CASE REPORT

ECG changes in hyperemesis gravidarum

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SUMMARY

This is a case report of a 30-year-old patient presenting at advanced gestation with hyperemesis, who developed a prolonged QT interval secondary to electrolyte imbalance during recovery. This potentially fatal complication should be considered in all patients with hyperemesis gravidarum, especially after a prolonged period of starvation. We hope to highlight the importance of ECG monitoring and careful prescribing in such cases, something that is not considered in current guidelines.

BACKGROUND

Hyperemesis is a common condition affecting 1% of pregnant women, usually in early pregnancy. The pathophysiology is likely oversecretion of beta human chorionic gonadotropin (bHCG) by the placenta, and is worse in multiple pregnancies. It rarely causes harm to the fetus, and 90% of cases resolve by 20 weeks.¹

This case presentation is of particular interest due to the patient's ECG changes following refeeding. A prolonged QT interval on ECG can occur as a complication of electrolyte imbalance, drugs, and underlying heart conditions. This abnormality can lead to arrhythmia including Torsade de pointes. Torsade will revert spontaneously to sinus rhythm or can degenerate to ventricular fibrillation and potentially cardiac arrest.²

This case provides a number of learning points, in particular regarding the appropriate investigations and management of a rare complication of an obstetric disorder.

CASE PRESENTATION**Presenting complaint**

This primiparous patient presented 24 weeks pregnant with severe vomiting and reduced oral intake for 1 week, on a background of known hyperemesis gravidarum with recurrent hospital admissions since the beginning of pregnancy. The vomiting was associated with severe epigastric pain. Fetal movements were reported as normal.

Background

She had previously completed a tapering regimen of steroids for hyperemesis gravidarum with improvement in symptoms. She was investigated for a raised serum alanine aminotransferase during this pregnancy, presumed to be due to recurrent vomiting, with a liver ultrasound scan demonstrating two gallstones of 6 and 4 mm. She was known to suffer from gastritis prior to pregnancy, and had completed treatment for pulmonary tuberculosis years previously. She had no cardiac history and no

other medical or surgical history. She was taking omeprazole, cyclizine, metoclopramide, and Pregnacare (containing vitamin D, folic acid and vitamin B12) on admission. Dating and anomaly scans were normal.

On examination

She was showing signs of dehydration with dry mucus membranes and a tachycardia. She was otherwise haemodynamically stable and afebrile. Her chest was clear, abdomen was soft, but there was some tenderness over the epigastrium. Calves were soft and non-tender.

INVESTIGATIONS**Bedside tests**

Urine dip on admission showed ketones++++ and protein+. Urine protein: creatinine ratio was normal therefore ruling out pre-eclampsia. ECG on admission had shown a normal QTc (<460 ms). This investigation was repeated due to abnormal serum electrolyte results following oral intake (potassium 3.0 mmol/L, calcium 1.94 mmol/L, calcium adjusted 2.14 mmol/L, phosphate 0.76 mmol/L). This ECG demonstrated a prolonged QTc of 510 ms, meaning that the patient was at high risk of Torsade de pointes. Apart from this finding, there were no other ECG changes. She was consequently moved to the high-dependency unit on the ward with continuous cardiac monitoring.

Blood results

Serum electrolytes were measured daily. A full liver screen was normal except for positive Epstein Barr Virus IgG and IGM. Serum alanine aminotransferase and serum amylase were consistently high throughout admission, presumed to be secondary to chronic vomiting. She also had a short synacthen test that demonstrated a normal cortisol response.

DIFFERENTIAL DIAGNOSIS**Vomiting and epigastric pain**

With symptoms increasing in severity despite maximal medical treatment, and worsening epigastric pain, other teams were involved in this patient's case. One point that had previously been overlooked was a chronic mild rise in amylase, which along with a history of gallstones and a raised alanine aminotransferase led to investigation to rule out chronic pancreatitis. However, inflammatory markers were within normal range and previous ultrasound of the pancreas was unremarkable. Other differential diagnosis included gastritis, which was ruled out with normal gastroscopy. Another differential was adrenal insufficiency secondary to previous tuberculosis, as a previous

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episode of persistent vomiting had been quelled by a short course of steroids. A short synacthen test also ruled this out. The diagnosis of hyperemesis gravidarum was eventually settled on for this patient, and on balance a second course of steroids was deemed beneficial, after a multidisciplinary team discussion.

Long QTc

The cause of this patients' long QTc on ECG may have been secondary to electrolyte imbalance (hypokalaemia, hypomagnesaemia, and hypocalcaemia), or drugs (including antiemetics). Other causes of long QTc include acute myocardial ischaemia, hypothermia and elevated intracranial pressure. However, these were less likely as she had not reported any further symptoms or shown signs of these conditions. Congenital long QT syndrome was also unlikely due to previous normal ECG's and no past syncope or cardiac history.

TREATMENT

Management of this patient's condition involved a number of teams and healthcare professionals.

Obstetric team

At this gestation this patient was treated in an obstetric ward. She was resuscitated with intravenous fluids (sodium lactate compound solution) and managed with antiemetics (metoclopramide, cyclizine, ondansetron) and analgesia including morphine, meperidine (pethidine) and paracetamol (acetaminophen). Venous thromboembolism prophylaxis included antiembolism stockings and enoxaparin. After 5 days, intravenous access became problematic, and the decision was made to insert a peripherally inserted central catheter. A strict fluid balance chart was initiated. We monitored her baby with regular fetal heart monitoring and obstetric ultrasound to measure growth, fetal Doppler and amniotic fluid volume.

Gastroenterology team

As management for hyperemesis had failed, the medical team became involved in this case to investigate other causes of persistent vomiting. Intravenous proton pump inhibitor was prescribed (pantoprazole) alongside ranitidine and peptac liquid (sodium alginate, sodium bicarbonate and calcium carbonate). During the second gastroscopy, a nasojejunal tube was placed in view of improving her nutrition.

The medical team was also involved in electrolyte replacement and monitoring (including monitoring ECG changes). She was diagnosed with refeeding syndrome following nasojejunal tube insertion and an increase in oral intake. ECG demonstrated a long QTc (510 ms), resulting in cardiac monitoring in a high-dependency unit with intravenous replacement of calcium on multiple occasions. Potassium was first replaced intravenously and later orally with Sando-K (potassium bicarbonate and potassium chloride), alongside magnesium aspartate sachets, and phosphate and calcium tablets.

Managing this patients' long QTc was supportive. However, some patients with long QT syndrome may be managed with β -blockers by a cardiologist, reducing the risk of arrhythmias via adrenergic blockage. An implantable cardioverter-defibrillator or pacing is recommended in some high-risk patients.³

Dietician

A feed regimen was planned in view of improving this patients' nutrition. The dietician recommended daily refeeding blood tests including serum phosphate, calcium, magnesium and

potassium. Intravenous Pabrinex (vitamins B and C) was given twice a day throughout her stay.

OUTCOME AND FOLLOW-UP

After 13 days as an inpatient (in both high-dependence unit (HDU) and on the ward), this patient began to recover and was once again able to increase her oral intake. She was discharged home once her QTc on ECG normalised and serum electrolytes were within normal range. She was sent home with antiemetics, ranitidine and magnesium supplements.

Follow-up for this patient included an obstetric ultrasound scan at 28 weeks gestation to check the growth of the baby, as it is possible that this may have been affected by her extended illness. An antenatal clinic appointment was secured to see an obstetric consultant and review her condition, as well as recheck abnormal liver function tests and electrolytes.

DISCUSSION

National Institute for Health and Care Excellence (NICE) guidelines for hyperemesis gravidarum recommend hospital admission with persistent severe symptoms after 24 hours of oral medication.⁴ Oral promethazine or cyclizine are considered first-line antiemetics, followed by metoclopramide, prochlorperazine, or ondansetron.⁴ Concerning features requiring specialist obstetric advice include medical comorbidities, weight loss, and raised urinary ketones.⁴ Guidance for managing hyperemesis affecting oral intake includes monitoring weight; urinalysis for ketones; assessing for dehydration; ultrasound scan; and assessing electrolyte imbalance.⁴ NICE guidelines recommend assessing for hypokalaemia and hypocalcaemia or hypercalcaemia. However, there is no mention in the guidelines about refeeding syndrome and other electrolytes that are important to monitor including phosphate, magnesium and calcium.⁴

Recently updated 'Green Top' Guidelines from the Royal College of Obstetrics and Gynaecology mirror the NICE guidance. Additionally, there is suggestion to monitor calcium and phosphate in patients with hyperemesis.⁵ Electrolyte imbalance is considered in the guidance; however, consequences of electrolyte imbalance are once again overlooked, including any suggestion for ECG monitoring or refeeding syndrome.⁵ This is despite cases of refeeding syndrome secondary to hyperemesis being published in previous years.⁶ This case report described a patient of similar age and risk factors, including nasojejunal feeding; however, it does not discuss ECG abnormalities. No similar case reports discuss ECG changes secondary to refeeding syndrome in hyperemesis gravidarum.

Refeeding syndrome occurs when a patient increases oral intake following prolonged starvation. This is because, during starvation, insulin production decreases and protein and fat stores are catabolised for energy, resulting in reduced electrolyte concentrations intracellularly. With increased oral intake comes increased metabolism of carbohydrates requiring insulin, which leads to hypophosphataemia and results in electrolyte imbalance and refeeding syndrome.

A major complication of electrolyte imbalance is conduction abnormalities and arrhythmias, including a prolonged QTc as seen in this patient. Patients who are fed intravenously or through a nasogastric or nasojejunal tube are at high risk of refeeding syndrome, as seen in this presentation. Management includes observation and electrolyte replacement intravenously or orally.⁷

It is also important to consider other causes of long QTc in this patient, including drugs. Prescribing in pregnancy can be challenging, and in hyperemesis we may often need to prescribe multiple drugs for patients with known or expected electrolyte disturbances. In this case, ondansetron was prescribed which is

known to cause long QTc, and therefore could have had fatal consequences. The Food and Drug Administration (FDA) (US FDA) suggests that high intravenous doses (32 mg) of ondansetron can affect the electrical activity of the heart to prolong the QT interval and predispose to arrhythmia.⁸

Prolonged QTc is caused by delayed repolarisation of the heart muscle following a cardiac cycle. Long QTc increases the risk of developing Torsades de pointes, which can result in syncope, or even ventricular fibrillation resulting in sudden death. Patients with anorexia are at high risk of conduction abnormalities and arrhythmias due to electrolyte imbalance, through the same mechanisms as hyperemesis. In this patient, the cause of long QTc is likely multifactorial, including electrolyte abnormalities, and drugs including ondansetron and domperidone.^{9 10} Another minor consideration is that some evidence suggests that QT interval may be physiologically longer in pregnant women compared with non-pregnant women (but still within normal range).¹¹

Finally, another important consideration in hyperemesis gravidarum and refeeding syndrome is nutrient replacement, including thiamine and B12. The dietician recommended Pabrinex

during the period of starvation; this is due to the association of low thiamine in hyperemesis gravidarum with Wernicke's encephalopathy.¹²

Contributors SJM is the primary author of this manuscript. PC acted as the study supervisor.

Competing interests None declared.

Patient consent Obtained.

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Learning points

The main learning points from this case include:

- ▶ Consider refeeding syndrome and electrolyte abnormalities in all obstetric patients with severe hyperemesis.
- ▶ Consider monitoring electrolytes routinely, especially when there has been an extended period of starvation (ie, over 5 days).
- ▶ Consider ECG monitoring in patients with deranged electrolytes, due to the risk of long QTc.
- ▶ Be aware of drug interactions and side effects when prescribing, especially in the context of electrolyte abnormalities.

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