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Case Report

Acute Fatty Liver of Pregnancy, a Diagnostic Challenge Compared to Other Causes of Disseminated Intravascular Coagulation. Case Report and Literature Review

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Abstract

Background: Acute fatty liver of pregnancy (AFLP) is considered a rare and life-threatening obstetric emergency that generally affects pregnancies in the third trimester, as well as in the postpartum period. Its incidence is reported to affect 1 in every 100,000 pregnancies. This pathology is characterized by acute liver failure, which is preceded by fatty infiltration of the liver. Associated with high rates of maternal and perinatal morbidity and mortality of up to 80% when it occurs.

Clinical Case: 21-year-old patient, who enters a first-level health care unit with a third trimester pregnancy and labor, as well as an attack on her general condition, nausea, vomiting, mild jaundice generalized abdominal pain, as well as laboratory studies with anemia, thrombocytopenia, leukocytosis and hypoglycemia. After vaginal birth it began with transvaginal hemorrhage, final quantification of blood loss at 1,550 ml. Referred for advanced life support to a higher health center, upon arrival with multidisciplinary management in the Intensive Care Unit (ICU) with progressive hemodynamic deterioration, the time of death being declared later, in whom a diagnostic necropsy was performed, with histopathological report of AFLP.

Conclusion: It is considered an extremely rare, but potentially fatal complication, with serious consequences for both the mother and the fetus. Faced with a pregnant patient who triggers a clinical picture highly suspicious of AFLP, based mainly on compliance with > 6 of the Swansea criteria, always taking into account that not in all cases it presents as a single entity, and can be correlated with other pathologies that complicate the second and third trimesters of pregnancy.

Keywords: *Acute Fatty Liver of Pregnancy; Liver Dysfunction; Disseminated Intravascular Coagulation; Obstetric Hemorrhage; Maternal Morbidity and Mortality*

Abbreviations

AFLP: Acute Fatty Liver of Pregnancy; ICU: Intensive Care Unit; DIC: Disseminated Intravascular Coagulation; LCHAD: Long Chain 3-Hydroxyacyl CoA Dehydrogenase; TCA: Tricarboxylic Acid; ATP: Adenosine Triphosphate; RRT: Renal Replacement Therapy; Hb: Hemoglobin; Hct: Hematocrit; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; DHL: Lactic Dehydrogenase; BT: Total Bilirubin; BD: Direct Bilirubin; BI: Indirect Bilirubin; TP: Prothrombin Time; TTP: Thromboplastin Time Partial

Introduction

AFLP is considered a rare and life-threatening obstetric emergency that generally affects pregnancies in the third trimester, however, cases have been reported in the second trimester, as well as in the immediate puerperium (postpartum). Its incidence is reported to affect 1 in every 100,000 pregnancies in developing countries, although in countries like the United States it ranges between 1 in every 7,000 to 15,000 pregnancies. This pathology is characterized by acute liver failure, which is preceded by fatty infiltration of the liver [1].

Associated with high rates of maternal and perinatal morbidity and mortality. In the last decades, this rate reached such important and alarming figures of up to 80% [2]. Currently, these figures vary widely, with maternal mortality reported to be less than 18%, and perinatal mortality less than 23% [3]. This decrease compared to retrospective studies is mainly attributed to earlier diagnosis and better management of multiple maternal conditions [4].

Up to 80% of patients affected with AFLP present persistent nausea and vomiting, lethargy, abdominal pain and jaundice, and only a smaller number of patients may develop pancreatitis, the above with respect to the clinical presentation [5]. Regarding the biochemical presentation; AST and ALT levels have been reported with elevations of up to 10 times the upper normal limit [6]. The clinical presentation, as well as the biochemical and laboratory findings, are of vital importance when it comes to differentiating AFLP from other diseases that are equally related to pregnancy, with a very similar form of presentation, but with particularities that they do different things, among which intrahepatic cholestasis of pregnancy, HELLP syndrome and preeclampsia (PE) stand out.

Disseminated intravascular coagulation (DIC) in pregnancy represents around 5% of all cases of DIC, a higher statistic in countries considered developing, hospitalizations of up to 12.5 per 10,000 pregnant patients (0.13%) have been reported are afflicted by DIC [7]. Although the numbers are low, patients with serious pregnancy complications, such as AFLP, placental abruption, HELLP syndrome, or amniotic fluid embolism, represent a very high risk of development, reported even above 20% [8].

In this article we present the case of a patient who developed AFLP in the third trimester of pregnancy, with a fatal outcome. The objective of this review is to evaluate the literature available in electronic databases, including case series, incidence reports, clinical course and treatment results, with the aim of expanding knowledge regarding this topic, as well as emphasizing that a complete and timely diagnostic approach, as well as the availability of resources in the postpartum period, are essential for an accurate and timely diagnosis, which is vital for choosing the specific and appropriate treatment, thus improving the prognosis of patients, mainly in the face of this pathology with such high morbidity and mortality.

Clinical Case

A 21-year-old patient, originally from a rural area of the state of Michoacán, Mexico, with a positive genetic load for type II diabetes mellitus and chronic systemic arterial hypertension, with a history of only three hospitalizations for the resolution of vaginal birth, without complications. She denied knowing any medical, chronic, or degenerative illnesses. With menarche at 13 years of age, irregular menstrual cycles, beginning of active sexual life at 17 years of age, three sexual partners since then, three pregnancies, three births.

Referred from a primary care rural health center, with vague and scarce data on obstetric care prior to her referral. The resolution of the pregnancy was reported 16 hours prior to her arrival, where it was reported that she was admitted to the hospital to conduct labor vaginally, at that time with a pregnancy of 38.3 weeks of gestation (SDG), labor in the active phase, general malaise and vomiting on different occasions. Due to the time of admission and the availability of hospital resources, only basic laboratory studies were performed; positive hemotype O, glucose 69 mg/dl, creatinine 0.9 mg/dl, platelets 122,000/uL, hemoglobin 9.3 g/dl, hematocrit 30%, leukocytes 15,000/uL, no admission clotting times reported.

Conduction of labor began, with resolution vaginally four hours later, active management of the third stage of labor with Oxytocin was indicated, obtaining a male newborn, weighing 3,250 grams, height 50 cm, APGAR 08- 09, silverman 0-0, an initial bleeding of 350 ml was quantified, two hours later she underwent surgery to perform bilateral tubal occlusion, and subsequently went to rooming-in for recovery, almost immediately she developed excessive transvaginal bleeding, according to the reference, secondary to uterine hypotonia, staggered uterotonic medications were applied; ergometrine, carbetocin, misoprostol, without obtaining a response, so clamping of the uterine arteries was performed with the Zea technique, with a decrease in transvaginal bleeding, with an estimated quantification of 1,200 ml, total blood losses up to that point of 1,550 ml, it was started water resuscitation with 1,500 ml of crystalloid solutions, as well as transfusion of two erythrocyte concentrates, and was presented to state support for referral to a third level of care.

Upon arrival at our hospital, a patient was found with the following vital signs: blood pressure 90/54 mmHg, heart rate 132 palpitations per minute, respiratory rate 24 per minute, SaO_2 of 94%, temperature of 34c, with paleness and marked jaundice of the skin and integuments, patient oriented, conscious, soft, flat, depressible abdomen, with uterus involute below the umbilical scar, painful on deep palpation in the epigastrium, vaginal examination with presence of serohematic lochia, without evidence of bleeding active, 3 second capillary refill. A FAST ultrasound was performed, which was reported as positive, so under suspicion of hemorrhage in the abdominal cavity, it was protocolized with laboratory studies and she was immediately taken to the operating room to perform an exploratory laparotomy. The admission laboratory studies are explained in table 1. As an intraoperative finding, only the presence of free peritoneal fluid, with serous characteristics, of approximately 700 ml, was reported; no source of active bleeding was found.

Subsequently, and given the severity of the clinical condition, it was decided to admit her to the intensive care unit (ICU) for advanced life support management. Upon admission with mean arterial pressure (MAP) of 54 mmHg with vasopressor support at 0.3 mcg/kg/min, tachycardic, pale, jaundiced, orointubated, VMC was placed with low parameters, hypoventilated lung fields, as well as pleural effusion. At that moment in transfusion, to complete 6 fresh frozen plasmas, 3 cryoprecipitates, 3 globular packets, 2 bottles of fibrinogen, it is important to mention that since her arrival the transfusion of blood components and blood products began. After analysis of laboratory studies, the need for a greater contribution of fibrinogen, platelets, and blood products was documented. A nephrology evaluation was requested for AKIN 3 acute renal failure; a furosemide challenge was previously performed, which was negative. And new laboratory studies are obtained, presented in the same way in table 1. The nephrology service commented on the persistence of anuria for more than 24 hours, with an acid-base state of uncompensated metabolic acidosis of the hyperchloremic type due to delta gap, and hyperlactatemia type A. Therefore, she is considered a candidate for renal support therapy with continuous renal replacement therapy (RRT). However, when she encountered DIC, resolution was initially expected with the administration of blood products, to later place a Niagara catheter and start continuous RRT.

However, and despite adequate life support, 19 hours after admission, she presented hemodynamic deterioration, with hypotension of 54 mmHg, for which she was managed with increased vasopressor, respiratory deterioration, desaturation 64%, alveolar hemorrhage, with increased provision of FiO_2 to 100%, as well as titration of PEEP up to 16 cmH_2O, at that time with norepinephrine at 0.45 mcg/

Parameters	Results			
	Income	Entrance to ICU	12 Hours of Admission	19 Hours of Admission
Platelets	30,000/uL	22,000/uL	55,000/uL	66,000/uL
Hb	5.9 g/dl	9.8 g/dl	6 g/dl	7.8 g/dL
Hto	21.3%	29.7%	18%	23.4%
Leukocytes	23.9/uL	18.7/uL	10.8/uL	9.4/uL
Glucose	62 mg/dl	166 mg/dl	126 mg/dl	133 mg/dl
Creatinine	2.77 mg/dl	4 mg/dl	3.08 mg/dl	2.94 mg/dl
Urea	123.6	202.2	241	231
Triglycerides	267 mg/dL	242 mg/dL	221 mg/dL	196 mg/dL
DHL	2,197 A/L	4,340 A/L	4,143 U/L	3,997 U/L
AST	402 U/L	1,453 U/L	1,662 U/L	1,564 U/L
Other	214 U/L	662 U/L	667 U/L	642 U/L
BT	6.33 mg/dL	7.99 mg/dL	7.21 mg/dL	7.46 mg/dL
BD	5.09 mg/dL	5.86 mg/dL	4.55 mg/dL	5.41 mg/dL
BI	1.24 mg/dL	2.13 mg/dL	1.66 mg/dL	1.97 mg/dL
TP	48.6 seg	23.5 seg	17.1 seg	14.7 seg
TTP	123.2 SEG	65.9 seg	53.4 seg	49.2 seg
INR	3.9	1.79	1.28	1.09
Fibrinogen	40 mg/dL	201 mg/dL	306 mg/dL	387 mg/dL
Dimer D			> 10	> 10

Table 1: *Report of laboratory studies and their evolution.*

Hb: Hemoglobin; Hto: Hematocrit; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; DHL: Lactic Dehydrogenase; BT: Total Bilirubin; BD: Direct Bilirubin; BI: Indirect Bilirubin; PT: Prothrombin Time; TTP: Partial Thromboplastin Time.

kg/min, vasopressin 0.3 ml/hr, with data of extreme hypoperfusion, motling score 4 points, with capillary refilling of 10 seconds, it was escalated to norepinephrine 16 ml/hour 0.32 mcg/kg/min, with vasopressin 10 ml/hr, mechanical ventilation with high parameters, IU 0.02 ml/kg/min until that moment a total of 2 platelet aphereses were transfused, 17 fresh frozen plasmas, 13 erythrocyte concentrates, 18 cryoprecipitates. Thirty minutes later, she had no pulse, advanced cardiopulmonary resuscitation was started without recovery of spontaneous circulation and pulse, and time of death was declared. After signing informed consents, a Necropsy was performed, with findings described in table 2, illustrated in images 1-8, as well as the final diagnoses presented in table 3.

Abdominal pain
Polydipsia or polyuria
Vomiting
Encephalopathy
Hypoglycemia < 72 mg/dL
Bilirrubina> 0.8 mg/dL
Uric acid > 5.7 mg/dL or 340 umol/L

Ascites
ALT > 42 U/L
Leukocytes > $11X10^9$/L
Ammonia > 66 umol/L
Creatinine > 1.7 mg/dL
TP: > 14s or DIC
Bright liver on ultrasound
Liver biopsy with report of microvesicular steatosis

Table 2: *Swansea criteria.*

ALT: Alanine Aminotransferase; TP: Prothrombin Time.

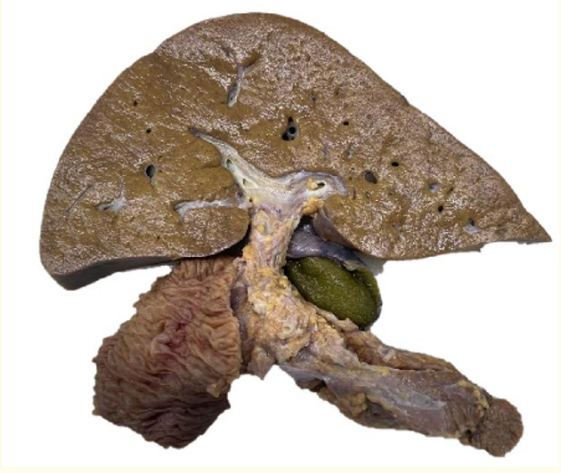

Image 1: *Surgical specimen with block dissection; liver parenchyma, gallbladder, pancreas and duodenal segment. Liver parenchyma with patent ducts and intrahepatic pathway.*

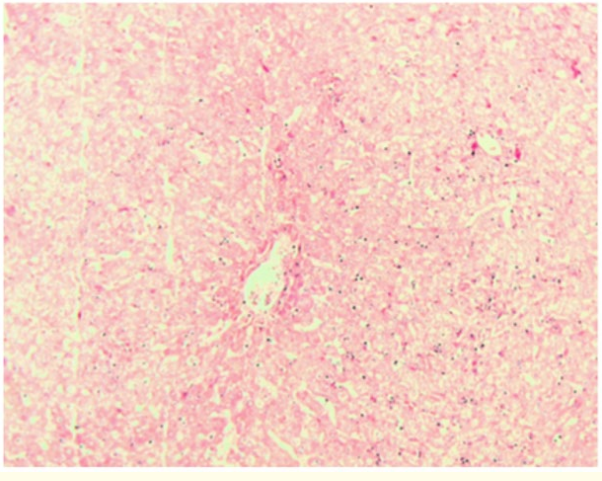

Image 2: *Photomicrograph stained with hematoxylin-eosin (H-E), where hepatic parenchyma with architectural loss is observed, attributable to data of hepatotoxicity.*

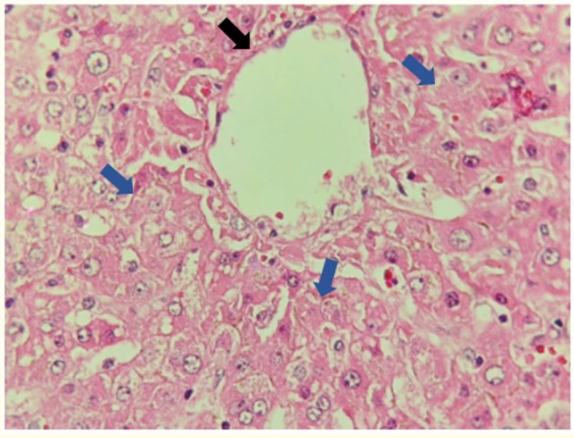

Image 3: *H-E stained photomicrograph showing a patent centrilobular vein (black arrow) without histological alterations and apoptotic hepatocytes (blue arrows).*

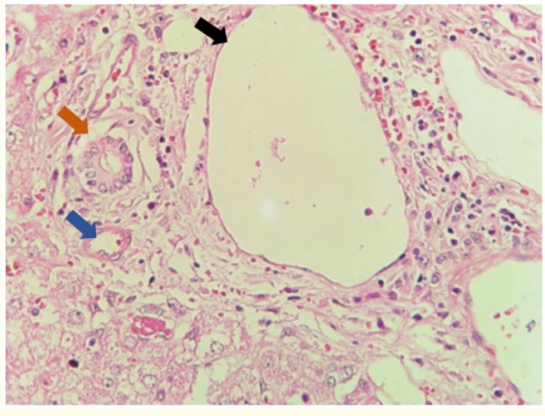

Image 4: *Photomicrograph stained with H-E, where the portal space consisting of the centrilobular vein (black arrow), artery (blue arrow) and cholangiolus (orange arrow) is found without histological alterations.*

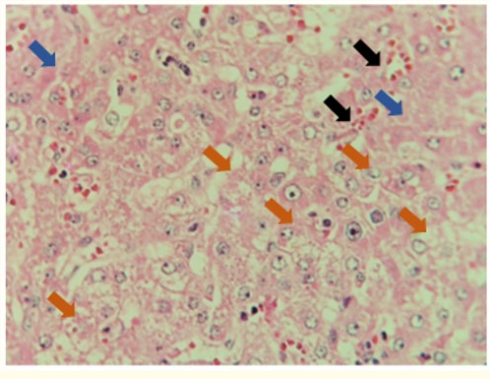

Image 5: *H-E stained photomicrograph with the presence of dilated sinusoidal spaces with the presence of erythrocytes (black arrow), apoptotic hepatocytes (blue arrows), intracytoplasmic microvesicles in hepatocytes (microvesicular steatosis) (orange arrows).*

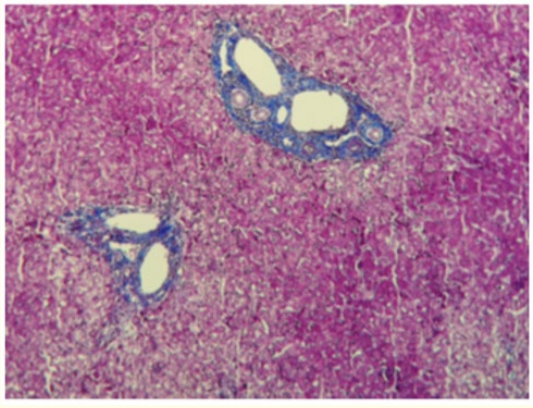

Image 6: *Negative Masson's Trichrome stain in liver parenchyma. Ruling out an inflammatory process.*

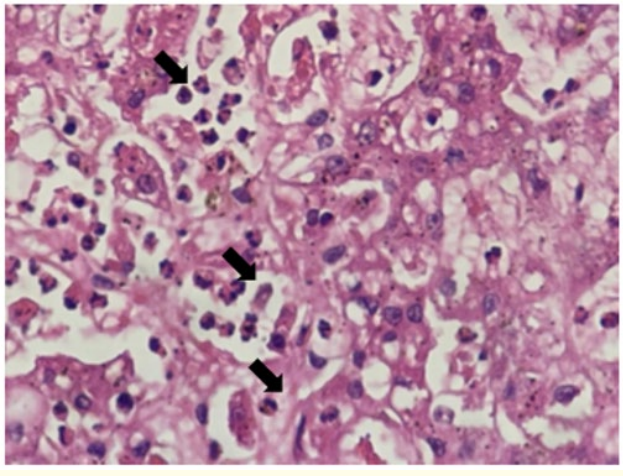

Image 7: *PAS (Periodic-Acid-Schiff) staining of the liver parenchyma. A predominantly acute inflammatory infiltrate is observed (black arrows), without dye affinity in intracytoplasmic microvacuoles of hepatocytes, ruling out a storage disease.*

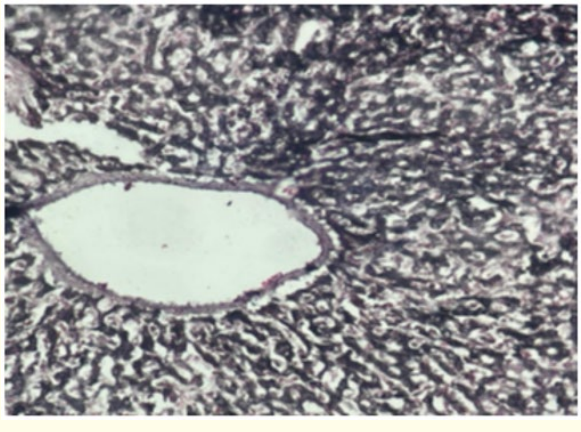

Image 8: ***F****rozen section of liver parenchyma stained with Sudan Black. Staining affinity in intracytoplasmic microvesicles of hepatocytes which correspond to neutral lipids, suggestive of microvesicular steatosis.*

- Acute fatty liver of pregnancy.
    - Coagulopathy due to consumption.
    - Multiple bleeding (Mediastinum, pericardium, lungs, digestive tract, and endometrium).
- Acute tubular necrosis.
- Chronic non-specific pyelonephritis.
- Chronic non-specific pancreatitis associated with edema and hemorrhage.
- Foci of insipient bronchopneumonia.
- Chronic passive congestion of the spleen.
- Chronic non-specific mumps.
- Regenerative changes in tongue epithelium.
- Chronic non-specific pancarditis.
- Acute ulcerated tracheitis.
- Chronic nonspecific esophagitis.
- Acute gastritis ulcer.
- Chronic non-specific periappendicitis.
- Chronic cholecystitis associated with necrosis and blood starvation.
- Chronic non-specific ileitis.
- Nursing mother.
- Follicular cysts on the ovaries.
- Postpartum uterus.
- Specific acute bleeding in the myometrium.
    - Bleeding in uterine parametrial vessels.
- Recent uterine venous thrombosis.
- Acute erosive cervicitis.
- Chronic non-specific vaginitis.
- Chronic focal nonspecific encephalitis.

Table 3: *Final necropsy findings (Final report).*

Materials and Methods

A search was performed in the Medline database via PubMed using the following terms: “acute fatty liver of pregnancy”, “hepatic dysfunction”, “disseminated intravascular coagulation”, “obstetric hemorrhage”, and “maternal morbidity and mortality”. The search was limited by the following filters: “Case Reports”, “Review”, “Systematic Reviews”, and “Books and Documents”, “Spanish and English”, editorials, reviews, duplicate articles were excluded and 31 studies were selected that will include women with the development of AFLP, and its different complications.

Results and Discussion

AFLP is a rare disease characterized by microvesicular fatty infiltration in the liver tissue [9]. Historically, the etiology of AFLP has been poorly understood, although there is currently evidence that relates it to mitochondrial dysfunction and affection, and impairment of fatty acid oxidation.

The liver is considered an organ that includes different metabolic pathways, such as those that synthesize glucose, lipids and ketones, which is why it has a significant number of mitochondrial metabolic pathways, such as the β-oxidation cycle, the acid cycle tricarboxylic acid (TCA), ketogenesis, respiratory activity and the synthesis of adenosine triphosphate (ATP) with the aim of developing and providing energy for different organic functions [10]. This organ faces constant mitochondrial remodeling, gene expression and morphology in the

face of an increase in metabolic demand, which represents a cornerstone in the pathogenesis of liver disease [11]. When mitochondrial homeostasis is related to subsequent organic dysfunction at the liver cellular level, specifically in the face of fatty liver disease [12]. This mitochondrial dysfunction is related to the subsequent development of reactive oxygen species (ROS), and direct exposure of the liver to oxidative stress produces inflammation of the liver tissue and fibrosis [13].

Disseminated intravascular coagulation (DIC) is considered a pathological alteration of hemostasis, producing systemic activation of coagulation, characterized by the generation and deposition of fibrin, as well as the formation of microvascular thrombi, which ultimately leads to multiorgan dysfunction. decreasing the platelet count to a critical level, thus producing excessive bleeding, as a consequence of this generalized coagulation, the platelet count continues to decrease, as well as the coagulation factors that are necessary to control this bleeding [14].

Risk factors and genetics related to AFLP

Different factors have been described that influence the development of AFLP, such as multiple gestations, male fetuses, obesity, fatty acid oxidation disorders in the fetus, etc [4].

It is believed that deficiency in fatty acid metabolism during pregnancy plays a fundamental role in the development of this pathology; different related genetic mutations have been described; Approximately 20% are associated with a homozygous long-chain mutation of 3-hydroxyacyl CoA dehydrogenase (LCHAD), which causes a fatty oxidation defect in fetal tissues, finally causing an accumulation of different metabolites toxic to the liver. Mother. The homozygous G1528C mutation, hemolysis, viral infections, HELLP syndrome, preeclampsia have also been associated with the development of AFLP [15].

Fetal LCHAD deficiency has been associated in up to 75% of cases in which AFLP developed in the third trimester of pregnancy [9]. In these cases, there is an almost 20-fold increase in fetal fat oxidation defects [16]. These defects have an autosomal recessive inheritance, so when present in the fetus, generally the mother will be a carrier of this disorder, making her susceptible to an overload of toxic free fatty acids [17].

Pathophysiology and mitochondrial dysfunction

A solid association has been described between the development of maternal AFLP and the alteration in the oxidation of fetal and placental fatty acids, there are different data that directly link long-chain LCHAD in fetal tissues with the development of AFLP in the mother at the end of pregnancy [18].

During a normal pregnancy, there are hormonal changes that are associated with a physiological decrease in the oxidation of long and medium chain fatty acids, thus causing an increase in the circulating level of maternal fatty acids during the three trimesters of pregnancy. This increases susceptibility to a load of free fatty acids that act as hepatotoxins in patients considered high risk [19].

Something that characterizes all cases of pregnancies affected by AFLP is multi-organ fatty infiltration. At the liver level, we speak of a generalized microvesicular fatty steatosis of the liver parenchyma. This microvesicular steatosis directly affects the hepatic production of cholesterol, fibrinogen and stress factors. coagulation and decreases the conjugation and clearance of bilirubin [9].

Currently, fetal fatty acid oxidation disorders are considered to be directly related to AFLP [20]. Deficiencies of the long-chain 3-hydroxyacyl-coenzyme A dehydrogenase enzyme lead to an accumulation of hepatotoxic metabolites of long-chain fatty acids in the fetus, which can pass into the maternal circulation, causing maternal hepatotoxicity and mitochondrial dysfunction [21]. This impairment and exposure to cytotoxic lipid peroxidation products can also depress metabolism at the cellular level and activate proinflammatory pathways [22]. The sustained increase in the levels of free fatty acids, such as arachidonic acid, serum nitrates and malondialdehyde, are

associated with increased oxidative and nitrosative stress within peroxisomes and mitochondria in patients with AFLP [21]. These high levels of free fatty acids increase the production of reactive oxygen species and the activity of caspase, which leads to the production of apoptosis at a different organic level, with liver tissue being more affected [21].

Clinical presentation and diagnosis

AFLP generally presents in the third trimester of pregnancy, an initial clinical picture tends to be vague and non-representative, including general symptoms such as epigastralgia, nausea and vomiting [17] that are associated with an increase in liver function tests. Cases have been reported in which they present asymptomatic hypertransaminasemia, only developing jaundice in severe cases [4]. In rare cases, signs and symptoms of acute liver failure may develop, including encephalopathy and bleeding secondary to coagulopathy; however, the latter have been reported to be observed 1 to 2 weeks after the first sign or symptom occurs.

Once the different mechanisms that cause the different forms of initial presentation have been raised, and since it is an entity with a high progression to fatality, severe hypoglycemia, acute pancreatitis, infection, acute renal failure are mentioned as some of the first complications. reported in these patients. On the other hand, hepatic encephalopathy, disseminated intravascular coagulation (DIC) and secondary hemorrhage are considered the most late complications. All of these complications occur in association with significant perinatal and maternal mortality. Rare cases have also been reported. in which diabetes insipidus develops [4].

Compared to AFLP, the diagnosis is made based on the clinical criteria; the biochemical presentation demonstrates compromise of the liver function tests. The severity of liver parenchymal dysfunction is not related to the degree of elevation of these tests, the platelet count is usually normal, except in cases complicated with DIC, blood urea nitrogen (BUN) and creatinine are generally normal. are found elevated. As liver function progresses and worsens, both hypoglycemia and encephalopathy with elevated ammonia develop. Currently, and although it is within the already established criteria, liver biopsy is not considered necessary, it can demonstrate infiltration of microvesicular fat in hepatocytes [23], the different imaging modalities are of little value to reach the diagnosis, but they are considered useful to rule out conditions such as hepatic ischemia, hepatic infarction, Budd-Chiari syndrome or hepatic hematoma/rupture [17].

Currently, the use of the Swansea criteria, including clinical symptoms, biochemical laboratory findings, and imaging findings, is recommended to make the diagnosis of AFLP (Table 2). A sensitivity of 100% and a specificity close to 60% has been reported when the use of the Swansea criteria is concerned, with a positive predictive value of approximately 85%, and a negative predictive value of 100% [15]. These will be considered positive for the diagnosis of AFLP when > 6 of the 15 previously mentioned criteria are met. Likewise, diagnostic suspicion is recommended when other diagnoses with a similar presentation have already been excluded.

Complications related to AFLP

These arise from liver dysfunction and affect different organs and systems, among which blood dyscrasias stand out, such as coagulopathy, thrombocytopenia, DIC and hemolysis [24]. Whatever the cause of this dysfunction, it is associated with a decrease in the production of different coagulation factors and procoagulant proteins, which leads to the development of coagulopathy in coexistence with hypercoagulability [25]. A reduction in fibrinogen levels, low levels of components of the antifibrinolytic pathway and regulation of tissue plasminogen activator are related, which promote hyperfibrinolysis and DIC [25].

Hemorrhage is commonly observed, as coagulopathy exacerbates common causes of obstetric hemorrhage, such as uterine atony, bleeding from surgical incisions, and injuries to sites adjacent to the resolution of pregnancy by any route. It has been reported that a little less than 70% of patients with AFLP will require transfusion of blood components and/or blood products during hospitalization. A small number of patients will require exploratory surgical reintervention due to bleeding from the abdominal surgical site [9]. Likewise, the presentation of non-obstetric hemorrhage has been described, mainly related to the upper gastrointestinal tract, such as esophagitis and ulcers [9].

Renal complications such as acute kidney injury up to the establishment of renal failure with the need to require renal replacement therapy [26]. In the context of acute liver failure, hepatorenal syndrome has been implicated in rare cases of renal dysfunction [19].

The development of encephalopathy is the defining feature of acute liver failure and has the potential to rapidly progress to seizures and coma [26]. When cerebral edema and increased intracranial pressure develop, it means a high risk of morbidity and mortality [27].

The development of pancreatitis is subsequent to the appearance of hepatic and renal dysfunction, which can be complicated by the appearance of pseudocysts with secondary infections, hemorrhagic pancreatitis and necrotizing pancreatitis. It has been suggested as an indicator of poor prognosis because it is associated with an increase in adverse outcomes [28].

In very severe cases, there is worsening of liver injury such as liver hematoma, liver rupture or infarction [29]. The development of acute portal hypertension further compromises maternal hemodynamics and directly contributes to multiorgan dysfunction [30]. Systemic infection such as sepsis, pneumonia, of the upper urinary tract, by dangerous and aggressive organisms such as *Clostridium difficile* and the development of peritonitis, have also been described [3]. Likewise, cases have been reported in which poor healing or seroma formation in the surgical wound results, as well as infection and tissue necrosis, depending on the weakened host immune response [19].

Causes of CID related to pregnancy

Related to pregnancy, different conditions have been described that triggered DIC when they occurred, among which the following stand out: placental abruption and postpartum hemorrhage in about 40%, explained by the severe hypoxia to which the patient is exposed after the pregnancy. hypovolemic shock, which results in the release of tissue factor from damaged cells, with consequent activation of coagulation, ultimately resulting in DIC, although it has also been proposed that it is due only to the loss of coagulation factors and platelets due to blood loss, which would lead to dysfunctional coagulopathy. Pregnancy-related hypertensive conditions have also been described, such as preeclampsia, eclampsia, and HELLP syndrome (hemolysis, elevated liver enzymes, thrombocytopenia), as well as AFLP, amniotic fluid embolism, and sepsis [31].

It is important to mention that the reaction after a transfusion can also trigger DIC, these are mainly due to ABO incompatibility, this can cause anemia, thrombocytopenia, suppuration of mucocutaneous sites and bleeding, these types of reactions are associated with a positive result in the direct Coombs test. Hemolytic transfusion reactions occur when there is an immunological incompatibility between the recipient of the transfusion, the red blood cells and the donor. The severity of this can range from mild hemolysis to DIC, shock, renal failure and death [31].

Likewise, DIC can also be caused by other entities that are not specific to pregnancy, such as sepsis, trauma, and cancer.

Hypertensive states of pregnancy and AFLP

There is a theory called superposition, which states that the diagnosis of one does not exclude the diagnosis of the other. In the face of severe hemolysis, elevated liver enzymes, thrombocytopenia and AFLP, they can become indistinguishable in some cases, even with a liver biopsy performed, it can be a challenge because the histological findings are very varied and can be misinterpreted. Interpret [15]. However, when we talk about a hypertensive state related to pregnancy (gestational hypertension, preeclampsia, preeclampsia with severity criteria or HELLP syndrome), they are characterized histopathologically by the presence of periportal hemorrhage and necrosis, compared to microvesicular steatosis, which characterizes and defines exclusively to the AFLP [26].

Driving

The main therapeutic action after the diagnosis of AFLP is the interruption of pregnancy by the route that best suits the couple; therefore, management aims at rapid and safe resolution for the mother and fetus. Preterm pregnancies may have a delay in the resolution of the pregnancy in order to complete a corticosteroid regimen in order to mature the fetal lung architecture and function; however, this action is not the most recommended compared to AFLP, given the risk. high that it implies for the binomial. With a high suspicion, taking a liver biopsy is not necessary, since it carries a higher risk of bleeding caused mainly by liver failure and DIC associated with AFLP [15].

With the development of different complications associated with AFLP, complete recovery is delayed, with up to weeks of evolution documented. Bringing TP levels to optimal levels is the first sign of liver recovery. In general, liver dysfunctions have not been reported after complete recovery. However, different authors believe otherwise, mainly when it comes to other organs. On rare occasions, pregnant patients who develop AFLP and severe acute liver dysfunction, with involvement of other organs, should be protocolized for a liver transplant, as the only opportunity for clinical and biochemical improvement.

AFLP has a recurrence of up to 20% in future pregnancies, the above supports the hypothesis that there is an underlying molecular mechanism that affects this recurrence, with the association between maternal AFLP and pediatric fatty acid oxidation defects [17].

Conclusion

AFLP is considered an extremely rare, but potentially fatal complication, with serious consequences for both the mother and the fetus. The pathogenesis of this entity is directly related to mitochondrial dysfunction associated with fetal deficiencies. The latest studies support the previous hypothesis originating from placental dysfunction and oxidative stress, thus causing cellular damage and mitochondrial dysfunction. When faced with a pregnant patient who triggers a clinical picture highly suspicious of AFLP, a correct and timely diagnosis should be considered as the cornerstone for the prognosis of the binomial, also being considered as a diagnosis of exclusion, and always taking into account that not in All cases present as a single entity, and can be correlated with other pathologies that complicate the second and third trimesters of pregnancy. In general, and not only in countries considered developing, it is important to train all levels of health care, with the precise intention of diagnosing, treating, and referring patients to health centers where they can provide adequate treatment and hemodynamic stability.

Conflict of Interest

There are no conflicts of interest.

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