DYSTONIA CAUSED BY USE OF PROCHLORPERAZINE IN HYPEREMESIS GRAVIDARUM

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INTRODUCTION

Nausea and vomiting are common symptoms in early pregnancy, but true hyperemesis gravidarum (HG) is rare. We present a multigravid patient with hyperemesis who showed mental status changes in the 12th week of pregnancy as a consequence of antiemetic therapy.

CASE REPORT

A 29-year-old lady presented to the gynaecology emergency unit with a ten-day history of worsening nausea and vomiting with reduced urine output despite taking oral antiemetics. Pregnancy test was positive. She had suffered similar symptoms in her first pregnancy. Her weight at booking was 51kg.

Clinical examination showed her to be severely dehydrated with heavy (3+) ketonuria, pulse rate 73/min, BP 110/70 mmHg. Systemic examination was normal. Blood results showed normal haematological, biochemical and thyroid indices. Pelvic ultrasound scan confirmed a single intrauterine pregnancy at eight weeks' gestation. She was managed with intravenous fluids and parenteral antiemetics (prochlorperazine and metoclopramide) and discharged two days later.

Following several admissions over the subsequent weeks (latest at 12 weeks gestation), she had become quite frail looking with 16% weight loss (43kg). Blood results showed hypokalaemia which was corrected. Parenteral vitamin B₁ (in order to prevent the development of Wernicke-Korsakoff syndrome (WKS), thiamine deficiency) and thromboprophylaxis was started. Naso-gastric tube feeding was commenced following a dietician review. She tolerated this for only 24 hours. She was only on prochlorperazine at this point.

In the four days following admission she gradually developed oro-facial dystonia, retracted upper lips, slow tongue movements, dysarthria, dysphasia and dysphagia. There was no facial weakness or postural disturbance. Cranial nerve, optic fundi, reflexes and power were all normal. There was no past history of neurological illness.

A neurologist diagnosed drug-induced dystonia secondary to prochlorperazine. This was discontinued and she was started on oral procyclidine, 5mg thrice daily. She showed dramatic improvement within two hours and was discharged home the following day. Review in the antenatal clinic two weeks later showed her to be in good health with complete resolution of symptoms. Her anomaly scan at 20 weeks was normal and the subsequent antenatal course was managed as low risk.

DISCUSSION

Nausea and vomiting during pregnancy is a common experience affecting 50% to 90% of all women. HG is the most severe form of nausea and vomiting occurring in pregnancy. Between 0.3% and 2% of all pregnant women suffer from the condition.

It is characterised by intractable nausea and vomiting leading to dehydration and ketonuria, electrolyte and metabolic disturbances, and nutritional deficiency with associated weight loss ($\geq 5\%$ body weight) that may require hospitalisation. The onset of symptoms is usually in the first trimester of pregnancy but the socioeconomic impact on time lost from paid employment or household work can be immense.

The cause of HG is poorly understood but it is essential to exclude other causes of similar symptoms (see table 1).

Causes of hyperemesis gravidarum molar pregnancy multiple pregnancy Other diagnoses with severe vomiting urinary tract infection acute pancreatitis cholecystitis
Laboratory tests to help with diagnosis and treatment may include full blood count serum electrolytes liver function tests thyroid function tests β -hCG (beta human chorionic gonadotrophin) amylase lipase pelvic ultrasound scan
<i>Table 1 Differential diagnosis of hyperemesis gravidarum</i>

Associated neurological signs in HG (WKS, or drug-induced following use of antiemetics leading to dystonic reactions, or oculogyric crisis in severe cases) may be secondary to thiamine (vitamin B₁) deficiency. Hyponatraemia and its rapid reversal may cause fatal pontine myelinosis.

WKS is a rare but known complication of severe HG caused by thiamine deficiency. There are only 49 published cases in the literature to date. The classic triad of symptoms – confusion, ocular signs and ataxia – were manifest in only 47% of patients (23 of 49). Other signs include nystagmus, headache, vertigo, altered consciousness, memory impairment. Of the 49 cases, the mean age was 27 years and the mean gestational age was 14 weeks. The overall pregnancy loss rate, directly (spontaneous fetal loss) and

indirectly (planned abortion) attributable to WKS, was 47% (23 of 49).

Diagnosis of WKS is clinical but can be confirmed by magnetic resonance imaging to rule out organic brain injury. Symptom resolution can take months and permanent impairment is common; indeed complete resolution occurred in only 14 of 49 cases so far. Prompt treatment with intravenous thiamine (vitamin B₁) and longterm oral supplements is recommended.

The second-line antiemetics are usually implicated in dystonic reactions with more severe reactions manifesting as oculogyric crisis. Examples are the phenothiazines, eg chlorpromazine, prochlorperazine and metoclopramide. These drugs cross the blood brain barrier acting centrally on the chemoreceptor trigger zone to produce their effects. Interestingly, there are also now case reports of similar reactions with ondansetron, a drug hitherto not thought to be implicated. Dystonic reactions which may be manifest include facial muscle spasms, tremors, involuntary movements and the distressing oculogyric crisis (OGC).

incredible restlessness
agitation
fixed eye stare
backward and lateral flexion of the neck
widely opened mouth
tongue protrusion
ocular pain

Table 2 Features of oculogyric crisis

OGC is a severe dystonic reaction to certain drugs or medical conditions. Features can be recurrent if there is continued exposure to the precipitating factor and may include those features and factors shown in tables 2 and 3.

Immediate treatment of drug-induced OGC can be achieved with intravenous benztropine or procyclidine, which are usually effective within five minutes, although may take as long as 30 minutes for full effect. Any causative new medication should be discontinued. The abrupt termination of the psychiatric symptoms at the conclusion of the crisis is most striking.

Drug related causes

neuroleptics
nifedipine
benzodiazepines
carbamazepine
tricyclics
metoclopramide

Other causes

multiple sclerosis
neurosyphilis
Tourette's syndrome
postencephalitic Parkinson's

Table 3 Factors predisposing to oculogyric crisis

FURTHER READING

Chiossi G, Neri I, Cavazzuti M, Basso G, Facchinetti F. Hyperemesis gravidarum complicated by Wernicke encephalopathy: background, case report, and review of the literature. *Obstet Gynecol Surv* 2006;61(4):255-68

Rabenda-Lacka K, Wilczyński J, Breborowicz GH, Leśniak P, Jurga S, Radoch Z. Wernicke's encephalopathy due to hyperemesis gravidarum. *Ginekol Pol* 2003;74(8):633-7

Philip B. Hyperemesis Gravidarum: Literature Review. *Wis Med J* 2003;102(3):46-51

Spruill SC, Kuller JA. Hyperemesis Gravidarum complicated by Wernicke's Encephalopathy. *Obstet Gynecol* 2002;99: 815-7

Kuscu NK, Koyuncu F. Hyperemesis Gravidarum: Current concepts and management. *Postgrad Med J* 2002;78:76-9

Accetta SG, Abeche AM, Buchabqui JA, *et al.* Memory loss and ataxia after hyperemesis gravidarum: a case of Wernicke-Korsakoff syndrome. *Eur J Obstet Gynecol Reprod Biol* 2002;102(1):100-1

Sørensen HT, Nielsen GL, Christenson K, *et al.* Birth outcome following maternal use of metoclopramide. *Br J Clin Pharmacol* 2000;49(3):264-8

GEORGE CUP RESULT 2008

This year's George Cup Golf Competition was held on Saturday, 7th June, at Morecambe Golf Club. There was an excellent turnout with 24 golfers playing.

The competition results are as follows:

The George Cup

Ms Christine Bronder 43 points
Mr Sanj Prashar 34 points
Dr Malcolm Brown 33 points

The John Wilkie Quaiche

Ms Christine Bronder 22 points

The Phil Allen Plate

Mrs Lisa Higham 44 points

The Freend's Silla

Mr David Lavelle 33 points

An excellent day in glorious weather. Hopefully, next year's competition will be held at Heysham Golf Club.

Andrew Whitton, Golf Secretary