Original Article

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Pattern Recognition of MRI Findings in Patients with Non-Ketotic Hyperosmolar Hyperglycemic State- A Clinico-Radio-Biochemical Parameter Study

M. Dinesh[1], Anila Punchiry[2], Harshavardhan Balaganesan[3], Ram Gopal Karumuri[2]

[1]Assistant Professor, Department of Radiodiagnosis, Shri Satyasai Medical College and Research Institute, Ammapettai, Chengalpet, Tamilnadu, India, [2]Junior Resident, Department of Radiodiagnosis, Shri Satyasai Medical College and Research Institute, Ammapettai, Chengalpet, Tamilnadu, India, [3]Senior Resident, Department of Radiodiagnosis, Shri Satyasai Medical College and Research Institute, Ammapettai, Chengalpet, Tamilnadu, India.

Abstract

Background: Hyperosmolar hyperglycemic state is a complication of diabetes mellitus in which high blood sugar results in high osmolarity without significant ketoacidosis. The present study assessed MRI findings in patients with hyperosmolar hyperglycemic state. **Subjects and Methods:** 58 patients reported with hyperosmolar hyperglycemic state of both genders underwent MRI. **Results:** Out of 58 patients, males were 30 and females were 28. We found that clinical presentation were focal motor seizures in 25, multiple myoclonic jerks in 20, generalized tonic clonic seizures in 10 and complex partial seizures in 3 cases. The difference was non- significant (P> 0.05). The mean blood glucose level found to be 482.4 mg/dl, HbA1C was 12.1%, Na+/K+ level was 134.2/4.6 mmol/l and serum osmolarity was 305.8 mOsm/Kg. **Conclusion:** Clinical presentation were focal motor seizures, multiple myoclonic jerks, generalized tonic clonic seizures and complex partial seizures. T2/FLAIR was hyperintense, DWI showed restriction and SWAN was isointense.

Keywords: Focal motor seizures, multiple myoclonic jerks, non-ketotic, Hyperosmolar hyperglycemic state, Magnetic Resonance imaging.

Corresponding Author: Dr. Ram Gopal Karumuri, Junior resident, Department of Radiodiagnosis, Shri Satyasai Medical College and Research Institute, Ammapettai, Chengalpet, Tamilnadu, India.

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Introduction

Non-ketotic hyperosmolar hyperglycemic state (HHS) is a complication of diabetes mellitus in which high blood sugar results in high osmolarity without significant ketoacidosis. Symptoms include signs of dehydration, weakness, leg cramps, vision problems, and an altered level of consciousness.[1] Non-ketotic Hyperosmolar hyperglycemic state (NK HHS) is a life-threatening endocrine emergency that most commonly affects adults with type 2 diabetes mellitus. However, the incidence increased by 52.4% among children from 1997 to 2009.[2] NK HHS occurs in patients with type 2 diabetes who can still produce insulin (as opposed to diabetic ketoacidosis [DKA], which occurs in persons with type 1 diabetes and some with type 2 diabetes). The hallmarks of NK HHS include profound dehydration, marked hyperglycemia, variable degrees of neurologic impairment, and mild or no ketosis. Although DKA and HHS have been described as distinct entities, one-third of patients exhibit findings of both.[3]

The mortality rate from NK HHS ranges from 10% to 50%, which is considerably higher than that of DKA (1.2% to 9%). In children, the mortality rate from NK HHS may be as high as 60%. Mortality predictors include age, degree of dehydration, hemodynamic instability (hypotension, absence of reflex tachycardia), degree of consciousness, infection, and a history of cancer. Characteristic magnetic resonance imaging (MRI) findings in hyperglycemia-induced seizures include focal altered signal intensity, i.e., subcortical T2 hypointensity with gyral hyperintensity involving the cortex and cortical or leptomeningeal postcontrast enhancement.[4] The present study assessed MRI findings in patients with Non-ketotic hyperosmolar hyperglycemic state.

Subjects and Methods

The present study was conducted among 58 patients reported with Non-ketotic Hyperosmolar hyperglycemic state of both genders. All enrolled patients were made aware of purpose of the study and their written consent was obtained.

Demographic profile of patients was recorded. Parameters such as symptoms at presentation, history of diabetes, random blood sugar levels, serum electrolytes (sodium and potassium), blood urea, and HbA1C levels at presentation. The serum osmolality and blood urea nitrogen were calculated as follows- Serum osmolality (mOsm/kg = (2x

(Na {mmol/L} + K {mmol/L}) + (BUN {mg/dl}/2.8) + (glucose {mg/dl}/18). Blood urea nitrogen (mg/dl) = Urea (mg/dl)/2.14

All the patients underwent MRI on a 1.5 Tesla super conducting magnet, Phillips Achieva scanner including conventional sequences (T1 weighted image [T1W], T2W, and fluid-attenuated inversion recovery [FLAIR]) and advanced sequences (diffusion-weighted imaging [DWI] and susceptibility-weighted angiography [SWAN]), Magnetic resonance angiogrpahy(MRA). Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

Total- 58		
Gender	**Males**	**Females**
Number	30	28

[Table 1] shows that out of 58 patients, males were 30 and females were 28.

Table 2: Clinical presentation of patients

Clinical presentation	Number	P value
Focal motor seizures	25	0.14
Multiple myoclonic jerks	20	
Generalized tonic clonic seizures	10	
Complex partial seizures	3	

[Table 2, Figure 1] shows that clinical presentation were focal motor seizures in 25, multiple myoclonic jerks in 20, generalized tonic clonic seizures in 10 and complex partial seizures in 3 cases. The difference was non- significant (P> 0.05).

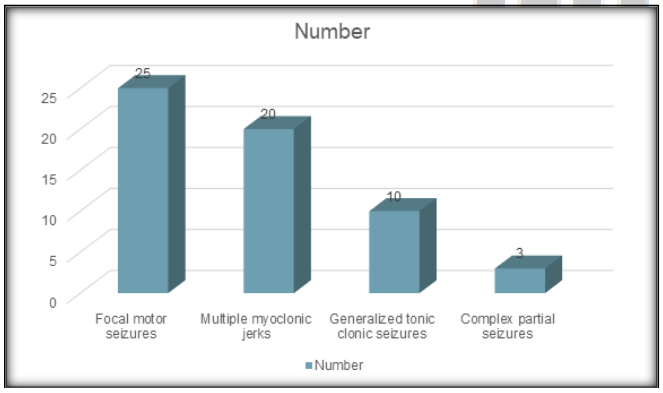

Figure 1: Clinical presentation of patients

Table 3: Assessment of laboratory findings

Laboratory findings	Values
Blood glucose (mg/dl)	482.4
HbA1C (%)	12.1
Na+/K+ (mmol/l)	134.2/4.6
Serum osmolarity (mOsm/Kg)	305.8

[Table 3] shows that mean blood glucose level found to be 482.4 mg/dl, HbA1C was 12.1%, Na+/K+ level was 134.2/4.6 mmol/l and serum osmolarity was 305.8 mOsm/Kg.

Table 4: Assessment of MRI findings

Location	Variables	Findings
Cortex	T2/FLAIR	Hyperintense
	DWI	Restriction
	SWAN	Isointense
Subcortical white matter	T2/ FLAIR	Hypointense
	DWI	Isointense
	SWAN	Hypointense

[Table 4] shows MRI findings in patients with hyperosmolar hyperglycemic state.

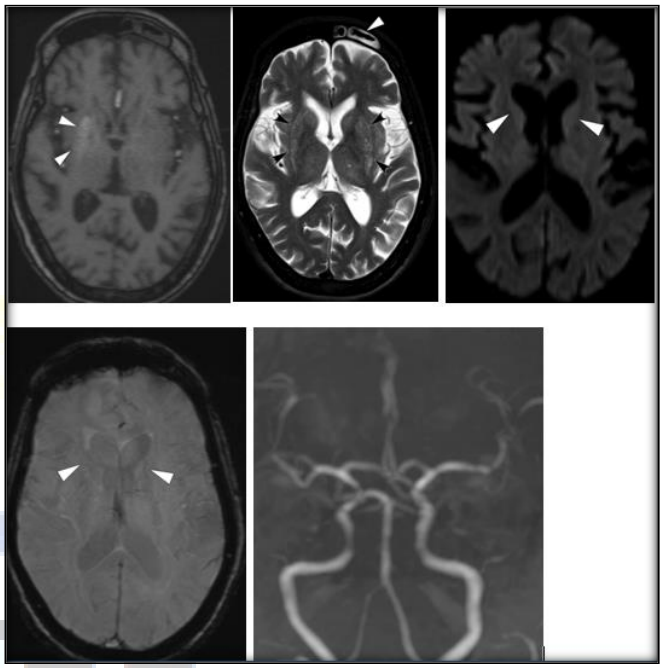

Figure 1: A 75 year old female presented to the emergency department with recent episode of focal motor seizures and unsreponsiveness, on presentation laboratory investigations showed blood glucose level of 460mg/dl & no ketone bodies in urine.

Non contrast MRI brain was performed with T1, T2, DWI, SWI & MRA images in sequential order depicting an areas increased signal intensity (white arrows) in right lent form and caudate nucleus (basal ganglia) with mild hyper intensity on T2 image (black arrows) showing no evidence of true diffusion restriction or abnormal blooming foci on SWI (white arrows). A normal appearing time of flight MRA image ruling out the vascular possibility.

Discussion

Non-ketotic hyperglycemia-induced seizures are refractory to antiepileptic medications, account for 15–40% of seizures in patients with NK HHS, and are commonly focal motor seizures and epilepsia partialis continua. NKHHS can be precipitated by infections, medications, nonadherence to therapy, undiagnosed diabetes, substance abuse, and coexisting diseases. Infections are the leading cause (57%

of cases); pneumonia, often gram-negative, is the most common infection, followed by urinary tract infection and sepsis.[5] Poor adherence to diabetes medication causes 21% of NK HHS cases. Other causes include myocardial infarction, cerebrovascular accident, pulmonary embolism, and mesenteric artery thrombosis. Psychoactive medications, especially second-generation antipsychotics, cause glucose elevations, insulin resistance, and diabetes independent of weight gain. Older adults with type 2 diabetes (sometimes undiagnosed) are at higher risk of NK HHS because they often take dehydrating medications (e.g., diuretics) and may be unable to adequately communicate their symptoms if they live alone or in a nursing home.[6] The present study assessed MRI findings in patients with hyperosmolar hyperglycemic state.

In present study, out of 58 patients, males were 30 and females were 28. We found that clinical presentation were focal motor seizures in 25, multiple myoclonic jerks in 20, generalized tonic clonic seizures in 10 and complex partial seizures in 3 cases. Lammouchi et al,[7] in their study twenty-four patients were included. On imaging, posterior cerebral region was predominantly involved, with parietal involvement in 83.3%, followed by occipital, frontal, and temporal involvement in 33.3% patients compared with occipital in 58.3%, parietal in 45.8%, and frontal and temporal in 16.6% of patients in previous literature. The subcortical T2 hypo-intensity was present in 83.3% of the patients, cortical hyper-intensity in all patients, and restricted diffusion in 66.6% of the patients in our study compared with subcortical T2 hypo-intensity in 95.8% of the patients, cortical hyper-intensity in 62.5%, and restricted diffusion in 58.3% of the patients in previous literature. Although many etiologies present with subcortical T2 hypointensity, cortical hyperintensity, restricted diffusion, and postcontrast enhancement on MRI, the clinical setting of seizures in a patient with uncontrolled hyperglycemia, hyperosmolar state, and absence of ketones should suggest hyperglycemia-induced seizures to avoid misdiagnosis, unnecessary invasive investigations, and initiate timely management.

We found that mean blood glucose level found to be 482.4 mg/dl, HbA1C was 12.1%, Na+/K+ level was 134.2/4.6 mmol/l and serum osmolarity was 305.[8] mOsm/Kg.The exact pathophysiology leading to seizures in the hyperglycemic hyperosmolar state is not entirely understood. One of the postulated mechanisms is a decrease in the levels of gamma-aminobutyric acid (GABA) because of depression in glucose utilization and Krebs cycle, thereby elevating alternate pathways of glucose metabolism.[8] These metabolic changes lead to the production of succinic acid from GABA using the succinic–semialdehyde pathway, which supplies up to 40% of the energy requirements of brain tissue. This decrease in the levels of GABA leads to a reduction in the seizure threshold and proconvulsive state.[9] In contrast, diabetic ketoacidosis has an antiepileptic effect as ketone bodies supply most of the energy requirements of neural tissue. Adenosine triphosphate-sensitive potassium channels (KATP) with diminished levels of GABA have been incriminated for the effects of increased extracellular glucose levels leading to neuronal hyperexcitability, neuropropagation, and seizures.[10]

Although a few studies reported no significant abnormalities in the MRI, subcortical T2 hypo-intensity, cortical hyper intensity with restricted diffusion, and cortical or leptomeningeal postcontrast enhancement, predominantly involving parietooccipital region are characteristic findings reported in Non-ketotic hyperglycemia-induced seizures.[11] Most of the previous studies on MRI changes in peri-ictal period, post generalized tonic-clonic seizures, or status epilepticus reported subcortical T2 hyperintensity and in contrast, most studies reported subcortical T2 hypointensity in Non-ketotic hyperglycemia-induced seizures. The exact pathophysiology leading to subcortical T2 hypo-intensity is not known and many hypotheses have been put forward. The transient deposition of free radicals and/or iron because of excitotoxic axonal damage during hyperglycemia-induced seizures and intracellular dehydration in glial and supporting tissues are postulated mechanisms for subcortical altered signal intensity.[12]

Conclusion

Authors found that clinical presentation were focal motor seizures, multiple myoclonic jerks, generalized tonic clonic seizures and complex partial seizures. MRI findings were T1 hyperintense &T2/FLAIR mild hyperintense, DWI showed no true restriction and SWI showed no evidence of hemorrhage.

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