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Case Report

Paroxysmal exercise induced dyskinesia and writer's cramps in twin siblings with SLC2A1 mutation

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ABSTRACT

Paroxysmal exercise induced dyskinesias (PED) are rare disorders with recurring episodes of sudden involuntary movement disorders precipitated by physical exercise. It had been reported that less than 20% of PED patients carry an SLC2A1 mutation encoding GLUT 1 of whom 49 patients have been identified worldwide We hereby reported a case of twin siblings, 23 year old male with no antecedent other past illness and family history presenting with writer's cramps and paroxysmal exercise induced dyskinesia attributed to milder phenotype of glucose transporter type 1 deficiency with the heterozygous exon-6 SLC2A1 gene mutation. Ketogenic diet in these patients may help in these cases.

Keywords: Paroxysmal exercise induced dyskinesia, SLCA2A1 mutation, Writer's cramps

INTRODUCTION

Paroxysmal dyskinesias are rare disorders with recurring episodes of sudden involuntary movement disorders which may be choreic, dystonic or mixture of both.[1] These are further classified into three subtypes: paroxysmal kinesigenic dyskinesia (PKD), paroxysmal non-kinesigenic dyskinesia (PNKD) and exercise-induced (PED) dyskinesia.[2]

PED is usually lower-limb dystonia precipitated by sustained walking or running. The underlying aetiology of PED is quite heterogenous, most being sporadic.[3] Familial cases with heterozygous missense mutations in SLC2A1, encoding for glucose transporter type 1 (GLUT-1) and few with mutations in the GTP cyclohydrolase 1 gene (GCH1) and mitochondrial short-chain enoyl-CoA hydratase 1 deficiency (ECHS1D) have been associated.[4] It has been reported that less than 20% of PED patients carry an SLC2A1 mutation of whom 49 patients have been identified worldwide.[5]

We hereby reported a case of twin siblings, 23 year old male with no antecedent other past illness and family history presenting with writer's cramps and paroxysmal exercise induced dyskinesia attributed to milder phenotype of Glucose transporter type 1 deficiency with the heterozygous exon- 6 SLC2A1 gene mutation.

CASE REPORT

The twin brothers had normal birth and developmental history. At the age of 13 years, they noticed after working in fields (harvesting crops) in the month of April, while returning back to home, with prolonged walking their feet twisted inwards or outwards. If they continued walking, they had to drag their feet. So, they used to rest for twenty to thirty minutes after which they could walk again for one hour. These symptoms involved either foot at a time. Later they observed while playing cricket continuously for 6-7 hours, they had similar complaints of twisting feet which persisted with activity for about 10 minutes. They used to take rest for 15 minutes and then again continued. Similar complaints also noted by them

while paddling bicycles. Since past 6 months they felt that these movements had aggravated. Initially 2 to 2.5 km walk precipitated these twisting movements but now one of them was observing symptoms after prolonged walking for 1 km also.

Since the age of 19 years one of them observed twisting of hands with prolonged writing also. While he was writing for his graduation examinations, he felt that after continuously writing for 1 hour, his right hands repeatedly twisted and he had to take rest for about 15 minutes only then he was able to resume his exam. He was still having these symptoms with prolonged writing but no similar complaints with shaving. There was no h/s/o any distal weakness, seizures, myoglobinuria, myotonia or second wing phenomenon.

On examination, MMSE-30/30, no cranial nerve abnormality, no pyramidal signs, no extrapyramidal or cerebellar signs noted. Limb dystonia and writer's cramp noted on prolonged exertion.

On evaluation, viral markers HIV/HBsAg/anti-HCV were non-reactive. USG abdomen-normal study. Slit lamp examination for KF rings negative. MRI brain suggestive of normal study. Nerve conduction tests suggestive of normal motor, sensory and F wave. Rest investigations were also normal (Table 1).

Table 1: Biochemical parameters of the patient.

Parameters	Patient value	Normal range
Complete hemogram	Haemoglobin-16.6 gm/dl	13.8 to 17.2 gm/dl
	Total leucocyte count-5.3×10^9/l	4.5-11.0×10^9/l
	Platelet count-160×10^9/l	150-450×10^9/l
Renal function tests	Blood urea-28 mg/dl	20-40 mg/dl
	Serum creatinine-1.2 mg/dl	0.9-1.3 mg/dl
Liver function tests	ALT-37 U/l	7-55 U/l
	AST-38 U/l	8-48 U/l
	Alkaline phosphatase-108 U/l	35-130 U/l
	Bilirubin (T)-0.8 mg/dl	0.3-1.2 mg/dl
Serum electrolytes	Sodium-144 mmol/l	135-148 mmol/l
	Potassium-4.6 mmol/l	3.5-5 mmol/l
	Calcium-10 mg/dl	8.6-10.3 mg/dl
Blood sugar fasting	90 mg/dl	70-100 mg/dl
Thyroid profile	T3-168 ng/dl	100-200 ng/dl
	T4-7.2 µg/dl	5-12 µg/dl
	TSH-3.1 mU/l	0.4-4.0 mU/l
Serum total creatine phosphokinase levels	165 IU/l	20 to 200 IU/l

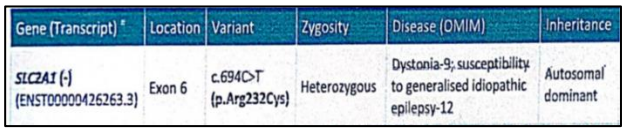

Figure 1: Genetic testing of the patient.

Genetic testing for dystonia gene revealed heterozygous mutation in exon 6 of SLC2A1 gene (c.694C>Tp.Arg232Cys) (Figure 1). They were started on ketogenic diet (high fat, low carbohydrate). Avoiding precipitating events, like prolonged physical exercise, was advised to prevent attacks.

DISCUSSION

Glucose transporter type 1 deficiency syndrome (GLUT1DS) are neurometabolic disorder with a treatable etiology.[6,7] Leen et al described two phenotypes: (1) the classical phenotype (84%) with seizures, developmental delay, microcephaly; (2) a non-classical phenotype (16%) with movement disorders without epilepsy, early-onset absence epilepsy, PED.[8] A ketogenic diet has been effective in management of patients with GLUT1 DS.[9,10]

CONCLUSION

Our case highlights that paroxysmal exercise induced dyskinesia can be presenting with a number of different disorders. Recognition of underlying etiology and timely management with ketogenic diet may be beneficial.

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