

**Peripartum jaundice is not always pregnancy-related: : an illustrating case
report**

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Abstract :

Background: Leptospirosis is a widespread zoonotic disease that presents significant diagnostic challenges, particularly during pregnancy where its symptoms may mimic conditions such as HELLP syndrome, acute fatty liver of pregnancy (AFLP), and sepsis. Early and accurate diagnosis is critical for optimal maternal and fetal outcomes, especially in resource-limited settings.

Case Report: A 35-year-old primiparous woman in her 36th week of gestation presented with abdominal pain and hypertension. Initial suspicions of HELLP syndrome led to an emergency cesarean section. Postpartum, she developed seizures and jaundice, necessitating intensive care. Extensive investigations revealed elevated procalcitonin levels, which, although nonspecific, guided the diagnosis of leptospirosis when other etiologies were excluded. The diagnosis was confirmed by serological testing. Comprehensive management included supportive care, antibiotics, and hematoma drainage, resulting in full recovery.

Conclusion: This case highlights the diagnostic complexity of leptospirosis in pregnancy and the importance of a high index of suspicion. Procalcitonin, while not definitive, can assist in guiding diagnostic efforts and assessing disease severity. A comprehensive, multidisciplinary approach is essential for timely diagnosis and effective management, particularly in settings with limited access to advanced diagnostic tools.

Keywords:

Leptospirosis, Peripartum jaundice, Acute fatty liver, hellp syndrome,

Introduction :

Leptospirosis is considered as most widespread zoonotic disease in the world. Its impact on pregnant women carries ominous implications, often resulting in serious risks for both the fetus and the mother. Adding to the complexity, its clinical presentation often mirrors a spectrum of other infections, including viral, bacterial, and parasitic, alongside complications such as acute fatty liver, pregnancy-induced hypertension, and HELLP syndrome. Unraveling this diagnostic intricacy becomes paramount in ensuring timely and effective interventions for maternal and fetal well-being.

Case presentation :

A 35 year old woman, primiparous in 36th week of gestation, was admitted to the obstetrical emergency department with abdominal pain, vomiting and high blood pressure.

Devoid of any medical or surgical history, with no recent travel, animal contact, fever, or history of Moroccan or Moorish baths in the last fifteen days, she underwent blood tests revealing a hemoglobin of 9 g/dL, total white blood cells at $29,9 \times 10^9/L$, platelets at $161 \times 10^9/L$, lactate dehydrogenase (LDH) of 1667 U/L. Liver function tests showed aspartate transaminase (AST) 109 U/L and alanine transferase (ALT) 103 U/L. Prothrombin ratio was at 40 % and an international normalized ratio (INR) of 2,1. Kidney function tests showed an urea of 0.93 g/L and creatinine of 36 mg/L while the proteinuria/creatinuria ratio in the urine sample was negative.

Suspecting HELLP syndrome due to the clinical presentation, the patient underwent an emergency cesarean section, delivering a healthy male with Apgar scores of 7 and 10 at 1 and 5 minutes, respectively.

Two days post-delivery, she developed seizures and jaundice, necessitating intensive care unit (ICU) admission.

The initial assessment revealed a confused, disoriented patient (grade 3 hepatic encephalopathy) with a Blood Pressure of 125/63, a heart rate of 80 beats per minutes, and a polypnea of 35 breaths per minute.

Further examinations uncovered abdominal distension, extensive ecchymosis lesions, and a hematoma around the C-section scar (figure 1) . The ocular examination found no conjunctival suffusion .

Hematological analysis displayed a decline in hemoglobin to 5.6 g/dL, an increase in white blood cell count to $44.83 \times 10^9/L$, and a drop in platelet count to $159 \times 10^9/L$.

Additionally, there was a deterioration in renal function, instances of hypoglycemia, and an elevation in inflammatory markers, with C-reactive protein (CRP) measuring at 127.9 mg/L and procalcitonin at 19.87 ng/mL.

An abdominal ultrasound revealed a steatotic liver of normal size, a large peritoneal effusion, and no dilation of the hepatic bile ducts. The spleen and kidneys appeared normal.

Considering the elevated procalcitonin levels, an extensive infectious workup was undertaken. The chest X-ray revealed no abnormalities, while cytobacteriological analyses of urine, ascitic fluid, and vaginal swab yielded negative results.

The viral serology tests for hepatitis A, B, C, and E, as well as cytomegalovirus and herpes simplex virus, all returned negative results. Due to the unavailability of leptospirosis-specific diagnostic tests in our region, samples for serological analysis, including the Microscopic Agglutination Test (MAT) and Enzyme-Linked Immunosorbent Assay (ELISA), were sent abroad.

At this stage, given the context of postpartum acute liver failure and the presence of 10 elements out of the 12 Swansea criteria , the most likely diagnosis was acute fatty liver of pregnancy.

Two days following her admission to the ICU, the patient developed respiratory distress associated with hemoptysis and an increase in the size of the hematoma. Though no hemodynamic instability was observed, and there was no requirement for vasoactive drugs, management included symptomatic treatment, non-invasive ventilation, euglycemia maintenance, albumin infusion, transfusion with red blood cells and fresh frozen plasma, empirical antibiotics (Ceftriaxone 2 g per day, which were maintained throughout her treatment), and the surgical drainage of the hematoma

Later , the leptospirosis IgM antibodies by ELISA were positive at 1/400 dilution and the diagnosis of leptospirosis (Weil's syndrome) was then confirmed.

During her stay in the ICU, the patient's neurological and respiratory status improved, her jaundice disappeared and her liver and kidney function returned to normal. She was then discharged from the ICU at day 21 .

Discussion :

Leptospirosis is a zoonotic disease of global importance, occurring in urban environments of industrialized and developing countries, as well as in rural regions worldwide. It is estimated that there are more than 500,000 severe cases of leptospirosis per year worldwide, with a fatality rate that may

exceed 10%. These figures are likely to be underestimated due to the lack of awareness of the disease, diversity of symptoms, and relatively inaccessible and insufficiently rapid diagnostics.[1]

Humans act as incidental hosts within a transmission cycle primarily involving both wild and domestic animals. Several hundred serovars have been described among pathogenic leptospires. The animal reservoir, mainly rodents, excretes leptospires in its urine, thus contaminating the water environment and spreading the disease to other animals or humans.

The clinical presentation is biphasic. The first phase is the "anicteric phase," typically lasting about 1 week, during which the patient presents with fever, chills, headache, anorexia, diarrhea, abdominal pain, nausea, vomiting, severe myalgia, and conjunctival suffusion or hemorrhage; 90% of patients recover during this phase. In about 10% of cases, symptoms reappear within 1 to 3 days after initial improvement, advancing to a more severe condition known as "Weil's disease," which carries a mortality rate of up to 40% [2]. It may manifest as multiorgan failure characterized by acute renal failure, acute respiratory distress syndrome (ARDS) with pulmonary hemorrhages, and disseminated intravascular coagulation (DIC)[3-4]. A systematic review found that the incidence of leptospirosis is lower during pregnancy compared to the general population, with no difference in clinical presentation[5].

This clinical presentation can closely resemble pregnancy-related conditions such as pre-eclampsia, HELLP syndrome, AFLP, and cholestasis gravidarum. Additionally, it may mimic non-pregnancy-related conditions like viral hepatitis or sepsis. The overlap in symptoms and laboratory findings, combined with the absence of specific diagnostic criteria, often complicates accurate differentiation[6].

In our case, the patient was diagnosed as an AFLP having fulfilled 10 of the 12 Swansea criteria, highlighting the fact that these criteria has low specificity and positive predictive value among pregnant women with AFLP[7]. The elevated procalcitonin was the only sign that could not be explained and that guided us toward leptospirosis. While procalcitonin does not confirm leptospirosis, it serves as a valuable marker in directing further investigations and can even be used to assess the severity of leptospirosis[8].

Leptospirosis is confirmed through cultures, gene amplification from bodily fluids (blood, urine, or cerebrospinal fluid), or serological tests such as MAT and ELISA, though these are often restricted to specialized laboratories. When diagnosed early, leptospirosis in pregnancy is highly treatable and does not necessitate pregnancy termination, provided there is close fetal monitoring.

Management includes supportive treatment for liver, renal, and coagulation dysfunctions, along with antibiotic therapy such as penicillins or cephalosporins for 7 days. Doxycycline is contraindicated

during pregnancy and should be avoided in such cases Corticosteroids may be beneficial in some cases[4].

Conclusion :

The presented case underscores the potential for leptospirosis to manifest with unusual subtlety in pregnant women. Vigilance and a high index of suspicion are crucial for early identification, particularly considering the challenges associated with its elusive presentation. Diagnosis proves challenging, especially in low-income countries where lab results may not always be readily available. Procalcitonin, while not specific to leptospirosis, can guide clinicians toward the diagnosis and aid in assessing its severity, particularly when liver biopsy feasibility is compromised due to coagulopathy. This emphasizes the imperative need for a comprehensive and nuanced diagnostic approach in recognizing and managing leptospirosis in pregnant individuals.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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None

References :

[1] Abela-Ridder B., Sikkema R., and Hartskeerl R.A ,“Estimating the burden of human leptospirosis.” *International journal of antimicrobial agents* vol. 36 Suppl 1 (2010): S5-7.
doi:10.1016/j.ijantimicag.2010.06.012

[2] Puliyaath, G., Singh, S. Leptospirosis in pregnancy. *Eur J Clin Microbiol Infect Dis* **31**, 2491–2496 (2012). <https://doi.org/10.1007/s10096-012-1625-7>

[3] Bharti, A. R., Nally, J. E., Ricaldi, J. N., Matthias, M. A., Diaz, M. M., Lovett, M. A., Levett, P. N., Gilman, R. H., Willig, M. R., Gotuzzo, E., Vinetz, J. M., & Peru-United States Leptospirosis

Consortium (2003). Leptospirosis: a zoonotic disease of global importance. *The Lancet. Infectious diseases*, 3(12), 757–771. [https://doi.org/10.1016/s1473-3099\(03\)00830-2](https://doi.org/10.1016/s1473-3099(03)00830-2)

[4] Karnik, Niteen D, and Aditi S Patankar. “Leptospirosis in Intensive Care Unit.” *Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine* vol. 25,Suppl 2 (2021): S134-S137. doi:10.5005/jp-journals-10071-23852

[5] Selvarajah S, Ran S, Roberts NW, Nair M (2021) Leptospirosis in pregnancy: A systematic review. *PLOS Neglected Tropical Diseases* 15(9): e0009747. <https://doi.org/10.1371/journal.pntd.0009747>

[6] Rath W, Tsikouras P, Stelzl P. HELLP Syndrome or Acute Fatty Liver of Pregnancy: A Differential Diagnostic Challenge: Common Features and Differences. *Geburtshilfe Frauenheilkd.* 2020;80(5):499-507. doi:10.1055/a-1091-8630

[7] Casey, L. C., Fontana, R. J., Aday, A., Nelson, D. B., Rule, J. A., Gottfried, M., Tran, M., Lee, W. M., & Acute Liver Failure Study Group (2020). Acute Liver Failure (ALF) in Pregnancy: How Much Is Pregnancy Related?. *Hepatology (Baltimore, Md.)*, 72(4), 1366–1377. <https://doi.org/10.1002/hep.31144>

[8] Crouzet, J., Faucher, J., Toubin, M., Hoen, B., & Estavoyer, J.M. (2011). Serum C-reactive protein (CRP) and procalcitonin (PCT) levels and kinetics in patients with leptospirosis. *European Journal of Clinical Microbiology & Infectious Diseases*, 30, 299-302. <https://doi.org/10.1007/s10096-010-1088-7>

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Figures :



Figure 1 : image showing hematoma around caesarean scar after drainage

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