poor visual responsiveness and almost no emotional expressions, Parent also reported the death of first sibling with similar symptoms in infancy.

Past Medical History

A male child, has a history of normal full term vaginal delivery with acceptable birth weight. Except for two to three episodes of epileptic seizure; no significant history reported by parents. No familial history of seizure, but the death of elder sibling in neonatal age. Parents reported consanguineous marriage took place five years back.

On Physical Examination

On physical examination, minor developmental delay in milestone and hypotonia was noted, fairly low hair growth on the head without any lesions. The skin shows barely apparent pink rash over the entire body which was ignored and mistaken by parents as skin complexion.

On Clinical Examination

Child presented with mild febrile condition and chest congestion with a breathing difficulty. Muscle tone was less than normal and had poor reflexes. Head circumference - low, little to no visual response, but Ophthalmic finding was normal.

Laboratory Reports

Primary Laboratory investigation revealed Plasma glucose, urea and creatinine within normal reference range. Blood gas analysis indicated normal anion gap metabolic acidosis. Serum lactic acid level was elevated, Serum ammonia level was normal. Based on symptoms and primary laboratory reports strong suspicion for the possible metabolic disorder was raised.

Fresh Urine and plasma sample was sent to look for any inborn error of metabolism at Department of Biochemistry of a private medical college hospital.

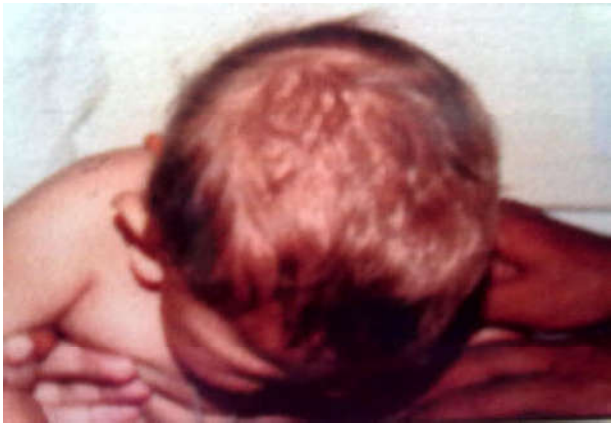

Fig. 1: Scnty hair growth

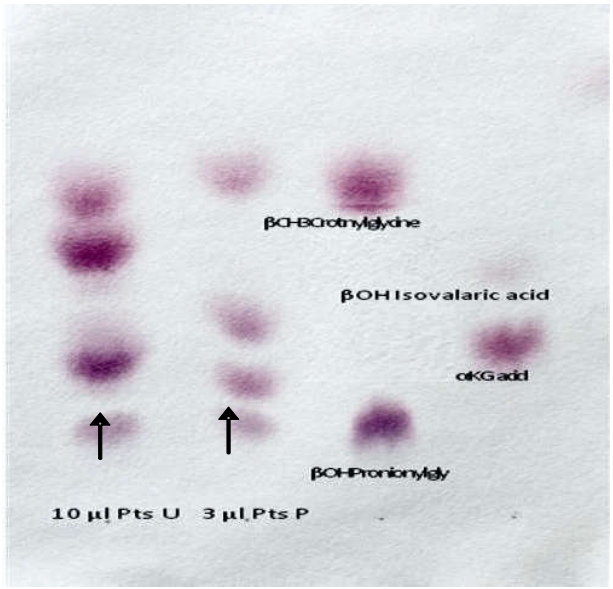

Fig. 2: Chromatogram of organic acid by Ninhydrin stain

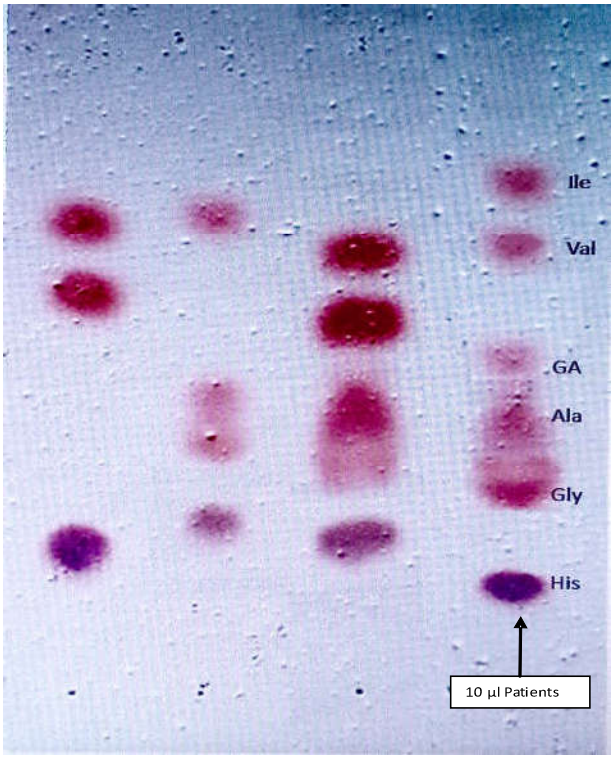

Fig. 2: Thin Layer Chromatography (Silica gel) Plate of patients urine

The urine sample was analyzed for aminoaciduria, glycosuria, ketouria and organicaciduria as a part of simple metabolic screening. The results of chemical tests performed on urine sample indicated presence of organicaciduria which was supported by thin layer chromatography of plasma and urine sample. Initially thin layer chromatography [Figure 3] for amino acid indicated a marked increased on glycine, Isovaline and Alanine along with Histidine and Glutamic acid. Elevated level of Alanine (2.2 fold), Histidine (2 fold) and valine (1.75fold) are reported in biotinidase deficiency by Kalayci O (1994) [5]. TLC for organic acids pointed out the presence of β-OH isovalericacid, β-methyl-crotonylglycine β-hydroxypropionyl glycine and α-ketoglutaric-acid [Figure 2]. Chemical tests and TLC for carbohydrates remained negative.

As a confirmatory test Serum Biotinidase levels were analyzed at specialized laboratory and result was in concordance with our findings.

Discussion

Common features of Biotinidase deficiency include seizures, hypotonia, ataxia, breathing problems, hearing loss, skin rashes, alopecia and developmental dealy. A patient having seizure which is non-responsive to routine anticonvulsant therapy strongly

suspect biotinidase deficiency. Characteristic symptoms such as alopecia, skin rash could also manifest in zinc deficiency which should be kept in mind [6]. Since there was no history of dietary indiscretion, zinc deficiency was ruled out. Biotinidase releases free biotin from its complex Biocytin. Biotin acts as coenzyme in carboxylase catalyzed reactions. Deficiency of biotin will influence on metabolism, as a result increased organic acids like propionyl glycine, Isovalaric acid, 2-oxaloglutaric acid or 3 – hydroxyl isovalaric acid are excreted in urine. Organic aciduria is heterogeneous group of inborn error of metabolism, biochemically describe by 1] abnormal metabolites or 2] pathologically high concentration of normal metabolites [7]. Organic acids are water soluble compounds containing one or more carboxyl group along with other keto or hydroxyl group. They are intermediate metabolites of amino acids, carbohydrates, lipids, nucleic acids and steroids. Due to impaired pyruvate carboxylase lactic acidosis may also result.

Treatment

After complete review of physical symptoms, Clinical findings and laboratory reports, our patient was diagnosed as biotinidase deficiency. Serum biotinidase activity was low. Patient was put on Mega dose of Biotin (20 to 40mg/day) which responded positively and symptoms were normalized within four days. The patient was observed for four weeks after suspension of supplemented biotin dose, as expected reappearance of symptoms confirmed biotinidase deficiency. Parents were instructed and counseled for lifelong biotin supplementation. The patient was discharged after one more week observation at hospital.

Conclusion

Biochemical diagnosis of individual organicacidemia ultimately relies on urine organic acid analysis. TLC being a simple screening method gives valuable information within minimum time and help clinicians to treat the patient before any complication sets in.

Conflic of Interest and Ethical Approval

The present study was on urine sample where no procedure was performed on patient. The study was approved by institutional ethical committee. None of the participants in this study have expressed conflicting of interest. The patient being child informed consent was obtained from patient's parents. We express our thanks to the patient's parent for permitting us in the study and presentation of this case in a scientific community.

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