Acute Fatty Liver in Twin Pregnancy

Suneetha GANTA MRCOG
Janani IYER MRCOG
Department of Obstetrics and Gynaecology, South Tyneside NHS Foundation Trust, South Shields, United Kingdom
Balaraj GOVINDAN FRCA
Department of Anaesthesia, South Tyneside NHS Foundation Trust, South Shields, United Kingdom
Shamma AI-INIZI FRCOG
Department of Obstetrics and Gynaecology, South Tyneside NHS Foundation Trust, South Shields, United Kingdom

Acute fatty liver of pregnancy (AFLP) is a rare but potentially fatal complication of late pregnancy. Various conditions such as haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome can produce hepatic impairment. The liver dysfunction associated with AFLP can cause significant hypoglycaemia and raised ammonia levels, which may help to distinguish it from pre-eclampsia and the HELLP syndrome. We present an atypical case of AFLP in a twin pregnancy who presented with severe hepatic and renal impairment, severe coagulopathy leading to hepatic coma and adult respiratory distress syndrome. There was no hypoglycaemia at presentation and the serum ammonia level was not high, indicating that the diagnosis of AFLP cannot be excluded just because these two aforementioned features are absent.
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Case Report

A 43-year-old Caucasian woman in her second pregnancy was admitted at 35 weeks of gestation. She had had a previous uncomplicated vaginal delivery and an unremarkable medical and surgical history. For her current spontaneous, diamniotic, dichorionic twin pregnancy, she had received uncomplicated consultant-led antenatal care, and an antenatal visit at 34 weeks' gestation had been unremarkable. At presentation she had noticed gradual onset of constitutional symptoms with increasing weakness, tiredness, and sleepiness, but she was well-oriented. However, she was deeply jaundiced, cyanosed, and had bilateral leg oedema. Initial investigations yielded deranged liver and renal function test results, coagulopathy, and thrombocytopenia (Table), but arterial blood showed no evidence of acidosis with normal blood sugar and serum ammonia levels. On admission her blood pressure was slightly elevated, her reflexes were brisk, and she had proteinuria. After review by the obstetrician, the differential diagnosis was acute fatty liver of pregnancy (AFLP) or severe haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome with pre-eclampsia and disseminated intravascular coagulation (DIC) with multi-organ failure. Accordingly, multidisciplinary input involving an anaesthetist, haematologist, and paediatrician was obtained.

The obstetrical treatment plan entailed expeditious Caesarean delivery because of the patient's deteriorating clinical and biochemical features and cardiotocography traces showing fetal tachycardia, reduced variability, and atypical variable decelerations since her initial evaluation. Under the circumstances, urgent delivery was indicated though the patient was not in labour. Steroids to enhance fetal lung maturity were not given due to the gestational age and the need for urgent delivery. Four units of fresh frozen plasma and 3 units of packed red blood cells were given in the operating theatre. The Caesarean delivery was performed under general anaesthesia as regional analgesia was not advised by the anaesthetist due to the patient's coagulopathy and DIC. Anaesthesia involved use of intravenous fentanyl, midazolam, sodium thiopental, and inhalation of methoxyflurane.

The procedure was otherwise uneventful and two healthy live female babies (weighing 2.2 kg and 2.3 kg with Apgar scores of 5/8 and 5/9, respectively) were delivered. The first twin had arterial pH of 7.12, base excess of -9.9 and venous pH of 7.17, base excess -8.8. For the second twin the corresponding results were 7.08, -10.9 for arterial and 7.16, -9.0 for venous. Both twins were admitted for observation to the special care baby unit for 5 days, and later both were found to test negative for long-chain 3-hydroxyacyl coenzyme A dehydrogenase deficiency. The patient herself was transferred to intensive therapy unit for postoperative

Correspondence to: Dr Shamma Al-Inizi
Email: shamma.al-inizi@stft.nhs.uk

Table. Results of blood tests

Test	At presentation (normal range / level)	Postnatal day 1	Postnatal day 2
Haemoglobin (g/L)	115 (115-165)	97	75
Platelets (/mcl)	74,000 (150,000-450,000)	69,000	52,000
Urea (mmol/L)	15 (2.5-7.8)	20	28
Creatinine (μmol/L)	306 (50-120)	407	440
Alkaline phosphatase (U/L)	429 (30-130)	444	459
Alanine aminotransferase (U/L)	314 (5-35)	333	347
Blood sugar (mmol/L)	4.2 (3.0-7.8)	1.9	2.9
Serum bilirubin (μmol/L)	172 (0-21)	179	190
Prothrombin time (secs)	29.7 (9-14)	32	39
Partial thromboplastin time (secs)	60.3 (23-35)	64	66
Fibrinogen (μmol/L)	4.4 (5.9-17.6)	5.9	5.6
Sodium (mmol/L)	137 (133-146)	147	152
Potassium (mmol/L)	6 (3.5-5.5)	6.4	6.9
International normalised ratio	3 (1)	1.9	1.8

recovery, and a few hours later she was extubated.

On the following day (i.e. postnatal day 1), she became drowsy and confused, and had blurred vision. Blood tests continued to show deranged liver and renal function, as well as DIC (Table). She started to have abdominal distension, decreased oxygen saturation, and became hypotensive. She had some hypoglycaemic episodes (Table). She became encephalopathic and had deteriorating multi-organ impairment for which she was seen by a hepatologist. She was started on inotropes, intubated, and ventilated because of adult respiratory distress syndrome (ARDS). The differential diagnosis at this stage was AFLP and eclampsia with cerebral involvement. However, as the patient showed clear signs of AFLP with liver failure and hypoglycaemia, the multidisciplinary team including the hepatologist was in favour of AFLP, especially as the patient had a low blood pressure and no urine protein. Brain computed tomographic scan was normal. As advised by the haematologist, further transfusion of blood products was undertaken due to ongoing coagulopathy. Chest X-ray showed bilateral pneumonia, possibly related to general anaesthesia, though no aspiration was suspected or confirmed. Alternatively, there could have been generalised clinical and biochemical deterioration due to AFLP and ARDS, low immunity, multi-organ failure, and having had a Caesarean section. She received intravenous broad-spectrum antibiotic cover with piperacillin / tazobactam (4.5 g 8-hourly) as advised by the microbiologist. The patient also received a single prophylactic dose of intravenous co-amoxiclav 1.2 g, in accordance with the local Caesarean section protocol. Her serum ammonia level was still normal, and ultrasound of the liver and computed tomography of the abdomen showed non-specific fatty changes in the liver with mild ascites. At the same time she also had stigmata of liver failure (hepatic flap, spider naevi, and other features of encephalopathy), as well as DIC and renal impairment. Hemofiltration was performed to improve her renal function. Twelve days later her liver, renal, respiratory functions and coagulopathy gradually started to improve. She was then extubated and transferred to a liver unit for continuous supportive management as her liver function remained mildly deranged for 2 months. Her renal function then returned to normal. During the course of her recovery, she developed myopathy causing mobility problems for which she received rehabilitation exercises and prolonged physiotherapy. Following 3 weeks in the liver unit, she was discharged home in a good condition. She was strongly advised against becoming pregnant again owing to the recurrent nature of her disease and its implications on her health and pregnancy. Contraception was discussed. She declined hormonal contraception and sterilisation and continued to consider condoms, in the expectation that her husband was to have a vasectomy.

Discussion

Significant hepatic dysfunction in pregnancy has been reported in AFLP and the HELLP syndrome. Liver involvement with the HELLP syndrome complicates 3-10% of patients with pre-eclampsia. AFLP is a life-threatening condition which mostly occurs in the third trimester, is commonly associated with pre-eclampsia

(50-100%), and is more common in nulliparous and twin pregnancies. Evidently, it displays no racial or geographical predilections[1-5]. AFLP and HELLP syndrome manifest specific patterns, whilst they share many clinical and laboratory similarities. Not surprisingly, early differentiation of the two conditions may be difficult. Notably, HELLP syndrome is more frequent than AFLP (1:5000 vs. 1:13000)[1,3]. A comprehensive review of the United Kingdom Obstetric Surveillance System identified 57 cases out of 1,132,964 maternities. Nearly a fifth of these were in twin pregnancies, confirming a much greater risk[6].

Using the Swansea criteria, we anticipated the possible diagnosis of AFLP in this case. Seven criteria were present in this case including encephalopathy, elevated bilirubin level of >14 μmol/L, hypoglycaemia (blood sugar <4 mmol/L), ascites on ultrasound, elevated transaminases, renal impairment with creatinine level of >150 μmol/L, and coagulopathy (prothrombin time >14 seconds or activated partial thromboplastin time >34 seconds). Liver imaging is helpful in the diagnosis of AFLP when taken together with some Swansea criteria like ascites. However, liver biopsy is the gold standard but it was not performed in this case due to the patient's deteriorating condition and the presence of significant coagulopathy. The definitive management of both conditions entails rapid delivery of the fetus and supportive care, which results in a significant decrease in maternal and perinatal mortality[1,3,4,7-10].

The HELLP syndrome usually has an acute onset and is not associated with liver failure even though the transaminase levels may be high; the international normalised ratio and blood sugar levels are within normal limits. Postpartum resolution rather than exacerbation of the condition ensues. Moreover, it is more frequent in multiparous women due to endothelial dysfunction, and around 38% of the patients develop DIC that also contributes to acute renal impairment[3,11]. Patients with AFLP are more likely to show signs of liver failure with coagulopathy, hypoglycaemia, encephalopathy, high serum ammonia levels, and renal impairment. The coagulopathy in HELLP syndrome is mainly due to platelet dysfunction, whereas in AFLP it is due to low concentrations of clotting factors due to failure of hepatic synthesis. In our case, the clinical features of severe liver dysfunction appeared at 35 weeks' gestation in a twin pregnancy, together with the clinical laboratory evidence of deranged renal function, hepatic encephalopathy, and late-onset hypoglycaemia, all of which favour the diagnosis of AFLP over HELLP syndrome. At presentation, the absence of hypoglycaemia together with normal serum ammonia levels caused some difficulty in the diagnosis.

This case illustrates that although the pathophysiology of AFLP and HELLP syndrome differs, it is still difficult to differentiate these two conditions at presentation, especially if blood sugar and ammonia levels are normal, as these parameters are commonly used to distinguish the two conditions. Thus, a high index of suspicion for both conditions is essential. Early recognition, immediate multidisciplinary management, and expeditious delivery are the most appropriate care pathways to interrupt disease progression.

Declaration

No conflicts of interests were declared by authors.

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