A novel GLUT-1 mutation in a patient with apparently normal cerebrospinal fluid glucose level

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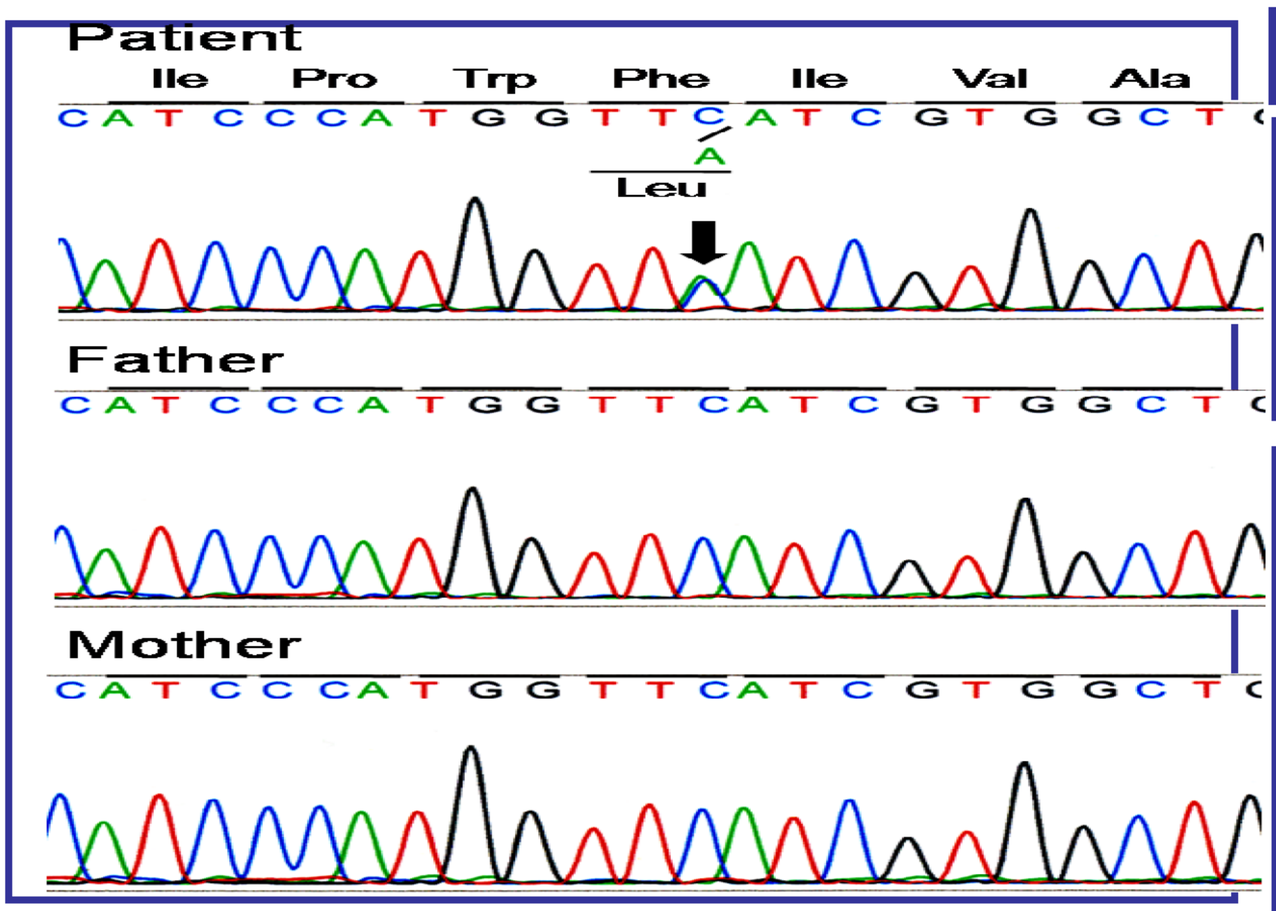
OBJECTIVES

Glucose is the main energy source for the brain's cells. Glucose transporter 1 (GLUT1), encoded by the SLC2A1 gene, is a membrane protein that plays an essential role in the transport of glucose across the blood-brain barrier. A mutation in GLUT-1, so-called GLUT-1 deficiency syndrome (GLUT-1 DS; OMIM #606777), results in low levels of glucose in the cerebrospinal fluid despite normoglycemia.. GLUT-1 deficiency causes a series of symptoms that may differ considerably from one patient to another.

CASE

A 17 year-old boy was born to healthy non-consanguineous parents after an uneventful pregnancy with normal birth weight and head circumference. He had a infantil seizure at one of age. The patient continued to have seizures with same frequency and duration until 17 years old of age. Blood investigations revealed normal hemogram and biochemistry The seizures did not respond to anticonvulsants, including levetiracetam ,carbamazepine or valproic acid.. Brain MRI and electroencephalogram yielded no specific findings.



RESULTS

Cerebrospinal fluid :
Lumbar puncture revealed normal glucose concentration in the CSF in the setting of normoglycemia (blood glucose, 93mg/dl ; CSF glucose 47mg/dl, and CSF to blood glucose ratio 0.50).

Mutation analysis
The patient had a heterozygous missense mutation in SLC2A1 (c.1167C>A, numbered according to Genebank accession no. NM_006516.2, p.Phe389Leu). Testing of the patient's parents confirmed that the SLC2A1 mutation occurred de novo. The mutation was predicted to be damaging by both PolyPhen-2 and SIFT.

DISCUSSION

GLUT-1-deficiency syndrome is a unusual metabolic encephalopathy that is not recognized and possibly underdiagnosed. A low cerebrospinal fluid glucose concentration in the absence of hypoglycaemia is not a mandatory feature of of this syndrome. It is essential to include GLUT-1 syndrome in the differential diagnosis of patients with seizures that are unresponsive to treatment
Our patient helps to clarify the phenotype of GLUT-1 deficiency more clearly and reveals a new pathogenic mutation.

References

Ticus I, Cano A, Villeneuve N, Milh M, Mancini J, Chabrol B. [GLUT-1 deficiency syndrome or De Vivo disease: a case report]. Arch Pediatr. 2008 Aug;15(8):1296-9

Wang D, Pascual JM, Yang H, Engelstad K, Jhung S, Sun RP, De Vivo DC. Glut-1 deficiency syndrome: clinical, genetic, and therapeutic aspects. Ann Neurol. 2005 Jan;57(1):111-8.

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