


# Perinatal Pyogenic Liver Abscess: A Rare Entity and First Reported Case of *Klebsiella pneumoniae*

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## Abstract

### Keywords

- ▶ pyogenic liver abscess
- ▶ liver abscess
- ▶ pregnancy
- ▶ sepsis
- ▶ perinatal infection

**Introduction** Pyogenic liver abscess (PLA) is a rare clinical entity, occurring in ~2.3 per 100,000 patients. Perinatal PLA syndromes are exceedingly rare with just seven previously described cases in the literature and no prior *Klebsiella*-associated reports. **Case** A 29-year-old gravida 2 para 1 woman at 11 weeks gestation reporting fever, body aches, and headache. Search for an infectious source identified a 4-cm liver abscess. Percutaneous drainage confirmed *Klebsiella pneumoniae* infection. The patient was treated with antibiotics until imaging verified complete resolution of the abscess. **Conclusion** PLA is an uncommon etiology of sepsis in pregnancy. A thorough workup until a source was identified resulted in accurate diagnosis. This allowed for directed therapy and prompt recovery, undoubtedly contributing to favorable pregnancy outcomes in this first report of *Klebsiella*-associated perinatal PLA.


Cryptogenic pyogenic liver abscess (PLA) describes those cases with unknown etiology and can be thought of as primary PLA rather than secondary to hepatobiliary disease, gastrointestinal infection, or intra-abdominal infection. Cryptogenic invasive PLA (CIPLA) describes the involvement of septic emboli to the brain, eyes, lungs, heart, joints, fascia, or other distant organs. Monomicrobial CIPLA secondary to *Klebsiella pneumoniae* (CIKPLA) is endemic to Taiwan with additional cases described in other Eastern countries, but just one case described in the United States and no prior reports in or around pregnancy.<sup>1</sup> On the other hand, cryptogenic noninvasive PLA (CNPLA) is usually associated with bacteremia without septic seeding. Monomicrobial CNPLA secondary to *K. pneumoniae*, while rare, has been described in Western countries, though only in patients of Asian or Hispanic descent and never in the puerperium. To our knowledge, pregnancy-related cryptogenic PLA has not been previously described in the medical literature.

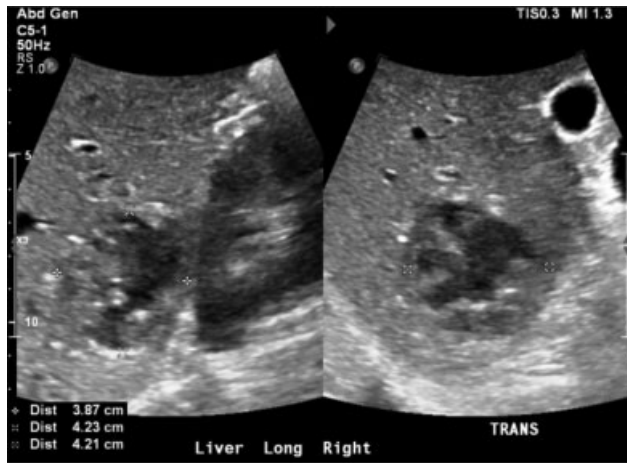
We report here a case of monomicrobial CNPLA in pregnancy secondary to *K. pneumoniae* in a patient of Asian descent with no other risk factors.

## Case

A 29 year-old gravida 2 para 1001 of Filipino descent presented to the emergency department at 11 weeks and 1 day of gestation complaining of fever, myalgias, malaise, and headache. She reported no other symptoms and denied any sick contacts. Her medical history included childhood asthma with no current inhaler use. Her obstetric history was pertinent for an uncomplicated term spontaneous vaginal delivery three years prior. Her remaining history was unremarkable aside from reported allergy to penicillin. She had lived in the United States for 7 years and denied any recent travel.

On presentation, her vital signs were notable for blood pressure ranging 90–100/50–70 mm Hg, heart rate 100 to 120 bpm, oxygen saturation 93% to 100% on room air, and initial temperature of 38.7°C with maximum temperature of 39.6°C. Physical examination was unremarkable and without

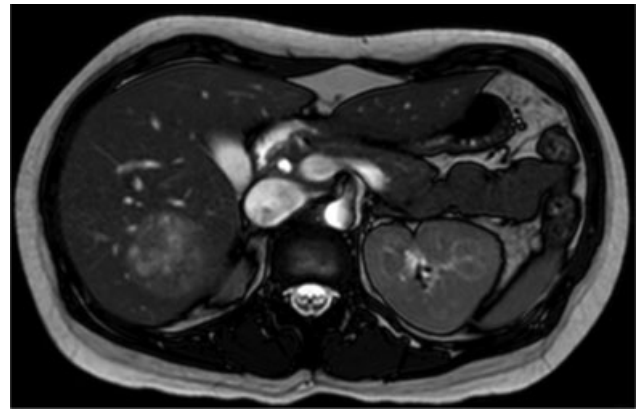
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**Fig. 1** Our patient's right upper-quadrant (RUQ) ultrasound demonstrated a  $3.9 \times 4.2 \times 4.2$  cm echogenic and irregular lesion within the right lobe of the liver adjacent to the right kidney. The partially ill-defined peripheral rim and absence of internal blood flow were suspicious for an early pyogenic abscess, and less likely a hypovascular tumor.

meningeal signs. Fetal heart rate was assessed by abdominal ultrasound at 160 to 170 bpm. Initial laboratory analysis was unremarkable including absence of leukocytosis (WBC 9.4), as well as normal renal and hepatic function. Urinalysis was also normal. Chest X-ray was without evidence of acute cardiopulmonary process. Blood and urine cultures were obtained. A lumbar puncture revealed cerebral spinal fluid cytology that was within normal limits. Serum gram stain quickly resulted gram-negative rods. BioFire FilmArray (BioFire, Salt Lake City, UT) blood culture identification panel, a rapid polymerase chain reaction (PCR) test, resulted presumptive *K. pneumoniae* within 1 hour of testing. The patient was subsequently treated with intravenous (IV) ceftriaxone 2 g every 24 hours and admitted to the hospital for continued evaluation and treatment. Final blood culture speciation and sensitivities resulted heavy growth of pan-sensitive *K. pneumoniae*, while final urine and cerebral spinal fluid cultures remained negative.

Over the next 24 hours, the patient underwent thorough evaluation for the source of her *K. pneumoniae* bacteremia. This work-up included a right upper-quadrant ultrasound that was notable for a  $3.9 \times 4.2 \times 4.2$  cm lesion within the right lobe of the liver (►Fig. 1). The liver lesion was predominantly echogenic with an irregular, ill-defined peripheral rim and no internal blood flow. Due to concerns for an abscess, Infectious Disease was consulted and recommended addition of IV metronidazole 500 mg every 8 hours to the patient's antibiotic regimen, as PLA is most often polymicrobial. The patient also underwent stool evaluation for ova and parasites since parasitic liver abscesses remain more common worldwide than PLA. The patient next underwent magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) that confirmed the right hepatic lobe lesion noted by the ultrasound that was consistent with pyogenic abscess (►Fig. 2). No additional infectious focus or abnormality was noted on MRI of the abdomen and pelvis.



**Fig. 2** Follow-up magnetic resonance imaging (MRI) of the abdomen/pelvis in our patient demonstrated a  $4.0 \times 4.6 \times 4.0$  cm inferior hepatic lobe focus that was most consistent with pyogenic abscess, confirming the previous ultrasound results.

The patient underwent ultrasound and fluoroscopy-guided percutaneous aspiration of the liver abscess with drain placement by Interventional Radiology. Culture confirmed monomicrobial infection with pan-sensitive *K. pneumoniae*. To rule out invasive PLA, the patient underwent echocardiogram and ophthalmologic examination, which were both normal. Ultimately, the patient was diagnosed with cryptogenic noninvasive PLA (CNPLA) secondary to *K. pneumoniae*. Prior to discharge on hospital day number 5, the patient underwent peripherally inserted central catheter (PICC) placement due to plans for prolonged antibiotic therapy. The IV ceftriaxone 2 g daily was continued and she was transitioned to *per os* (PO) metronidazole 500 mg three times daily.

After a total of two weeks of antibiotic therapy, the patient followed-up with Infectious Disease. The IV ceftriaxone and PO metronidazole as well as the PICC line were discontinued and the patient was transitioned to PO cefixime 400 mg daily. The plan was to continue antibiotic therapy until complete resolution of the abscess. After a total of four weeks of antibiotic therapy (two weeks IV and two weeks PO only), the patient underwent MRI confirming resolution of the abscess and the drain and antibiotics were discontinued at ~15 weeks of gestation.

For the remainder of the pregnancy, the patient was followed in the high-risk obstetric clinic. She had an uneventful antenatal course with term delivery at 37 weeks and 6 days gestation following presentation in labor with spontaneous rupture of membranes. She delivered a healthy female infant weighing 3,635 g with Apgars 8 and 9 at 1 and 5 minutes, respectively. The patient and newborn were discharged home together on postpartum day 1.

The patient followed-up with Infectious Disease at ~8 weeks postpartum and was incidentally found to have a mild transaminitis (alanine aminotransferase [ALT], of 43 U/L compared with patient's baseline of 16 U/L) that was expectantly managed with complete resolution at 8 months postpartum. In the 10 months since her delivery, the patient has received treatment via incision and drainage for a subcutaneous abdominal abscess (no cultures obtained) and nares

abscess (oxacillin-resistant *Staphylococcus aureus*). She was also recently evaluated by her primary care physician for epigastric pain felt most likely to be secondary to acid reflux, but for which abdominal imaging was pursued given her prior history and was subsequently normal. She is scheduled for annual follow-up with Infectious Disease.

## Discussion

Pyogenic liver abscesses are much more common in Eastern compared with Western countries, with 82% of cases occurring in Taiwan.<sup>1</sup> The majority of cases are polymicrobial and occur in elderly men with diabetes mellitus who also have underlying hepatobiliary or gastrointestinal disease. Monomicrobial infection represents a minority of PLA. *K. pneumoniae* infection, specifically, was once a rare finding in Western cases of monomicrobial PLA; however, rates are increasing and now account for up to 40% of cases in certain areas of the United States. Interestingly, United States' cases of monomicrobial PLA secondary to *K. pneumoniae* have only been described in patients of Asian or Hispanic descent. This finding suggests that geographical residence as well as genetic susceptibility play a role in this poorly understood predisposition.<sup>2,3</sup>

Overall, monomicrobial CNPLA secondary to *K. pneumoniae* remains a rare condition worldwide with most cases clustering in Southeast Asia. In the United States, these cases differ from polymicrobial PLA as they are most often community-acquired, rarely associated with diabetes or identifiable hepatobiliary or gastrointestinal disease, and generally have a good clinical outcome if promptly diagnosed and treated. Unlike CNPLA, cryptogenic invasive PLA (CIPLA) is highly associated with distant seeding and is nearly exclusively found in Taiwan. While the pathogenesis of this finding is most likely multifactorial and related to race, environment, and underlying disease (e.g., diabetes mellitus), the precise explanation for the endemic nature of CIPLA to Taiwan remains poorly understood.<sup>4</sup> Like CNPLA, CIPLA cases are increasingly associated with *K. pneumoniae*, rising from 30% in the 1980s to 80% of cases in the 1990s.<sup>1</sup>

Symptoms of monomicrobial CNPLA are frequently nonspecific and routine laboratory evaluation is often nondiagnostic, particularly in cases of noninvasive disease. Rapid diagnosis is critical as associated bacteremia can progress to sepsis if left untreated, with subsequent increase in morbidity and mortality. In the pregnant patient, sepsis is additionally associated with worsening outcomes including two times greater risk for preterm delivery and five times higher rates of perinatal mortality.<sup>5</sup> Accurate recognition necessitates a thorough work-up to include blood cultures and directed testing based on patient history and ultimately requires abdominal imaging for the diagnosis.

Antibiotic treatment of bacteremia-associated PLA is imperative and should be initiated within 60 minutes of presentation, particularly if there are concerns for sepsis.<sup>6</sup> Most often this requires initiation of broad-spectrum antibiotic coverage prior to receiving final culture results. While gram stain and/or cytology can direct therapy, precise

speciation usually requires 24 to 48 hours. However, newer PCR techniques have allowed for rapid preliminary speciation, as was the case for our patient. Available testing using these highly multiplexed PCR assays of blood, cerebral spinal fluid, and gastrointestinal and/or respiratory samples can provide preliminary results for many infections within 60 minutes.

Following initiation of antibiotics, a work-up for the source of bacteremia is necessary. In our patient, the full fever work-up was unremarkable and required additional imaging. With pulmonary and genitourinary sources ruled out, evaluation for possible intra-abdominal etiology was pursued via abdominal ultrasound. Extrapolated data from non-pregnant patients has shown abdominal ultrasound to be an effective screening tool for PLA, with greater than 85% sensitivity.<sup>7</sup> Subsequent imaging, via CT or MRI, is often completed when PLA is suspected to both confirm ultrasound findings and assess for the underlying source of the abscess as most causes are secondary to underlying hepatobiliary disease or intra-abdominal infection. PLA often requires drainage of the abscess and necessitates prolonged antibiotic therapy.

Once cryptogenic PLA has been diagnosed and targeted treatment is initiated, it is important to evaluate for invasive infection. Septic emboli most commonly occur in the eyes (endophthalmitis) but have also been described in the lungs, brain, heart, kidneys, and colon. Necrotizing fasciitis, although rare, has also been reported. Additionally, there have been rare cases of suspected cryptogenic PLA with underlying subclinical malignancy, particularly colorectal cancer. In one study, colonoscopy detected underlying cancer in 25% of patients with cryptogenic PLA secondary to *K. pneumoniae* and was most common among patients of Asian descent with diabetes mellitus.<sup>8</sup> Therefore, colonoscopy should be performed in patients with risk factors and in those with concerning symptoms and/or imaging. Also, recurrent cryptogenic PLA may be a harbinger of underlying colorectal cancer.<sup>9</sup>

Very few cases of perinatal PLA cases have been described, with exceedingly rare occurrence in Western countries (– **Table 1**). These cases were found to be secondary to other infections; specifically *Streptococcus anginosus* in a case subacute cholecystitis secondary to local perforation of the gallbladder in a Canadian patient at 30 weeks of gestation<sup>10</sup> and methicillin-resistant *Staphylococcus aureus* (MRSA) in an American patient at 33 weeks who was treated for multiple subcutaneous MRSA abscesses four weeks prior.<sup>11</sup> Our case is the first to our knowledge reporting a case of cryptogenic PLA in pregnancy and is most accurately described as noninvasive. Our Filipino patient had no underlying medical conditions that would have otherwise put her at increased risk for PLA.

## Conclusion

Pyogenic liver abscess remains a very rare cause of bacteremia and/or sepsis in pregnancy, particularly in Western countries. Given the diversity of the United States population

**Table 1** Previously reported perinatal pyogenic liver abscesses

Study (reference)	Country	Perinatal period	Abscess culture	Risk factor(s)	Comments
Naveau et al, 1983 <sup>12</sup>	France	Second trimester	<i>Brucella</i> spp.	<ul style="list-style-type: none"> <li>Consumption of unpasteurized goat's milk and cheeses in pregnancy</li> </ul>	<ul style="list-style-type: none"> <li>Bacteremia initially treated with outpatient antibiotics</li> <li>Returned for evaluation 2 weeks later with worsening symptoms and underwent laparoscopic drainage</li> <li>Spontaneous vaginal delivery at term</li> </ul>
Lindgren et al, 1996 <sup>13</sup>	Austria	27 weeks gestation	<i>Listeria monocytogenes</i>	<ul style="list-style-type: none"> <li>Consumption of raw fish</li> </ul>	<ul style="list-style-type: none"> <li>Primary cesarean delivery (CD) performed on day of admission due to fetal distress</li> <li>Computed tomography (CT) guided aspiration of abscess on postpartum day 9</li> <li>Surgical drainage of persistent abscess on postpartum day 19</li> </ul>
Kopernik et al, 1998 <sup>14</sup>	Israel	Immediately postpartum	Sterile	<ul style="list-style-type: none"> <li>Three week history of malaise, nausea/vomiting and epigastric pain prior to admission for labor</li> </ul>	<ul style="list-style-type: none"> <li>Received broad spectrum antibiotics in labor for chorioamnionitis</li> <li>Underwent CT guided abscess drainage with drain placement x5 days</li> </ul>
Ibis et al, 2005 <sup>15</sup>	Turkey	3 weeks postpartum	Sterile	<ul style="list-style-type: none"> <li>Postpartum endomyometritis with <i>E. Coli</i> bacteremia</li> <li>Severe portal and mesenteric vein thromboses with septic emboli to liver</li> </ul>	<ul style="list-style-type: none"> <li>Received broad spectrum antibiotics prior to ultrasound guided abscess drainage</li> <li>Found to be antithrombin III and protein S deficient, treated with anticoagulation in addition to antibiotics</li> </ul>
Sherer et al, 2010 <sup>11</sup>	United States	33 weeks gestation	Methicillin-resistant <i>Staphylococcus aureus</i>	<ul style="list-style-type: none"> <li>Treated for multiple subcutaneous MRSA abscesses 4 weeks prior, presumed to have led to hematogenous spread</li> </ul>	<ul style="list-style-type: none"> <li>Interventional radiology (IR) declined drainage in pregnancy due to location of abscess</li> <li>Primary CD at 34 weeks due to worsening maternal status</li> <li>Underwent postpartum CT guided abscess drainage</li> </ul>
Yüksel et al, 2013 <sup>16</sup>	Turkey	23 weeks gestation	<i>Escherichia coli</i>	<ul style="list-style-type: none"> <li>Treated for presumed gastroenteritis and possible nephrolithiasis 1 week prior to admission</li> <li><i>E. Coli</i> positive blood and stool cultures</li> </ul>	<ul style="list-style-type: none"> <li>Rapidly developed sepsis and disseminated intravascular coagulopathy (DIC)</li> <li>Underwent ultrasound guided abscess drainage during admission</li> <li>Elective CD at 38 weeks</li> </ul>
Zipori et al, 2017 <sup>10</sup>	Canada	30 weeks gestation	<i>Streptococcus anginosus</i>	<ul style="list-style-type: none"> <li>Local perforation of underlying subacute cholecystitis</li> <li><i>S. anginosus</i> bacteremia</li> </ul>	<ul style="list-style-type: none"> <li>Underwent ultrasound guided abscess drainage during admission</li> <li>Spontaneous vaginal delivery at 41 weeks</li> <li>Postpartum follow-up with general surgery for underlying cholelithiasis</li> </ul>

with high rates of patients of Asian and Hispanic descent, PLA should be considered in cases of sepsis where common sources have been ruled out even in the absence of underlying risk factors like diabetes, hepatobiliary disease, or gastrointestinal disease. Once recognized, targeted antibiotic therapy and drainage of the abscess will lower the maternal morbidity and mortality and decrease the subsequent risk of pregnancy complications.

The opinions expressed herein are those of the authors and do not reflect the official policy or position of Madigan Army Medical Center, the Department of the Army, the Department of Defense or the United States Government.

#### Financial Disclosures

None.

#### Précis

Perinatal pyogenic liver abscess is a rare but dangerous etiology of maternal sepsis, requiring thorough infectious work-up and prompt treatment to improve maternal-fetal outcomes.

#### Teaching Points

Pyogenic liver abscesses are an uncommon etiology of fever in the puerperium and are often associated with nonspecific symptoms that overlap common pregnancy complaints.

Accurate diagnosis of a pyogenic liver abscess requires thorough fever workup until a source is identified. Astute obstetric care and a multidisciplinary approach can allow for prompt diagnosis and directed therapy, improving outcomes for both mother and fetus.

#### Note

This article was presented at the American College of Obstetricians and Gynecologists Annual Clinical and Scientific Meeting, Austin, Texas, April 2018.

#### Conflict of Interest

None.

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