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CASE REPORT

Atypical Case of Acute Fatty Liver of Pregnancy

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حالة لا نمطية للكبد الدهني الحاد في الحمل

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الملخص: يُعَدّ الكبد الدهني الحاد في الحمل من الحالات الطارئة التي تهدد الحياة. تشمل الأعراض الأكثر شيوعا: التوعك والغثيان والتقيؤ والألم الشرسوفي يتبعها اليرقان. ينبغي إجراء التشخيص مبكرا والإسراع بالعلاج والرعاية نظرا لارتفاع معدل وفيات الأمهات وحديثي الولادة. ندرج هنا وصف لحالة لا نمطية من الكبد الدهني الحاد في الحمل ونناقش العلاج والمضاعفات لهذه الحالة النادرة من الاضطراب.

مفتاح الكلمات: الكبد الدهني الحاد في الحمل ؛ النزف بعد الولادة؛ تخثر الدم داخل الأوعية، تقرير حالة، عُمان.

ABSTRACT: Acute fatty liver of pregnancy (AFLP) is a life threatening obstetric emergency. The most common presentation is malaise, nausea, vomiting and epigastric pain followed by jaundice. Due to high maternal and perinatal mortality, early diagnosis, prompt delivery and supportive care are required. We report an atypical case of AFLP and discuss the management and complications of this rare obstetric disorder.

Keywords: Acute fatty liver of pregnancy; Postpartum haemorrhage; Disseminated intravascular coagulation; Case report; Oman.

Acute fatty liver of pregnancy (AFLP), a life threatening obstetric emergency, was first described by Sheehan in 1940.[1] The most common presentation is malaise, nausea, vomiting and epigastric pain followed by jaundice. Laboratory tests usually demonstrate high bilirubin levels, deranged liver and renal functions, coagulopathy and hypoglycaemia. At presentation, one should keep in mind other pregnancy related liver diseases that mimic AFLP such as HELLP syndrome: haemolysis (H), elevated liver enzymes (EL) and low platelet count (LP), and intrahepatic cholestasis of pregnancy. Liver biopsy is the gold standard for diagnosing AFLP, but due to the presence of coagulation abnormalities diagnosis is usually made by clinical and laboratory findings. Bleeding and disseminated intravascular coagulation (DIC) are one of most common complications.

Case Report

A 36 year-old healthy woman, gravida 3 para 2, presented to a peripheral hospital at 34 weeks gestation with a 3-day history of malaise, nausea, vomiting and abdominal pains. Her pregnancy had been uncomplicated. On admission, her vitals appeared to be stable, but her blood pressure was 150/90 mmHg with no proteinuria. The results of the complete blood count was as follows: haemoglobin 13.4 g/dl; white blood count 22 x 10^9/L, and platelets, 227 x 10^9/L. The biochemical markers were as follows: total bilirubin 122.8 µmol/L; serum aspartate aminotransferase (AST) 118.9 IU/L; serum alanine aminotransferase (ALT) 129.8 IU/L, and creatinine 158.5 µmol/L. The coagulation profile was as follows: prothrombin time (PT) 13 sec; activated partial thromboplastin time (APTT) 41 sec.

The patient underwent an emergency caesarean section because of a non-reassuring fetal heart tracing. The outcome was a live male baby with good Apgar scores. The next day, the patient started bleeding profusely through the vagina and her haemoglobin dropped to 4.9 g/dl; the platelet count was 25 x 10^9/L and fibrinogen 0.5 g/L. She was assessed, but no cause of bleeding identified. She was taken to the operating room and an exploratory midline laparotomy was performed. No

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source of bleeding was identified intraoperatively and the abdomen was packed, closed and an intraperitoneal drain was inserted. A hysterectomy was not performed and no other intervention was done.

The patient was then transferred to the intensive care unit (ICU) at Sultan Qaboos University, tertiary hospital, Oman, after receiving a total of 10 units of packed red blood cells, 19 units of fresh frozen plasma, 7 units of cryoprecipitate and 7 units of platelets. She was ventilated and was on intravenous dopamine infusion. The patient was bleeding profusely from her intraperitoneal Jackson-Pratt (J-P) drain. The laboratory findings on admission at our hospital were as follows: Hb 12.4 g/dl; platelets 56 x 10^9/L; PT 23 sec; APTT 40 sec; fibrinogen 1.5 g/L; total bilirubin 155 µmol/L; AST 123 IU/L; ALT 123 IU/L, and creatinine 163.9 µmol/L. The patient required further replacement of blood products. At our hospital, she received a total of 5 units of packed red blood cells, 5 units of fresh frozen plasma, 11 units of cryoprecipitate and 10 units of platelets. Two units of recombinant activated factor VII (rFVIIa) were given to her and the bleeding lessened thereafter. She was taken to the operating room 24 hours after admission for removal of the abdominal packs. At the time of surgery, it was noted the abdominal packs were foul smelling and adherent to the serosal layers. The abdominal wall was bruised, but no active bleeding was observed. Since there was no active bleeding, a hysterectomy was not performed, the packs were removed and abdomen was irrigated well and closed in layers. During the patient's ICU stay, she was on intravenous labetalol infusion for 48 hours to control her blood pressure. She was extubated on day 4 and moved to the ward on day 8 of admission.

The patient's status improved gradually, but she remained severally jaundiced with high bilirubin levels, mainly of the conjugated type (maximum total bilirubin level of 280), raised liver enzymes remaining in the hundreds and hypoalbuminemic (15 g/dl). Viral hepatitis screening was done, but was negative. The dilemma was the amount of serous fluid drainage, first from the J-P drain that was removed on day 8 of admission and then from the patient's wound site. Clinical assessment and several investigations were performed including creatinine levels of the draining fluid, intravenous pyelogram, and ultrasound and computed tomography (CT) scans of the abdomen that excluded wound dehiscence, urinoma and seroma. On the bases of her clinical presentation including her signs, symptoms, massive bleeding and laboratory findings, the diagnosis of AFLP was made and supportive care continued. Further investigations with liver ultrasound and CT scans did not show evidence of fatty changes of the liver and a liver biopsy was not performed.

On day 18 of admission, the patient was febrile and her wound grew a *Pseudomonas* species infection that was treated with intravenous antibiotics (meropenem). On day 21 of admission, complete wound dehiscence was found and an emergency surgery was performed. It was noted during the surgery that there were lots of adhesions, the liver was frozen with multiple adhesions, the bowel was inflamed and the rectus fascia was not healthy. After adhesiolysis and extensive washing of the abdominal cavity with normal saline, a mass closure of the abdomen was performed using tension sutures. Postoperatively, the patient did well. The wound healed with the assistance of the vacuum assisted closure (VAC) system. The sutures were removed after 4 weeks and she was discharged home. She was monitored closely in the outpatient clinic and on her six weeks follow-up, the liver enzymes, bilirubin and albumin levels were normal and she was off antihypertensive medications.

Discussion

Hypertensive and liver disorders of pregnancy comprise a spectrum of conditions associated with adverse fetomaternal outcomes.[1] The patient's initial presentation may vary during the antepartum, intrapartum and even the postpartum period. Clear understanding of the pathophysiology and mechanism of these disorders in pregnancy is very important. Although severe preeclampsia is commoner than AFLP and other liver disorders related to pregnancy, our patient's presentation and laboratory test results were in favour of an AFLP diagnosis. Ch'ng *et al.* first set the Swansea criteria for diagnosing AFLP that have been used by many institutions.[2,3] Six or more of the following features are used to diagnose AFLP in the absence of other explanation: vomiting; abdominal pain; polydipsia/polyuria; encephalopathy;

elevated bilirubin >14 μmol/L; hypoglycaemia <4 mmol/L; elevated urate >340 μmol/L; leukocytosis >11x10^9/L; ascites or bright liver on ultrasound; elevated tramsaminases; elevated ammonia >47 μmol/L; renal impairment creatinine >150 μmol/L; coagulopathy (PT >14 sec or APTT >34 sec), or microvesicular steatosis on liver biopsy. Using these criteria we anticipated the diagnosis of AFLP. The patient had vomiting, abdominal pain, elevated bilirubin and transaminases, elevated creatinine and coagulopathy at presentation. A patient with severe preeclampsia/HELLP will usually present with proteinuria.

AFLP was first described by Sheehan in 1940.[1] The aetiology of the disease is unknown with an incidence of 1 in 10,000 to 1 in 15,000.[5] It is a life threatening obstetrical emergency that can lead to high maternal and perinatal morbidity and mortality. Due to the development of more rapid diagnosis tools and early termination of pregnancy, the maternal mortality rate due to this disease has decreased from 80–85% to 7–18% and the fetal mortality rate from 50% to 9–23%.[6-8] The disease usually presents in the first pregnancy and in the third trimester with a mean gestational age of 34–37 weeks.[9,10] The signs and symptoms at initial presentation may vary, making the diagnosis of this disease difficult, or there might be delay in diagnosis. Similarly, the differential diagnosis may be difficult in a patient with abnormal hepatic function in pregnancy since a number of pathologies such as HELLP syndrome, viral hepatitis and hormone-induced cholestasis share some of the same symptoms and signs.

The diagnosis of AFLP remains challenging since there is no specific non-invasive diagnostic test to identify it. Ultrasound and CT scans of the liver have been used, but the specificity and sensitivity of these studies are insufficient to make a diagnosis and the likelihood of false negative results is high.[11] Our patient had normal liver ultrasound and CT scan results.

Liver biopsy is the gold standard test, but it is invasive and requires a patient with normal coagulation status.[4,5,12] The clinical presentation of both AFLP and HELLP syndrome are very similar but nausea, vomiting, epigastric pain and jaundice are more commonly seen in AFLP patients.[5] Although AFLP is an uncommon disease, our patient's presentation and the development of jaundice with chronic hypoalbuminemia made this diagnosis more likely. Moreover, the patient developed DIC requiring massive blood transfusion (total of 76 units), making the diagnosis of AFLP more likely. DIC is seen in about 80–100% of patients with AFLP as opposed to 21% of patients with HELLP syndrome.[5,12-14] The DIC might be a severe and potentially fatal complication of AFLP. The main cause of the coagulopathy leading to DIC in patients with AFLP is the severe hepatic dysfunction. It is less likely to be a complication for patients with other obstetrical or medical disorders such as HELLP syndrome. Early identification and correction of the coagulopathy before any obstetrical procedure is very important. When the patient presented to our ICU, after having two surgeries within 24 hours, it was very difficult to make the decision to take her back to the operating room to control her bleeding. We continued replacing her with blood products and decided to give her rFVIIa and observe if the latter would control the bleeding. Fortunately, the bleeding settled and the patient stabilised after receiving two doses of rFVIIa.

There are an increasing number of case reports in the literature describing the successful "off-label" use of rFVIIa (NovoSeven, Novo Nordisk, Denmark) in the treatment of massive postpartum haemorrhage (PPH) refractory to conventional medical and surgical therapy.[15] The rationale for the use of rFVIIa in this setting is based on the observation that it directly activates factor X on the surface of activated platelets at the site of injury, factors VIII, and IX. This results in a "thrombin burst" with the conversion of prothrombin into large amounts of thrombin and the local formation of a stable fibrin clot that may control bleeding.[16] A recent systematic review was undertaken by a group in Italy looking at the effects and role of rFVIIa in patients with massive PPH.[17] Nine studies met the inclusion criteria and there were 272 patients involved. The group made the following recommendations: 1) Consider the use of rFVIIa in cases of massive PPH refractory to medical therapy including replacement of other blood products and even after a conservative/invasive surgical approach such as internal iliac or uterine artery ligation fails; 2) Consider a second dose of rFVIIa (90 mg/kg IV bollus over 3–5 min) if there is no response after 20 minutes from the first dose, and 3) If bleeding

persists after 2 doses of rFVIIa, consider performing a hysterectomy.

Conclusion

Despite the critical condition at presentation, and the complications she went through such as DIC, chronic hypoalbuminemia, infection and burst abdomen, our patient finally went home in a good condition. Early diagnosis of obstetrical emergencies, prompt therapy, adequate supportive care and a multidisciplinary approach are the key elements for a good outcome.

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