Hyperemesis Gravidarum is a Syndrome of Metabolic and Endocrine Disturbances: A Case Description

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Abstract Hyperemesis gravidarum is a clinical syndrome characterized by excess vomiting, dehydration and weight loss associated high human chorionic gonadotropin levels, usually occurring in the first trimester of gestation. It often presents with severe electrolyte imbalance, mental confusion and may be associated with thyroid dysfunction. We are describing the management of one such case riddled with multiple metabolic events.

Keywords Hyperemesis gravidarum · Hyponatremia · Transient hyperthyroidism of hyperemesis gravidarum (THHG) · Wernicke's encephalopathy · Central pontine myelinolysis

Introduction

Hyperemesis gravidarum (HG) is a clinical syndrome characterized by excess vomitings, dehydration and weight loss with elevated human chorionic gonadotropin (hCG) levels, usually occurring early trimesters of gestation. It is often associated with metabolic and nutritional disturbances and leads to significant fetomaternal morbidity. Here, we describe a typical case of HG with a plethora of metabolic, endocrine and neurological events.

Case Report

A 22 year old gravida (G2, P1) with 24 weeks of amenorrhoea presented with convulsions, delirium followed by unconsciousness. She was admitted in critical care unit for management. On examination, she was unconscious and dehydrated, but responding to deep painful stimuli. There was history of intractable vomiting (4–6 times/day), anorexia, loss of weight since 12 weeks. She was given parenteral fluids, frequently since 8 weeks due to severe restriction of oral liquid and calorie intake. At present admission, she was started on 5 % dextrose and normal saline for rehydration. Her investigations revealed hyponatremia of 123 mmol/L (139–145) and hypokalemia of 3.0 mmol/L (3.5–5.5). Arterial blood gas (ABG) analysis showed pH of 7.58 (alkalosis), HCO₃ was 28 mEq/L, pCO₂ of 56 mmHg and pO₂ of 110 mmHg. On systemic evaluation, there was no icterus and liver function tests were within normal limits (total bilirubin = 1.6 mg %; SGOT = 41 IU/L; SGPT = 54 IU/L; ALP = 126 IU/L). There were no signs of urinary tract infection and urinalysis was normal. Ultrasound abdomen showed single live fetus of 23 weeks gestation and no evidence of molar degeneration. Serum HcG titer was 8,243 mIU/mL.

In view of weight loss and palpitations, thyroid function test was done. Reports were suggestive of hyperthyroidism with serum thyroid stimulating hormone (TSH) = 0.06 mIU/mL (0.4–5.5), total triiodothyronine (T3) = 321 pg/mL (90–200) and total thyroxine (T4) = 18 ng/mL (8–15). But, T3/T4 ratio was <20:1 and hyperthyroid features were subtle leading to differential diagnosis of transient hyperthyroidism of hyperemesis gravidarum (THHG). As we suspected it to be gestational thyrotoxicosis, we have not started antithyroid drugs. Random blood sugar was 81 mg/dL and glycosylated hemoglobin of 7 % (4–6)

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suggested mild impaired glucose tolerance, though there was no past history of diabetes mellitus or gestational diabetes. Urinary ketones was +++ but urinary glucose was negative, which could be suggestive of prolonged starvation and catabolism in the apparent absence of diabetic ketoacidosis. She was started on fluid replacement with 5 % dextrose, 3 % hypertonic saline and potassium chloride (60 mmol/day) for correction of fluid and electrolytes. Antiemetics in the form of ondansetron 16 mg/day was given in divided doses. Urine output, electrocardiogram and serum electrolytes were monitored 6th hourly. There was gradual improvement in hydration and conscious states. Hyponatremia was corrected over 4 days duration with oral salt replacement from third day of admission. By third day, she regained consciousness, but developed horizontal nystagmus and complaining of diplopia. We suspected Wernicke's encephalopathy (WE) and provisionally started thiamine injections of 100 mg/day. On sixth day she was made ambulant, but was suffering from ataxia and mental confusion. No cerebellar or extrapyramidal signs were present. Tendon reflexes were normal. She was discharged on seventh day with the advice of oral thiamine supplementation, anti-emetics and salt intake. At the time of discharge, her serum sodium level was 148 mmol/L and potassium was 3.8 mmol/L. But, on 16th day she was admitted with left hemiparesis and aphasia following intractable vomitings for 2 days. Clinical history revealed that she defaulted with the advised medications at discharge. She was again started on parenteral fluids, anti-emetics and re-evaluated. Serum sodium was 124 mmol/L (139–145) and hypertonic saline was given slowly to correct hyponatremia.

Magnetic resonance imaging (MRI) of brain showed evidence of central pontine myelinolysis (CPM) (Figs. 1, 2, 3). Thiamine injections were given at the dose of 100 mg/day for subsequent 10 days. She recovered from motor weakness and aphasia by 19th day. She was diagnosed to be having WE secondary to HG and thiamine deficiency. On 23rd day, she complained of decreased fetal movements and ultrasound confirmed the diagnosis of an intrauterine death followed by termination. Her nystagmus and cognitive skills improved over following 4 weeks, but with mild residual ataxia. On 26th day, she was discharged on 10 mg of thiamine per day, dietary advice and psychological counseling. All the important clinical events are depicted in Fig. 4.

Discussion

The incidence of HG is variable with hospitalization rate of 0.5–0.8 % and repeat hospitalization rate of 20 % in subsequent pregnancies [1, 2]. HG usually occurs in the early trimesters of gestation and the etiology of HG is enigmatic, but the implicated causes are hormonal hCG, prolactin,

Fig. 1 T1-weighted sagittal MRI image of brain showing hypointense patch of CPM (arrow)

Fig. 2 T2-weighted sagittal MRI image of brain showing hyperintense patch of CPM (arrow)

thyroxine, estrogen, leptin, placental growth hormone) [3]; ethnicity; neurological and psychosomatic component. HG can lead to weight loss, dehydration, hyponatremia, hypokalemia, alkalosis and in severe cases, metabolic acidosis. Life-threatening complications such as renal failure, esophageal rupture, WE and neurological sequelae are reported in intractable cases. The most frequent clinical

Fig. 3 T1-weighted axial MRI image of brain showing hypointense CPM (arrow)

Fig. 4 A First day of admission; B regained consciousness; C patient was ambulant; D discharged; E Re-admitted with hemiparesis; F recovered; G fetal death; H recovered from WE

features of WE are confusion, ataxia and ophthalmoplegia. In their review of 49 cases of WE, Chiossi et al. [4] showed that 50 % of the patients had ataxia, nystagmus and mental confusion. Long term sequelae such as ocular palsies, blindness, convulsions and coma have been reported. But, early and aggressive treatment of WE with thiamine aids in complete patient's recovery [5].

THHG is a self-limiting condition, which resolves spontaneously with adequate control of hyperemesis and anti-thyroid drugs are not indicated [6]. Though differentiation between Graves' disease and THHG is not easy, several diagnostic clues such as past history, T3:T4 ratio is >20 and palpitations in Graves' disease helps in diagnosis of the cause of thyrotoxicosis. The CPM usually occurs due

to hyponatremia [7], rapid correction of hyponatremia or chronic alcoholism [8]. But, in our case hyponatremia was corrected gradually, but the clinical features of CPM and encephalopathy improved fast with thiamine supplementation. There are reports of CPM associated with WE in literature [9] and few reports show that CPM is completely reversible, though radiologic normalization takes many months [10]. Thus, it was highly suggestive of WE associated polyneuropathy as the cause of CPM in our case.

A very high index of suspicion is required to diagnose the associated metabolic disturbances and encephalopathy. The clinical scenario with plethora of events such as emaciation, dehydration, dyselectrolytemia, hyperthyroidism, alkalosis, ketonuria, hyperbilirubinaemia and encephalopathy justifies the status of HG as a syndrome with grave prognosis. Fortunately, all the above metabolic and endocrine disturbances are reversible with early and aggressive treatment. An interdisciplinary approach constituting an endocrinologist, obstetrician, physician and intensivist is needed to prevent fetal-maternal morbidity and mortality.

Conflict of interest The authors declare that they have no conflict of interest to disclose.

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