Case report

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Acute fatty liver of pregnancy: A case report

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Abstract

***Introduction*: Acute fatty liver of pregnancy (AFLP) is considered an uncommon but grave complication occurring typically in the third trimester of pregnancy. AFLP can clinically range from presenting vague symptoms to causing acute liver failure and, ultimately, death if untreated.**

***Objective*: Report the findings that allowed the diagnosis and prompt treatment of AFLP by the Obstetric Intensive Care Unit of a patient who went to a second-level hospital in the state of Sinaloa.**

***Methods and results*: A search was performed using PubMed, Europe PMC, and EBSCO on the diagnosis and management of AFLP. Seven articles were found from 2017 to 2022, of which information was drawn, conclusions, and recommendations were made.**

***Conclusions*: AFLP is a rare entity that simulates the intrahepatic cholestasis of pregnancy, preeclampsia, and hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome. Due to the difficulty of performing a liver biopsy, the diagnosis is made based on the Swansea criteria. This includes various characteristic symptoms, laboratory, and imaging findings.**

Introduction

Acute fatty liver of pregnancy (AFLP) is a rare condition that occurs mainly during the 30th to 38th weeks of pregnancy or after childbirth. In the absence of timely diagnosis and treatment, this condition can be fatal. (1,2) It was first described by Sheehan in 1940 as "acute hepatic jaundice". (3,4) Currently, AFLP affects approximately 1:7,000 to 1:20,000 pregnancies and has an 18% mortality rate. Death is caused mainly by sepsis, renal failure, circulatory collapse, pancreatitis, and gastrointestinal bleeding, (1) in addition to disseminated intravascular coagulation (DIC), which is the primary complication of this condition. (3)

AFLP is still not fully understood. It has been demonstrated, however, that microvesicular fat accumulates at the level of the cytoplasm of hepatocytes without causing inflammation or necrosis. These histological findings are predominantly present at the acinar zone 2 and 3 of the liver. Consequently, as microvesicular fat accumulates, beta-oxidation gets disrupted. (5) Interestingly, during pregnancy, some products of gestation present a deficiency of the 3-hydroxyacyl-CoA dehydrogenase of long-chain fatty acids, which induces an oxidative defect of the long-chain fatty acids, leading to the characteristic clinical manifestation of AFLP. (2,5)

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Several risk factors for AFLP include nulliparity, multiple gestations, morbid obesity, advanced maternal age, and male fetuses. Furthermore, due to the clinical similarity of AFLP with preeclampsia, eclampsia, and hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, it is necessary to rule out these differential diagnoses when suspecting AFLP. (5) Additionally, the Swansea criteria (**Table 1**), as well as the absence of any other explanation for liver failure, must be met in order to make a diagnosis of AFLP. (1,3) The gold standard for diagnosing AFLP is liver biopsy, which is not readily available in all hospitals. (1,5) Terminating the pregnancy and providing supportive care are the definitive treatments. (3)

Case presentation

A 22-year-old woman with a history of C-section seven years ago presented to our hospital at 38.1 weeks gestation by the last menstrual period date. Due to compromised fetal well-being, the patient underwent amniorrhexis, and meconium fluid ++/+++ was obtained. Posteriorly an emergency C-section was performed on the patient due to a rapidly decreasing fetal heart rate. A male newborn with a weight of 2940 g, length of 48 cm; activity, pulse, grimace, appearance, respiration (APGAR) score 1-7, and Silverman scores 1 was delivered. Soon after, the patient experienced transient uterine atony; therefore, she received treatment with carbetocin and misoprostol.

After surgery, the patient's blood pressure increased to 144/88 mmHg, she became oliguric with a diuresis of 0.4 ml/kg/hour, and elevated transaminases were identified (alanine aminotransferase [ALT] 393.3 IU/l, aspartate aminotransferase [AST] 202.3 IU/l). Preeclampsia with severity features was the most likely diagnosis. Later, she got admitted to the Intensive Care Unit (ICU), where she received nifedipine and metoprolol as part of her treatment. There, a liver ultrasound was performed without abnormal findings. On her second day in the ICU, the patient presented a decreased blood glucose level of 57 mg/dl.

On the third day of her ICU stay, acute fatty liver disease of pregnancy was suspected based on positive Swansea criteria (8 of 14 criteria for diagnosis [**Table 1**]). She had non-tense ascites on physical examination. Her urinary output was adequate. A proteinuria result of 170 mg/24 hours was obtained. The patient required intravenous albumin, vitamin K, and fresh frozen plasma three units. As a result of rapidly decreasing hemoglobin, abdominal and pelvic tomography was also indicated (**Table 2**). The abdomen and pelvis tomography revealed a hematoma and free fluid. As a result, an exploratory laparotomy was indicated, with intraoperative findings of a hematoma in the Retzius space of 15x15 cm and approximately 800 cc of hemoperitoneum. In this procedure, uterine arteries were ligated using the O'Leary technique. A total of three units of red blood cells and two units of plasma were transfused during the procedure. During her second day in the ICU, the patient still had a tympanic abdomen, probably due to ascites. Her urinary output was 1.56 ml/kg/hour. However, a cholestatic pattern was detected in the biochemical profile (**Table 2**). During the fourth to the tenth days of hospitalization, her condition improved, she was experiencing minimal pain in the surgical wound, her blood pressure was under control, and her urinary output was 1.5 ml/kg/day on average. Additionally, renal function improved, although bilirubin levels decreased, transaminases remained elevated, coagulation times were prolonged, and hemoglobin was low. Due to persistent anemia, two units of red blood cells and one unit of fresh plasma were transfused (**Table 2**). Prophylactic enoxaparin, albumin, L-ortidine L-aspartate, dexamethasone, and ursodeoxycholic acid were given, and antibiotic therapy was changed to ertapenem as part of the critical care treatment. In light of the patient's current status, the liver biopsy was postponed.

After day 11, the patient was transferred from the ICU to the obstetric ward to continue her treatment, where her laboratory results improved (**Table 2**). On days 12 and 17, the patient remained asymptomatic, ambulatory, and with controlled blood pressure measurements. Following clinical improvement, the patient was discharged with ambulatory management of hematinic and nifedipine 30 mg every eight hours.

Discussion

AFLP is a pathological condition that rarely occurs but can be fatal if undiagnosed. Usually, this condition occurs during the third trimester or early puerperium. It is a diagnosis of exclusion after gestational intrahepatic cholestasis, preeclampsia, eclampsia, and HELLP syndrome are ruled out since all these entities affect liver enzymes. (1) AFLP has non-specific symptoms and behaves like severe preeclampsia with abdominal pain, encephalopathy findings, epigastric pain, vomiting, nausea, and malaise; its most severe manifestation is liver failure, eventually leading to death. (1,3)

Clinical information specific to gestational age must be considered when making a differential diagnosis. For instance, during gestational intrahepatic cholestasis, alkaline phosphatase (ALP), gamma-glutamyl

transpeptidase (GGT), bile acids, and transaminases increase during the second or third trimester of pregnancy, with pruritus as an initial manifestation in the hands and feet which later generalizes. (5) This case report presents a patient with elevated ALP and transaminase levels. However, the transaminase levels were not significant or associated with pruritus to meet the diagnosis criteria for intrahepatic cholestasis.

In this case, preeclampsia was excluded since the diagnosis criteria were not entirely met. In particular, the presence of proteinuria equal to or greater than 300 mg/24 hours, as well as target organ damage criteria was not proven. Thus, ruling out preeclampsia as the primary diagnosis. (4,6)

In spite of the clinical similarities between HELLP syndrome and AFLP, the presence of hypoglycemia rules out HELLP as the cause of the clinical manifestations. Additionally, eight of the 14 Swansea criteria were met, indicating AFLP as the most likely diagnosis. In spite of this, a liver biopsy, the gold standard for diagnosing this disease, could not be performed due to the severity of the patient's condition. (3,4)

In accordance with best practice guidelines for antimicrobial management, in this case, the antimicrobial agent was switched from third-generation cephalosporin to carbapenem due to the local resistance profile in our hospital. In addition, transfusion of blood derivatives was dictated by anemia and thrombocytopenia. As the patient had compromised liver function, L-ortidine L-aspartate and ursodeoxycholic acid were prescribed, and thromboprophylaxis was indicated since she met more than 5 Caprini criteria.

Conclusions

AFLP is a rare condition that shares similarities with other diseases, such as preeclampsia, HELLP syndrome, and intrahepatic cholestasis. Moreover, the definitive diagnosis is made by assessing the clinical and biochemical parameters, as well as the Swansea criteria. The latter is a valuable tool, especially when the liver biopsy has to be postponed due to the patient's condition, as in this case.

Table 1. Swansea criteria for diagnosis of AFLP

1. Vomiting
2. Abdominal pain
3. Polydipsia/polyuria
4. Encephalopathy
5. Hyperbilirubinemia (total bilirubin greater than 0.82 mg/dl)
6. Hypoglycemia (glucose less than 72 mg/dl)
7. Hyperuricemia (uric acid greater than 5.7 mg/dl)
8. Leukocytosis (greater than 11,000 cells/ul)
9. Ascites or "hepatic hyperechogenicity on abdominal ultrasound"
10. Hypertransaminemia (AST or ALT greater than 42 IU/l)
11. Elevated ammonium (greater than 47 umol/l)
12. Acute kidney injury (creatinine greater than 1.7 mg/dl)
13. Coagulopathy (prothrombin time greater than 14 seconds or activated partial thromboplastin time greater than 34 seconds)
14. Microvesicular steatosis in liver biopsy

Legend: AFLP=acute fatty liver of pregnancy; AST=aspartate aminotransferase; ALT=alanine aminotransferase.

Table 2. Laboratory results

	Admission delivery room	Post-partum results	ICU								
			Day 1	Day 2	Day 3	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11
Hb, g/l	13.5	13	10.9	8.0	9.3	9.4	9.8	9.8	7.9	9.9	10.6
WBC, $x10^9$/l	-	11.7	22.6	19.3	10.6	14.0	11.06	7.1	12.6	13.0	13.4
Plat, $x10^9$/l	154	152	125	11	95	84	91	95	83	106	214
PT, sec	24.9	24.9	32.8	39	39	35	14.8	16	20	15.1	14.6
PTT, sec	29.2	53	66.2	49	58	30	32.4	32.2	44.7	32.9	28
ALP, UI/l	-	664	515	510	496	-	-	396	330	-	320
Alb, mg/dl	-	2.8	3.6	3.25	3.3	-	-	3.7	-	-	3.8
ALT, UI/l	393.1	-	254	139.2	78	73	91	98	-	-	110
AST, UI/l	202.2	-	124	63	60	66	109	85	-	-	76
TB, mg/dl	9	-	4	3.7	8.04	6.8	6.78	4.4	-	1.5	1.3
DB, mg/dl	4.5	-	3.98	3.6	7.1	5.9	6.6	4.3	-	4.0	3.2
IB, mg/dl	4.5	-	-	0.12	-	0.81	0.14	0.19	-	0.2	0.6
LDH, mg/dl	361	361	477	388	372	367	314	320	305	312	315
Na, mEq/l	136	136	115	120	135	140	142	138	135	137	135
K, mEq/l	4.1	4.1	3.5	3.31	4.0	3.5	3.8	4.2	4.1	3.9	4.7
Ca, mg/l	8.9	10	9.4	7.4	7.5	8.3	7.2	8.3	8.0	8.8	8
Mg, mEq/l	1.84	1.8	1.9	4.71	3.5	2.0	2.9	2.02	2.5	2.0	2.6
Cl, mEq/l	-	106	98	92.1	92	93.5	-	100	99.2	102.3	101
PO4, mg/dl		4.6	-	-	-	2.9	-	3.6	-	-	-
Gluc, mg/dl	-	57	63	65	50	126	125	162	127	113	95
Cr, mg/dl	-	1.1	1.25	1.8	0.98	0.6	0.62	0.67		0.62	0.6
BUN, mg/dl		20	24	22	26	25	30	28	25	28	29
Urea, mg/dl	-	40	39	42	45	39	39	35	30	36	39
Uric acid, mg/dl	-	-	5.8	5.6	5	4.8	-	4.2	-	3.9	3.5
Procalcitonin, ng/dl	-	-	48	93.11	61.89	-	-	-	-	1.37	-

Legend: Hb=hemoglobin; WBC=white blood cells; Plat=platelets; PT=prothrombin time; PTT=partial thromboplastin time; ALP=alkaline phosphatase; Alb=albumin; ALT=alanine aminotransferase; AST=aspartate aminotransferase; TB=total bilirubin; DB=direct bilirubin; IB=indirect bilirubin; LDH=lactic dehydrogenase; Na=sodium; K=potassium; Ca=calcium; Mg=magnesium; Cl=chloride; PO4=phosphorus; Gluc=glucose; Cr=creatinine; BUN=blood urea nitrogen; ICU=Intensive Care Unit.

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