Acute Pancreatitis in a Pregnant Woman with Acute Fatty Liver Dystrophy. A Case Report

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Abstract

Acute fatty liver and acute pancreatitis rarely complicate pregnancy. Acute pancreatitis may appear isolated but when it is subsequent to acute fatty liver of pregnancy the evolution is in many cases fatal. We report the case of a 26-year-old primigravida, at 25 weeks' gestation, who developed acute fatty liver of pregnancy and acute pancreatitis after an acute viral upper respiratory tract infection, with an unfavorable evolution to death. Establishing the diagnosis was very difficult and it was confirmed only at laparotomy.

Key words

Pregnancy - acute viral upper respiratory tract infection - acute fatty liver of pregnancy - acute pancreatitis

Introduction

Acute pancreatitis (AP) represents a rare complication during pregnancy. Most frequently, it is caused by gallstones or alcohol abuse (1). The association with acute fatty liver of pregnancy (AFLP) represents an extremely severe complication, fatal in most cases (2). AP during pregnancy causes serious problems regarding diagnosis and treatment (3).

Case report

A 26-year-old primigravida, at 25 weeks' gestation, was admitted to a first level care unit for: dry coughing, pyrexia, dyspnea, nausea (02.02). The laboratory investigations revealed anemia (Hb=6g/dl, Ht=27%), without any other pathological results. The case was interpreted as: 25 weeks pregnancy in evolution; acute viral upper respiratory tract infection; severe anemia. Antibiotic and symptomatic treatment was initiated, the evolution being favorable. On the 7th day after admission, the patient developed malaise, pyrexia, nuchal rigidity, hyporeflexia but with stable haemodynamics and normal blood pressure. Meningism was suspected and the patient was transferred to a third level Infectious Disease Clinic (09.02) for further investigation and treatment.

The clinical examination at admission revealed a moderately altered general status, pale skin and mucosa, afebrile, mild dyspnea, stable haemodinamics, vesicular murmur with basal right lung crepitations. The pulmonary X-ray showed no pathological findings. The cardiological examination established a small pericardial collection. The laboratory examinations revealed an inflammatory syndrome (ESR=75/100 mm, leucocytes 11,400/mm3 with neutrophyles 87.3%, fibrinogenemia 410 mg/dl, positive C reactive protein), hepatocytolisis (AST=453 U/dl, ALT=131U/dl), total bilirubin 0.43 mg/dl, anemia (Hb=5g/dl, Ht=24%), blood urea nitrogen (BUN) 50.4 mg/dl, creatininemia 2.35 mg/dl, negative markers for hepatitis viruses. No changes at lumbar puncture, urinalysis, pharynx exudate examination. The rheumatoid factor was negative, ASLO < 200 IU. Abdominal ultrasonography showed moderate hepatomegaly and normal aspect of the kidneys, portal vein and spleen. The obstetrical examination revealed a 26 weeks' pregnancy in evolution. The diagnosis was pericardial effusion; hepatorenal syndrome; severe anemia. Antibiotics (in triple association) and also antipyretic and hepatoprotective treatment were administered. The anemia was corrected by erythrocyte transfusion, the patient's status improving. During the following days (12.02), her status deteriorated again with stupor, agitation and worsening of the laboratory studies: total bilirubin 1.36 mg/dl, AST 665 U/dl, ALT 185 U/dl, BUN 114 mg/dl, APPT 31.5", INR 1.32. An AFLP was suspected and the patient was urgently transferred to a third level Clinic of Obstetrics and Gynaecology (13.02).

At admittance, the examination of the patient revealed profoundly altered general status, stupor, pale skin, scleral jaundice, normal blood pressure, normal body temperature, anuria for the last 24 hours. It was interpreted as AFLP,

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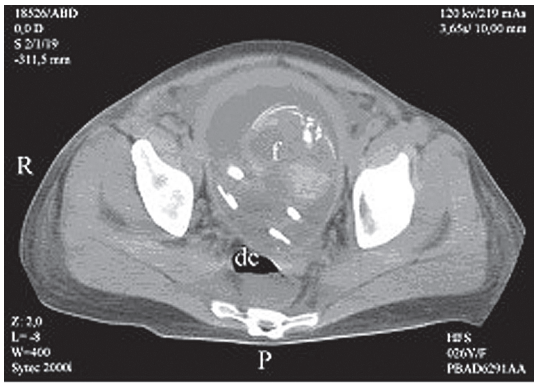

Fig.1 Pregnant uterus (f - fetus, dc - Douglas collection).

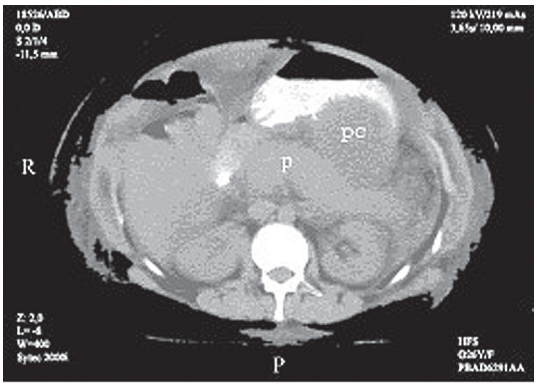

Fig.3 Peripancreatic collection (p - pancreas, pc- peripancreatic collection).

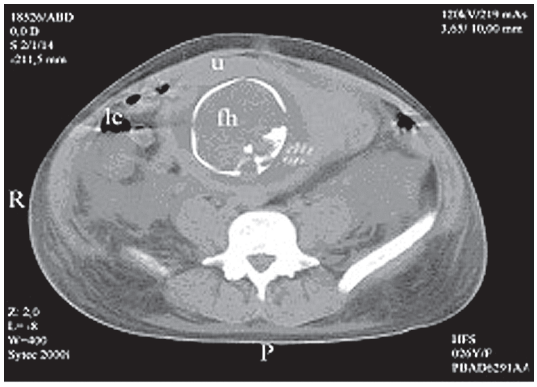

Fig.2 Pregnant uterus (u - uterus,fh - fetal head,lc - liquid collection).

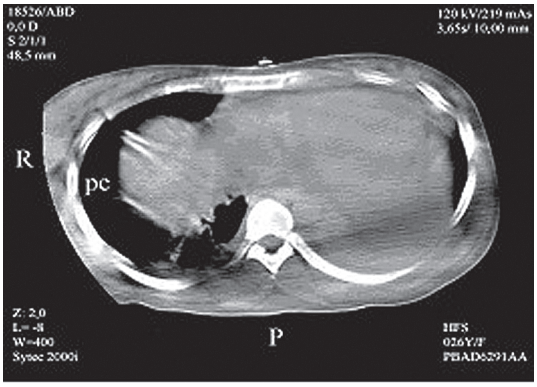

Fig.4 Right pleural effusion (pc - pleural collection).

associated with acute renal failure and anemia. A few hours after admittance, the patient developed vomiting, meteorism, abdominal tenderness, positive Blumberg sign. Laboratory examinations revealed a BUN 268 mg/dl, creatinine 2.6 mg/dl, thrombocytes 264,000/mm3, leucocytes 31,100/mm3, Hb 11.2 g/dl, Ht 35%, hepatocytolisis, metabolic acidosis (pH 7.222, anion gap -17.3 mmol/L), serum amylases 623 U/dl, urinary amylase 886 U/dl. Another abdominal US was performed suspecting acute pancreatitis, and this evidenced stillbirth. The abdominal and thoracic CT revealed pregnant uterus (Figs.1,2), diffuse enlargement and irregular pancreatic outline, peripancreatic fluid collection (Fig.3), ascites (Figs.1,2), thick peritoneum, edema of the intestinal walls, right pleural effusion (Fig.4). After surgical examination which confirmed the acute abdomen, the patient underwent urgent laparotomy (13.02). This revealed hemorrhagic peritoneal fluid, fundus of uterus at the ombilicus level, focal enzymic necrosis of the epiploon, masive edema of the peritoneum, pancreatic edema with thickened capsula and peripancreatic collection, enlargement of the liver, gallbladder distension without stones. A pancreatic axial capsulotomy was performed, then drainage of the retroperitoneal fluid, caesarian section (dead fetus weighting about 800 g), lavage and multiple drainages.

Postoperatively, the status of the patient continued to worsen despite intensive care measures, and cardio-pulmonary arrest, refractory to resuscitation developed. Death was declared at 30 hours after intervention.

The necropsy report confirmed the acute pancreatitis, acute fatty liver dystrophy, pulmonary edema, cerebral hemorrhage.

Discussion

Acute fatty liver of pregnancy occurs in 1/1,000-1/13,000 (4,5) pregnancies and it usually complicates gestation as part of pregnancy induced hypertension or HELLP syndrome (21). In 39% of the cases it appears secondary to a urinary or respiratory infection (2). An infectious trigger was also found in our case. Any other cause has not been found.

Regarding pathophysiology, recent studies suggest that AFLP is caused by a mitochondrial defect. The long chain 3-hydroxyacil-CoA-dehidrogenase deficiency in mitochondria determines long and medium chain fatty acids accumulation into the cell. This defective enzyme is determined by a gene mutation (E47Q) (6) with an incidence of 1:150-1:200 in population. Alternatively, pregnancy may itself affect mitochondrial function. Other hypotheses favor above-normal (for pregnancy) level of estrogens potentiating the effects of an otherwise tolerable hormonal insult to mitochondria in the third trimester.

Clinically, the onset is between the 30th and 38th weeks of gestation. In a few cases, the onset of the disease has been noted in the 2nd trimester, as was in our case. Classically, it presents with malaise, nausea, vomiting, abdominal pain, fever, headaches and pruritus. Often jaundice is noticed only

after delivery. The symptoms of the disease are not specific, appearing in many digestive diseases. The diagnosis was obvious only when complications developed; the patient was admitted to a gynecologic care unit presenting encephalopathy and renal failure. Complications cited in the literature are (7): hepatic encephalopathy (13%), hypoglycemia (55%), renal failure (50%), coagulopathy (96%), disseminated intravascular coagulopathy (55%) and pre-eclampsia (50%). Sepsis leads to significant mortality. The biochemical changes in our patient were represented by raised serum transaminases, elevated serum ammonia, lactic acidosis, uric acid, hyperbilirubin and hypoglycemia. The coagulation times were prolonged. Coagulation disorders, elevated serum transaminases and disseminated intravascular coagulopathy are secondary to septic complications (7). Symptomatic and liver protective treatment was administered to our patient. The use of liver transplantation in AFLP is controversial (9). Pereira *et al* (7) suggested that transplantation should be reserved for those with liver rupture complicated by hepatic necrosis, in the presence of hepatic encephalopathy, and in case of a severe metabolic acidosis, together with worsening coagulopathy. It is uncommon for AFLP to recur in subsequent pregnancies; to date, four cases are reported in the literature (10, 11).

The association of AFLP and AP in pregnancy is a very rare situation. In the last 15 years only a few cases have been reported in the literature. Acute pancreatitis complicates 1/1,000-1/3,000 pregnancies (1,12). Acute pancreatitis is most frequent in women with multiple pregnancies (72%), especially in the second trimester of the pregnancy (1), as in our case. None of the main predisposing conditions of AP in pregnancy (cholelithiasis, hypertryglyceridemia) were found in our patient.

Pathophysiologically, pregnancy creates a series of favorable conditions for the occurrence of AP (3,13):

1. hyperlipidemia, secondary to physiological increase of estrogen levels (14).The level of triglycerides required to induce acute pancreatitis is between 750-1000 mg/dl (15);

2. high blood progesterone level which causes increased lipase and trypsin secretion. It also causes spasms of Oddi's sphincter and hypotonia of pancreatic ducts (16);

3. immunological processes which normally occur during pregnancy represent a risk factor for acute pancreatitis.

Association of AP was not recognized because of the similar symptoms of both entities. It is important to mention the presence of pleural effusion, described in 10% of AP (unknown cause). The laboratory examinations suggestive for AP were the increased serum and urinary amylase levels, and also of the amylase level in the peritoneal fluid. Hyperamylasemia is not specific for AP; it also increases in cholecystitis, bowel obstruction, and ruptured ectopic pregnancy. An elevated amylase level was shown to have a diagnostic sensitivity of 81%, and when adding lipase, a sensitivity of 94% (17). The abdominal ultrasound and computed tomography also suggested AP in our patient.

The criteria for differential diagnosis between several digestive emergencies were evaluated, as shown in Table 1 (20). There have been patients who underwent exploratory laparotomy for establishing the cause of the acute abdomen, as in our case.

Table I Differential diagnosis of biliary tract diseases in pregnancy (20)

	Clinical features	Ultrasonography	Serum transaminase level	Serum bilirubin level	Serum amylase and lipase levels
HELLP, hemolysis, elevated liver enzyme levels, low platelet count syndrome					
Biliary colic	Abdominal pain, nausea, vomiting, no fever	Gallbladder sludge or stones, no biliary ductal dilation, normal gallbladder wall thickening	Normal	Normal	Normal
Acute cholecystitis	Abdominal pain, nausea, vomiting, fever, Murphy's sign	Abnormal gallbladder wall thickening, pericholecystic fluid, sonographic Murphy's sign	Mild elevation	Normal	Normal
Acute cholangitis	Abdominal pain, fever, jaundice, mental status changes	Biliary ductal dilation	Mild elevation	Elevated	Normal
Acute pancreatitis	Abdominal pain, nausea, vomiting, mild fever	Can show biliary sludge or stones	Mild elevation	Mild elevation unless biliary obstruction also present	Elevated
Acute fatty liver of pregnancy	Right upper abdominal quadrant pain, mental status changes, renal failure	Can show fatty infiltration of the liver	500 U/l	<85 m M	Normal
HELLP syndrome	Abdominal pain, hypertension, peripheral edema, thrombocytopenia	Can be normal	500 U/l	<85 m M	Normal

Medical management included intravenous fluids, nasogastric suctioning, total parenteral nutrition, use of analgetics and and antibiotics (17). Actually, the recommended therapy in biliary pancreatitis is endoscopic retrograde cholangio-pancreatography (ERCP) followed by endoscopic sphincterotomy. This technique has good results with rapid resolution of symptoms, it is less invasive than surgery and has a low rate of complications. The reported efficacy is 95% (12,18,19).

In a series of 12 cases of AP in pregnant women with AFLP, Moldenhauser *et al* (2) found the following complications: encephalopathy (50%), respiratory failure (17%) and acute renal failure (33%). Elevated serum lipase were found in 91%. Imaging techniques (ultrasound and computed tomography) were accurate in only 7 cases (58%).

Pancreatitis in pregnancy is associated with a high maternal death rate and fetal loss rate. These rates are declining in case of earlier diagnosis of the disease (17). The pathogenesis of this association is vague, although AP typically appears after severe AFLP and renal failure.

In conclusion, the particularities in our patient were: the onset of AFLP at an unusual gestational age, the acute viral infection being the only recognizable trigger factor of AFLP, and the diagnostic difficulties of the associated AP, which imposed an exploratory laparotomy.

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