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CASUISTIC PAPER

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Non-ketotic hyperglycemia and diabetic striatopathy – a rare presentation with hemichorea-hemiballismus

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ABSTRACT

Introduction and aim. Non-ketotic hyperglycemia (NKHG), also known as hyperosmolar hyperglycemic state (HHS) is a serious metabolic complication of diabetes mellitus (DM).The mortality rate can be up to 20% and this is much more higher than that of diabetic ketoacidosis (DKA). It is usually precipitated by an event such as pulmonary/urinary infection, myocardial infarction (MI) or stroke. In this state of metabolic derangements, central nervous system (CNS) manifestations including altered mental status with or without focal neurological deficits are prominent clinical presentations. On the other hand, HHS may also be complicated with various other CNS events. Herein, a quite rare presentation of HHS with hemichorea – hemiballismus in a 71 year old female patient with type 2 DM is presented.

Description of the case. A 71-year-old female patient type 2 DM presented to our emergency department with progressive involuntary movements on the right upper and lower extremities accompanied by semiconsciousness during the last 24 hours. On neurological examination, cranial nerves and cerebellar signs were found to be normal, as the deep tendon reflexes. However, involuntary non-rhythmic writhing movements at rest were present on her right sided extremities. The fingerstick evaluation showed marked hyperglycemia (HG). The laboratory findings were characterized with high blood glucose level without obvious acidosis compatible with HHS. In urine analysis, glucosuria without significant ketonuria was detected. On head CT, subtle hyperdensity was noted in the left neostriatal regions without any mass effect or perilesional edema, compatible with left sided diabetic striatopathy (DS).

Conclusion. Diabetic striatopathy is a quite rare presentation of HHS with hemichorea – hemiballismus. The characteristic computed tomograhy (CT) findings of associated striatopathy should be differentiated from vascular lesions that may also present with unilateral findings in the course of HHS and should not be overlooked in diabetic patients to recognise the ongoing HHS before the coma precedes.

Keywords. diabetic striatopathy, hemiballismus, hemichorea, hyperdense basal ganglia

Introduction

Non-ketotic hyperglycemia (NKHG), also known as hyperosmolar hyperglycemic state (HHS) is a serious metabolic complication of diabetes mellitus (DM). It is particularly seen in elderly diabetic women, mostly with T2DM but can also occur in type 1 DM. It was first described by Won Frerichs and Dreschfeld in 1880s.[1] It is a potentially fatal complication which can progress to coma, which is called as non-ketotic hyperosmolar coma (NKHC). The mortality rate can be up to 20% and this is much more higher than that of diabetic ketoacidosis (DKA).[2,3] It is usually precipitated by an event such as pulmonary/urinary infection, myocardial infarction (MI) or stroke. HHS is characterized with

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profound hyperglycemia (HG) without significant ketoacidosis & Kussmaul breathing or fruity urine. In HHS, high blood glucose level leads to severe dehydration and increased osmolarity resulting in decreased circulation with compromised end organ perfusion. As a response to decreased cerebral blood flow, the brain starts to produce osmotically active organic substances (idiogenic osmoles) in order to ensure intracellular volume by preventing fluid from moving into the extracellular space from the intracellular space.[4] In this state of metabolic derangements, central nervous system (CNS) manifestations including altered mental status with or without focal neurological deficits are prominent clinical presentations. On the other hand, HHS may also be complicated with various other CNS events, some of which are early presenting clinical manifestations before the coma.

Aim

Herein, we aimed to present a quite rare presentation of HHS with hemichorea - hemiballismus in a 71-year old female patient with type 2 DM.

Description of the case

A 71-year-old female patient with hypertention, hypercholesterolemia and long-standing poorly controlled type 2 DM presented to our emergency department with progressive involuntary movements on the right upper and lower extremities that started 4-5 days ago and were accompanied by semiconsciousness during the last 24 hours. There were no history of movement disorders, previous history of stroke or trauma. She was ill appearing with findings of dehydration including hypotension (105/65 mmHg), tachycardia (113/minute) and weak pulses. The skin and the oral mucosa were all dry with poor skin turgor. Her body temperature was raised (38.3°C). On neurological examination, cranial nerves and cerebellar signs were found to be normal, as the deep tendon reflexes. However, involuntary non-rhythmic writhing movements at rest were present on her right sided extremities. The fingerstick evaluation showed marked HG. The laboratory findings were characterized with high blood glucose level (524 mg/dL) without obvious acidosis (pH: 7.347 and HCO_3: 12 mmol/L) compatible with HHS. Serum sodium (Na^+) level was 131 mg/dl with increased anion gap of 20 mmol/L. The low level of Na was compatible with pseudohyponatremia and the corrected level was calculated as 137.8 mg/dL. The serum osmolarity was calculated as 345 mOsm/L. The other electrolytes including potassium (4.6 mg/dL), phosphorous and magnesium were all in the normal ranges, except the increased level of Cl (113 mg/dL). The creatinine, urea and uric acid levels were elevated reflecting prerenal azotemia. In urine analysis, glucosuria without significant ketonuria was detected. The white blood cell count (WBC) was increased ($25x10^3$/μL) with neutrophil predominance (90%) in addition to increased level of procalcitonin (6.45 μg/L), which reflects a pyogenic infection. Neither pneumonia on chest computed tomography (CT) nor urinary tract infection in urine analysis were detected, but methicillin resistant staphylococcus aureus (MRSA) was established in the blood culture analysis (Table 1).

Table 1. The laboratory values

	Patient's results	Normal reference values
Blood glucose	524 mg/dL	74-100 mg/dL
pH	7.347	7.37-7.45
HCO_3	12 mmol/L	21-26 mmol/L
Na^+	131 mmol/L	136-145 mmol/L
K^+	4.6 mmol/L	3.5-5.1 mmol/L
Cl^-	113 mmol/L	95-105 mmol/L
WBC	$25x10^3$/uL	$3.8\text{-}10x10^3$/uL
neutrophils	90%	45-78 %
procalcitonin	6.45 μg/L	0-0.5 μg/L

On head CT, there were no intracranial hemorrhage or cerebral edema. However, when looked at carefully, subtle hyperdensity was noted in the left neostriatal regions without any mass effect or perilesional edema, compatible with left sided diabetic striatopathy (DS) which explains the right sided hemichoreic movements (Fig. 1). She was managed with wide spectrum intravenous antibiotherapy in addition to isotonic fluid and insulin to correct the HG with close monitoring of the glucose level. Her clinical findings were resolved upon glucose control completely at first month on clinical follow up.

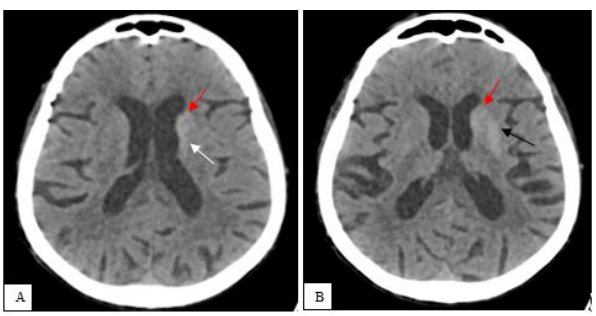

Fig. 1. Head CT showing subtle abnormal hyperdensity involving the left striatal regions; The head of caudate nucleus (a,b; red arrow), the body of caudate nucleus (a,white arrow) and putamen (b, black arrow)

Discussion

HHS is defined as plasma glucose level greater than 600 mg/dL, plasma effective osmolarity greater than 320 mOsm/L at the absence of significant ketoacidosis.[5] In the pathophysiology, the main underlying factor is decreased utilization of glucose in peripheral tissues

caused by the deficient effect of insulin. The resultant HG becomes more pronounced with gluconeogenesis and glycogenolysis by the release of counter-regulatory hormones as a response to tissue starvation, as in the pathogenesis of DKA. Also, increased serum osmolarity causes free water to be withdrawn from extracellular space and excreted in the urine, along with glucose and electrolytes, resulting in dehydration.[6] In HHS, as insulin is still produced, ketogenesis is greatly inhibited, and thus ketonemia & acidosis. In severe HG, the osmotic gradient leads to passage of intracellular water into the extracellular space resulting in Na^+ level to be measured incorrectly low, which should be corrected to assess the severity of dehydration and to adress the management. On the other hand, the anion gap must be calculated by using the measured Na^+ level instead of the corrected Na^+ and if it is found to be increased as in our patient, the cause is lactic acid production from compromised end-organ perfusion, which is also the cause of mild acidosis in HHS, if present.[7] Acute neurological manifestations in HHS are not uncommon. First of all, patients are at increased risk of thromboembolic events due to hyperosmolarity. Moreover, the earliar stages of HHS, may be complicated with various CNS events. Seizure is seen in up to 25% of the cases and is called as nonketotoic hyperglycemic seizure.[8] Much more rare than this, hemichorea-hemiballismus may also be the early presentation in HHS. It is also called as nonketotic hyperglycemic hemichorea, chorea-hyperglycemia-basal ganglia syndrome or DS. It is more commonly reported in elderly type 2 diabetic female patients as compared to males, and more frequently in Asian patients, which may suggest a genetical predisposition or may be a publication bias.[9,10] The neostriatum is composed of caudate nucleus and putamen, which involve in voluntary motor control and timing of the movement among many other functions. Hemichorea-hemiballismus is unilateral involuntary and non-rhytmic movements on one side of the body caused by contrlateral disorders of the neostriatum. DS is a very rare cause of hemichorea-hemiballismus associated with contrlateral neostriatal imaging abnormalities.[9,11] A metanalysis reported bilateral chorea with bilateral neuroimaging abnormalities in a small subset of the cases. Hemichorea with ipsilateral neuroimaging findings was very rare which was seen in only 2% of the patients while 98% of the cases had contrlateral findings.[9] Although the exact pathogenesis is not clear, the augmented sensitivity of dopaminergic receptors in neostriatum due to decline in the estrogen receptors is considered regarding the higher prevelance in elderly women.[12] Cerebrovascular insufficiency causing transient ischemia and petechial microhemorrhages were also proposed as the underlying causes. Additionally, secondary metabolic changes like depletion of gamma-aminobutyric acid and acetylcholine associated with metabolic acidosis secondary to shifting of cerebral metabolism to anaerobic pathway is also considered.[13-15] Neuroimaging findings are very typical and include contrlateral hyperdensity in the neostriatum on CT and corresponding T1w hyperintensity on magnetic resonance imaging (MRI) in the same areas.[13,15-17] Although the precise pathophysiological causes of these neuroimaging abnormalities are also not clear, petechial microhaemorrhages due to regional blood-brain barrier disruption induced by hyperviscosity resulting in erythrocyte diapedesis was suggested.[18] In addition, mineral deposits, myelin destruction and infarction with astrocytosis were also proposed.[13,17,19] Petechial microhemorrhages can explain the characteristic CT finding but some reports including susceptibility images show that hemorrhages are not present consistently. Calcification is another explanation for CT hyperdensity but reversibility of the imaging findings makes this also unlikely. Therefore, reactive astrocytosis and an abundance of gemistocytes was suggested as the most possible underlying mechanism to explain the high T1 signal on the MRI and protein desiccation during Wallerian degeneration to explain CT findings.[17] Neuroimaging studies are crucial in the evaluation of acute onset hemichorea-hemiballismus in order to differentiate vascular lesions which may also present as a unilateral basal ganglia findings. The hyperdensity conforming to the shape of the caudate nucleus and the putamen with no perilesional edema and no mass effect on CT is very characteristic to distinguish DS from hemorrhage involving basal ganglia. DS is also differentiated from a striatocapsular infarct caused by the occlusion of middle cerebral artery (MCA) by the sparing of the anterior limb of the internal capsul.[9] Besides, on CT the abnormality is not hyperdense in case of ischemic infarction and instead, faint hypodensity may present. The reversibility of neuroimaging findings upon correction of HG in contrast to the vascular lesions is the other characteristic feature of DS and usually seen on follow up imaging studies. The time for the resolution of the imaging findings was reported as three months for CT and over eight months on MRI in a study.[13] Unfortunately, our patient had no follow up imaging studies till the three monts after her presentation to show the reversibility. In addition, electroencephalography had not been performed during the clinical follow up of the patient to evaluate the changes. In the management of DS there is no need for specific treatment. The prognosis is excellent in most of the cases and clinical findings resolve with the correction of HG – hyperosmolarity. In a case series, the complete resolution of the chorea was shown in 74% of the patients over a period of one hour to ten months.[9] However, some patients may require dopamine antagonists for the relief of the longstanding symptoms. The other important aspect of HHS regarding neurological complications is the

prevention of cerebral edema during management. The serum osmolarity should be decreased so rapidly that it does not exceed the rate at which the brain can remove the idiogenic osmoles. Therefore blood glucose level should be closely monitored and should be prevented from sudden drop.

Conclusion

In conclusion, hemichorea-hemiballismus syndrome can be encountered as an early presenting clinical manifestation in HHS and imaging plays an important role in dfiferentiation of DS from vascular lesions which may also occur in the course of HHS as a triggering factor or as a complication related with hyperosmolarity and may also present with unilateral imaging findings. It should not be overlooked in diabetic patients to recognise the existing HHS and to prevent coma.

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Declarations

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Author contributions

Conceptualization, B.E. and H.Ö.; Methodology, B.E. and T.O.K.; Formal Analysis, B.E., N.K. and H.Ö.; Investigation, B.E. and T.O.K.; Writing – Original Draft Preparation, B.E. and T.O.K.; Writing – Review & Editing, B.E. and T.O.K.; Supervision, B.E. and H.Ö.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The data sets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Ethics approval

Not applicable.

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