Classic Imaging Features of L-2-Hydroxyglutaric Aciduria in Young Adult Presenting as Seizures Associated with Fever

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Abstract

L-2 Hydroxyglutaric aciduria is a rare metabolic disorder which is autosomal recessive in inheritance. It is characterised by the increased urinary excretion of L-2 hydroxyglutaric acid and the diagnosis is based on the increased levels of the L-2 hydroxy glutaric acid in the urine, serum & CSF. This is a neurometabolic disorder which is associated with slowly progressive psychomotor delay since childhood. We report a case of an 18 –year old female who presented at the emergency department with seizures, fever and on imaging show classic features.

Keywords: Febrile seizures, L-2-hydroxyglutaric aciduria, subcortical white matter

Introduction

The L-2-hydroxyglutaric aciduria is a rare metabolic disorder which is autosomal recessive in inheritance. The first case was described in 1980.[1] It is characterized by the increased urinary excretion of L-2 hydroxyglutaric acid, and the diagnosis is based on the increased levels of the L-2-hydroxyglutaric acid in the urine, serum, and cerebrospinal fluid. This is a neurometabolic disorder which is associated with slowly progressive psychomotor delay since childhood. We report a case of an 18-year-old female who presented at the emergency department with seizures associated with fever.

Clinical Details

A 18-year-old female patient was admitted to medicine department with fever and seizures. The patient's attendant described that there was a history of the similar episode of seizure 5-year back. The patient was a preterm child with a history of asphyxia. There was a history of delayed achievement of the developmental milestone that is the patient started sitting at the age of 1 year and walking at the age of 3 years. The physical examination of the patient revealed the cerebellar signs in the form of ataxia, slurring of speech, and horizontal nystagmus. The patient was doing routine work normally up to the age of 12 years, after that she started decline in motor and cognitive functions. Now for the past 2 years, she does not take bath and combs her hair herself. She has difficulty in using knife and scissors. She does not know day, month, and year. There was no history of similar complaints within the family. For further workup, the noncontrast computed tomography (CT) head was done. The various findings on the CT head were diffuse, hypodensities in the white matter (WM) of the bilateral cerebral hemispheres predominantly in the subcortical location [black arrow in Figure 1a and b]. The deep as well as periventricular WM is spared [white arrow in Figure 1c and d]. For further evaluation, magnetic resonance imaging (MRI) brain was done. The various imaging features revealed on MRI were bilaterally symmetrical T2-weighted/fluid-attenuated inversion recovery (T2/FLAIR), hyperintense lesions in the dentate nuclei [Figure 2a and d], caudate nuclei, and bilateral lentiform nuclei [Figure 2b], with mild cerebellar atrophy.

The T2/FLAIR hyperintense lesions were also seen in the subcortical WM [Figure 2c and f, inserts C1 and f1]. The brain stem, thalami, and the periventricular WM were spared [Figure 2b and c]. All routine biochemical and hematological findings were within normal limits as shown in Table 1.

Based on the neuroimaging findings, the possibility of L-2-hydroxyglutaric aciduria was kept, and urine analysis was done. It has shown that the urinary excretion of L-2-hydroxylglutaric aciduria was 1256 mg/g creatine (normal values <10 mg/g creatine).

Discussion

L-2-hydroxyglutaric aciduria is a rare neurometabolic disorder which is caused due to mutation of gene L-2-hydroxyglutarate dehydrogenase (L-2 HGDH). This disorder is inherited as an autosomal recessive trait. The product of this gene is

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L-2 HGDH, which catalyzes the conversion of L-2 OHG to 2-ketoglutarate.[2,3] It has been found that the accumulation of L-2 OHG is toxic to WM which myelin vacuolation.[4] There is an increased excretion of L-2 OHG in the urine, in the affected patients. In healthy individuals, L-2 OHG acid is present in urine in D and L configurations equally.

The symptoms usually appear in early childhood. The various clinical signs and symptoms are delayed developmental milestones, cerebellar signs, extrapyramidal symptoms, and mental retardation. The patient may present with the clinical progressive neurological symptoms and seizures. On MRI imaging, this disorder has characteristic features. There is symmetrical involvement of the subcortical WM. The T2/FLAIR hyperintense lesions are seen in the bilateral cerebral hemispheres predominantly in subcortical WM with sparing of the deep and periventricular WM.[4-6] The T2/FLAIR hyperintense lesions are also seen in the bilateral dentate, caudate, and lentiform nuclei with sparing of the thalami.[7] With the progression of the disease, there may be atrophy of the brain parenchyma. The rare form of hydroxyglutaric aciduria is L-2-hydroxyglutaric aciduria; it presents early with symptoms such as hypotonia, cardiomyopathy, seizures, and visual failure.[8]

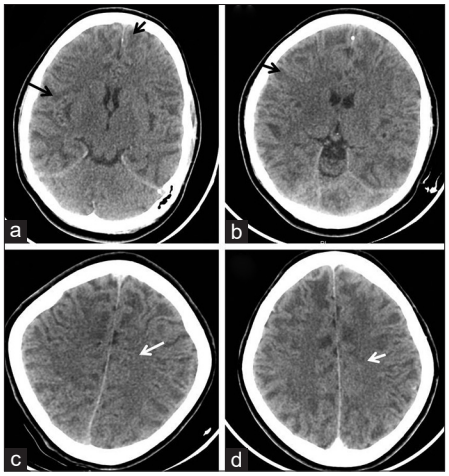

Figure 1: Axial noncontrast computed tomography head images showing diffuse hypodensities in the bilateral cerebral hemispheres (black arrow in a and b) with sparing of periventricular and deep white matter (white arrow in c and d)

The other differentials of this disorder include Canavan disease and Kearns–Sayre syndrome. In Kearns–Sayre syndrome, there are bilaterally symmetrical lesions of the globus pallidus and subcortical WM. The caudate nucleus and the brainstem and thalamus are also affected in most patients. In our case, there is a sparing of brainstem and thalami. In Canavan disease, the bilaterally symmetrical signal intensity abnormalities of cerebral WM are seen, preferential subcortical localization with the involvement of globus pallidus and sparing of the putamen and caudate nucleus.

Our case is unique, presenting in adulthood with fever-associated seizures and ataxia. The imaging revealed classic CT and MRI features. We suggest that the young adults presenting with leukodystrophy-like features on imaging with fever and seizures, the possibility of rare metabolic disorder, that is, L-2-hydroxyglutaric aciduria should be suspected.

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

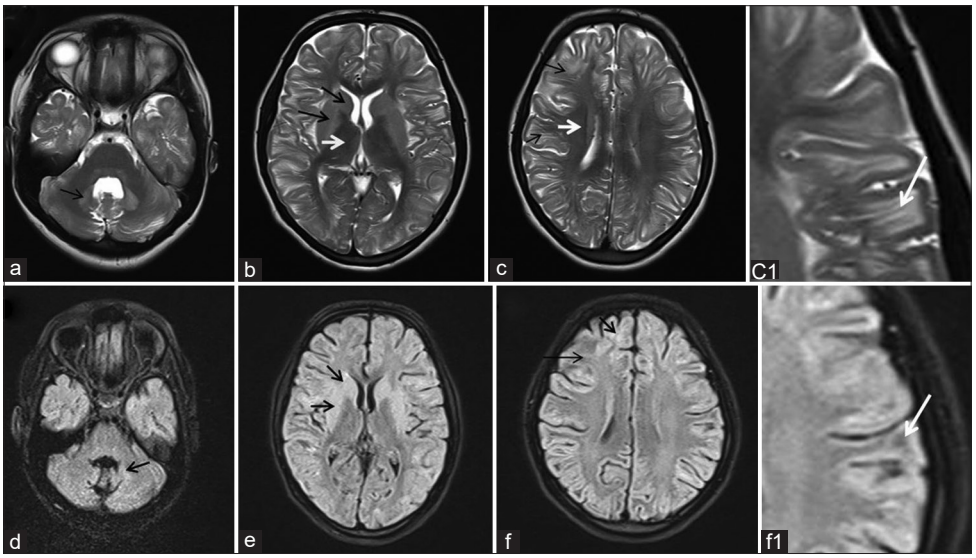

Figure 2: Axial T2-weighted/fluid-attenuated inversion recovery images showing bilaterally symmetrical T2-weighted/fluid-attenuated inversion recovery hyperintense lesions in the dentate nuclei (black arrow in a and d), caudate nuclei and bilateral lentiform nuclei (black arrows in b and e), subcortical white matter (black arrows in c and f, with white arrow in insert C1 and f1), sparing of bilateral thalami and periventricular white matter (white arrows in b and c)

Table 1: Biochemical and hematological Tests

Test	Results
Hemoglobin	12.8 g/dl
Total leukocyte count	8900/µl
Platelet count	1.5 lacs/µl
ESR	05 mm at 1h
Random blood sugar	130 mg/dl
Blood urea	32 mg/dl
Serum creatinine	0.9 mg/dl
Sodium	136 mmol/L
Potassium	3.7 mmol/L
Chloride	89 mmol/L
Serum bilirubin	
Total	1.5 mg/dl
Direct	0.4 mg/dl
Alanine transaminase	27 U/L
Aspartate transaminase	57 U/L
Alkaline phosphatase	82 U/L
Serum protein	
Total	8.6 g/dl
Albumin	4.9 g/dl

ESR=Erythrocyte sedimentation rate

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.

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Conflicts of interest

There are no conflicts of interest.

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