Fatal Herpetic Hepatitis in Pregnancy

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ABSTRACT
Background: Disseminated herpetic infections during pregnancy have been reported in the literature.
Case: This case presentation describes a pregnant patient who presented with fever, elevated liver enzymes, and upper abdominal tenderness and succumbed from fulminant herpetic hepatitis.
Conclusion: Early diagnosis and treatment are essential because of the high mortality rate.

KEY WORDS
Herpes simplex virus, thrombocytopenia, pregnancy

CASE REPORT
The patient was a 20-year-old white female, G1P0, with an intrauterine pregnancy at 32 weeks gestation by ultrasound examination performed in the referring hospital on October 14, 1991. The patient was seen by her primary physician in the emergency room at the referring hospital 1 week prior to transfer. She was diagnosed with a urinary tract infection and was treated with Septra. The patient continued to experience a febrile course and was admitted to the referring hospital where her temperature was found to be 39.6°C. Her blood pressure was 90/60 and her pulse was 98.

The patient's medical history was negative for diabetes mellitus, hypertension, asthma, hepatitis, and thyroid and kidney disease. She denied the use of tobacco, alcohol, and illicit drugs.

The initial physical examination revealed a patient who was not icteric and not dehydrated. Right upper quadrant tenderness was found. Mild uterine tenderness was also noted. Occasional uterine contractions were noted. Her cervix was 1 cm dilated and 25% effaced with intact membranes.

Initial laboratory values showed a white blood cell (WBC) count of 4,000 with 64% polys, 18% bands, and 12% lymphocytes. The platelet count was 124,000, and hematocrit 36.8%. Liver enzymes showed an ALT of 1,062, ALP of 204, AST of 2,031, and lactate dehydrogenase (LDH) of 1,918. A liver ultrasound was obtained and did not show any gallstones. Hepatitis B surface antigen was negative. The patient's prenatal laboratory results showed her to be human immunodeficiency virus (HIV) negative. Differential diagnosis included hemolytic uremic syndrome, acute fatty liver, and hepatitis.

The patient was treated with magnesium sulfate tocolysis for the uterine contractions and was transferred to the tertiary care hospital on December 22, 1991. On her arrival at the tertiary care hospital, her temperature was 38.3°C, her pulse was 108, and her blood pressure was 110/60. A repeat physical examination showed the lungs to be clear. Abdominal palpation showed definite right upper quadrant tenderness. The lower abdomen and uterus were non-tender to palpation. The patient...
was alert and oriented. Her cervix was 1 cm di-
lated, long, and posterior.

Laboratory examination showed the WBC count
to be 2,800, platelets 86,000, PT and PTT within
normal limits, fibrinogen 386, and bleeding time
4.5 min. A urinalysis showed 2+ ketones but no
evidence of bile, blood, nitrates, or leukocyte es-
terases. Two to 4 WBCs were noted with a rare red
blood cell (RBC). Repeat chemistry panel showed
an AST of 4,053 and an LDH of 12,255. Biliru-
bin was 1.0. Bacterial cultures were obtained of the
urine, blood, cervix, and amniotic fluid.

An internal medicine consultation was requested
soon after the patient's arrival at the tertiary care
hospital.

The assessment of the patient was 1) fever of
unknown origin; 2) epigastric pain, rule out gas tri-
tis, gastric reflux, and hepatic enlargement; 3)
thrombocytopenia; and 4) elevated liver enzymes.
The patient was started on ceftriaxone and tobramy-
cin. Magnesium sulfate was continued at 2 g/h.
TORCH titers were ordered. Twelve hours after
her admission, the patient's physical examination
had not changed. The patient complained of hun-
ger and thirst. She was no longer contracting. The
cervix was unchanged. The uterus was non-tender.

Ultrasound examination showed the fetus to be
consistent with 32 weeks gestation. A liver and
spleen ultrasound did not show enlargement of ei-
ther organ. The chest X-ray was also normal. Re-
peat laboratory data showed the WBC count to be
3,200, platelets 90,000, uric acid 5.9, total biliru-
bin 1.2, amylase <30, LDH 18,574, AST 5,498,
and ALT 2,254. Gram stain of the amniotic fluid
was returned as negative for organisms and WBCs.

The differential diagnosis was expanded to include
possible cholangitis. The patient was started on in-
travenous metronidazole for coverage of anaerobic
bacteria. A gastroenterological consultation was ob-
tained. The impression was that the patient had
common bile duct stones with cholangitis, rule out
pancreatitis, rule out hepatitis. IgG TORCH titers
were returned with a positive titer for cytomegalov-
irus. IgM titers were not returned initially. All
bacterial cultures were negative.

The patient remained on continuous fetal moni-
tor. Approximately 30 h after admission, the pa-
tient developed persistent late decelerations. There
were no uterine contractions noted by the patient;
however, contractions were picked up by the fetal
monitor. The patient was treated with 3 doses of
subcutaneous terbutaline but persisted in having
contractions. A cesarean section was planned due to
the persistent late decelerations. A coagulation sur-
vey and CBC were obtained prior to surgery. Plate-
lets were 27,000 and PT and PTT were both mark-
edly elevated. Bleeding time was now 10 min. The
patient was transfused with 2 units of fresh frozen
plasma and 10 units of platelets. An emergency
cesarean section was performed under general anes-
thesia with delivery of a viable female infant weigh-
ing approximately 1,800 g, Apgar 6/8. The pla-
centa showed evidence of retroplacental hemato-
ma consistent with placental abruption.

Postpartally, the PT and PTT remained ele-
vated. Fibrinogen was 177 and platelets 53,000.
Four hours postoperatively, the patient began to
have a large amount of vaginal bleeding. The uter-
ine fundus was firm on examination. Repeat coagu-
lation studies showed prolonged PT and PTT, fi-
brinogen of 90, and platelets of 40,000. The patient
was transfused with 10 units of platelets and 1 unit
of fresh frozen plasma. She became disoriented and
developed labored respirations. Arterial blood gases
showed a pH of 7.27, PCO₂ of 18, po₂ of 89,
bicarbonate of 8, oxygen saturation of 97% with
base excess of 16.3.

The impression at this time was metabolic acido-
sis secondary to sepsis vs. hepatitis. Antibiotics were
continued. The patient was transfused with 8 units
of packed RBCs, 9 units of fresh frozen plasma,
and 10 units of platelets, but continued to bleed
profusely. Twenty-four hours postoperatively, the
patient became unresponsive to pain, and her urine
output dropped to 0. She experienced a grand mal
seizure and her pupils were noted to be fixed and
dilated. Two successive electroencephalograms were
read as flat line. The patient's ventilator support
was removed on December 27, 1991. TORCH
IgM titers were returned only after the patient had
become unresponsive and were found to be positive
for herpes simplex virus (HSV) type I and type II.
A repeat HIV was negative. Epstein-Barr virus
IgM was also negative. The patient was negative
for leptospriosis.

An autopsy was performed and was limited to the
thorax and abdomen at the family's request. Autopsy
findings were consistent with herpetic hep-
atitis with fulminant hemorrhagic hepatitis necro-
sis. Figure 1 demonstrates hepatic necrosis with
herpetic inclusions. Herpetic inclusions were also identified in the endocervical glandular epithelium.

**DISCUSSION**

Fourteen cases of herpetic hepatitis have been reported in the literature. Herpetic hepatitis is a difficult diagnosis to make because of confusion with pregnancy-specific hepatic disorders, such as HELLP syndrome (hemolysis, elevated liver function tests, low platelets) and acute fatty liver of pregnancy. Herpetic hepatitis is extremely rare, with a maternal mortality rate of 43%. The high mortality rate may be due to a defect in the cell-mediated response in the pregnant patient.

There are several distinguishing characteristics of herpetic hepatitis as stated in the literature. These include onset of disease in the 3rd trimester, a prodromal illness, vulvar or oropharyngeal vesicular lesions, primary HSV infection, and anicteric presentation. The patient in this case had the above presentations; however, she had no obvious vesicular lesions. The postmortem examination did show evidence of an endocervical herpetic infection.

Of the 14 patients reported in the literature, 6 of them died. Four patients treated with parenteral acyclovir survived and 2 of the patients treated with the antiviral agent vidarabine also survived; however, 5 of 7 patients who did not receive antiviral therapy died. Parenteral acyclovir has been shown to be efficacious in the treatment of disseminated HSV. Not only has acyclovir improved maternal morbidity rates, but it also has been shown to improve neonatal HSV infection.

Herpetic hepatitis is a difficult diagnosis to make. Disseminated herpes has a high mortality rate in pregnant patients. It is essential to make a diagnosis in order to institute therapy. HSV hepatitis should be included in the differential diagnosis of hepatic dysfunction in the 3rd trimester. The pregnant patient with a primary HSV lesion should be closely watched for any evidence of disseminated disease. Diagnosis can be made by liver biopsy to confirm the presence of herpetic intranuclear inclusion bodies. Once the diagnosis is made, acyclovir can be initiated to significantly reduce maternal mortality.

**REFERENCES**

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