Gigantic Liver Abscess in Pregnancy: A Rare Case

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ABSTRACT

Liver abscess (LA) is defined as a suppurated cavity caused by invasion and multiplication of microorganisms within liver parenchyma. Incidence of LA is rare with 20/100,000 admissions. Etiology of LA can be bacterial, parasitic, mixed or more rarely fungal. Amoebic liver abscess (ALA) is one of the most sequelae invasive amoebiasis with 44.1% LA in patients were caused by ALA. Early treatment initiation is important to avoid the potential risks of preterm delivery, fetal infection, perinatal mortality, multi-organ dysfunction, sepsis, septic shock, and even maternal death.

Methods this research was case report: A 27 year old patient diagnosed with G1P0A0L0 16-17 weeks of pregnancy with LA, previously the patient went to Emergency room with complaint of upper right abdominal pain since a week and getting worsed since 1 day. The patient also complaint fever and swelling at the right abdomen. From physical examination found swelling and tenderness in the right abdomen, palpable flat surface mass and dim percussion. From an ultrasound examination is a single intrauterine live fetus, gravid 16-17 weeks according to biometry, a hypoechoic mass appeared measure 11.6 x 9.6 cm, suspected liver abscess. Then she underwent laparoscopy abscess drainage with digestive surgery collaboration, from histopathology the result was chronic inflammation acute exaserbation might from liver abscess. Liver abscess (LA) during pregnancy is an extremely rare condition. Pregnancy has been described as a risk factor for LA because of immunological changes. Imaging modalities should be chosen with caution in the pregnant patient.
I. INTRODUCTION

Liver abscess is defined as a pus-filled mass in the liver, it can develop from injury to the liver or an intraabdominal infection spread from portal circulation (7). The majority etiology of liver abscess are categorized into pyogenic or amoebic, and minority is caused by parasites and fungi. Amoebic liver abscess (ALA) are most caused by Entamoeba histolytica, while pyogenic liver abscess (PLA) are usually polymicrobial, but some organisms are seen like Escherichia coli, Klebsiella, Streptococcus, Staphylococcus, and anaerobes.(8)

Liver abscess remains an important clinical problem with a significant mortality rate in both developing and developed countries. It can occur as a complication of various intraabdominal infections; by hematogenous spread via the portal vein of the gastrointestinal tract; or, it can develop after a traumatic injury to the liver. ALA is an important cause of space-occupying hepatic lesions; especially in developing countries accounts for 3-9% of all cases of amoebiasis. This infection is caused by the protozoa Entamoeba histolytica which ascends to the portal vein system. It also has been estimated that 10% of the world's population infected with Entamoeba histolytica and endemic within tropical and subtropical region(9)

Liver abscess also the most common type of visceral abscess. In one study intraabdominal abscess, pyogenic liver abscess accounted for 48% of visceral abscesses and 13% of intraabdominal abscesses. The annual incidence of pyogenic liver abscess is estimated at 2.3 cases per 100,000 population and is higher in men than in women (3.3 vs 1.3 per 100,000).9 Pyogenic liver abscess (PLA) is a significant health problem, with the highest incidence reported in Asia. Endemic to Taiwan, the incidence of PLA is steadily increasing, most recently 15.45/100,000 population in 2011. Although less common in North America, PLA still has an estimated incidence of between 2.3 and 3.6/100,000 population in Canada and the United States. In addition, this condition is associated with significant morbidity and has a mortality risk of between 6 and 10%.10

The etiologies of liver abscess may include lithiasic biliary disease (cholecystitis, cholangitis), intra-abdominal collections (appendicitis, sigmoid diverticulitis, Crohn's disease), and bile duct ischemia secondary to pancreatoduodenectomy, liver transplantation, interventional techniques (radiofrequency ablation, intra-arterial chemo-embolization), and/or liver trauma. Less commonly, liver abscess can occurs after septicemia in either healthy or preexisting liver disease (gall cyst, hydatidiform cyst, cystic or necrotic metastasis).1

Because clinical and laboratory findings are usually non-specific, misdiagnosis is common, but early diagnosis and treatment are essential because of the high perinatal mortality rate in untreated cases. Another problem with the onset of ALA in pregnancy is the possibility of progression to severe sepsis or septic shock which is associated with an increased rate of preterm delivery, fetal infection, multiple organ dysfunction syndrome, and death.11

II. METHODS

Case report according to our case report, that can be helpful in term of providing surgeon and maternal-fetal medicine specialist for diagnostic, management and prognostic information for counseling families. Furthermore, it was recently established a multidisciplinary clinic that was composed by specialists from areas, including surgeon and maternal-fetal medicine. This case provide us to makes a more in depth evaluation of liver abscess in pregnancy.

III. RESULT

The following case is reported regarding Mrs. A 27-year-old woman came to the emergency department Dr. M. Djamil Hospital with the main complaint of severe right upper abdominal pain since 3 days before being admitted to the hospital. Right abdominal pain has been felt since 1 week, the pain gets worse when the patient takes a breath. The patient also complained of fever
since 3 days. No nausea and vomiting, no shortness of breath. The patient is pregnant with her first child with a gestational age of 16-17 years. There is no past history of disease. From Physical Examination vital signs were within normal limits, with a normal female body appearance. The patient's BMI of 23.4. Head and neck examination did not reveal webbed neck or facial malformations. Physical examination of the chest, lung, and heart was also normal. On abdominal examination, there was tenderness and a palpable mass in the upper right region. Vaginal toucher didn’t performed. From abdominal ultrasound examination revealed BPD 2.51 cm, HC 8.99 cm, AC 9.75 cm, FL 1.47 cm, FHR 166 bpm and EFW 112 grams. Ultrasound results also showed a hypoechoic appearance with an internal echoabscess measuring 11.65 cm x 9.65 cm. From an ultrasound examination was a single intrauterine live fetus, gravid 16-17 weeks according to biometry, a hypoechoic mass appeared to measure 11.6 x 9.6 cm, suspected liver abscess. Laboratory examination results obtained hemoglobin 11 g/dl, leukocytes 12,700/mm3, platelets 141,000/mm3, hematocrit 32%, leukocyte type count obtained bacofil 0%, eosinophils 0%, segment neutrophils 82%, lymphocytes 4%, and monocytes 15%. Patient was diagnosed with G1P0A0L0 16-17 weeks of pregnancy with liver abscess.

Figure 1 Ultrasound Examination

The patient underwent laparoscopic abscess drainage with digestive surgery collaboration. At the time of operation, a cystic mass was found in the liver, aspiration was performed to remove black liquid. Histopathological examination showed the distribution and grouping of lymphocytes, PMN leukocytes, some macrophage plasma cells against a background of
erythrocytes. From histopathology the result was chronic inflammation, acute exacerbation, might be from liver abscess.

![Figure 2 Diagnostic Laparoscopy](image)

**IV. DISCUSSION**

The three main forms of liver abscess, classified by etiology, are as follows: (1) Pyogenic abscess, which is most commonly polymicrobial, accounts for 80% of cases of liver abscess in the United States, (2) Amoebic abscess due to Entamoeba histolytica accounts for 10% of cases, (3) Fungal abscess, most often due to Candida species, accounts for less than 10% of cases.12 Liver abscess is associated with significant morbidity, mortality and increased consumption of health resources. Several studies report the incidence of liver abscess to be 1.1-3.3 per 100,000 person-years in the Western general population. Liver abscess, which is highly endemic in Taiwan, has an incidence of 11.5–17.5 per 100,000 person-years. In addition, renal failure is a significant risk factor for liver abscess.13 Men are affected more often than women. Age plays a factor in the type of abscess that develops. People aged 40-60 years are more prone to developing liver abscesses that are not the result of trauma.7 Liver abscess is a very rare pathology that occurs in pregnancy. It is often a diagnostic and therapeutic challenge, and can even be a cause of maternal death. Amoebic liver abscess is the most common cause of liver abscess in developing countries whereas in developed countries pyogenic liver abscess is the most common. Pregnancy has been described as a risk factor for the development of invasive amoebiasis and the management of these patients is complex.14 Amoebic liver abscesses (ALAs) are the most commonly extraintestinal manifestation of human invasive amebiasis, which results from Entamoeba histolytica which spreading extraintestinally.15 Entamoeba histolytica is an anaerobic parasitic invasive enteric protozoan, and its infections correlate to high mortality and morbidity rates. This protozoan can causes 40,000-100,000 deaths each year, ranking only behind malaria in patient mortality.16 Amebiasis also still has high rate of
incidence, and its remains a public health concern in low- and middle-income developing countries in the tropics, especially crowded environments, lacking in adequate sanitation such as clean water due to the oral-fecal route of this pathogen transmission (including ingestion of food or water that contains cysts from this protozoan). On the other hand, amebiasis is rarely seen in wealthier countries but the epidemiologically increase with recent immigrants from endemic regions (or travelers returning from a long-term stay in an endemic region).

The route of transmission of E. histolytica that leads to ALA still cannot be explained completely, but broadly, after E. histolytica breaches the host’s innate defenses, invading the intestinal mucosa, and also its trophozoites can enter the circulatory system. They are then filtered in the liver and produce abscesses and can develop further into severe invasive diseases, such as ALAs. On the other hand, immune-compromised individuals and/or momentaneous immune modulation in humans have been reported to increase both bacterial and viral infections and related diseases. ALA may arise because of an impairment of the anti-E. histolytica immune system, and the immune evasion action of pathogens in humans.

In Western countries, 80% of liver abscess is bacteria. They can occur in the course of intraabdominal biliary infection contaminating the bile duct at the same time or can be secondary seeding through the portal venous system of non-biliary infection (appendicitis or sigmoiditis). Liver abscess may also complicate surgical procedures (pancreatoduodenectomy, or liver transplantation) or hepatobiliary procedures (radiofrequency ablation and/or intra-arterial chemoembolization). Less commonly, liver abscess develops after hepatic trauma or arterial embolization for trauma. Some liver abscesses are also secondary to extraabdominal infections contaminating the liver parenchyma or pre-existing liver lesions (biliary cysts, hydatidiform cysts or necrotic metastases), most commonly via the hematogenous route. Unlike liver abscess which complicates stomach infections, liver abscess of arterial origin is most often monomicrobial with positive blood cultures.

The pathogenesis of amoebic liver abscess (ALA) is different from that of pyogenic liver abscess (PLA). ALA, which is caused by an intestinal protozoa, Entamoeba histolytica can induce liver apoptosis and the latter is a suppurative infection of the liver parenchyma. Confirmatory diagnosis is important, although difficult in resource-limited settings, as it leads to appropriate management. A pyogenic abscess is defined as a collection of pus consisting of many inflammatory cells, mainly neutrophils and tissue debris. Infection is associated with necrosis due to inflammation of the surrounding tissue. The word abscess may represent a misnomer when used to define a pathological process caused by E. histolytica in the liver. In the case of ALA, hepatocyte cell death occurs both by apoptosis and necrosis. It is generally agreed that there are no inflammatory cells due to lysis of neutrophils by protozoa which form non-purulent “anchovy paste” abscesses.

In general, the signs, symptoms, and laboratory findings of liver abscess are nonspecific, making the diagnosis sometimes difficult. Approximately 70% of cases of liver abscess are diagnosed within 2 weeks, and 43% of cases are diagnosed more than 2 weeks after the onset of symptoms. The clinical features of pyogenic and amoebic liver abscess are indistinguishable. Important signs and symptoms of liver abscess are abdominal pain and hepatomegaly. Other signs and symptoms that may appear include fever, abdominal pain especially in the right hypochondriac region, nausea and vomiting, night sweats, weight loss, diarrhea, cough, jaundice, changes in lung appearance such as right pleural effusion, hepatomegaly, ascites and confusion.

The diagnosis of ALA is made through combination of characteristic findings, imaging and serologic testing. Crucial predictors of ALA may include habitual alcohol consumption, low socioeconomic status, or recent immigrants from endemic regions. A number of diagnostic tools are available for diagnosis, especially imaging and serology. ALA has a cystic intrahepatic cavity that is usually indistinguishable from other causes of liver abscesses. The majority of ALAs are solitary lesions, there can be also occasionally multiple lesions, and more often found in the right lobe than the left.
On ultrasound, ALA lesion is a round well-defined hypoechoic mass. After healing, the periphery of the abscess may calcify and form a round, thin rim. But the imaging findings are not specific enough to make a diagnosis and must be interpreted in conjunction with either serological or serum antigenic confirmation. Serology is focusing primarily on detecting E. histolytica using PCR or enzyme-linked immunosorbent assay.15 Data reported that total of 99% of patients with amoebic liver abscesses will develop detectable antibodies to E. histolytica, although the test may be negative in the first seven days of illness. The antibodies are detectable at presentation in 92%-97% of patients with amoebic liver abscesses. Recently, the XEh Rapid® IgG4-based rapid dipstick test for rapid detection of ALAs (based on detecting the anti-E. histolytica pyruvate phosphate dikinase IgG4 antibody) demonstrated high diagnostic specificity in infected patients (97%-100%), with diagnostic sensitivity varying between 38% and 94%.23

It is difficult to distinguish ALA from pyogenic liver abscesses using only clinical, laboratory, and imaging findings. In order to diagnose the various ALA-related complications, computed tomography (CT) scans serve as an ideal tool.24 CT findings can determine different morphological types of ALA and to determine any differences in their clinical features. ALAs were found have three CT morphological types. Type I abscesses (66% of the total) have walls that were either absent or incomplete as well as peripheral septa and edges that are ragged and exhibit enhancement that is both irregular and interrupted. Type I abscesses had an acute presentation alongside severe disease with laboratory were significantly deranged, and higher incidences of rupture. This type I abscesses was prompted percutaneous drainage to be carried out immediately in 81% cases.25 Type II abscesses (28% of the total) have complete walls with both peripheral hypodense halo and rim enhancement. Type III abscesses (6% of the total) demonstrate walls but without enhancement. The type II and III abscesses feature delayed presentations, with near-normal laboratory findings and mild to moderate disease.25 Otherwise, according to American College of Obstetricians and Gynecologists (ACOG) guidelines still recommend ultrasound and MRI as the modalities of choice in the pregnant patient.26 Additionally, diagnosis is also possible through abdominal ultrasound and echography-guided liver puncture. If liver abscess fluid bacterial cultures remain negative, amoebic abscess should be considered as a possibility, even if the patient has no personal history of tropical or subtropical travel.27
Pyogenic liver abscess is diagnosed based on clinical signs and symptoms, laboratory results and radiological examination. Symptoms commonly found in pyogenic abscess are fever, right upper quadrant abdominal pain, decreased appetite, and weight loss. From the physical examination we can find an enlarged liver, jaundice and sometimes decreased breath sounds in the lower lobe of the right lung. Just like clinical symptoms, laboratory tests are also not specific for the diagnosis of PLA. The most frequent findings are increased ALP, leukocytosis, and a nonspecific increase in fibrinogen during pregnancy. Infection-induced increases in ALT and thrombocytopenia have also been reported. The sensitivity of ultrasound for the diagnosis of PLA was reported to be 85.8%. The clinical incidence of PLA varies from region to region but has been reported to be 11 cases per million people per year.

Blood cultures are positive in 50% of cases, especially when the cause of the liver abscess is hematogenous spread. Aspiration culture of liver abscess is very important in diagnosis and treatment. Approximately 30% of liver abscess cultures are negative, this may be due to administration of antimicrobial therapy prior to examination of the abscess culture. A positive result in a patient who has received antimicrobial therapy prior to culture examination may indicate the presence of an antibiotic-resistant pathogen. Pus aspiration in pyogenic liver abscess looks purulent and has a foul smell macroscopically, whereas amoebic liver abscess is generally brownish in color, viscous and odorless.

Most features of our case can be regarded as typical for ALA such as right upper quadrant pain, fever and hepatomegaly. On abdominal ultrasound results showed a hypoechoic appearance with an internal echoabscess measuring 11.65 cm x 9.65 cm, while laboratory with leukocytosis without eosinophilia. In this case, pregnancy may be presented as a predisposing factor in reactivation of amoebic infection. The presence of a fetus requires an altered immunological response and results in a variety of immunomodulating processes with measurable changes in cellular and humoral immunity. While pregnancy cannot be regarded as a state of systemic immunosuppression, there are measurable changes of cellular immune response to pathogens and the self, for example from T-helper 1 (Th1)- to T-helper 2 (Th2)-lymphocytes, increasing B-cell activation and production of antibodies while decreasing cytotoxic T-cell responses. While, humoral changes also decreased release of chemokines and growth factors such as tumor necrosis factor (TNF-), IFN-, interleukin (IL)-15, vascular endothelial growth factor A (VEGF-A), and chemokine (C–C motif) ligand 2 (CCL2). Immunological changes are also facilitated by increased production of steroid hormones, progesterone and estrogen as pregnancy takes its course. High progesterone levels also drive T helper cell differentiation towards the anti-inflammatory Th2-phenotype and secretion of anti-
inflammatory cytokines including IL-4, IL-5, and IL-10; they also drive differentiation of macrophages to a state coined M2 phenotype, associated with healthy, full-term pregnancies. In contrast, M1 macrophage phenotype is associated with elevated secretion of IL-12 and TNF and associated with preterm birth. Similar roles are employed both by estradiol and estriol, where high concentrations are also associated with an anti-inflammatory phenotype in cellular immunity. Management of ALA consists of medical management, radiological drainage, and surgical management. In the absence of formal management guidelines, evidence to guide treatment decisions, such as timing and indications for radiological intervention, is limited. Tissue amebicides such as nitroimidazoles form the mainstay of management of all patients with ALA. Oral or intravenous (IV) administration (in patients who cannot take [PO]) of metronidazole results in resolution of fever, toxemia, and pain in 80% of the 90% of patients with ALA without complications within 48 to 72 hours of treatment. Tinidazole is better tolerated and has the advantage of a shorter duration of treatment. Indications for liver abscess drainage along with medical management are: (1) left lobe liver abscess, (2) abscess with a thin border of liver parenchyma (<10 mm) around it, (3) multiple liver abscesses, (4) impending rupture recognized on imaging, and (5) nonresponse to medical therapy after 3 to 5 days.

Metronidazole should cover Entamoeba histolytica. The duration of treatment varies but is usually from two to six weeks. After initial intravenous treatment, the oral route can be used safely in most cases to complete treatment. Culture results help narrow down the organisms, so that empirical treatment is no longer needed, as it can lead to antibiotic resistance. Anaerobes are difficult to cultivate, so sometimes they have to be treated for the entire course empirically. For stable patients, antibiotics can be given post-drainage to improve culture results for appropriate treatment. Empirical antifungal treatment is essential in immunosuppressed patients at risk for chronic disseminated fungemia. Sometimes if the patient is too sick for drainage, antibiotics are used only for treatment, but this is a less desirable method.

Metronidazole and the structurally similar tinidazole are therapeutic agents used for the treatment of acute E. histolytica infections. Metronidazole is the treatment of choice for pregnant women. Metronidazole is a US Food and Drug Administration (FDA) pregnancy category B drug, is generally well tolerated and although crosses the placenta does not appear to have significant embryotoxic effects. The initial situation with delayed serologic results requires adjunctive therapy with i.v. ceftriaxone. Differentiation between amoebic and bacterial liver abscess by clinical and imaging findings is not possible and bacterial abscesses may be caused by bacteria unresponsive to metronidazole such as Enterococcus spp. or Klebsiella spp., which warrant the use of broad-spectrum antibiotics such as third-generation cephalosporins. The second anti-amoebic agent required specifically for eradication of intraluminal entamoebic cysts and therefore the holistic treatment of amebiasis is paromomycin aminoglycoside, an FDA pregnancy category C drug.

Drainage is required and can be performed under US or CT. Needle aspiration (sometimes repeated) may be necessary for abscesses less than 5 cm, but catheterization may be necessary if the diameter is larger. Percutaneous drainage with catheter placement is probably the most successful procedure for abscesses larger than 5 cm. Laparoscopic drainage is also sometimes used. Surgery is necessary for peritonitis, thick-walled abscesses, ruptured abscesses, multiple large abscesses, and previous failed drainage procedures. The operation is performed either by a transperitoneal approach or by a posterior transpleural approach. The first approach drains the abscess and allows for undetected exploration of the ulcer, whereas the second is better for posterior abscesses. Size, location, and stage help determine a successful treatment plan. When previous biliary procedures have been performed, endoscopic retrograde drainage cholangiopancreatography (ERCP) may be used. Liver abscesses that are not drained can cause sepsis, peritonitis, and empyema.

The management of pyogenic liver abscess in pregnancy is complicated, because general and obstetric risks need to be considered before proceeding with any intervention. A pregnant woman
with PLA and poor prognostic factors ideally requires a laparotomy at the end of the third trimester. For all abscesses that cannot be drained during laparotomy or patients who are unfit for laparotomy during late pregnancy, ultrasound-guided drainage combined with broad-spectrum antibiotic coverage is the method of choice. In the early first, second and third trimesters, ultrasound-guided drainage may be used as first-line management, with patients followed up closely; and the same was done in this case after multidisciplinary consideration.7 PLA may occur in the setting of infection of the stomach/biliary tree or in the presence of systemic bloodstream infection. Patients with PLA usually have more pronounced systemic features with multiple liver abscesses on imaging than patients with ALA. Unlike ALA, the principal treatment of PLA involves drainage of the abscess, appropriate use of antibiotics, and control of the primary source of infection. Antibiotics are given for 2-6 weeks. Antibiotics that can be given are third generation cephalosporins, Aminoglycosides, Piperacillin tazobactam, Carbapenems, Vancomycin (if you suspect gram positive), and Metronidazole (for anaerobic coverage).33 Empirical antibiotic coverage is especially important when the organism is unknown. Antibiotics should cover Enterobacteriaceae, anaerobes, streptococci, enterococci, and Entamoeba histolytica. These antibiotic regimens include a cephalosporin plus metronidazole, a beta-lactam beta-lactamase inhibitor plus metronidazole, or a synthetic penicillin plus an aminoglycoside and metronidazole. Alternatively, fluoroquinolones or carbapenems can be substituted for cephalosporins or penicillins if allergic or unavailable. 33 Liver abscess during pregnancy is an extremely rare condition that poses a diagnostic and therapeutic challenge. Because clinical and laboratory findings are usually non-specific, misdiagnosis is common, but early diagnosis and treatment are essential because of the high perinatal mortality rate in untreated cases. Another problem with the onset of liver abscess in pregnancy is the possibility of disease progression to severe sepsis or septic shock which is associated with increased rates of preterm birth, fetal infection, multiple organ dysfunction syndrome, and death.6 Early treatment initiation is important to avoid the potential risks of preterm delivery, fetal infection, perinatal mortality, multi-organ dysfunction, sepsis, septic shock, and even maternal death. Sepsis and septic shock during pregnancy can be fatal, whatever the source, and early stabilization, fluid resuscitation, and prompt administration of broad-spectrum antibiotics are essential. Simultaneous efforts should be directed at finding the source of infection (genito-urinary, respiratory, gastrointestinal, etc.), which should be prioritized. The pus needs to be drained along with initiation of appropriate antibiotics. From an obstetric point of view, premature or prolonged rupture of membranes and chorioamnionitis must be ruled out and a proper history and vaginal examination are essential for the same; as they can be a common source of infection, especially during late pregnancy.34

V. CONCLUSION
ALA during pregnancy is an extremely rare condition that poses a diagnostic and therapeutic challenge. Imaging modalities should be chosen with caution in the pregnant patient. American College of Obstetricians and Gynecologists (ACOG) guidelines recommend ultrasound and MRI as the modalities of choice. Management of liver abscess consists of medical management, radiological drainage, and surgical management. Needle aspiration (sometimes repeated) may be necessary for abscesses less than 5 cm, but catheterization may be necessary if the diameter is larger. Percutaneous drainage with catheter placement is probably the most successful procedure for abscesses larger than 5 cm. Laparoscopic drainage is also sometimes used. The management of pyogenic liver abscess in pregnancy is complicated, because general and obstetric risks need to be considered before proceeding with any intervention.
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