A case of hyperosmolar hyperglycaemic state with involuntary movements – diagnostic dilemma and clinical considerations

Hanisah Abd Hamid[1], Nor-Aini Umar[1], Hanita Othman[1], Srijit Das[2]

[1]Department of Pathology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia
[2]Department of Anatomy, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

Submitted: 17 August 2009
Accepted: 14 September 2009
Arch Med Sci 2010; 6, 6: 987-990
DOI: 10.5114/aoms.2010.19315
Copyright © 2010 Termedia & Banach

Corresponding author:
Assoc. Prof. Dr.
Nor-Aini Umar, MD, DCP
Department of Pathology
Universiti Kebangsaan
Malaysia Medical Centre
Jalan Yaacob Latiff, Bandar
Tun Razak
56000 Cheras, Kuala Lumpur
Malaysia
Phone: +6 03 914 553 76
Fax: +6 03 917 382 55
E-mail: nau@ppukm.ukm.my

Abstract

Hyperosmolar hyperglycaemic state (HHS) is a medical emergency which needs immediate medical intervention. A 37-year-old Chinese woman with a history of hypertension attended the Emergency Department. She had a two-day history of involuntary movement, i.e. chorea of the upper limbs, preceded by a one-week history of upper respiratory tract infection. She also had polyuria and polydipsia, although she was never diagnosed as diabetic. The main aim of reporting the present case was to highlight the importance of biochemical investigations involved in the diagnosis of involuntary movements.

Key words: hyperglycaemic hyperosmolar state, involuntary movement, treatment

Introduction

Seizures are common presenting manifestations in patients with non-ketotic hyperglycaemic (NKH) hyperosmolar state [1]. Previous research reports have labelled diabetic ketoacidosis (DKA) and the hyperosmolar hyperglycaemic state (HHS) as important life-threatening emergencies with a mortality rate of HHS reaching up to 9.2% [2].

A 37-year-old Chinese woman attended the emergency department of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) with complaints of involuntary movement, i.e. chorea of the upper limbs. The preliminary investigations showed hyperosmolarity and hyperglycaemic state that led to an early diagnosis of acute on chronic renal failure. Interestingly, the involuntary movements disappeared with adequate treatment of the metabolic state. The importance of an early diagnosis of HHS with all possible biochemical investigations is discussed in the present paper. We also stress the fact that by focusing on the clinical presentation alone, one may delay arrival at a proper diagnosis of HHS. An early biochemical investigation regarding estimation of glucose may be necessary.

Case report

Prior ethical consent was obtained to report this case report. A 37-year-old Chinese, unmarried woman with a history of hypertension was brought in to the Emergency Department of UKMMC with a two-day history of involuntary movements of the upper limbs, i.e. chorea, preceded by a one-week history of upper respiratory tract infection. She also complained of

Table I. Biochemical investigations performed on admission

Parameter	Result
Creatinine (62-106 μmol/l)	229
Sodium (135-150 mmol/l)	127
Potassium (3.5-5.0 mmol/l)	4.0
Urea (2.5-6.4 mmol/l)	21.8
Magnesium (0.60-1.10 mmol/l)	1.43
Phosphate (0.71-1.36 mmol/l)	1.91
Total protein (67-88 g/l)	81
Albumin (35-50 g/l)	35
ALP (32-104 U/l)	192
ALT (< 44 U/l)	47
Cr. Ca 2 (2.14-2.58 mmol/l)	2.60
Cholesterol (< 5.7 mmol/l)	11.94
HDL (> 1.20 mmol/l)	1.42
LDL (< 3.80 mmol/l)	1.83
TG (< 1.40 mmol/l)	19.12
HBA_{1c} (4.4-6.4%)	15.9
FBS (3.0-6.7 mmol/l)	35.9
CRP (0-0.5 mg/dl)	7.08
ESR (1-20 mm/hr)	96
ABG	
BE (–3 – +3)	–3.5
PCO_2 (35–45)	93.1
PH (7.35–7.45)	7.39
PO_2 (65–100)	66.9
SBC (22-26)	21.5
Urine dipstick	Glu3+ Blood 1+ PH 6.5 Leu 2+
Urine ketone	+
Protein creat. index (< 0.02 g/mmol)	0.05
Urine sodium (mmol/l)	24
Urine osmolality (50-1200 mOsm/kg)	550
Serum osmolality (275-295 mOsm/kg)	358
ACTH random (0-46 pg/ml)	19.60
Cortisol random(am) (68-469 nmol/l)	639
PTH (1.3-7.6 pmol/l)	12.7

polyuria and polydipsia. There was a history of loss of appetite and weight.

Examination revealed a mildly dehydrated patient, who was otherwise alert and oriented. She was afebrile (37.5°C) with blood pressure recording of 130/90 mm Hg; heart rate of 70 beats/min and oxygen saturation (SaO_2) of 93% under 3 litres via nasal prongs. Her weight and height were 71 kg and 156 cm, respectively. The waist circumference was 108 cm with the body mass index (BMI) being 29. She had truncal obesity, buffalo hump and cushingoid facies (moon face with acne).

Her respiratory examination showed bilateral lung crepitations with inspiratory rhonchi and a prolonged expiratory phase. Involuntary movements of both upper limbs were diagnosed as chorea. On examining the central nervous system, including the visual field, reflexes were found to be unremarkable. There were generalized multiple white patches on both upper and lower limbs.

As displayed in Table I, the baseline biochemical investigations showed severe hyperglycaemia (35.9 mmol/l), high serum osmolality (358 mOsm/kg), elevated urea: creatinine ratio (> 30 : 1), trace ketonuria with normal arterial blood gases (pH 7.39, bicarbonate 21.5).

On admission, all the laboratory investigational values were consistent with HHS. Her fasting blood sugar showed severe hyperglycaemia (35.9 mmol/l) that suggested undiagnosed diabetes melitus (DM). This was further supported by her initial glycated haemoglobin, which showed severe chronic hyperglycaemia (15.9%). Fasting lipid profile revealed severe hypertriglyceridaemia (19.12 mmol/l).

A diagnosis of acute on chronic kidney failure due to severe dehydration secondary to HHS was made and the patient was transferred to the medical ward. She was aggressively rehydrated with intravenous fluid. Insulin infusion was instituted with strict monitoring of glucose and input output chart. A central venous pressure line was inserted to monitor the intravascular volume. Intravenous Augmentin and azithromycin treatment with 8 hourly Ventolin nebuliser for pneumonia was carried out. Interestingly, the chorea resolved completely with appropriate treatment.

Discussion

This case in the young patient was unique as the involuntary movement, i.e. chorea, was the main presenting symptom of the HHS with previously undiagnosed type 2 DM. We arrived at the diagnosis of type 2 DM. Other differential diagnosis could include type 1 DM, diabetes insipidus and diabetic ketoacidosis.

The high osmolarity contributed to the neurological symptoms observed in HHS. These focal neurological symptoms can include myoclonic jerks, chorea, nystagmus, and Babinski's signs, seizures and stroke [3]. Interestingly, the focal neurological deficit reversed completely with adequate treatment and correction of the metabolic abnormalities. Delayed treatment could result in mental obtundation with less than 20% of patients

presenting with coma [3]. However, there are many disorders that could also present with similar neurological changes apart from HHS. Thus, by focusing solely on the clinical presentation one may delay the diagnosis of HHS unless the glucose level is obtained early in the presentation.

HHS is a serious acute metabolic complication of diabetes mellitus. Higher HHS mortality rates compared to DKA (i.e. between 10% and 50%) are reported to respond to appropriate treatment [4]. HHS can also be the initial presentation of diabetes in 30% to 40% of patients, especially in the elderly, obese and those with decreased renal function [4, 5]. HHS is more common in type 2 DM as compared to type 1 DM [3, 4]. As per earlier reports, successful treatment of DKA and HHS needs immediate correction of dehydration, hyperglycaemia, and electrolyte imbalances; proper identification of co-morbid precipitating events; and also frequent patient monitoring [6]. An earlier protocol stated that the initial laboratory investigation in patients with suspected DKA or HHS should focus mainly on the plasma glucose, blood urea nitrogen/creatinine, serum ketones, electrolytes, osmolality, urinalysis, urine ketones, initial arterial blood gases, complete blood count with differential, and electrocardiogram [7]. Interestingly, in the present case, the patient had all possible risks of developing HHS.

HHS classically presents with an insidious onset of osmotic symptoms, i.e. polyuria and polydipsia, that occur for several weeks, followed by signs and symptoms of profound dehydration. In the present case, the patient was not known to be diabetic. Thus, there was under-recognition of signs and symptoms of uncontrolled diabetes, thereby leading to the development of HHS.

Initial physical examination revealed that the patient was afebrile despite her underlying pneumonia and urinary tract infection. HHS might have caused peripheral vasodilatation, thereby explaining the afebrile condition of the patient. In addition, obesity and diabetic dermatopathy indicated insulin resistance in this patient. However, all these clinical presentations of HHS might be similar to DKA, and a definite diagnosis must be confirmed through laboratory investigation. We advocate that the precipitating causes and other co-morbidities associated with HHS should also be included as part of the initial laboratory evaluation.

The classical picture of HHS in this patient included insidious onset of osmotic symptoms, i.e. polyuria and polydipsia, followed by signs and symptoms of profound dehydration. The under-recognition of the signs and symptoms of uncontrolled diabetes contributed to the development of HHS.

On the day of admission, measured serum osmolality (358 mOsm/kg) was high, corresponding to urine osmolality (550 mOsm/kg). Presence of high urinary sodium with severe hyperglycaemia indicated osmotic diuresis, which was consistent with the symptoms (i.e. polyuria and polydipsia). There was an osmolar gap as there was a discrepancy between the measured (358 mmol/l) and calculated serum osmolality (316 mmol/l) as a consequence of severe dehydration and hyperlipidaemia.

The renal function test revealed acute on chronic kidney failure as her previous creatinine level was 136 μmol/l at the time when the diagnosis of hypertension was made. During the current admission, her renal profile values were: sodium 127 mmol/l; potassium 4.0 mmol/l; serum urea and creatinine of 21.8 and 229 μmol/l, respectively giving a urea : creatinine ratio more than 30 : 1. This indicated pre-renal azotaemia as a consequence of severe dehydration. This was further supported by her urine : serum osmolarity ratio of more than 1.5 : 1. Furthermore, the magnesium (1.43 mmol/l), phosphate (1.91 mmol/l), and calcium (2.60 mmol/l) were also raised. Her corrected sodium (Table I) was normal (136 mmol/l) even though the measured sodium was low (127 mmol/l), which indicated pseudohyponatraemia due to the presence of severe hyperglycaemia and hypertriglyceridaemia.

The liver function test showed mild hypo-albuminaemia (35 g/l) that was most likely due to underlying chronic illness or diabetic nephropathy with evidence of significantly increased protein creatinine index. Her total protein and transaminase enzyme, ALP and ALT (81 g/l, 192 U/l, 47 U/l) were raised on initial presentation due to dehydration. Mildly elevated alkaline phosphatase was attributed to the dehydration or secondary to renal osteodystrophy. This was further confirmed by her serum calcium, which markedly decreased (1.87 mmol/l) after the aggressive treatment, which revealed the true hypocalcaemia as a complication of chronic kidney disease and increase of para-thyroid hormone level (12.7 pmol/l).

Arterial blood gas was normal (pH 7.39, bi-carbonate 21.5) and it ruled out DKA. Inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were markedly elevated because of ongoing infection or in-flammation. Urinalysis showed marked glycosuria (3+), leukocytosis (2+) with trace ketonuria. Full blood count showed relative polycythaemia (Hb 17.1) with haematocrit (48.5%) as a con-sequence of severe dehydration. White cell count (WBC) was high (18.8×10^9 mm^3) with pre-dominantly neutrophils, suggestive of infection. Blood culture was negative while urine culture revealed significant growth of *Candida* species indicative of urinary tract infection

Chest X-ray was suggestive of pneumonia. In conclusion, based on the above biochemical and

microbiological findings, this patient had developed acute on chronic kidney failure secondary to severe dehydration due to HHS precipitated by pneumonia and urinary tract infection.

HHS is the most serious complication of diabetic decompensation, which is associated with high mortality. Glucose levels, serum osmolality, and blood pH and serum bicarbonate level with or without ketones confirmed the biochemical diagnosis of HHS. In addition, calculation of the effective osmolarity and corrected sodium and potassium values could help the clinician to guide the treatment and identify any precipitating illness. HHS is a preventable disease, so we advocate that early diagnosis and identification of patients at risk with consistent hyperglycaemic state monitoring may be necessary.

References

1. Schomer DL. Focal status epilepticus and epilepsia partialis continua in adults and children. Epilepsia 1993; 34: S29-36.
2. MacIsaac RJ, Lee LY, McNeil KJ, Tsalamandris C, Jerums G. Influence of age on the presentation and outcome of acidotic and hyperosmolar diabetic emergencies. Intern Med J 2002; 32: 379-85.
3. Nugent BW. Hyperosmolar hyperglycemic state. Emerg Med Clin North Am 2005; 23: 629-48.
4. Chiasson J, Aris-Jilwan N, Belanger R, et al. Diagnosis and treatment of diabetic ketoacidosis and the hyperglycemic hyperosmolar state. CMAJ 2003; 168: 859-66.
5. English P, Williams G. Hyperglycaemic crisis and lactic acidosis in diabetes mellitus. Postgrad Med 2004; 80: 253-61.
6. Kitabchi AE, Nyenwe EA. Hyperglycemic crises in diabetes mellitus: diabetic ketoacidosis and hyperglycemic hyperosmolar state. Endocrinol Metab Clin N Am 2006; 35: 725-51.
7. American Diabetes Association. Hyperglycemic crises in diabetes. Diabetes Care 2004; 27: S94-102..