A Dual Diagnosis in the Puerperium: Severe Endometritis Complicated by Leptospirosis-Induced Weil's Syndrome

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ABSTRACT

Endometritis is defined as the inflammation of the endometrium and myometrium. Social factors can predispose to concomitant tropical infections, and diseases such as leptospirosis can have overlapping symptoms. We present the case of a 19-year-old female who had an urgent cesarean section, had a poor clinical course with jaundice, acute kidney injury, and coagulopathy requiring a second surgical time, and underwent an urgent hysterectomy for severe and irreversible endometritis. Additionally, leptospirosis-induced Weil's syndrome was confirmed by serology (positive IgM) due to the presence of systemic alterations that could not be explained by a gynecologic condition alone. Endometritis has identifiable risk factors, and a typical antibiotic regimen is usually sufficient to prevent complications. However, severe cases can still occur despite treatment. This case highlights the diagnostic challenge of differentiating severe sepsis due to obstetric syndromes and zoonotic diseases such as leptospirosis, which can mimic gynecologic diseases and delay diagnosis and treatment. Analyzing each case is crucial to identifying unusual pathologies in pregnant patients and preventing adverse outcomes.

Keywords: Endometritis; Hysterectomy; Leptospirosis; Pregnancy complications

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Introduction

During pregnancy, there can be multiple maternal and perinatal complications that can lead to life-threatening conditions that may have a direct or indirect association with age, especially at extreme ages (≤19 years old and ≥35 years old) (1). One of them is endometritis, defined as the inflammation of the endometrium and myometrium caused by an infection of the superficial epithelium with multiple microorganisms, including aerobes and anaerobes (2). The route of infection can be ascending through the cervix and vagina or secondary to endometrial surgical interventions such as a cesarean section (2). The infection can be acute or chronic, and treatment includes antimicrobials against the most common pathogens; in cases of unresponsiveness, a surgical procedure may be necessary (3). Furthermore, acute and chronic endometritis are related to amenorrhea, infertility, and poor reproductive outcomes (4).

Along with intrinsic pregnancy risks, social factors like low socioeconomic status, poor health care access, and poor control of infectious diseases can lead to extra complications in pregnant women. Leptospirosis, a preventable infectious disease caused by spirochete bacteria, is spread through the urine of infected animals and is more common among low-income groups (5). There is no clear data on leptospirosis in pregnant women. One systematic review estimates its incidence at 1.3 per 10,000 women with fever or jaundice (5). Screening for leptospirosis is not mandatory during pregnancy, as it is not part of the TORCH congenital infections (6). Still, leptospirosis can lead to systemic complications. The most severe stage, Weil's syndrome, is rare and features renal dysfunction, high bilirubin, and coagulopathy (7).

This study presents a case of a young woman in her first pregnancy with acute endometritis and severe postpartum

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complications due to Weil's syndrome, highlighting the need to consider zoonoses as possible life-threatening conditions after childbirth.

Case Report

A 19-year-old female from a rural zone at 39 weeks and 1 day into her first pregnancy, without relevant medical history, consulted the emergency room for 24 hours for subjective fever and asthenia. Initial physical examinations were normal, with vital signs of blood pressure of 115/81 mmHg, 78 beats per minute, 18 breaths per minute, and a temperature of 36.6 degrees Celsius. Irregular uterine dynamics were reported, with a fetal cardiac frequency of 142 beats per minute, a 32 cm uterine height, and no cervical changes. In addition, jaundice was documented. The first labs showed an elevated white blood cell count and a platelet count of 132,000 mm³, indicating thrombocytopenia despite the normal decrease in platelets in the third trimester; hypoglycemia; abnormal renal and hepatic laboratory values; and arterial blood gases showing non-compensated metabolic acidosis and hyperlactatemia (Table I).

Due to these findings, abdominal sepsis was suspected, and an emergency cesarean was performed. Intraoperative findings include peritoneal free fluid, a moderate amount of intense yellow color in the bilious aspect, and an edematous appendix, which necessitated an intraoperative call to the general surgery team, who performed an appendectomy without complications. In addition, they suggest performing a total abdominal ultrasound scan, with the only additional finding of fatty liver. After the surgical procedures, the initial diagnosis proposed was abdominal sepsis with renal vascular and liver compromise; she was transferred to the intermediate care unit (IMCU), where she was initially managed with piperacillin-tazobactam 4.5 g intravenous (IV) every 6 hours and later added metronidazole 500 mg IV every 8 hours. While hospitalized in the IMCU, the patient continued to exhibit laboratory abnormalities across multiple systems (Table I). Other laboratory results included a D-dimer of 3659 ng/mL (NR: < 0.50 ng/mL), positive dengue IgM antibodies of 1.33 (NR < 0.688), elevated Gamma-Glutamyl Transpeptidase of 522 U/L (NR 0 to 30 U/L), and positive 24-hour urine proteins of 432 mg (NR: < 80 mg/dL). Here, an initial hypothesis was documented: the possibility that she may have eventually developed pre-eclampsia. However, blood pressure readings in the hypertension range were never recorded, either during prenatal checkups or during hospitalization.

The patient continued hospitalization and was treated by the emergency medicine, general surgery, and gynecology and obstetrics departments. First, the general surgery team requested multiple studies and suspected biliary origins. Computed tomography (CT) of the abdomen showed pneumobilia as the only positive finding in the biliary tract and multiple post-surgical findings (Figure 1). Based on these findings, the general surgery team ruled out cholangitis; however, the emergency medicine team still insisted on this hypothesis and requested a magnetic resonance cholangiography (MRCP), which reported that the patient had acute edematous pancreatitis, with a lot of free fluid in different compartments, vesicular subserosal edema connected to biliary mud, and widespread steatosis in the liver.

Table I: *Laboratory test record*

	Normal values	Pre-CS	First day post-CS	Fifth day post-CS	Tenth day post-CS and pre-TAH	First day post-TAH	Fifth day post-TAH	Eighth day post-TAH
White blood cell	4,500-11,000 mm³	17,260	32,470	20,340	18,900	19,300	13,300	18,800
Neutrophils	50-70%	73.8	79	70.9	92	91	78	75
Lymphocytes	30-45%	15.6	14.9	20.6	-	-	14	-
Haemoglobin	12-16 g/dL	12.3	11	9.1	6.3	10.7	8.8	6.2
Haematocrit	37-47%	37.1	32.9	26.6	18.4	30.7	26.2	-
Platelets	150,000-400,000mm³	132,000	117,000	88,000	120,000	130,000	427,000	665,000
Glucose	77-99 mg/dL	63.4	-	78.8	132	135	96	-
Creatinine	0.5-1.10 mg/dL	2.16	1.92	1.41	-	0.85	0.74	0.49
Blood urea nitrogen	8-20 mg/dL	12.7	13.2	43.3	-	15	9	11
AST	10-40 U/L	115	66	106	-	77	63	66
ALT	10-40 U/L	148	70	60	-	50	60	53
Total bilirubin	0.3-1.0 mg/dL	7.83	6.07	8.55	4.75	3.92	3.31	1.61
Direct bilirubin	0.1-0.3 mg/dL	5.59	4.61	5.74	2.98	2.6	2	0.84
Alkaline phosphatase	30-120 U/L	617	-	-	-	322	306	276
Lactic acid	0.7-2.1 mmol/L	9.4	2.6	1.8	-	0.9	-	-
Lactate dehydrogenase	80-225 U/L	593	600	838	273	-	-	-
Procalcitonin	≤0.10 ng/mL	-	2.13	-	-	-	-	0.46
Prothrombin time	11–13 seconds	23.7	25.9	20.3	17.9	-	-	10.9
INR	2-3	2.05	2.28	1.70	-	-	-	1
Thromboplastin time	25–35 seconds	44.08	56	42.8	34.9	-	-	25.4
C-reactive protein	0.3-1 mg/dL	< 6	-	24	-	-	13.6	-

CS: Cesarean section. TAH: Total Abdominal Hysterectomy. Source: own elaboration.

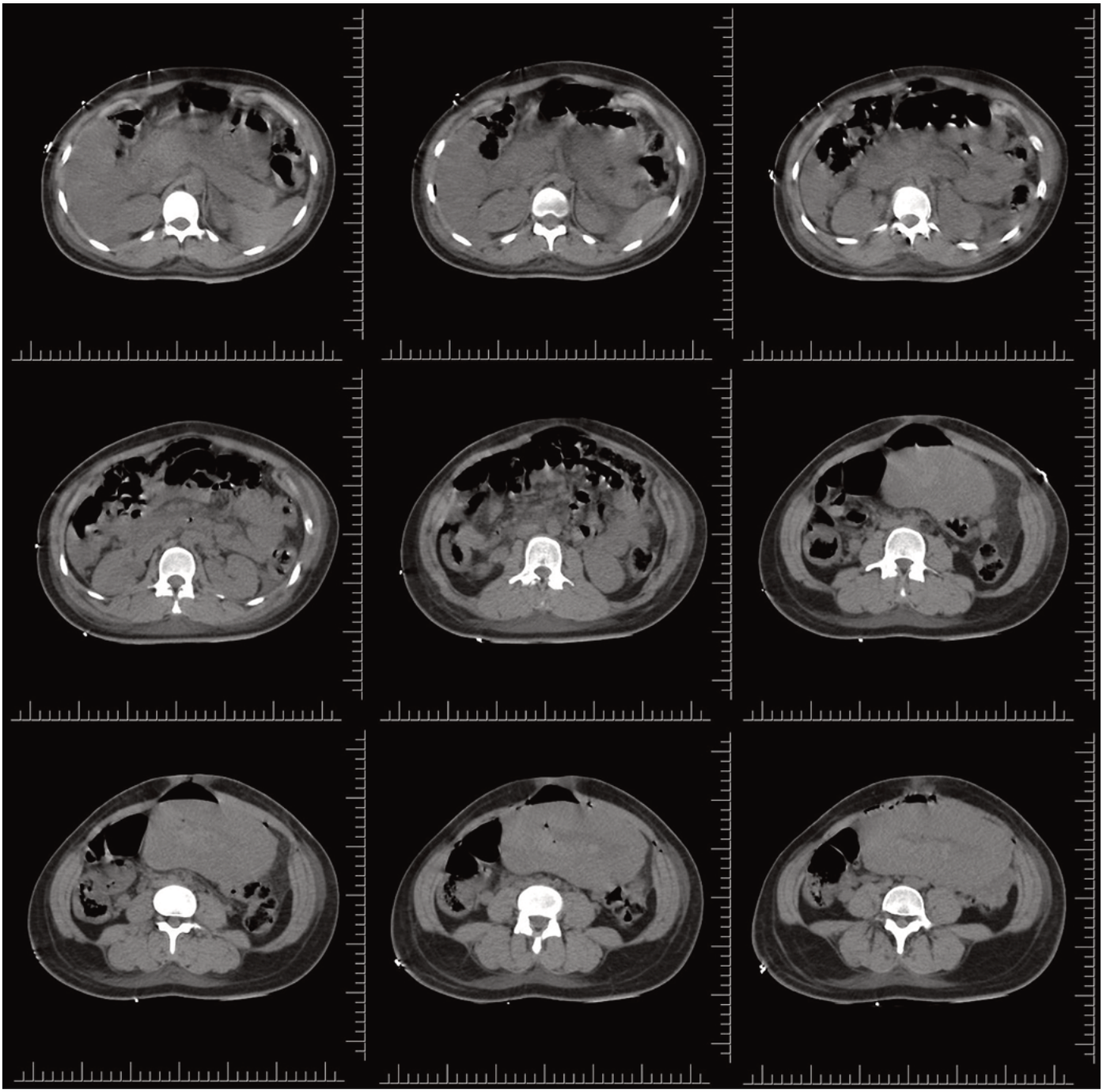

Figure 1: *Transversal slices of simple computed tomography of the abdomen showing pneumobilia, prominence of the body and tail of the pancreas, post-surgical pneumoperitoneum, free fluid in the perisplenic space, in the splenorenal recess, and in both paracolic gutters; a uterus in a puerperal state with the presence of hyperdensities likely containing blood; and soft tissue edema and emphysema in the hypogastrium.*

During hospitalization, no hypertensive readings were detected, but the patient continued to show inadequate clinical and laboratory findings with abdominal pain, ascites, and highlighted jaundice. After this, the emergency and general surgery staff agreed on cholangitis as the primary diagnosis, and an endoscopic retrograde cholangiopancreatography (ERCP) was performed. No defects were observed in the bile duct, with clear bile and no cholangitis. After ruling out cholangitis, the medical team had not yet identified the primary disease. The patient continued to experience clinical deterioration, prompting the gynecology and obstetrics team to consider target organ damage (TOD) in the kidneys, which was not related to hypertensive disorders of pregnancy. Therefore, HELLP syndrome was considered as a potential primary diagnosis. Six days after admission to the institution, the same number of days after the emergency cesarean section, the patient was referred to a major complex hospital to continue treatment in an intensive care unit (ICU).

While hospitalized in the ICU, medical staff documented acute severe pancreatitis and anasarca and considered depletion management before considering surgery. Additionally, due to adequate uterine involution, non-fetid lochia, and a cervical neck without changes, they ruled out endometritis or any other infectious process of gynecological origin but requested a soft tissue ultrasound for assessment of the surgical wound due to persistent abdominal pain with poor modulation. The ultrasound revealed a heterogeneous collection containing liquid and hypoechoic punctiform echogenic material, extending along the surgical scar and indicating a hematoma. In addition, severe anemia (6.3 g/dL) was reported (Table I). With these findings, the possibility of abdominal bleeding was proposed, and an exploratory laparotomy was requested. The exploratory laparotomy found 1000 cc of blood and 2000 cc of ascitic fluid. Moreover, they found irreversible alterations at the endometrial level, compatible with postpartum endometritis and infectious processes, due to hypoperfusion. They performed an emergency obstetric hysterectomy and bilateral salpingectomy. The patient continued being treated in the ICU with laboratory follow-up (Table I), and during her stay, the medical staff considered multiple diagnoses, including an incomplete HELLP syndrome (altered laboratories without hypertensive disorder associated with pregnancy), a thrombotic microangiopathy (positive direct Coombs, high lactate dehydrogenase, and hemolytic anemia with a blood transfusion requirement), and tropical diseases (dengue and malaria), all of which were posteriorly ruled out. Due to an inconclusive diagnosis, additional studies were performed, including an IgM test for leptospirosis, which was confirmed by a second laboratory test. On the eighth day after TAH, an infectologist was consulted; he considered Weil's syndrome due to the patient's laboratory and clinical findings that could not be explained by gynecological or obstetric conditions alone; he suspended piperacillin-tazobactam and switched to ceftriaxone 1 g IV every 12 hours. In addition, a new blood transfusion was requested due to an increase in hemoglobin to 10 g/dL. The patient continued her hospital stay. With improved laboratory and imaging results, she was transferred to a general hospital for further care. Currently, she continues to complete at least 10 days of the ceftriaxone regimen.

Discussion

Traditionally, endometritis is classified as acute (≤ 30 days) or chronic (> 30 days). Furthermore, some authors incorporate a third type, postpartum endometritis. In contrast, some authors categorize postpartum endometritis as a subtype of acute endometritis (8). Regarding acute endometritis, more than 85% of cases are caused by sexually transmitted infections (STIs), with Chlamydia trachomatis being the most frequent, followed by Neisseria gonorrhoeae and bacteria associated with bacterial vaginosis. Known risk factors included a previous history of STIs, high-risk sexual behaviors, age under 25, and a history of gynecologic procedures. The incidence of acute endometritis in developing countries is approximately 32% and is highly related to pelvic inflammatory disease (PID) (8).

Chronic endometritis is often associated with other bacterial infections. The primary causative organisms found include Streptococcus species, followed by Enterococcus faecalis and Escherichia coli. Risk factors for chronic endometritis are numerous and include multiparity, previous abortions, the use of intrauterine devices (IUDs), and abnormal uterine bleeding (AUB). The statistics of chronic endometritis are extremely difficult to estimate, but some studies reported an estimated incidence of 30% in patients with recurrent pregnancy loss (8). In general, treatment includes antibiotics directed to the usual bacteria according to the main classification. Clindamycin and gentamicin together are a suitable combination for the treatment of endometritis (3). In our case, the first approach was compatible with a sepsis of abdominal origin requiring an urgent cesarean section; however, despite the antibiotic regimen, the patient continued to worsen her vital signs and alter laboratory results, and she was presented with numerous complications, such as acute pancreatitis, acute kidney injury (AKI) alterations, and a high suspicion of biliary obstruction. It was after the second surgical procedure that the medical staff considered severe endometritis with irreversible changes and intra-abdominal bleeding, so they decided to perform an urgent hysterectomy as a definitive treatment.

Other risk factors for endometritis include lower socioeconomic status, a high body mass index, prolonged membrane ruptures, persistent genital manipulation, and other types of gynecological and obstetric infections (8). Furthermore, between one and four percent of patients with endometritis have complications, including pelvic peritonitis, abscess, septicemia, and septic shock (8). Besides, women with a diagnosis of endometriosis have an increased risk of other gynecologic diseases, such as PID, lower genital tract infection, infections at the surgical site after gynecologic procedures like a caesarean section, and poor reproductive outcomes, with infertility being the worst scenario (4,9). Our patient had a torpid evolution after the caesarean section; the systemic alterations (renal, hepatic, and circulatory) were not exclusively compatible with endometritis; however, in spite of the clinical findings and the laboratory test results, her diagnosis was late due to postpartum complications that could have covered up the endometriosis diagnosis, which was finally performed intraoperatively, where the requirement of hysterectomy in a 19-year-old patient precludes further gestation.

The low socioeconomic status can lead to infectious diseases that may hinder the correct approach to the patient, especially in the pregnant or early postpartum population. Different authors have identified that some tropical infectious diseases can mimic obstetric conditions,such as pre-eclampsia, acute fatty liver disease (AFLP), and HELLP syndrome

(5,7,10). Leptospirosis is a zoonotic disease caused by spirochetes of the genus Leptospira. It is diagnosed by ELISA or agglutination tests, considering that up to 80% of blood cultures remain sterile (5). The first systematic review of leptospirosis in pregnancy reveals an estimated incidence of 1.3 per 10,000 women with fever or jaundice. While it is often anicteric and self-limiting with fever, constitutional symptoms, and conjunctival hemorrhages, severe cases of leptospirosis (5–10%) present jaundice and life-threatening conditions such as pulmonary hemorrhage, meningitis, renal failure, and hemodynamic collapse (10).

Severe leptospirosis is also known as Weil's syndrome, which can perfectly overlap the signs, symptoms, and laboratory abnormalities presented in HELLP syndrome (10). Numerous differential diagnoses were considered in other case reports of leptospirosis in pregnancy. Selvarajah et al. reported that, among the 35 cases analyzed, three were considered pre-eclampsia as a differential diagnosis, six acute fatty liver of pregnancy, and nine HELLP syndrome, with this being the most frequently reported differential diagnosis (5). In our patient, the presence of fever, thrombocytopenia (up to 88,000 mm^3), AKI, hyperbilirubinemia, and a constellation of findings demanded that we rule out HELLP syndrome. However, the absence of hypertension and the degree of renal and hepatic impairment were more suggestive of a systemic infectious process. The initial treatment with a broad-spectrum antibiotic regimen, including piperacillin-tazobactam, covers the causal agents of endometritis, but it is not the first-line in cases of severe leptospirosis.

Normally, penicillin is the antibiotic of choice for the treatment of leptospirosis; in the general population, mild leptospirosis can be treated orally with amoxicillin; other options include doxycycline, azithromycin, or intravenous ampicillin; moderate and severe leptospirosis require intravenous treatment with penicillin G, ampicillin, or ceftriaxone (11). In pregnancy, no studies assess the effects of antibiotics on maternal and fetal outcomes or disease prognosis. Doxycycline should be avoided in pregnancy due to the potential risk to the fetus (12). Selvarajah et al. reported that ampicillin was the most commonly used regimen in pregnant women, followed by ceftriaxone and penicillin G in severe cases (5). In our case, when the medical team realized that the patient came from a remote area with a disadvantaged socioeconomic status and limited access to potable water sources, the risk of leptospirosis was clear, and the serology confirmed the need to change the antibiotic treatment. The transition to ceftriaxone signified a significant improvement in the patient's clinical condition. Notice that most patients present with risk factors or exposure to leptospirosis (5). A thorough interrogation, without overlooking sociodemographic factors, is crucial for early identification of the disease.

Speaking of fetal outcomes in reported cases of leptospirosis in pregnancy, the literature is scarce; however, the first systematic review of leptospirosis in pregnancy reported that 20 (57%) cases included were reported as fetal deaths and 15 (43%) were reported as live births; of them, 8 (53%) presented preterm birth and the 7 (47%) remaining were term births. The study concluded that the second trimester had a higher incidence of fetal death than the third trimester (5). Regarding maternal outcomes, 4 (11%) cases were reported as deceased, whereas 31 (89%) survived (5). In our case, fortunately, no fetal or maternal deaths were reported. However, the patient presented multiple health events and an irreversible outcome regarding her reproductive status at an early age. This reflects non-fatal but significant outcomes for the reported case.

Conclusions

Endometritis is a common condition, particularly among high-risk populations. Analyzing each case and the individual risk factors is essential for identifying unusual pathologies in pregnant patients that may go unnoticed and delay appropriate treatment. This case highlights an important aspect of managing obstetric patients: the need to employ a broad differential diagnosis, particularly in endemic regions. The co-existence of a gynecological disease and leptospirosis-induced Weil's syndrome is extremely rare and can mimic life-threatening gynecologic diseases such as HELLP syndrome. Prompt diagnosis and conservative treatment are crucial to avoiding major complications and unwanted outcomes, such as poor reproductive outcomes.

Declarations

Ethics approval and consent to participate: Informed consent was obtained from the patient before publishing this article. All procedures were performed in accordance with the Declaration of Helsinki.

Availability of data and materials: The data supporting this study are available through the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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