Hepatic capsular rupture in pregnancy

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Abstract

The syndrome of haemolysis, elevated liver enzymes and low platelets is a rare condition specific to pregnancy, affecting approximately 5–20% of all pre-eclamptic pregnancies. Described here is a woman in her first pregnancy, who experienced an intrauterine death following a significant hepatic haematoma and capsular rupture, in the absence of classical clinical features suggestive of pre-eclampsia. The events that followed suggested haemolysis, elevated liver enzymes and low platelets syndrome as the likely diagnosis. The patient's clinical course highlights the difficulties that may be encountered when making decisions about pregnant women with complicated medical and obstetric issues.

Keywords

Liver failure, acute, pregnancy, haemolysis, elevated liver enzymes and low platelets syndrome

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Introduction

The syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP) is a condition specific to pregnancy, first described by Weinstein¹ in a subgroup of women with pre-eclampsia.¹ It is a rare condition, estimated to affect approximately 5–20% of all pre-eclamptic pregnancies, but more commonly in those in whom pre-eclampsia develops at an early gestation.² In the most recent report of maternal deaths in the UK (2011–13), pre-eclampsia and related conditions were associated with six maternal deaths (0.25 per 100,000 maternities).³ The specific cause of death in these cases was not further elucidated, but the most recent previous report to document the exact causes of death included a total of 19 women who died in the UK of hypertensive disorders of pregnancy in the triennium 2006–2008. Three died of hepatic complications including capsular rupture, necrosis and fulminant liver failure and the remainder died as a result of either pulmonary or cerebral complications.⁴

Described here is a woman in her first pregnancy, who experienced an intrauterine death following a significant hepatic haematoma and capsular rupture, in the absence of classical clinical features suggestive of pre-eclampsia. The events that followed suggested HELLP syndrome as the likely diagnosis. Her second pregnancy is also discussed. The patient's clinical course highlights the difficulties that may be encountered when making decisions about pregnant women with complicated medical and obstetric issues.

Case

A 31-year-old female presented to her local hospital in the 31st week with a five-day history of severe right upper quadrant and epigastric pain, and recent onset vomiting. Fetal movements were reduced. Her pregnancy had been uncomplicated except for a recent *Escherichia coli* urinary tract infection, for which she had received amoxicillin. Other than well-controlled asthma (which had remained stable during her pregnancy), she was previously fit and well. On presentation, her blood pressure was 110/70 mmHg, she had a sinus tachycardia at a rate of 115 beats per minute and urinalysis showed 4+ proteinuria and 2+ blood. Abdominal examination revealed right upper quadrant tenderness. A gravid, non-tender uterus was palpable, but no fetal heart was heard on auscultation. The remainder of the examination was normal. Of note, there was no PV bleeding, she was not icteric and there was no peripheral oedema. Initial laboratory tests are shown in Table 1.

Abdominal ultrasound confirmed an intrauterine fetal death. Extensive free fluid was noted in the peritoneum, with an abnormal appearance of the parenchyma within the superior portion of the right lobe of the liver. A subsequent computerised tomography (CT) scan of the abdomen revealed a large hepatic subcapsular haematoma, with associated disruption of the capsule and significant intra-abdominal free fluid (Figure 1). The parenchyma of the surrounding liver appeared heterogeneous, consistent with infarction. The CT also demonstrated the consequential hepatomegaly was significant enough to cause compression of the intrahepatic portion of the inferior vena cava and hepatic veins with venous engorgement of the lower abdominal viscera. The patient was transferred to our centre for assessment and possible hepatobiliary intervention.

The patient was admitted to the intensive care unit on arrival. She was alert, communicative and not confused. She continued to report severe, right upper quadrant pain. Arterial blood gas analysis breathing oxygen 4 L/min revealed a severe metabolic acidosis with partial respiratory compensation (pH 7.16 (normal range for pregnancy 7.35–7.45), PaCO₂ 2.19 kPa (3.7–4.3), PaO₂ 17.7 kPa (12.7–14.0), bicarbonate 8.7 mmol/L (18–22) lactate 16.1 mmol/L (<1), potassium 7.4 mmol/L (3.5–5.0), base excess –22 mmol/L (+2 to –2)).

Her clinical condition deteriorated rapidly. She became anuric, hypotensive and coagulopathic (prothrombin time 17 s, activated partial thromboplastin time 56 s, platelets 78 × 10⁹/L) and required haemofiltration, intravenous noradrenaline and resuscitation with blood products including packed red blood cells and fresh frozen plasma. In view of her unstable clinical condition, emergency delivery was not undertaken. Following discussion with the regional liver unit, a plan was made to treat life-threatening hyperkalaemia with haemodiafiltration and then transfer urgently to the specialist centre for ongoing management.

After a period of continuous venovenous haemodiafiltration (35 ml/kg, lactate-free buffer) and reduction of serum potassium concentration, the patient was transferred uneventfully to the regional liver centre. On arrival, the patient underwent laparotomy,

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Table 1. Admission blood tests.

Test (normal ranges for pregnant women ⁵)	Result
Haemoglobin (11.0–14.0 g/dl)	9.3
White cell count (6.0–16.0 × 10 ⁹ /L)	23.3
Platelets (150–400 × 10 ⁹ /L)	143
Prothrombin time (9.0–12.0 s)	14.5
Activated partial thromboplastin time (20–30 s)	37.8
Creatinine (44–73 µmol/L)	108
Bilirubin (3–16 µmol/L)	12
Alanine transaminase (6–32 units/L)	284
Alkaline phosphatase (133–418 units/L)	265

Figure 1. CT abdomen with contrast.

Portal phase axial CT of the upper abdomen demonstrating free fluid in the left and right subphrenic spaces (4 and 2, respectively). The fluid is of higher attenuation than water (cf. stomach contents) in keeping with intraperitoneal blood. There is a large subcapsular haematoma in the liver (3), with capsular rupture (1).

evacuation of haematoma and packing of her liver as well as an upper segment caesarean section. There was no evidence of placental abruption at operation, and no structural abnormality of the liver was seen. She returned to the ICU with a laparostomy in situ and remained intubated and mechanically ventilated. She required ongoing vasopressor support and haemofiltration and was given an infusion of syntocinon, broad spectrum antibiotics and empirical antifungals. Twenty-four hours post-operatively, the lactic acidemia persisted, and she was listed for liver transplantation. After three days, she returned to theatre for pack removal and her abdomen was closed, as there was no evidence of further bleeding. In light of this, she was taken off the transplant list. Liver biopsy was performed, whilst she was still at the liver unit. This was reported to show significant perivenular and mid zonal necrosis with features of ischaemia, findings not consistent with acute fatty liver of pregnancy (AFLP). She subsequently developed persistent hypertension and tachycardia, despite optimal analgesia, which responded well to beta-blocker therapy. She was extubated on day 10 and made a subsequent gradual recovery, with normalisation of liver and renal function. Post-mortem examination of the infant was performed and showed a normally grown infant with evidence of acute hypoxia as the cause of death.

Two years later after careful pre-pregnancy counselling, she became pregnant again. She was prescribed low dose aspirin from 12 weeks of gestation. Antiphospholipid antibodies were negative. Her antenatal

course was entirely straightforward until 30 weeks of gestation, where she developed hypertension, proteinuria and peripheral oedema. Oral methyldopa was commenced, and she was admitted for inpatient monitoring. She received parenteral betamethasone to aid fetal lung maturation in case emergency delivery was required. Seven days after the onset of hypertension, routine cardiotocography showed pathological changes consistent with fetal distress and so she underwent an emergency lower segment caesarean section under spinal anaesthesia. A female infant weighing 1.56 kg (50th centile) was delivered and taken to the Special Care Baby Unit. The Apgar score was 10 at 1 and 5 min, and umbilical blood gases were normal. The procedure was complicated by major haemorrhage and placenta accreta at the site of the uterine scar. Haemostasis was achieved after manual removal of the placenta, inflation of a Rusch balloon and placement of a brace suture. She received 7 units of packed red blood cells, 7 units of fresh frozen plasma and one pool of platelets during the procedure as the estimated blood loss was 5.5 litres. Her post-operative course was complicated by labile blood pressure and a post-operative ileus, which settled with conservative management and she was discharged seven days post caesarean section. The patient wished to avoid further pregnancies given the life-threatening nature of the surgical and medical complications that had occurred, thus planned to take the progesterone-only pill.

The fragmented placenta was sent for histological analysis. This showed villi more mature than expected for the gestational age, suggestive of maternal underperfusion, but the changes were not thought to be severe. There was no evidence of chorioamnionitis.

Discussion

Diagnosis

Acute liver failure in pregnancy. Acute liver failure is characterised by derangement of liver synthetic function, manifest as abnormal clotting, hypoalbuminaemia and hypoglycaemia, typically with a marked lactic acidosis. In a series reviewing all admissions to a tertiary liver centre with pregnancy-related acute liver failure, nearly half of cases had HELLP (26 of 54 women) and the majority of the remainder had AFLP.⁶ This latter condition is characterised by microvesicular steatosis and may be associated with heritable disorders of fatty acid metabolism. Whilst the patient we describe met some of the Swansea criteria for the diagnosis of AFLP, such as abdominal pain, acute kidney injury and leucocytosis, none of these is specific for the diagnosis.⁷ The lack of hyperbilirubinaemia or hypoglycaemia, coupled with a liver biopsy performed at a tertiary liver centre that did not find features suggestive of AFLP, led to the exclusion of this diagnosis in the first pregnancy. However, AFLP must be considered in any pregnant woman with acute liver failure.

Hepatic haematoma and capsular rupture. Hepatic haematomata can develop in the absence of underlying pathology but are much more commonly associated with an underlying abnormality of structure (e.g. adenoma, malignancy, haemangioma) or coagulation. The majority of cases in pregnancy occur in the presence of HELLP, though there are two reports in women with AFLP.^{8,9} There have only been a small number of cases reported of pregnant women with spontaneous haematoma and capsular rupture with no evidence of underlying structural, coagulation or hypertensive disease.^{10–14}

HELLP syndrome. HELLP syndrome is seen in a subgroup of women with pre-eclampsia and arises from the same pathological processes. It is associated with maternal morbidity including acute renal failure, hepatic haematoma, pulmonary oedema, cerebral haemorrhage and disseminated intravascular coagulation. HELLP is a significant cause

of fetal morbidity, including intrauterine growth restriction, fetal distress, preterm birth and stillbirth.

At presentation, hypertension and proteinuria are not present in all cases of HELLP; they aid the diagnosis if present, but do not exclude the diagnosis if absent.^{15,16} It is, however, unusual for capsular rupture to be the first feature of the condition as it was in this patient.

Subsequent pregnancies are infrequently complicated by HELLP (the quoted rate is 2–19%), but a higher incidence of pre-eclampsia is reported.¹⁵ The development of early onset pre-eclampsia in this patient's second pregnancy further supports the diagnosis of HELLP syndrome in the first.

Management

Delivery. The only curative intervention for HELLP is delivery, but risks must be weighed up against those of emergent delivery in an inadequately resuscitated woman, as this risks further deterioration in the maternal condition. Delivery can be either vaginal or by caesarean section; the decision for this is individualised and depends on many factors in addition to the maternal condition, including gestation, previous pregnancies and their mode of delivery. Avoidance of surgical delivery is generally preferred after an intrauterine death. In this case, a caesarean section was performed because the patient was critically unwell and already undergoing laparotomy.

Antihypertensives. Not all women with HELLP syndrome develop hypertension. If present, this should be treated with antihypertensives such as labetalol, nifedipine or methyldopa, as recommended in NICE guidelines.¹⁷

Coagulopathy. Disseminated intravascular coagulation can occur in HELLP syndrome, but a coagulopathy may also follow acute hepatic rupture. The impaired synthetic function of the liver coupled with the ongoing loss of haemostatic factors results in severe coagulopathy. A multifaceted approach to treatment is required, incorporating strategies to optimise synthesis (vitamin K) whilst transfusing patients with blood and plasma components to restore circulating levels to near normal values.

Other measures. N-acetylcysteine is a standard part of the management of paracetamol-induced hepatotoxicity. It was not administered in this case but is increasingly being used in non-paracetamol-induced acute liver failure, including acute liver disorders of pregnancy, in an attempt to minimise free-radical damage to hepatocytes. A recent meta-analysis included four trials and a total of 331 non-pregnant patients with non-paracetamol-induced acute liver failure and showed improved survival for both patients with native liver and liver transplant recipients.¹⁸

Interventional radiology and surgery. The options for intervention include liver packing, partial resection, embolization and hepatic artery ligation.

Liver transplantation. The standard criteria used to assess whether a transplant is needed in non-pregnant patients were shown to be unreliable in this group of patients.^{6,19} It is therefore important to discuss these complex and challenging patients with specialist liver units early, as the decision to proceed to liver transplantation needs to be made on a case-by-case basis by an appropriately equipped multidisciplinary team.

Conclusions

Hepatic haematoma and capsular rupture in pregnancy is a condition which exemplifies the management challenges that a critically ill obstetric patient poses. Multidisciplinary involvement is crucial as there are many different aspects that need to be considered, including if, when, and how to perform an emergency delivery and whether to transfer to a specialist centre.

Once the episode has been dealt with, it must be remembered that there will be understandable anxiety from both patient and healthcare providers with respect to future pregnancies. Pre-pregnancy counselling needs to be holistic, to ensure that all medical and surgical aspects are appropriately addressed, in addition to the potential psychological impact on both the mother and her partner of another complicated pregnancy.

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