International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

Acute Fatty Liver of Pregnancy, a Diagnostic Challenge: Case Report and Literature Review

Edgar Allan Villagómez Mendoza, Jaime Edgar Martínez Niño

Department of Obstetrics and Gynecology

General Hospital of Ecatepec Dr. José María Rodríguez, State of México.

Corresponding Author: Edgar Allan Villagómez Mendoza

Email contact: allan.villagomez.m@gmail.com

Abstract

The acute fatty liver of pregnancy (AFLP) represents an obstetric emergency that may cause multiple organ failure due to the risk of the delayed diagnosis and unpredictable progression. This is the case report presented to our hospital. Given the low incidence, we demonstrate the importance of the "Swansea criteria" to determine a diagnosis and early treatment.

Keywords

Acute fatty liver of pregnancy, liver disease, and pregnancy, intrahepatic cholestasis.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

I. Introduction

Acute fatty liver represents an unusual obstetric emergency, characterized by liver failure and increased maternal morbidity and mortality. Due to the nonspecific clinical evolution of this disease, the initial approach to the early diagnosis and clinical management is proportional to the maternal-fetal benefit.

Approximately 1 case of acute fatty liver occurs in 7,000 to 20,000 pregnancies. Although appearance is characteristic in the third trimester of pregnancy, cases of gestational age less than 28 weeks gestation and a maternal death rate of up to 24% and fetal death of 40% have been reported. The associated risk factor includes a mitochondrial defect in the beta-oxidation of fatty acids which is related to an enzyme deficiency responsible for approximately 20% of AFLP cases. Potential risk factors for AFLP include; prior episode of AFLP, preeclampsia or HELLP syndrome, male fetal sex and low body mass index (BMI <20 kg/m2), multiple gestation and Fetal long-chain 3-hydroxyacyl CoA dehydrogenase deficiency [1].

The exact pathogenesis is not clear. Related literature review indicates that it is more likely due to heterozygous long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCHAD) deficiency. Approximately 20 percent of AFLP is associated with LCHAD deficiency.

LCHAD deficiency is autosomal recessive in inheritance and mothers are often found to be heterozygous for the affected mutation.

LCHAD, that is found on the mitochondrial membrane, is involved in the beta-oxidation of long-chain fatty acids and catalyzes a step in beta-oxidation of mitochondrial fatty acids in which 3-ketoacyl-CoA is formed from 3-hydroxyacyl-CoA. In the fetus, who is homozygous for LCHAD mutation, the fetoplacental unit cannot perform this step therefore, levels of intermediate products of fatty acid metabolism increase and enter the maternal circulation. This contributes to long-chain metabolites accumulating in maternal blood and hepatocytes thus resulting in toxic effects. This results in hepatic strain leading to the development of AFLP.

The responsible gene for LCHAD has been isolated, and the most common mutation found in acute fatty liver of pregnancy is the E474Q missense mutation.
G1528C mutation has been associated with the development of HELLP syndrome and preeclampsia which share several phenotypic features with AFLP.
Apart from G1528C mutation, deficiencies of fetoplacental mitochondrial oxidation due to short-chain acyl-CoA dehydrogenase deficiency, medium-chain acyl-CoA dehydrogenase deficiency, carnitine palmitoyltransferase deficiency, mitochondrial trifunctional protein deficiency, and deficiency of long-chain 3-hydroxyacyl-coenzyme A (CoA) dehydrogenase have also been associated with the development of AFLP [2, 3].

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

The clinical manifestations are variable, frequently occurring in the third trimester between 30-38 weeks of gestation and/or 4 days postpartum. Non-specific initial symptoms are nausea, vomiting, anorexia, abdominal pain especially in upper hemiabdomen, in epigastrium and / or right hypochondrium, headache, polydipsia with or without polyuria. It may coexist with HELLP syndrome in 20% of cases and 20-40% of patients with preeclampsia.

Some other signs and symptoms are attributed to liver failure such as jaundice, ascites, encephalopathy, disseminated intravascular coagulopathy, and hypoglycemia. Most patients affected by acute kidney disease and often progress to multiorgan failure. Patients may develop diabetes insipidus due to a decrease in arginine vasopressin levels, as well as acute pancreatitis that occurs more frequently in the setting of liver and kidney failure.

The laboratory findings include elevations in transaminases 5-10 times higher than upper reference limit of normal and usually less than 1000 U / L, elevated serum bilirubin levels, low serum glucose, elevated serum creatinine, leukocytosis, urate level elevation, prolongation of coagulation parameters and INR, reduced antithrombin level, thrombocytopenia, low fibrinogen, and proteinuria. however, it is necessary to know the physiological changes of pregnancy to determine the cut-off points and pregnancy-associated alterations if present any.

Imaging studies such as ultrasound may describe non-specific changes, fatty infiltration, which causes an increase in the echogenicity of the liver parenchyma. Magnetic resonance imaging or computed tomography can be performed as diagnostic aids, however, the histopathological study, liver biopsy is the gold standard to accurately determine the diagnosis.

Histologic findings suggestive of AFLP include microvesicular infiltration of fatty acids in hepatocytes and frothy appearance of cytoplasm due to the fat droplets surround centrally located nuclei. The fatty infiltration is more prominent in the central and mid zonal parts of the lobule. A liver biopsy can provide a definitive diagnosis, but the presence of coagulopathy and difficulties in performing a liver biopsy in the antenatal mother are challenges that impact obtaining histological confirmation of AFLP in a suspected patient.

The diagnosis is based on the clinical appearance of the symptoms such as nausea, vomiting, abdominal pain and anorexia, however, associated physiological changes of pregnancy may delay the suspected diagnosis if treating physicians is not aware of such physiological changes and alterations. Likewise, the association with Preeclampsia or HELLP syndrome sometimes can make its diagnosis extremely difficult as there is a large clinical overlap between AFLP, HELLP syndrome, and severe preeclampsia.

The Swansea criteria as validated in a cohort study includes symptoms, laboratory findings,

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

and imaging, which are a diagnostic model for AFLP (Table 1).

The score obtained for each item awarded is 1 point. As depicted by a research study in which Swansea criteria were applied to women with suspected pregnancy-related disease who underwent biopsy, the presence of ≥6 abnormal variables had a positive predictive value of 85 percent and negative predictive value of 100 percent for finding microvesicular steatosis [4,5].

The management plan involves prompt delivery once a patient is diagnosed with AFLP. Primary medical management is to stabilize the patient mainly by the critical care support. It is important to assess the patient with Swansea criteria. The delivery should not be delayed as delivery initiates the resolution of this life-threatening disease, as in patients with HELLP syndrome and severe preeclampsia. During the monitoring, plasma glucose concentration assessment for diagnosing hypoglycemia and tests for coagulation parameters to monitor coagulopathy should be requested approximately every 6 hours. In addition to monitoring laboratory studies, Model for End-stage Liver Disease (MELD) score should be followed since a high MELD score (particularly MELD ≥30) is associated with risk of maternal complications., If worsening of coagulopathy is documented then it is an indication for expedited liver transplant evaluation, therefore the management has to be multidisciplinary with Intensive care unit support [6,7]

Fetal monitoring with fetal well-being tests such as cardiotocographic recording should be continuous, abnormal fetal heart rate patterns would impact the urgency of delivery. Magnesium sulfate can be administered for fetal neuroprotection in pregnancies < 32 weeks of gestation [8]. Each case should be individualized to determine the route of delivery. Delivery is expedited if there is the risk of rapidly progressing maternal/fetal decompensation [9].

Vaginal birth can be expedited with labor induction if successful delivery can be achieved within 24 hours and AFLP is not rapidly progressing within this time frame however if there is a concern about rapidly progressing maternal/fetal decompensation, then performing a cesarean delivery is a reasonable option rather than labor induction. Special attention should be given to correcting any coagulopathy before performing surgery while stabilizing the patient.

Generally, the acute fatty liver resolves after delivery and in most patients, liver functions return to normal within 7-10 days postpartum. Liver chemistries, creatinine, and coagulation tests are monitored every six hours until a clear downward trend is observed, and the frequency of testing can be reduced afterward. Recurrence has been reported in the subsequent gestations, however, the risk of exact recurrence is not yet established. Therefore, patients with a history of acute fatty liver should be referred to maternal-fetal medicine specialist for counseling if they consider future pregnancy [10].

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

II. Case Report

21-year-old patient, primigravida with a 34-weeks' gestation presented with diffuse abdominal pain, accompanied by nausea reaching vomiting on 10 occasions. Hospital admission was advised, with a presumptive diagnosis of threatened preterm labor. However, there were found no compatible cervical changes for threatened preterm birth during the hospital stay. Vital signs Blood pressure 100 / 70mmHg, Heart rate 92 bpm, Breathing frequency 20 breaths per minute Temperature 36.5C, laboratories reported; glucose 65mg / dL, creatinine 1.46mg / dL, total bilirubin of 1.2mg / dL, Aspartate aminotransferase 469U / L, Alanine aminotransferase 590U / L, Lactate dehydrogenase442U / L, Hemoglobin17.2g / dl, Hematocrit 48.8%, platelets 285,000/mm3, leukocytes 9.45x109/L Urine analysis without evidence of proteinuria, prothrombin time 13.9 seconds, International Normalized Ratio R 1.12, Study protocol was established with a diagnosis of intrahepatic cholestasis of pregnancy vs gallstones Evaluation was requested by Internal Medicine Specialist who suggested complete evaluation protocol for probable hepatopathy of viral origin, however patient underwent significant biochemical deterioration and reported to have glucose 45mg / dl, creatinine 2.5mg / dl, total bilirubin 1.9mg / dl, Aspartate aminotransferase 497U / L, Alanine aminotransferase 427 U / L, prothrombin time of 14.3 seconds, International Normalized Ratio 1.15, leukocytes of 23x109/L. Analysis of patient with Swansea's criteria was performed which scored at least 10 points, the emergency code is activated, cesarean section was indicated, the surgical intervention course went without complications, resulting in a newborn was male delivered with a height of 43cm weight 1985grams, 36 weeks, Apgar 8/9 without complications, the patient had puerperium without any complication, with evidence of notable improvement in biochemical markers. The patient was discharged 4 days postpartum after clinical improvement.

II. Discussion

Acute fatty liver is a serious entity with increased maternal and fetal morbidity and mortality particularly when the physician does not have a high index of suspicion for its diagnosis. Literature review shows that the maternal and perinatal mortality have greatly decreased, to approximately 18% and 23%, respectively, with the help of prompt diagnosis and treatment.

Our case report indicates that although the patient was admitted with suspected threatened preterm labor, the diagnosis was altered to AFLP because of evaluation tests and assessment. Swansea Criteria was one important assessment tool that assisted us to diagnose our patients promptly. Liver biopsy was not performed in our patient who was evaluated through Swansea criteria which further helped us in patient's management subsequently. It is worthy to note that patient improved clinically, and biochemical markers for liver functions returned to normal in postpartum period. We could not exclude viral hepatopathy because of the unavailability of required reagents for viral hepatitis panel in

our setup and we couldn't do it through external source because of the economic limitations. Because of the absence of hypoglycemia, coagulopathy, and presence of transaminases level of less than 1000 U/L in our patient, we did not suspect viral hepatitis induced acute liver injury. Presumptive diagnosis of preeclampsia/HELLP syndrome could have been another possibility. AFLP may coexist with HELLP syndrome in 20% of cases and 20-40% of patients with preeclampsia which is the diagnostic challenge for physicians. Our patient was normotensive and without any evidence of proteinuria and hemolysis, we did not have a high suspicion of thrombotic microangiopathy as seen in severe preeclampsia/HELLP syndrome.

III. Conclusion

The acute fatty liver of pregnancy is an obstetric emergency, with an unpredictable progression therefore, early diagnosis is essential. However, it becomes difficult to diagnose it as it shares clinical features with other common disorders such as Preeclampsia and HELLP syndrome. Prompt suspicion and early recognition are cornerstones of the management of patients with AFLP. Multidisciplinary management and emergent careful delivery of the baby is carried out in patients with risk of developing rapidly progressive maternal/fetal decompensation caused by this life-threatening disease. Due to the risk of recurrence in a subsequent pregnancy, women with a history of AFLP should be co-managed with a maternal-fetal medicine specialist for counseling, if they are planning to have a pregnancy in the future.

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

VI. References

[1] Nelson D, et al. Acute fatty liver of pregnancy: clinical outcomes and expected duration of recovery. Am J Obstet Gynecol 2013: 209: 456

[2] Ibdah J, et al. A fetal fatty-acid oxidation disorder as a cause or liver disease in pregnant women. N Engl J Med 1999: 340: 172

[3] Knight M, et al. A prospective national study of acute fatty liver of pregnancy in the UK. Gut 2008: 57: 951

[4] Lee R, et al. Acute fatty liver or pregnancy, jan 2020, www.uptodate.com

[5] Tran T, et al. ACG clinical guideline: Liver Disease and pregnancy, Am J Gastroenterol 2016: 111: 176

[6] Lorenzo A, et al. Acute fatty liver of pregnancy: an unusual diagnosis in obstetrics, Clin Invest Gin Obst. 2005; 32 (1): 27-9

[7] Muñoz T, et al. Acute fatty liver of pregnancy and HELLP syndrome: diagnostic and therapeutic aspects, Gastroenterol. latinoam 2013; Vol 24, Suppl. No. 1: S 123-S 126

[8] Crowther C, et al. Magnesium sulphate at 30 to 34 weeks' gestational age: neuroprotection trial (MAGENTA) - study protocol. BMC Pregnancy Childbirth. 2013 Apr 9; 13: 91. doi: 10.1186 / 1471-2393-13-91.

[9] Bacq Y. Liver diseases unique to pregnancy: a 2010 update. Clin Res Hepatol Gastroenterol 2011; 35: 182.

[10] Westbrook RH, Dusheiko G, Williamson C. Pregnancy and liver disease. J Hepatol 2016; 64: 933

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/

Table 1. Swansea criteria

Vomiting
Abdominal pain
Polydipsia / Polyuria
Encephalopathy
Bilirubin>0.8mg/dL
Hypoglycemia <72mmg/dL
Leukocytosis>11,000/microL
Transaminase >42U/L
Elevated ammonia (>47 micromol/L)
Uric acid >5.7mg/dL
Acute renal injury or creatinine>1.7mg/dL
Coagulopathy or prothrombin time>14 seconds
Ascites or bright liver echotexture on ultrasound
Microvesicular steatosis reported in biopsy

International Journal of Obstetrics and Gynaecology Research (IJOGR)
Vol. 6 (2020) No.4, pp. 787-794
http://www.ijogr.com/