Acute Fatty Liver of Pregnancy: A Rare Case Further Complicated with Disseminated Intravascular Coagulation

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Abstract
Introduction: An acute fatty liver of pregnancy is a rare and potentially deadly pregnancy complication. A case of acute fatty liver of pregnancy that is complicated with disseminated intravascular coagulation is hereby presented.
Case Report: A 27-years old, 36 weeks pregnant female is presented with jaundice, elevated LDH and liver enzymes, and thrombocytopenia. An emergency obstetric ultrasonography examination found an unremarkable pregnancy without a placental abruption. The patient was managed conservatively and she delivered 6 days after the presentation. The neonate was treated in the neonatal intensive care unit due to a meconium aspiration. The patient suffered from a continued uterine bleeding and she was managed with the Sayeba's technique. The laboratory work-up showed a disseminated intravascular coagulation with anemia and thrombocytopenia. The patient was treated with a packed red cell and fresh frozen plasma transfusion. The patient required an intensive care treatment.
Discussion: An acute fatty liver of pregnancy is a potentially deadly complication of pregnancy and it requires a multidisciplinary, intensive support. The acute fatty liver of pregnancy symptoms are similar to those of a HELLP syndrome. An acute fatty liver of pregnancy requires a prompt delivery followed with a intensive support. Complications of an acute fatty liver of pregnancy include a hepatic failure and a disseminated intravascular coagulation which should be managed accordingly.
Conclusion: An acute fatty liver of pregnancy requires a prompt diagnosis and treatment to achieve the best possible maternal outcome.

Keywords: acute fatty liver of pregnancy, disseminated intravascular coagulation, pregnancy complications

Acute Fatty Liver of Pregnancy: Kasus Jarang Dengan Komplikasi Koagulasi Intravaskular Diseminata

Abstrak
Pendahuluan: *Acute fatty liver of pregnancy* adalah komplikasi kehamilan yang langka dan dapat mematikan. Laporan ini memaparkan sebuah kasus *acute fatty liver of pregnancy* dengan komplikasi koagulasi intravascular diseminata.
Laporan Kasus: Seorang perempuan berusia 27 tahun, hamil 36 minggu datang dengan icterus, peningkatan kadar LDH dan enzim hati, serta trombositopenia. Pemeriksaan ultrasonografi obstetric di IGD menemukan kehamilan tanpa komplikasi dan tanpa solusio plasenta. Pasien ditatalaksana secara konservatif dan melahirkan 6 hari pasca-perawatan. Neonatus dirawat di ruang rawat intensif karena aspirasi meconium. Pasien mengalami perdarahan uterus dan ditatalaksana dengan kondom Sayeba. Pemeriksaan laboratorium menunjukkan adanya koagulasi intravaskular diseminata dengan anemia dan trombositopenia. Pasien ditatalaksana dengan transfuse *packed red cell* dan *fresh frozen plasma*. Pasien memerlukan perawatan intensif.
Pembahasan: *Acute fatty liver of pregnancy* adalah komplikasi kehamilan yang dapat mematikan dan memerlukan tatalaksana intensif multidisipliner. *Acute fatty liver of pregnancy* memiliki gejala yang menyerupai sindrom HELLP. *Acute fatty liver of pregnancy* ditatalaksana dengan melakukan persalinan diikuti dengan terapi intensif. Komplikasi *acute fatty liver of pregnancy* meliputi gagal hepar dan koagulasi intravascular diseminata yang harus ditatalaksana dengan tepat.
Kesimpulan: *Acute fatty liver of pregnancy* memerlukan diagnosis dan tatalaksana yang cepat untuk meningkatkan luaran maternal.

Kata kunci: *acute fatty liver of pregnancy*, koagulasi intravascular diseminata, komplikasi kehamilan

Introduction

The acute fatty liver of pregnancy (AFLP) is a rare complication of pregnancy occurring in only about 1 per 7,000 to 1 per 16,000 pregnancies. Although the AFLP is rare, the mortality rate of AFLP is high: around 10-15% of mothers suffering and around 20% of neonates succumbed from the AFLP cases.[1–3] Acute fatty liver of pregnancy is a serious medical emergency requiring prompt management.[2,4]

The Swansea's criteria is commonly utilized clinical criteria to aid the diagnosis of acute fatty liver of pregnancy.[1,5,6] Nevertheless, both acute fatty liver of pregnancy and HELLP syndrome has similar presentations: vomiting, abdominal pain, jaundice, and hypertension.[6–8] In laboratory work-ups, both acute fatty liver of pregnancy and HELLP syndrome showed increased hepatic enzyme, thrombocytopenia, and might present with hyperbilirubinemia.[1,7]

The mainstay treatment of both acute fatty liver of pregnancy and HELLP syndrome is prompt delivery of fetus in conjunction with supportive maternal care, including correcting for coagulopathy, hypoglycemia, and other metabolic imbalances.[2,6,8] Acute fatty liver of pregnancy may also be complicated with disseminated intravascular coagulation (DIC).[3,4,9] The disseminated intravascular coagulation in acute fatty liver of pregnancy is thought to be caused by consumptive coagulopathy in conjunction with acidosis and endothelial injury.[8,9] In this report, we present a case of acute fatty liver in pregnancy (AFLP) complicated with disseminated intravascular coagulation (DIC).

Case Presentation

A 27-years old, 36 weeks singleton, G2P0A1 pregnant female was admitted to our Emergency Department with severe jaundice without vomiting. Patient was hypertensive (140/90 mmHg), but physical examination at presentation was otherwise unremarkable. At presentation, laboratory examinations revealed elevated AST (415.06 U/L), ALT (136.15 U/L), total bilirubin (335.2 µmol/L), indirect bilirubin (114.6 µmol/L), direct bilirubin (220.59 µmol/L), and serum LDH (584 U/L). At Emergency Department, the hemoglobin was 12.0 g/dL with total leukocyte at 11,050/mm^3 and platelet at 240,000/mm^3.

In our case, emergency obstetric ultrasonography was conducted in Emergency Department and confirmed 36 weeks singleton, otherwise unremarkable pregnancy with no placental abruption observed. Internal Medicine Department consult was obtained for suspicion of cholestatic jaundice of pregnancy. Patient was treated conservatively. Six days after presentation, patient spontaneously delivered 37 weeks female neonate, 2040 gram, Apgar 7/8, with signs of meconium aspiration. The neonate was treated in Neonatal Intensive Care Unit for meconium aspiration syndrome and discharged from the NICU after 3 days of treatments with no further complications.

Continued uterine bleeding in postpartum period was observed. Due to lack of severe bleeding, the patient was managed conservatively with tranexamic acid and placement of Sayeba's condom for 24 hours. The Sayeba's condom was removed without further bleeding. Serial laboratory examination showed progressively worsening anemia and thrombocytopenia, presumably due to disseminated intravascular coagulation. The elevation of serum LDH, bilirubin, and INR concurrent with thrombocytopenia and elevated hepatic enzymes give rise to suspicion of postpartum partial HELLP syndrome with disseminated intravascular coagulation. The DIC was confirmed in collaboration with the Internal Medicine Department through ISTH scoring

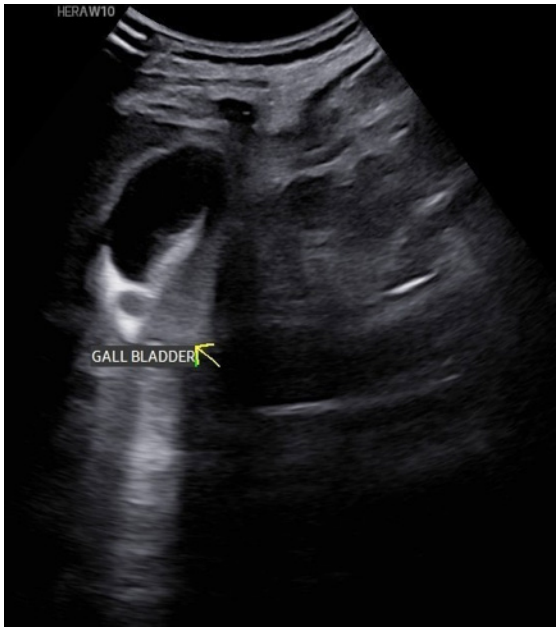

Figure 1 Gallbladder Emergency Maternal Obstetric Ultrasonography

Table 1 Summary of Treatments Administered

Days	Managements	Remarks
0	Initial assessment, observation	Internal Medicine Department consult
6	Spontaneous delivery	Postpartum hemorrhage observed
6	Tranexamic acid, placement of Sayeba's condom, starting antibiotics treatments	
7	Sayeba's condom removal	Sayeba's condom was removed after postpartum hemorrhage has been controlled
8	PRC and FFP transfusion, vitamin K	DIC confirmed, treatments administered in collaboration with the Internal Medicine Department
9	Placement of Sayeba's condom, ICU admission	Severe uterine hemorrhage secondary to DIC
9	Massive ascites	Internal Medicine Department consult
9	Tranexamic acid, FFP and PRC transfusion, albumin infusion	Worsening anemia secondary to uterine hemorrhage, hypoalbuminemia secondary to AFLP
11	Evacuation of blood clot from uterine cavity	
12	Patient discharged from the ICU	
15	Patient discharged from the hospital	

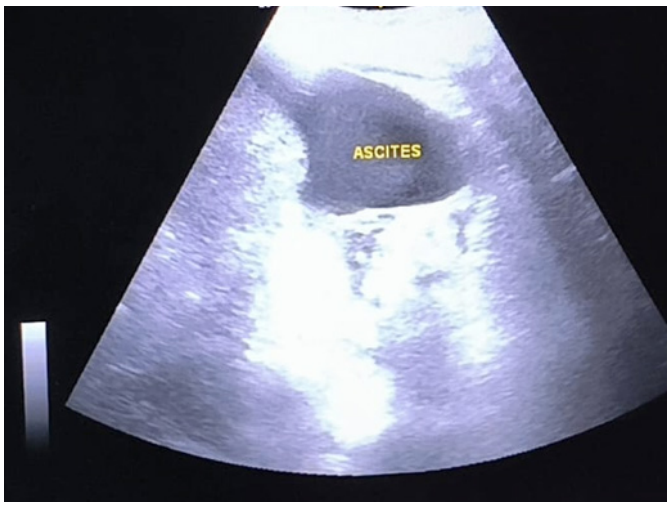

Figure 2 Massive Ascites Bedside Intensive Care Ultrasonography

system with total score of 6 (compatible with overt DIC).

Our patient underwent packed red cell transfusion for anemia in addition to fresh frozen plasma transfusion, vitamin K, and supportive measures after consulting with the Internal Medicine Department. On the third day after delivery, severe uterine hemorrhage was observed and Sayeba's condom was put back to control the bleeding. Laboratory examinations showed worsening anemia (hemoglobin 4.5 g/dL), thrombocytopenia (platelet 8,000/mm^3), hypoalbuminemia (2.0 g/dL), renal dysfunction (serum urea 91 mg/dL and creatinine 1.95 mg/dL), with elevated urate (9.0 mg/dL) and patient was admitted to Intensive Care Unit. Bedside abdominal ultrasonography in collaboration with the Internal Medicine Department revealed massive ascites in addition to blood clot in the uterine cavity. Patient underwent further FFP and PRC transfusion to manage the DIC in addition to albumin infusion to correct hypoalbuminemia.

After 2 days of intensive treatment, the patient condition had improved sufficiently to attempt for uterine cavity blood clot evacuation. The blood clot was evacuated uneventfully in the surgical theatre. After 3 days of ICU treatment, the patient was able to be discharged from the ICU. The patient was discharged from the hospital after 15 days of treatment.

Discussions

In our case, the elevated bilirubin, urate, and transaminases in conjunction with leukocytosis, thrombocytopenia, and coagulopathy is consistent with Swansea's criteria for acute fatty liver of pregnancy (AFLP).[1,5,6] Both acute fatty liver of pregnancy and HELLP syndrome shares similar and overlapping clinical presentation, including vomiting, abdominal pain, jaundice, and hypertension. Both acute fatty liver of pregnancy and HELLP syndrome also results in increased vascular permeability and circulatory shock due to plasma leakage.[6–8] Further confounding matters, both acute fatty liver of pregnancy and HELLP syndrome showed increased hepatic enzyme, thrombocytopenia, and might present with hyperbilirubinemia.[1,7] The confusion is evident in our case: hyperbilirubinemia and elevated liver enzymes results in difficulty differentiating postpartum partial HELLP syndrome and AFLP at the time before ICU admission.

Acute fatty liver of pregnancy is a rare complication of pregnancy, occurring in only about 1 per 7,000 to 1 per 16,000 pregnancies

and commonly found in third trimester. The AFLP involves fat microdeposit in the liver, causing decompensated liver function and subsequent liver failure. The maternal mortality rate of acute fatty liver of pregnancy is around 10-15% and fetal mortality rate is around 20%.[1–3] Acute fatty liver of pregnancy is medical emergency with risk factors including multigravida pregnancy, preeclampsia, multiple gestation, and male fetus. The risk factor of male fetus is not present in our case. Although the mechanism is still unclear,[2,4] The acute fatty liver of pregnancy is thought to be caused by inheritable mitochondrial enzymes deficiency causing fetal fatty acid oxidation and subsequent hepatotoxicity. The long-chain 3-hydroxyacyl-CoA-dehydrogenase (LCHAD) and mitochondrial trifunctional protein are responsible for fetal fatty acid oxidation. The fetal LCHAD deficiency is the most frequent risk factor of AFLP.[2–4] The mutation of *HADHA* and *HADHB* genes in chromosome 2p23.3 causes defect in subunit alpha and beta of mitochondrial trifunctional protein resulting in impaired mitochondrial long-chain fatty acids placental metabolism. The oxidative stress of the placenta arises from the accumulation of 3-hydroxy fatty acids, mitochondrial dysfunction, and resultant placental lipotoxicity. Subsequently, accumulated fatty acid intermediates in the third trimester causes maternal hepatotoxicity and hepatic failure[4,8] marked with elevated hepatic enzymes as evident in our case. The ascites in our case is thought to be related with the hypoalbuminemia present at the time of ICU admission.

Hepatobiliary ultrasonography is necessary to help to guide diagnosis. The acute fatty liver of pregnancy will show liver parenchymal heterogeneity consistent to fatty infiltration.[1,2] Liver biopsy might also be necessary in the times of diagnosis uncertainties.[8,10] Through the collaboration with the Internal Medicine Department we were able to visualize the massive ascites with bedside ultrasonography allowing the confirmation of AFLP.

The mainstay treatment of both acute fatty liver of pregnancy and HELLP syndrome is prompt delivery of fetus in conjunction with supportive maternal care, including correcting for coagulopathy, hypoglycemia, and sometimes plasmapheresis. As the last-ditch measure in case of liver failure, liver transplantation might be necessary.[2,6,8] Nevertheless, the American College of Gynecologists guidelines stated that the expectant management is sometimes reasonable when the both mother and the fetus is in the stable condition.[11] Delayed AFLP diagnosis is not uncommon, particularly due to the rarity of AFLP cases in clinical practice and overlapping symptoms with other conditions.[7,8] In our case, the maternal and fetal condition at admission and the delay of diagnosing AFLP led to the decision of expectant management. The diagnosis of AFLP in our case was only made after the delivery has occurred and the patient was admitted to the ICU.

The spontaneous recovery is rapid and complete in our case: the patient recovered spontaneously although the episode of DIC requiring an intensive treatment. The acute fatty liver of pregnancy will commonly recover spontaneously in the first month with supportive measures. The recovery is usually complete when no liver failure is present.[2,8] The disseminated intravascular coagulation (DIC) is also a known complication of ate stage of AFLP.[3,4,9] The DIC in AFLP is thought to be caused by consumptive coagulopathy in conjunction with acidosis and endothelial injury.[8,9]

The acute fatty liver of pregnancy is usually recovered spontaneously within one week after delivery with supportive treatment and correction of coagulopathy[2,4] as evident in our case. With the correction of coagulopathies through the FFP transfusion,

tranexamic acid, vitamin K injection, and Sayeba's condom method to control bleeding, our patient was able to be discharged after 3 days of intensive treatments.

The disseminated intravascular coagulopathy (DIC) itself is an acquired syndrome characterized by the systemic intravascular activation of coagulation causing damage to microvasculature and resultant organ disfunction. Overt bleeding observed in AFLP-related disseminated intravascular coagulation might be related with liver failure causing deficiency of procoagulant factors or thrombocytopenia secondary to decreased thrombopoietin synthesis. Further monitoring for microangiopathies and subsequent organ failures is necessary to guide further treatments.[12,13] When the disseminated intravascular coagulation is present, massive transfusion of fresh frozen plasma, platelet concentrates, and packed red cells is sometimes necessary to improve the outcome in cases of severe anemia or hemodynamic instability.[8,12,14,15] In our case, FFP and PRC transfusion was necessary to correct the DIC and to maintain adequate tissue oxygenation. Tranexamic acid and vitamin K injection was administered to support coagulation in of the DIC present. The disseminated intravascular coagulation in pregnancy is mainly treated through correcting the underlying cause, restoring the fluid balance, maintain tissue perfusion, and prevent hypoxia. Supportive treatment with multidisciplinary approach is invariably beneficial to improve patient outcome.[9,13,15] The collaboration with Internal Medicine Department in our patient proved beneficial in management of DIC. The Internal Medicine Department was able to provide valuable feedback and examination in addition to provide additional treatments.

The most serious consequence of acute fatty liver of pregnancy is hepatic failure. The hepatic failure in acute fatty liver of pregnancy is mainly managed similarly with non-pregnant cases.[16] Assessment for the acute liver failure includes screening for the hepatic encephalopathies, monitoring for coagulopathies and hepatic enzymes, and hyperbilirubinemia in addition to supportive treatments. Standard cares for hepatic failures also include continuous glucose infusion, prevention of stress ulcers, provision for N-acetylcysteine, and correcting any biochemical and fluid imbalances. In addition, avoiding hepatotoxic and nephrotoxic drugs are necessary to prevent further liver injuries.[17,18]

Conclusions

Acute fatty liver of pregnancy is a potentially deadly complication of pregnancy and requires multidisciplinary, intensive support for optimal management and maternal outcomes. Prompt diagnosis and treatment is the most critical step to recognize and achieve better maternal outcome, reduce the risk of further complications, and prevent maternal death. The difficulty in diagnosing acute fatty liver of pregnancy is more pronounced when non-specific symptoms are present; high index of suspicion is necessary to prevent delay in diagnosis and treatment. The acute fatty liver of pregnancy mainstay treatment includes prompt delivery of the fetus followed with intensive care and supportive measures. Complications of acute fatty liver of pregnancy includes hepatic failure and disseminated intravascular coagulation. Although acute fatty liver of pregnancy is a rare complication of pregnancy, the symptoms of acute fatty liver of pregnancy may mimic and overlap with another complication of pregnancy: HELLP syndrome.

Conflict of Interests

The authors declare no conflict of interests.

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