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Gluteric Aciduria Type 1 In Previously Normal Infant: A Case Report

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ABSTRACT

Gluteric aciduria type 1, a rare autosomal recessive genetic disorder which is caused by deficiency of Glutaryl CoA dehydrogenase leads to progressive neurological damage. 75% of the cases of gluteric acidemia type 1 present with macrocephaly and is the earliest and most consistent sign of the disease (1). Here we report a case of gluteric aciduria type 1 in a one year old male child without macrocephaly but typical clinical spectrum of the disease. 1 year old previously healthy and developmentally normal male child born of non consanguineous marriage was admitted in PICU with the complaints of fever, dystonia and progressive regression of normally achieved developmental milestones for which symptomatic management was started initially and the illness was diagnosed by the clinical picture of the disease, urinary gas chromatography and mass spectrometry. Treatment in the form of dietary modification with low lysine diet and carnitine therapy was started.

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Introduction

Gluteric aciduria type 1 is a rare genetic disorder that occurs approximately in 1 of every 100000 births (2). The affected gene is GCDH which encodes glutaryl CoA dehydrogenase is located on chromosome 19p13.2 causing defective degradation of lysine, hydroxylysine and tryptophane. Subsequent accumulation of intermediate breakdown products like glutaric acid, glutaryl CoA, 3-hydroxyglutaric acid, glutaconic acid which cause brain damage particularly affecting the basal ganglia and also produce carnitine deficiency which is required to detoxify glutaric acid (2). However it is different from type 2 glutaric acidemia which is caused by defect in electron transport system leading to defective ability of body to use proteins and fats for energy (3). Macrocephaly is one of the commonest and earliest finding of this illness, seen in approximately 75% cases (1). Early diagnosis and management can prevent the occurrence of irreversible brain injury and subsequent neurological sequel. We report a case without macrocephaly but with classical clinical progression.

Case Report

12 months old male child born to G3P2L2 mother of non consanguineous marriage with uneventful perinatal history. Child had normal developmental milestones till the onset of illness at 1 year of age when he suffered from acute illness of fever and abnormal body movements. It started with high grade intermittent fever followed by sustained twisting of all 4 limbs with tonic posturing lasting for 5-30 minutes associated with crying and subsided with sleep. Later on child stopped recognizing mother, not following commands with absent eye to eye contact and lost interaction with surroundings. There was no significant family history. On examination, child had all four limbs flexed with neck extended and head circumference 46 cm which was normal for the age and sex as per the population standards.

Neurological examination showed irritable child with dystonia, brisk deep tendon reflexes and upgoing plantar reflex. On further investigations, arterial blood gas suggested metabolic acidosis, later found to have elevated serum lactate and blood ammonia level. Contrast enhanced CT scan of head showed frontotemporal atrophy with increased extraaxial fluid with basal ganglia hypodensity suggesting gluteric aciduria type 1. Diagnosis was confirmed with urinary gas chromatography and mass spectrometry which showed elevated 3-hydroxyglutaric acid and gluteric acid in urine. After confirmation, child was started on low lysine diet and carnitine supplementation and kept under follow up.

Discussion

Gluteric aciduria type 1 is a defect in metabolism of amino acids; lysine, hydroxylysine and tryptophan (2). Though it's a rare disorder but improvement in health care and diagnostic support have led to early and better confirmation of the disease. Affected infants usually remain normal till 1-2 years of age with macrocephaly (4,5) which is a common finding. However the case reported here was presented with normal head size. The child remained asymptomatic and developmentally normal till the onset of illness. Disease usually appears after some minor catabolic insult like infection, recovery from the first attack usually occurs slowly but some residual neurologic abnormality like extrapyramidal movements may persist. Repeated attacks or severe catabolic condition leads to severe neurologic impairment from hypotonia, chorioathetosis to rigidity and dystonia. Here the child was apparently asymptomatic and developmentally normal, after single attack of some minor infective illness led to severe neurologic impairment. Death usually occurs in first decade of life as a result of one such episode. The disorder is characterised by high levels of glutaric acid and 3-hydroxyglutaric acid in urine, CSF and blood. Some cases may have elevated liver enzymes and hypoglycemia. Laboratory findings are insignificant in between attacks.

In “low excretors” intermediates may be elevated in spinal fluid only, and they require the enzyme activity measured in leukocytes Or cultured fibroblasts(2). Neuroimaging shows frontotemporal atrophy with basal ganglia lesions and increased extraaxial fluid. Low protein diet restricted in lysine, tryptophane and high doses of riboflavin and l- carnitine show decreased levels of intermediates but clinical improvement is variable(6,7).

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