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Case Report

Chorea Hyperglycemia Basal Ganglia Syndrome in a Young Patient with Type 1 Diabetes Mellitus: a Case Report

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HIGHLIGHTS

- Chorea hyperglycemia basal ganglia (CHBG) syndrome is a rare complication of uncontrolled diabetes mellitus.
- CHBG syndrome can affect young adults.
- Strict glycemic control will aid better prognosis and resolution of chorea.

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Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Chorea hyperglycemia basal ganglia (CHBG) syndrome is an uncommon manifestation of diabetes seen in patients with poor glycemic control. It is characterized by sudden onset of chorea with characteristic hyperintensities of the basal ganglia on brain magnetic resonance imaging. We report a case of a 31-year-old female patient with a history of type 1 diabetes mellitus, renal failure, and hypertension, who presented with acute symptoms of chorea involving both the upper and lower limbs with facial and cervical dystonia. Magnetic resonance imaging revealed bilateral hyperintensities of the globus pallidus and putamen. Control of blood glucose levels led to resolution of the choreic movements. In addition, follow-up magnetic resonance imaging studies revealed improvement in the hyperintensities of the basal ganglia bilaterally.

Keywords: Chorea; Basal Ganglia; Hyperglycemia

INTRODUCTION

Brain is susceptible to damage because of various metabolic disorders. Chorea hyperglycemia basal ganglia (CHBG) syndrome is a rare complication in diabetic patients with nonketotic hyperglycemia, with clinical features of sudden onset chorea [1]. Chorea is characterized by involuntary and irregular, non-rhythmic movements [2]. Patients with CHBG display typical hyperintense basal ganglia lesions on T1-weighted brain magnetic resonance imaging (MRI) [1].

Most reported cases of CHBG involve patients with Asian ethnicities, possibly because of underlying genetic predisposition [2,3]. This syndrome predominantly affects elderly women [1,3-5]. Furthermore, hemichorea with contralateral basal ganglia lesion is more common than that with bilateral involvements [1,3,4,6,7]. Herein, we report a case of CHBG which developed as an acute complication of diabetes mellitus in a young adult woman, with bilateral upper and lower limbs chorea and dystonic movements of the neck, face, and tongue.

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CASE REPORT

A 31-year-old woman visited the outpatient clinic of rehabilitation medicine with a chief complaint of new-onset generalized chorea for 2 weeks. She demonstrated involuntary choreic movements of both upper and lower limbs (the right side was more involved than the left). Facial dystonia with involuntary twitching, grimacing, protrusion of the tongue, and rapid involuntary neck rotation were also observed. These movements initially started in her right arm and subsequently progressed to the right leg, contralateral limbs, and face. It affected her daily activities of life but resolved when she was asleep.

She was diagnosed with type 1 diabetes mellitus at age of 10 years, and had hypertension and end-stage renal disease, which required continuous ambulatory peritoneal dialysis; she was waitlisted for donor kidney transplantation. Laboratory data revealed initial glucose level of 344 mg/dL and hemoglobin A1c (HbA1c) of 8.3%. Urine ketones were not detected. Review of past medical records showed that her previous HbA1c reading was 7.6%, 3 months ago, and the average serum glucose level measured at home for the last 3 months ranged between 300–350 mg/dL. Worsening HbA1c level was suggestive of poor glycemic control recently. The patient was prescribed a routine regimen of insulin injection; however, she frequently skipped the injections against medical advice.

Neurological examination did not reveal significant motor weakness. Before the onset of chorea, she was ambulated with an anterior walker because of generalized weakness and peripheral sensory polyneuropathy and was under continuous rehabilitation therapy in the outpatient clinic. Her deep tendon reflexes were normal. She scored 39.5 out of 120 on the Burke-Fahn-Marsden Dystonia Rating Scale in the movement section; more severe dystonic involvement was seen at the neck and right arm. On the Modified Barthel Index, she scored 34 out of 100, indicating severe dependency in routine activities of daily life; on the Berg Balance Scale, she scored 11 out of 56, indicating impaired balance and function. T1- and T2-weighted brain MRI images showed diffuse hyperintensities involving the bilateral basal ganglia regions, including the globus pallidus and putamen (Fig. 1). Diffusion-weighted brain MRI images showed no abnormally restricted diffusion which we could exclude ischemia.

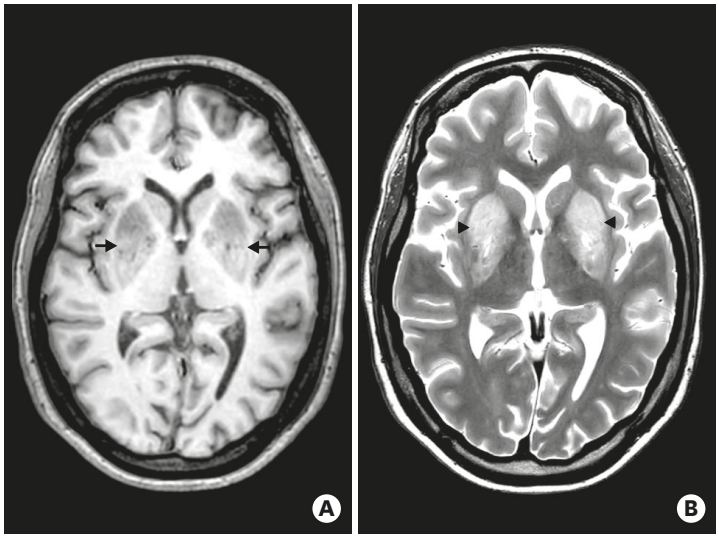

Fig. 1. (A) Hyperintensities involving bilateral basal ganglia including globus pallidus and putamen (black arrows) on T1-weighted image. (B) Corresponding T2-weighted image showing diffuse hyperintensities (arrowheads).

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Table 1. Abnormal findings in the genomic analysis of targeted sequencing of 370 genes

ACMG classification	Gene	Accession	Nucleotide	Zygosity	Disorder	Inheritance
VOUS	*DPM1*	NM_001317035.1	c.575+1G > C	Hetero	Congenital disorder of glycosylation	AR
VOUS	*DPM1*	NM_001317034.1	c.576G > C	Hetero	Congenital disorder of glycosylation	AR
VOUS	*PEX2*	NM_001079867.1	c.551G > T	Hetero	Peroxisome biogenesis disorder	AR
VOUS	*LMBRD1*	NM_018368.3	c.1192T > C	Hetero	Methylmalonic aciduria and homocystinuria	AR
VOUS	*PDP1*	NM_018444.3	c.1281G > A	Hetero	Pyruvate dehydrogenase phosphatatse deficiency	AR

ACMG, American College of Medical Genetics and Genomics; VOUS, variants of unknown significance; AR, autosomal recessive.

Comparison with a brain MRI image obtained 4 years ago, to evaluate generalized weakness, showed no basal ganglia lesions.

Genomic analyses of data from the targeted next-generation sequencing of 370 metabolic disease-associated genes identified variants with unknown significance in *DPM1, PEX2, LMBRD1,* and *PDP1* genes; however, no definite gene mutation causal to the metabolic disease was identified (Table 1). Electrodiagnostic study revealed demyelinating mixed peripheral sensorimotor polyneuropathy with axonal involvement, which was considered secondary to diabetic polyneuropathy (Table 2).

She was prescribed 12 units of regular human insulin injection. Rehabilitation therapy was continued for balance training and to alleviate dyskinetic movements. Symptomatic improvement was observed, with her glucose level improving to normal range. After 5 days of strict glycemic control, choreic movements of the 4 limbs, dystonic movements involving the neck muscles and perioral area, and tongue protrusion disappeared. Follow-up Burke-Fahn-

Table 2. Sensory and motor nerve conduction studies

Study	Stimulation site	Recording site	Latency (ms)	Amplitude (uV)	Velocity (m/s)
Sensory					
Rt. median	Wrist	3rd finger	4.9*	11.8*	
Lt. median	Wrist	3rd finger	No response		
Rt. ulnar	Wrist	5th finger	4.5*	9.0*	
Lt. ulnar	Wrist	5th finger	No response		
Rt. peroneal	Ankle	Lateral ankle	No response		
Lt. peroneal	Ankle	Lateral ankle	No response		
Rt. sural	Calf	Lateral ankle	No response		
Lt. sural	Calf	Lateral ankle	No response		
Motor					
Rt. median	Wrist	APB	5.8*	4.5*	
	Elbow	APB	11.6	4.4	41*
Lt. median	Wrist	APB	7.6*	0.6*	
	Elbow	APB	12.6	0.5	44*
Rt. ulnar	Wrist	ADM	4.6*	2.4*	
	Below elbow	ADM	13.1	1.2	28*
Lt. ulnar	Wrist	ADM	5.2*	0.5*	
	Below elbow	ADM	14.7	0.2	25*
Rt. peroneal	Ankle	EDB	No response		
Lt. peroneal	Ankle	EDB	No response		
Rt. peroneal	Ankle	TA	4.0	1.0*	
	Below fibular head	TA	6.4	0.6	37*
Lt. peroneal	Ankle	TA	3.6	1.2*	
	Below fibular head	TA	5.9	1.1	38*
Rt. tibial	Ankle	AH	7.8*	0.1*	
	Knee	AH	No response		
Lt. tibial	Ankle	AH	No response		

Rt., right; Lt., left; APB, abductor pollicis brevis; ADM, abductor digiti minimi; EDB, extensor digitorum brevis; TA, tibialis anterior; AH, abductor hallucis.
*Abnormal value.

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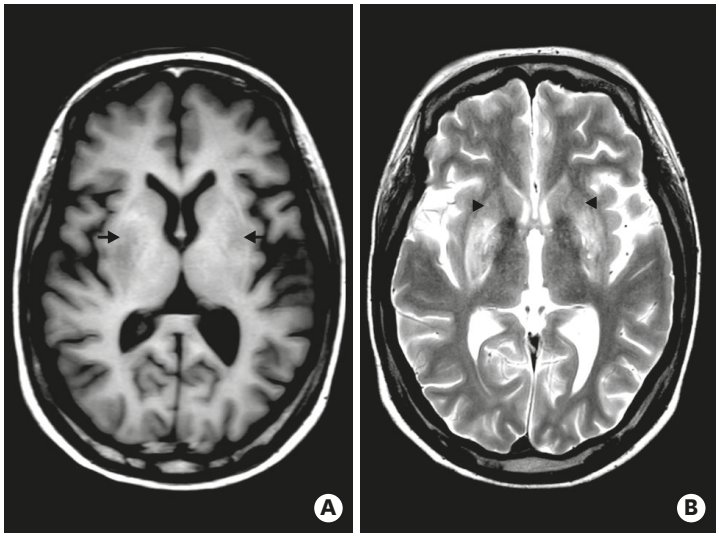

Fig. 2. (A) Follow-up T1-weighted images of brain magnetic resonance imaging showing decreased hyperintensities at bilateral globus pallidus and putamen (black arrows). (B) Corresponding T2-weighted image showing decreased hyperintensities (arrowheads).

Marsden Dystonia Rating Scale score improved to 0 after 2 weeks of glycemic control without any dyskinetic movements.

A follow-up brain MRI after 2 months of treatment showed improved hyperintensities at the bilateral globus pallidus and putamen; the difference was more significant on T2-weighted images (Fig. 2).

Informed consent for publication of the brain images was obtained from the patient. This study was approved by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital and requirement of written consent was waived (IRB No. 2019-11-006).

DISCUSSION

CHBG warrants awareness as a complication of diabetes mellitus, especially in patients with a long history of and poorly-controlled diabetes [1]. This case indicates that CHBG can also occur in young adults with continued diabetic history. Moreover, although unilateral involvement has been more commonly reported, this case had bilateral involvements [3,6].

T1-weighted brain MRI images of CHBG reveal characteristic hyperintense basal ganglia lesions. T2-weighted images show variable intensities of normal and hypo to hyperintense brain lesions; however, hypointense basal ganglia lesions have been most commonly reported [1,6]. Compared to acute phase brain MRI, the hyperintense lesions on T1-weighted images were reported to regress during remission phase, and the follow-up MRI studies have frequently shown the disappearance of basal ganglia hyperintensities [1,3,8]. Contrary to previously reported cases with hypointense or subtle hyperintense basal ganglia lesions on T2-weighted images, our case showed marked diffuse hyperintensities involving the basal ganglia on T2-weighted images. Furthermore, even though the choreic movements of the patient completely disappeared after glycemic control, hyperintensities in T2-weighted

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images remained with partial decrease of hypersignal in the follow-up brain MRI. Resolution of the brain images was slower than the clinical improvement.

The exact pathogenetic mechanism of CHBG remains unknown, and various hypotheses have been proposed [1,6,8,9]. The proposed mechanisms for hyperintense basal ganglia lesions in CHBG syndrome include deposition of myelin breakdown products, metabolic acidosis, petechial hemorrhage, calcification, or gemistocytosis due to ischemia [1,4-6,8]. Metabolic brain diseases can cause myelinolysis, releasing lipids, and consequently presenting abnormal signals on T1- and T2-weighted MRI [8].

Hyperglycemia is hypothesized to activate anaerobic metabolism [2,3,9]. During anaerobic metabolism, the brain metabolizes gamma-aminobutyrate (GABA) into succinic acid, which causes metabolic acidosis [3,9]. In nonketotic hyperglycemia, insufficient ketoacetate for GABA and acetylcholine re-synthesis can result in the lack of these neurotransmitters [3,9]. Depletion of GABA and acetylcholine within the basal ganglia may cause the onset of chorea [3,8].

In addition, hyperglycemia leads to increased viscosity of blood and disrupts the blood-brain barrier [2]. In cases of vascular insufficiency, this may cause transient ischemic injuries to the vulnerable striatum [2]. Previous single-photon emission CT studies have reported the hypoperfusion of these areas [6]. A combined interplay of these factors are believed to result in subsequent chorea and dyskinesia in patients with nonketotic hyperglycemia [2,6].

Previously published studies have frequently shown the rapid improvement of symptoms and favorable prognosis with the correction of hyperglycemia [5,7,8,10]. Our case revealed that the chorea originating from the hyperglycemia could be reversible within one week.

In conclusion, CHBG syndrome is an uncommon complication of uncontrolled hyperglycemia. Glycemic control is important even in young adults with type 1 diabetes mellitus. If patients with diabetes mellitus present with hyperkinetic movements, suspicion and early detection of CHBG syndrome would be important for the accurate diagnosis and treatment.

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