Case report

Idiopathic acute fatty liver of pregnancy: three cases including a subsequent normal pregnancy

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Acute fatty liver of pregnancy is a rare medical complication of late pregnancy and is associated with a high rate of maternal and fetal mortality. Prompt accurate diagnosis and institution of appropriate management should improve the prognosis. We report three cases and outline practical guidelines for diagnosis and management.

CASE 1

A 39-year-old patient in her eleventh pregnancy was admitted to the obstetric unit of another hospital at 34 weeks gestation with nausea, vomiting and malaise for two weeks, and jaundice for two days before admission. Although there was no previous history of pre-eclampsia, hypertension (170/100 mmHg) and mild oedema had been noted at 30 weeks for which she was treated with labetolol, chlorthalidone and diazepam. The day following her admission she became confused and unresponsive. Intrauterine death occurred and she was transferred to this hospital.

On arrival she was in circulatory collapse and made only unco-ordinated responses to painful stimuli. She was icteric but had no other stigmata of liver disease. She was profoundly hypoglycaemic, and following 50 ml of 50% dextrose intravenously her level of consciousness improved so that she mumbled responses to questions but remained drowsy (grade 3 hepatic encephalopathy). Normoglycaemia was maintained by continuous infusion of dextrose and the blood pressure was maintained by a dobutamine infusion. Initial investigations are shown in the Table. An electroencephalogram showed 2 - 3 Hz slow wave and triphasic activity consistent with hepatic encephalopathy. Examination of peripheral blood revealed giant platelets and normoblasts. A computerised tomogram (CT) showed diffuse abnormality of the liver with reduced attenuation over the liver of 19 Hounsfield units (normal 50 - 70), indicating fat infiltration. Eighteen hours after admission spontaneous labour began and progressed to a normal delivery of a stillborn male infant. Following delivery she rapidly improved and within an hour was able to answer rationally. Liver biopsy on the tenth
Laboratory results in three cases of acute fatty liver of pregnancy (normal range in brackets)

|                       | Case 1 | Case 2 | Case 3 |
|-----------------------|--------|--------|--------|
| **Serum values:**     |        |        |        |
| Bilirubin umol/l (3–18) | 140    | 185    | 224    |
| Aspartate transaminase U/l (10–40) | 357    | 139    | 373    |
| Alanine transaminase U/l (10–45) | 435    | 108    | 405    |
| Alkaline phosphatase U/l (35–120) | 681    | 375    | 533    |
| Gamma glutamyl transferase U/l (7–46) | 89     | 47     | 109    |
| Urate mmol/l (0·15–0·50) | 0·76   | 0·54   | 0·68   |
| Plasma glucose mmol/l | 53     | 64     | 24     |
| Prothrombin time — seconds (15–19) | 19     | 36     | 40     |
| White cell count 10^3/ul (411) | 18·4   | 14·4   | 28     |
| Platelet count 10^3/ul (150–400) | 250    | 60     | 98     |
| Coagulopathy           |        |        |        |
| (Disseminated intravascular coagulation) | No     | Yes    | Yes    |

Serology for hepatitis A and B and autoantibody screens were negative in all cases.

Postpartum day was consistent with resolving acute fatty liver of pregnancy with moderate accumulations of fat within hepatocytes, marked cholestasis and small foci of liver cell necrosis and regeneration. Serial CT scans showed progressive normalisation of the liver attenuation value which had risen to 48 Hounsfield units twenty days after delivery. She was discharged three weeks after admission and remains well.

CASE 2

A 25-year-old primagravida was admitted to the obstetric unit of another hospital at 36 + 4 weeks gestation. The first half of her pregnancy was complicated by severe hyperemesis and she had remained in hospital until 20 weeks, when the vomiting settled. On admission she was taking chlorpromazine 25 mg daily. Five days prior to admission vomiting had recurred and she had become jaundiced but had no abdominal pain or itch and was fully alert. The next day spontaneous labour began but emergency caesarean section was required for fetal distress. A live, heavily meconium-stained female infant was delivered: she required artificial ventilation for a period but then thrived. Postoperatively, the mother became drowsy and then unresponsive and was found to have a blood sugar of 0·7 mmol/l. Her level of consciousness responded to infusion of dextrose. There was bleeding from the surgical wound and disseminated intravascular coagulation was confirmed.

On transfer to this hospital, she was drowsy (grade 3 hepatic encephalopathy) and very icteric with a liver flap and mild foetor hepaticus. She was treated with fresh frozen plasma and cryoprecipitate along with a dextrose infusion. A CT scan showed diminished attenuation over the liver of 38 Hounsfield units (normal 50–70), consistent with fatty change. A transjugular liver biopsy performed five
days postpartum showed centrilobular fat accumulation which was mostly microvesicular, some focal cholestasis but no widespread necrosis or inflammation, the appearances being consistent with acute fatty liver of pregnancy. The bilirubin eventually peaked at 300 μmol/l fourteen days postpartum and all liver function tests subsequently returned to normal. She made an uneventful recovery and has remained well.

CASE 3

A 26-year-old primigravida was admitted to the obstetric unit of another hospital at 34 weeks gestation with a three week history of fatigue, nausea, vomiting and headaches. She was found to have hypertension, proteinuria and oedema, and was treated for pre-eclampsia with bed rest, hydralazine and diazepam. Her condition deteriorated and she became jaundiced. Six days after admission intrauterine death was diagnosed and she was transferred to this hospital.

She was deeply icteric but not initially encephalopathic and there were no other stigmata of liver disease. Coagulation screen indicated disseminated intravascular coagulation. CT scanning showed decreased liver attenuation of 29 Hounsfield units (normal 50–70) consistent with fatty infiltration. Labour was induced and a small-for-dates male stillbirth was delivered. Within hours of delivery the patient became drowsy and confused (grade 3 hepatic encephalopathy) and a liver flap was present. She was oliguric with a low urinary sodium consistent with functional renal failure of liver disease. She was treated with a continuous dextrose infusion, neomycin and lactulose via a nasogastric tube and four units of blood and fresh frozen plasma for postpartum haemorrhage associated with coagulopathy. She steadily improved. Percutaneous liver biopsy performed on the sixth postpartum day showed cholestasis and widespread microvesicular fatty change typical of acute fatty liver of pregnancy. She was discharged three weeks after admission but the serum bilirubin did not return to normal until nine months later. Two years later she again became pregnant. The pregnancy was without complication and her liver function tests were monitored at regular intervals and remained normal. Labour was induced at term and she had a normal delivery of a healthy baby girl. A CT scan on the day after delivery showed normal liver attenuation values.

DISCUSSION

Since first described in 1857 about one hundred cases of acute fatty liver of pregnancy have been reported.¹ The incidence of reported cases has risen in the last decade, probably as a result of improved antenatal surveillance, greater awareness of the diagnosis, and recognition that it is not an invariably fatal disease.² It is more common in twin and in male pregnancies. Historically, both maternal and fetal mortality were very high in this condition. In a series of twelve cases from the Royal Free Hospital in 1982 maternal mortality was 33% and fetal mortality was 67%.³

Although still a rare disease, it must always be considered in the differential diagnosis of jaundice or impaired level of consciousness in late pregnancy. Further improvement in prognosis depends on prompt accurate diagnosis and decisive management. In acute fatty liver of pregnancy there is usually a history of a prodromal malaise followed by rapid onset of nausea, vomiting and jaundice. Diminished level of consciousness can occur due to hepatic failure or hypoglycaemia when there is only slight jaundice. Prolongation of the prothrombin time in these circumstances indicates severe liver disease. Whilst abdominal pain
may occur, cholelithiasis can be excluded by ultrasound scan. Viral hepatitis can present similarly but the serum transaminases are usually very high in this condition compared to the nonspecific or cholestatic pattern seen in acute fatty liver of pregnancy. Cholestasis of pregnancy is characterised by itch and does not cause hepatic failure. Preceding pre-eclampsia is common (as in Cases 1 and 3), and it may be difficult to distinguish the liver disease of severe pre-eclampsia from acute fatty liver. Computerised tomography appears to provide a rapid non-invasive means of establishing the diagnosis and in all of our patients CT scans on the day of admission strongly indicated fatty infiltration of the liver. Use of CT scanning in Case 1 has previously been reported elsewhere. Neutrophilia, thrombocytopenia and abnormalities of the peripheral blood film including giant platelets, normoblasts and basophilic stippling are useful diagnostic indicators in acute fatty liver of pregnancy. Elevation of serum uric acid is usual.

The first principle of management should be to stabilise the patient and aim for delivery as soon as possible. Secondly, since hypoglycaemia is typical and may contribute to intrauterine fetal death, careful attention should be paid to maintaining normoglycaemia and large volumes of 10% or 50% intravenous dextrose may be required. As in Cases 2 and 3, bleeding may occur in association with disseminated intravascular coagulation but delivery should not be delayed on this account. However, bleeding should be treated in the usual way with fresh frozen plasma and platelets in addition to blood transfusion. Fresh frozen plasma and platelets should also be used to cover delivery where coagulopathy is present. Neonatal hypoglycaemia should be anticipated and promptly treated.

The aetiology of acute fatty liver of pregnancy remains unknown. It is one of a group of conditions with similar histological appearances of microvesicular fat accumulation within hepatocytes. These include Reye's syndrome in children, Jamaican vomiting sickness which is associated with a toxin in ackee fruit, and the fatty liver disease occasionally precipitated by sodium valproate and high doses of tetracyclines. Affected patients may have an underlying defect in fatty acid metabolising enzymes, and viral, toxic or nutritional factors may initiate the fatty change in susceptible patients.

In Case 3, pregnancy complicated by acute fatty liver resulting in stillbirth was followed by an uneventful pregnancy and normal delivery of a healthy baby. Burroughs et al reported seven subsequent normal pregnancies in four of their twelve patients. It appears that subsequent pregnancies carry no added risk of recurrence. Both liver function and histology rapidly return to normal in survivors.

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