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A STUDY ON NON-KETOTIC HYPERGLYCEMIA INDUCED MOVEMENT DISORDERS AND SEIZURES

Neurology

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ABSTRACT

Background: Non-ketotic hyperglycemia (NKHG) may increase the probability of movement disorders and seizures.
Methods: We describe a series of 18 patients admitted for seizures and movement disorders linked to NKHG.
Results: Ten patients developed movement disorders and eight others seizure disorder. Glucose levels varied 297 mg/dl to 597 mg/dl. All patients responded well to insulin therapy and nine of them needed anti-epileptic drugs.
Conclusion: Movement disorders or seizures in patients with NKHG could be misdiagnosed as neurological diseases. Blood glucose must be audited whenever patients with seizures or movement disorders are encountered, as the condition may quickly resolve when NKHG is controlled.

KEYWORDS

Hemichorea-Hemiballism, Non-ketotic hyperglycemi,a Movement disorders, Seizures

INTRODUCTION

The neurologic manifestations of diabetes are varied and include stroke, altered mental status, neuropathy, seizures, visual hallucinations, and movement disorders. Several movement disorders have subsequently been associated with hyperglycemia, with hemichorea-hemiballismus (HCHB) being the most common. Other involuntary movements seen in the setting of hyperglycemia can be due to seizures and can include generalized tonic-clonic seizures, focal seizures, and epilepsia partialis continua (EPC). It develops more quickly than other disorders of diabetes mellitus with hyperglycemia, but usually without evidence of ketosis. [1] Despite the long-standing documentation of these entities, their etiology remains poorly understood. The prompt institution of appropriate insulin therapy will improve prognosis and hasten recovery. [2]

MATERIALS AND METHODS

We performed a retrospective study of 18 patients referred to the Department of Neurology over a period of 5 years, on the basis of history, clinical features and neuroimaging findings consistent with seizures and movement disorders related to NKHG. Inclusion criteria – 1.NKHG- hyperglycemia with no evidence of ketosis, 2. Seizures that disappeared when hyperglycemia is controlled and 3. The absence of lesions in cerebral imaging that may explain seizures. Exclusion criteria – 1.Family or personal history of epilepsy, 2. Previous cranial trauma, 3. Preexisting neurological disorders associated with seizures and 4. Previous history of movement disorders. All patients underwent complete physical examination and routine laboratory analyses, including blood cell count, plasma glucose, serum electrolytes, renal, and liver tests. Urine samples were tested for glucose and ketones. Hourly monitoring of the plasma glucose was undertaken at the bedside using dextrostix. Diagnosis of NKHG was based on hyperglycaemia without ketoacidosis and no abnormalities in cerebral imaging and electroencephalogram (EEG). The medical records of the patients were reviewed for follow-up and response to treatment.

RESULTS

A total of 18 patients (7 men and 11 women) were included. The main clinical, blood investigation reports, neuroimaging findings, and treatment of the patients are summarized in table 1. The female to male sex ratio was of 1.57. The mean age at the onset of seizures and movement disorders was 66.17 years (range 51 – 86 years). The previous medical history of patients was noteworthy with diabetes mellitus in all cases and systemic hypertension in seven cases. Six patients experienced partial motor seizures, which were continuous (Epilepsia Partialis Continua) in two cases. Generalized tonic-clonic seizures were noted in two patients. Movement disorders were present in ten cases: the classical hemichorea- hemiballismus was seen in six patients, hemichorea in 2 patients and generalised chorea in two patients. The patients' vital signs were stable. The blood pressure was within the normal range in 13 patients even suffering from arterial hypertension during hospitalization. In the remaining 5 patients, elevated blood pressure was controlled easily with antihypertensives. 15 patients were conscious, and three was obtunded at admission. A thorough neurological examination was normal in 14 cases and revealed a post-ictal neurological hemiparesis (Todd's paralysis) in four patients. The paraclinical data revealed elevated plasma glucose in all patients. At admission, the plasma glucose levels varied from 297 to 587 mg% with a mean level of 430mg%. There was no evidence of ketosis in all urine samples. In addition, computed tomography brain was normal in ten patients. In the remaining 8 cases, CT brain showed classicial hyperdensity in Putamen and Caudate Nucleus. The interictal EEG was recorded in only 9 patients. It was normal in seven cases and bilateral epileptiform activity was noted in 2 patients.

Several amounts of physiological saline were infused as a first priority to relieve dehydration at the following rates: 1000-2000 ml in 1 h, 500-1000 ml considering the severity of renal failure in three patients. Potassium chloride was added in amount 10 mmol (mEq) per 500 ml of physiological saline as soon as the first dose of insulin was given, provided the ECG showed no peaks of T-waves. All our patients were administered immediately intravenous insulin with target capillary blood glucose ranged between 120 mg% to 160 mg%, to which eleven of them initially responded well. Monitoring of the plasma glucose was undertaken subsequently using dextrostix, and potassium deficiency was controlled every 4 h. The injections were repeated at hourly intervals until the plasma glucose had fallen below 160 mg%. When the acute symptoms of movement disorders and seizures relieved within a mean of 3 days (range 1-7 days), intravenous insulin was withdrawn and insulin was injected subcutaneously every 4 h. Sodium Valproate was prescribed during the hospital stay in four out of six cases of partial seizures (including one epilepsia partialis continua), in all two cases of generalised tonic clonic convulsions, and in three out of ten cases of movement disorders.

Table 1 - Clinical details of 18 patients with movement disorders seizures and related to non-ketotic hyperglycemia

No	Age/Sex	Duration of Diabetes	Type of movement disorder or Seizure	Blood sugar on admission	HbA1C	CT Brain findings	Treatment given	Symptoms vanishing after (days)
1	53/F	5	HCHB	523	14.3	HD Putamen and CN	Insulin	3
2	86/F	20	PMS in right hemi-face	496	14	Normal	Insulin, SVP	5
3	71/M	14	HCHB	387	12.5	Normal	Insulin, SVP	4
4	62/F	11	HCHB	333	14.8	HD Putamen and CN	Insulin	2
5	68/F	10	PMS on left upper limb	299	15.1	Normal	Insulin	1
6	59/M	7	EPC	297	14.3	Normal	Insulin, SVP, CLZ	7
7	74/M	20	GTCS	587	15.3	Normal	Insulin, SVP	5
8	70/M	17	HBHC	356	13.9	HD Putamen and CN	Insulin	1
9	66/F	10	HC	527	14.7	HD Putamen and CN	Insulin	2
10	65/F	12	HCHB	444	13.1	Normal	Insulin	1
12	69/F	13	PMS in righthemi-body	436	13.6	HD Putamen and CN	Insulin	4
13	59/F	11	GTCS	385	13.4	Normal	Insulin, SVP	3
14	52/F	14	GC	453	13.8	HD Putamen and CN	Insulin, SVP	5
15	70/F	15	HCHB	392	12.7	HD Putamen and CN	Insulin	1
16	60/M	10	PMS	507	14.5	Normal	Insulin, SVP	2
17	82/M	19	EPC	530	13.9	Normal	Insulin, SVP	3
18	74/F	20	HC	365	11.2	HD Putamen and CN	Insulin	2

CT: Computed tomography; HCHB: Hemichorea – Hemiballism; HC: Hemichorea; GC: Generalized Chorea; PMS: Partial motor seizures; GTCS: Generalized tonic-clonic seizures ; EPC: Epilepsia Partialis Continua; HD: Hyperdense; CN: Caudate Nucleus; SVP: Sodium Valproate; CLZ: Clonazepam

DISCUSSION

Involuntary movements and seizures associated with hyperglycemia have been well described in the neurology literature for over 50 years. These involuntary movements and seizures can be due to hereditary reasons, drugs, metabolic causes-hyperglycemia, thyroid/parathyroid disorders, infections, immunological and perinatal hypoxia. Metabolic cause is one of easily treatable and completely reversible cause of involuntary movements and seizures. Among the metabolic disorders, India has a high prevalence of diabetes mellitus [3]. Stroke and diabetes mellitus remain as the major causes of these disorders. Majority of the patients reported with movement disorders/seizures caused by non-ketotic hyperglycemia were Asians, due to possible genetic predisposition [4,5,6]. It can also be a presenting symptom of diabetes. The pathogenesis of movement disorders and seizures associated with non-ketotic hyperglycemia is poorly understood. In nonketotic hyperglycemia, the shift to anaerobic metabolism causes brain to utilize amino butyric acid which is synthesized from acetoacetate. Unlike in ketoacidosis, acetoacetate is rapidly depleted in nonketotic hyperglycemia causing cellular dysfunction. [7]

The female to male ratio remains controversial. It mostly occurs in females of 50- 80 years of age. The present series is consistent with literature, with a mean age at the onset of 66.17 years and the female to male sex ratio was 1.57.

NKHG in patients with diabetes mellitus has been shown to be associated with various movement disorders such as chorea, ballism, athetosis etc. either singularly or in combination (hemichoreahemiballism (HCHB), choreoathetosis) and showing either a generalized or lateralized distribution pattern.[8] These movement Disorders occur more commonly in those presenting with hyperglycemic hyperosmolar state than diabetic ketoacidosis. In our series, movement disorders were present in ten cases: the classical hemichorea- hemiballismus was seen in six patients, hemichorea in 2 patients and generalised chorea in two patients. The occurrence of seizures may also like all our patients, be a feature of NKHG in patients with known diabetes.Different types of seizures were noticed.[9] They are motor seizures usually focal, rarely generalized tonic-clonic seizures. Seizures associated with NKHG are often recurrent, and partial status epilepticus were observed.[10]

Elderly non-ketotic hyperglycemic diabetic patients presenting with hemichorea-hemiballism/focal seizures and showing hyperdensities in the contralateral basal ganglia on CT scan and high signal intensity in corresponding areas on T1-weighted magnetic resonance scans have been reported already.[12] There is much controversy regarding the cause of these imaging changes. Initially it was thought to be due to calcification.Chang and colleagues had postulated petechial haemorrhage to be the cause. Pathologic findings by stereotactic biopsy from the striatum revealed gliotic brain tissue with abundant gemistocytes suggesting that the hyperintensities in T1 could be due to the protein hydration layer inside the cytoplasm of the swollen gemistocytes, as is observed in cases of gemistocytic astrocytoma. [13]

The prognosis of seizures and movement disorders related to NKHG has been reported to be excellent [8,9,11]. When hyperglycemia is detected and corrected, the movement disorder usually resolves within few days and may not require symptomatic therapy. In our patients, hyperkinesia/seizures resolved dramatically after control of the hyperglycemia. This illustrates that acute movement disorders and seizures caused by hyperglycemia is a treatable disorder with a good prognosis. The symptoms are typically refractory to antiepileptic drugs but respond well to insulin therapy.Nonetheless, it requires sometimes the antiepileptic and neuroleptic drugs in movement disorders.[8,9,14] The antiepileptic drugs especially phenytoin may be harmful and inhibit the insulin secretion.In our series, the anti-epileptic drugs were prescribed in nine patients and have in most cases quickly achieved a satisfactory improvement. Clonazepam was prescribed in emergency settings to treat severe recurrent seizures that may disclose to status epilepticus. When seizures were typically spaced in time, we prescribed the sodium valproate. These antiepileptic drugs were thereafter withdrawn.

CONCLUSION

Involuntary movements and seizures associated with the hyperglycemic nonketotic state are well described in the neurology literature. It is important to recognize NKHG induced movement disorders and seizures as their management differs greatly from that used for “traditional” movement disorders and seizures. Treatment rests primarily on the reversal of hyperglycemia and the accompanying metabolic disturbances as opposed to the use of antiepileptics/ neuroleptics. The prognosis remains excellent, with the vast majority of patients showing complete resolution of involuntary movements and seizures within hours to a few days of correction of hyperglycemia.

REFERENCES

1. Scherer C. Seizures and non-ketotic hyperglycemia. Presse Med 2005; 34(15):1084-6. [In French].
2. Postuma RB, Lang AE. Hemiballism: revisiting a classic disorder. Lancet Neurol 2003; 2(11): 661-8.
3. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V.Diabetes Epidemiology Study Group in India.High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia.2001 Sep;44(9):1094-101.
4. Lin JJ, Lin GY, Shih C, Shen WC. Presentation of striatal hyperintensity on T1-weighted MRI in patients with hemiballism-hemichorea caused by non-ketotic hyperglycemia: report of seven new cases and a review of literature. J Neurol. 2001.Sep;248(9):750-5.
5. B Shalini,W Salmah , J Tharakan . Diabetic non-ketotic hyperglycemia and the hemichorea-hemiballism syndrome: A report of four cases , Neurology Asia 2010; 15(1) : 89 – 91
6. Hsu,J.L.; Wang,H.C.; Hsu,W.C. Hyperglycemia-induced unilateral basal ganglion lesions with and without hemichorea: PETstudy . Movement Disorders Group of Taiwan Neurological Society
7. Mihai CM, Catrinoiu D, Stoicescu RM. Atypical onset of diabetes in a teenage girl: A case report. Cases J. 2008;1:425
8. Lin JJ, Chang MK. Hemiballismhemichorea and non-ketotic hyperglycaemia. J Neurol Neurosurg Psychiatry 1994; 57(6): 748-50.
9. Lammouchi T, Zoghlami F, Ben SL, Grira M, Harzallah MS, Benammou S. Epileptic seizures in non-ketotic hyperglycemia. Neurophysiol Clin 2004; 34(3-4): 183-7.
10. Singh BM, Gupta DR, Strobos RJ. Nonketotic hyperglycemia and epilepsia partialis continua. Arch Neurol 1973; 29(3): 187-90.8.
11. Hennis A, Corbin D, Fraser H. Focal seizures and non-ketotic hyperglycaemia. J Neurol Neurosurg Psychiatry 1992; 55(3): 195-7.
12. Sanfield JA, Finkel J, Lewis S, Rosen SG. Alternating choreoathetosis associated with uncontrolled diabetes mellitus and basal ganglia calcifi cation. Diabetes care 1986; 9(1):100-1.
13. Abe K, Hasegawa H, Kobayashi Y, Fujimura H, Yorifuji S, Bitoh S. A gemistocytic astrocytoma demonstrated high intensity on MR images: protein hydration layer. Neuroradiology 1990; 32:166-7.
14. Ahlskog JE, Nishino H, Evidente VG, Tulloch JW, Forbes GS, Caviness JN, et al. Persistent chorea triggered by hyperglycemic crisis in diabetics. Mov Disord 2001; 16(5): 890-8.