An atypical presentation of acute fatty liver of pregnancy

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Acute fatty liver of pregnancy (AFLP) is an uncommon but life-threatening condition unique to pregnancy, affecting ~1 in 10 000 pregnancies, and is the most common cause of liver failure in pregnancy. Here the case is described of a 35-year-old patient who presented at 21 weeks' gestation complaining of vomiting, epigastric pain and food intolerance. During the course of her hospital stay of 31 days, she developed electrolyte imbalances and derangement in liver functions, with coagulopathy and bicytopenia. While she was being investigated for the cause of the biochemical abnormalities, she developed sepsis and anasarca, with a deterioration of her general condition, and it was decided to eliver the fetus. A diagnosis of AFLP was made on histological evaluation of a liver biopsy performed 3 days prior to delivery.

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Acute fatty liver of pregnancy (AFLP) is an uncommon but life-threatening condition unique to pregnancy, affecting ~1 in 10 000 pregnancies, and is the most common cause of liver failure in pregnancy.[1] AFLP carries a high maternal mortality rate of up to 75%, and a perinatal mortality rate of up to 85%, but with earlier diagnosis and the institution of timeous definitive management, i.e. delivery, these rates are reduced to 18% and 23%, respectively.[2] The condition usually presents in the third trimester of pregnancy, between 30 and 38 weeks' gestation, with a recurrence rate of 20% in subsequent pregnancies.[3] The diagnosis is based on the patient having at least six of the Swansea criteria, a combination of clinical and laboratory features (Table 1).[3,4]

The key to management of AFLP is timeous diagnosis and prompt termination of pregnancy or delivery, requiring a multidisciplinary approach in an intensive care unit.[2] Clinical recovery usually ensues in 3 - 4 days postpartum, but abnormalities in laboratory parameters may persist for much longer.[5]

Table 1. Swansea diagnostic criteria[3]

Laboratory	Clinical	Other
Bilirubin >14 µmol/L	Vomiting	Ultrasound showing ascites/ bright liver
Hypoglycaemia <4 mmol/L	Abdominal pain	Histology showing microvesicular steatosis
Uric acid >340 µmol/L	Polydipsia and polyuria	
Leukocytosis >11x10^6/L	Encephalopathy	
AST/ALT >42 IU/L		
Ammonia >47 µmol/L		
Creatinine >150 µmol/L		
Coagulopathy, PT >14 s		

AST= aspartate transaminase; ALT= alanine transaminase; PT= prothrombin time.

Case report

A 35-year-old nulliparous patient, with two previous first-trimester miscarriages, presented at 21 weeks' gestation with a history of vomiting, epigastric pain and food intolerance since the onset of the pregnancy. She was noted to be dehydrated, with a blood pressure of 99/50 mmHg and a heart rate of 80 beats per minute. Her glucose level was 5.6 mmol/L, and she had ketonuria. Biochemistry results showed hypokalaemia of 1.9 mmol/L and hypocalcaemia of 1.82 mmol/L. She was HIV-negative. An ultrasound showed a single intrauterine pregnancy, with a gestational age of 22 weeks and 4 days.

She was admitted with a diagnosis of hyperemesis gravidarum and treated with antiemetics, intravenous fluids and electrolyte replacement. Repeat liver function tests performed on the fifth day of admission revealed hypoproteinaemia with a total protein of 45 g/L and an albumin of 22 g/L. In addition, her liver function test showed the following: hyperbilirubinaemia of 33 µmol/L, aspartate transaminase of 389 IU/L, alanine transaminase of 1111 IU/L and serum creatinine level of 56 µmol/L. The viral hepatitis screen and screening for autoimmune conditions were negative (Table 2). An abdominal ultrasound showed a mildly echogenic liver, which is a feature that is not specific to AFLP, with no other pathology detected.

It was decided to manage the patient conservatively while investigating the cause of the electrolyte imbalance. There was a spontaneous improvement in her liver function tests (Table 2) on day 7 of admission, while the patient was still pregnant. On day 12 of admission, there was a rebound worsening of the liver function tests, which was complicated by anaemia, thrombocytopenia and coagulopathy, with a haemoglobin of 7.0 g/dL, a platelet count of 113 × 10^9/L and an international normalised ratio of 3.72. Although the patient had been normotensive throughout her admission, a differential diagnosis of HELLP syndrome – haemolysis, elevated liver enzymes and low platelets – was made. She then had a blood

transfusion and also received fresh frozen plasma. This was followed by an improvement in liver functions and electrolytes, and a return to normal coagulation within 24 hours.

On day 17 of the patient's admission, a liver biopsy was undertaken to determine the cause of her liver dysfunction. While awaiting the liver biopsy results, she developed signs of sepsis, and blood cultures grew Gram-negative bacilli, *Serratia marcescens*, which was sensitive to ertapenem. She also developed anasarca, and as a result of her deteriorating condition, a decision was taken to deliver the fetus. She delivered at 25w 3d gestation, and a live female was born, with a birth weight of 720 g. Unfortunately, the neonate died 4 days postpartum from complications of prematurity.

Histopathological evaluation of the core liver biopsy demonstrated ballooning and feathery degeneration of hepatocytes. Microvesicular steatosis was noted in approximately 80% of the liver core. There was evidence of both intra- and extrahepatic cholestasis (Fig. 1). A final diagnosis of AFLP was made.

Following delivery, there was a marked clinical improvement in the patient's condition, as well as improvement in her liver function tests. She was discharged after 30 days post admission, and was to follow up at the medical gastrointestinal outpatients' department.

Discussion

Our patient had an atypical presentation of AFLP. She presented at an early gestation of 22 weeks, whereas the average gestational age of presentation is in the third trimester, at a median gestational age of 36 weeks. It has also been reported in the puerperium, being diagnosed at an average of 4 days into the postpartum period.[6] She did not meet the required Swansea criteria for AFLP, as the most she had at any one time were five criteria, instead of the minimum of six. Her glucose levels and renal function remained normal throughout her hospital stay, and she was not encephalopathic at any point. There was also spontaneous improvement in her liver function half way through her admission, but it later deteriorated. However, the presence of microvesicular steatosis on core liver biopsy eventually confirmed the diagnosis of AFLP. The source of septicaemia in our patient could not be determined, as urine and sputa cultures did not grow the Gram-negative bacilli that were found on the blood culture. Septicaemia has been documented as one of the morbidities associated with AFLP.[6]

The Swansea criteria are a group of clinical and laboratory features gathered and used in the absence of any other explanation

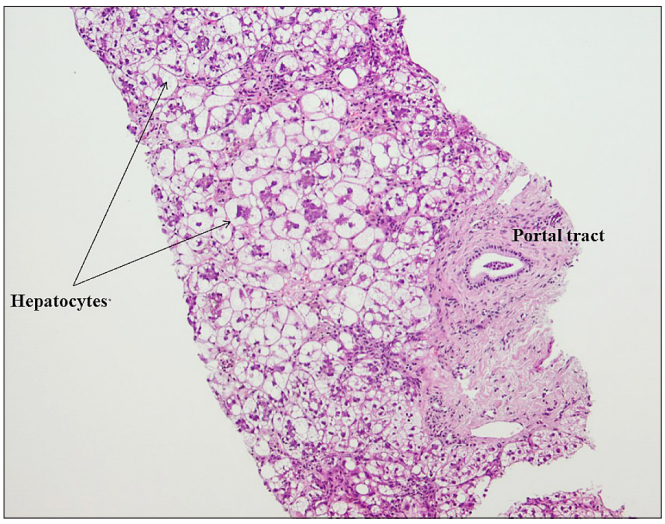

Fig. 1. Liver core biopsy showing a portal tract on the right. The hepatocytes show extensive feathery degeneration and ballooning (arrows). 2 μm section, original magnification ×100.

Table 2. Biochemistry and haematology results

	D0	D2	D3	D5	D6	D7	D8	D9	D12	D13	D15	D16	D18	D19
K^+ (mmol/L)	1.9	2.0	3.1	2.6	-	2.6	2.9	2.8	-	-	3.3	3.7	3.0	2.8
WCC	4.46	2.72	3.99	-	5.27	5.20		4.7	5.87	-	-	8.38	5.41	-
Hb (g/dL)	9.3	8.2	8.4	-	8.2	8.0		7.4	7.0	-	-	8.3	7.0	6.5
Platelets ($\times 10^9$/L)	170	154	116	-	188	203		224	113	-	-	133	14	118
TP (g/L)	-	-	-	45	-	45	-	41	37	35	42	44	37	-
Albumin (g/L)		21		22		19		21	15	15	18	18	15	-
ALT (IU/L)	-	-	-	398	-	339	-	220	805	508	308	251	128	136
AST (IU/L)	-	-	-	1111	-	689	-	301	3902	1157	355	210	93	165

K^+ = potassium; WCC = white cell count; Hb = haemoglobin; TP = total protein; ALT = alanine transaminase; AST = aspartate transaminase; D = day of admission.
Empty cells = not tested on the day.

Table 3. Liver disease related to pregnancy[8]

Hyperemesis gravidarum	Intrahepatic cholestasis of pregnancy	Pre-eclampsia or eclampsia	HELLP syndrome
• In first trimester • Excessive vomiting • Dehydration • Ketosis • Raised transaminases • Resolves by 20 weeks • Liver abnormality resolves when vomiting stops • Needs supportive management	• In second and third trimesters • Pruritus of palms and soles • Raised bile acids • Resolves with delivery • Jaundice in <25% of patients • Treated with UCDA	• Raised systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg occurring after 20 weeks • Hepatomegaly/ hepatocellular damage as part of liver dysfunction • Epigastric tenderness or RUQ abdominal pain • Delivery is the definitive treatment, from 34 - 37 weeks	• Presents between 28 and 36 weeks • Haemolytic anaemia • Raised transaminases • Low platelets • Raised LDH • Nausea/vomiting • RUQ or epigastric pain, malaise • Delivery is the definitive treatment • Resolves within 48 hours of delivery

UCDA = ursodeoxycholic acid; RUQ = right upper quadrant; LDH = lactate dehydrogenase.

for liver disease to diagnose AFLP. Developed in an obstetric unit in the City of Swansea in southern Wales in 1999 during a study of liver dysfunction in pregnancy, it has since been the standard for diagnosing AFLP with a positive predictive value of 85% and a negative predictive value of 100%.[7,8] There are often prodromal symptoms of vomiting, abdominal pain, polydipsia and encephalopathy.[6]

The pathophysiology of AFLP is thought to involve fetal deficiency of long-chain hydroxyacyl-CoA dehydrogenase (LCHAD). This is an enzyme involved in long-chain fatty acid metabolism. A deficiency leads to an accumulation of fetal and placental unmetabolised long-chain fatty acids in the maternal circulation, causing hepatotoxicity. The differential diagnoses for AFLP are varied, and must be considered. These can be determined by means of biochemical, serological and clinical parameters. Any pregnant woman with abnormal liver functions should undergo the same work-up as for non-pregnant women, as there may be a need for immediate intervention in order to preserve maternal and neonatal health. The liver dysfunction may be pre-existing and coincidental, not relating to pregnancy, such as biliary tract disease (for example, cholecystitis, cholangitis, cholelithiasis), liver masses and viral disease (such as hepatitis A, B, C or E) or may be related to pregnancy (Table 3).[8]

Imaging is a useful adjunct in ruling out other liver pathologies, such as biliary tract disease and liver masses. The 'bright liver' often reported in AFLP on ultrasound can also be found in other conditions of liver dysfunction, such as HELLP syndrome.[6,8] Magnetic resonance imaging has been shown to be useful in distinguishing other conditions such as HELLP syndrome from AFLP, and is safe to use in the second and third trimesters of pregnancy.[8,9] AFLP is a microscopic disease.[6]

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