Case Report
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Hypertriglyceridemia-induced acute pancreatitis in pregnancy causing maternal death

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Acute pancreatitis in pregnancy is rare and occurs in approximately 3 in 10,000 pregnancies. It rarely complicates pregnancy, and can occur during any trimester, however over half (52%) of cases occur during the third trimester and during the post-partum period. Gallstones are the most common cause of acute pancreatitis. On the other hand, acute pancreatitis caused by hypertriglyceridemia due to increase of estrogen during the gestational period is very unusual, but complication carries a higher risk of morbidity and mortality for both the mother and the fetus. We experienced a case of pregnant woman who died of acute exacerbation of hypertriglyceridemia-induced acute pancreatitis at 23 weeks of gestation. We report on progress and management of this case along with literature reviews.

Keywords: Acute pancreatitis; Hypertriglyceridemia; Maternal death; Pregnancy

Introduction

Acute pancreatitis occurring in pregnancy is a rare but dangerous disease [1]. The prevalence and mortality of acute pancreatitis in pregnant women and fetuses has decreased significantly from 21% in the past to 0% to 3% at present, however, without early diagnosis and adequate treatment the disease can induce various severe complications including shock, sepsis, and premature delivery in pregnant women and fetuses and may result in death [2,3]. Hypertriglyceridemia-induced acute pancreatitis in pregnancy usually occurs during the mid-trimester and thereafter, and it is known to be associated with an increase in estrogen related to lipid metabolism during pregnancy [4,5].

Case report

The patient was a 28-year-old woman with gravid 1, para 0. At 22 weeks and 6 days of gestation, she came to the emergency room of our hospital for severe epigastric pain which had occurred during the daytime of the same day and did not complain of nausea and vomiting. The patient had conceived monozygotic twins naturally and was under regular prenatal care at a private clinic.

The patient's weight was 70.5 kg, height was 163.1 cm, vital signs were normal. The patient had no specific past history and had not taken any drug recently. But her mother was taking medication under the diagnosis of hyperlipidemia.

There were moderate tenderness and rebound tenderness in upper abdomen. No cervical dilatation and effacement were observed during the pelvic examination. In fetus 1, heart sound was 152/min and presentation was cephalic, and in fetus 2, heart sound was 158/min and presentation was breech. There were no rupture of membranes and uterine contraction. So we ruled out the possibility of placental abruption and uterine rupture that could happen in second half

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Table 1. Laboratory test in case on emergency room

Variable	Result	Normal range
Triglyceride	10,392	28–200 mg/dL
Cholesterol	1,006	120–220 mg/dL
HDL-C	18	35–88 mg/dL
LDL-C	398	0–130 mg/dL
Amylase	337	30–118 U/L
Lipase	913	6–51 U/L
AST	27	10–40 U/L
ALT	35	5–40 U/L
Creatinine	0.4	0.5–1.2 mg/dL
Sodium	114	135–145 mEq/L
Potassium	3.7	3.5–5.5 mEq/L
Chloride	85	95–110 mEq/L
Calcium	3.2	8.2–10.8 mg/dL
Albumin	3.5	3.5–5.2 g/dL
Hemoglobin	10.9	11.5–15.5 g/dL
Leucocyte	17,850	3.7–9.5 $\times 10^3/mm^3$
Platelet	300,000	150–400 $\times 10^3/mm^3$
Glucose	207	70–100 mg/dL

HDL-C, high-density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; AST, aspartate aminotransferase; ALT, alanine amiontransferase.

of pregnancy.

As the patient showed lipemic in blood on emergency room, tests were performed after high-speed centrifuging. Blood tests; showed total cholesterol of 1,006 mg/dL, triglyceride 10,392 mg/dL, low-density lipoprotein 398 mg/dL, amylase 337 U/L, lipase 913 U/L, and blood glucose 207 mg/dL. The other results are normal (Table 1). The results of urine test showed glucose 4+ and protein 3+. As the pancreas was not seen clearly on abdominal ultrasonography, it was difficult to differentiate acute pancreatitis. In addition, gallstone and cholecystitis were not observed, and there was no specific finding except minimal fatty liver. Based on test results, we excluded the pregnancy-related liver disease, acute fatty liver and preeclampsia. We suspected acute pancreatitis and hospitalized the patient.

After admission, the patient complained of severe pain that made movement hardly possible, thus we started conservative treatments including intravenous fluid infusion, fasting, antibiotic, pain control, injection of insulin, and oxygenation. Fetal heart sounds were 150/min and 140/min.

Later on, the patient suddenly complained of severe pain and dyspnea. Her body temperature increased to 38.2°C and began to lose consciousness. As respiratory rate was 60/min and tachypnea continued, we studied her chest X-ray but it was not considered a respiratory problem. Results of arterial blood gas analysis were pH 6.984, PCO_2 49.1 mmHg, PO_2 42.1 mmHg, HCO_3 11.8 mmol/L, SO_2 51.9%, showing that metabolic acidosis was exacerbated. As the patient's vital signs were not measured and then cardiac arrest occurred, intravenous infusion of epinephrine and dobutamine was administered and then pulse was measured, but a convulsion soon followed and anticonvulsant drug $MgSO_4$ was administered.

Subsequently, the return of spontaneous circulation was confirmed by blood pressure 70/40 mmHg, pulse rate 134/min and respiratory rate to 25/min, but her consciousness was stupor. Heart sound was not heard for either of the two fetuses, and intrauterine fetal death was confirmed. The results of blood test at that time; showed that glucose had increased significantly to 474 mg/dL, serum amylase to 1,833 U/L and lipase to 1,863 U/L. Accordingly, it was believed to be hypertriglyceridemia-induced acute pancreatitis, in which pancreatic cells necrotized and, as a result, gestational diabetes occurred and exacerbated diabetic ketoacidosis and metabolic acidosis induced cardiac arrest. Extracorporeal membrane oxygenation was going to be applied, but was not effective due to high triglyceride level in the patient's blood. As a result, blood pressure could not be maintained and the patient died within 24 hours of admission.

Discussion

Acute pancreatitis is a disease with severe complications and high mortality. The most representative symptom of acute pancreatitis is severe epigastric pain, nausea, vomiting, and there can also be fever, tachycardia, hypotension, shock, etc.

It shows various patterns from interstitial pancreatitis with minimal symptoms that are healed spontaneously to necrotizing pancreatitis accompanied by severe systemic necrosis. To most common cause of acute pancreatitis is gallstone, followed by alcohol abuse [4]. To date, four genetic factors, which increase susceptibility to acute pancreatitis and control the severity of pancreatic damage, have been identified. They are cationic trypsinogen mutation (PRSS1m, R122Hm, and N291), pancreatic secretory trypsin inhibitor (SPINK1), CFTR,

and monocyte chemotactic protein (MCP-1) [6].

Test results may show the rise of serum amylase and lipase, and possibly the rise of leukocytosis, hypocalcemia, hyperbilirubinemia, low-density lipoprotein, etc. Imaging examinations such as ultrasonography and non-contrast magnetic resonance cholangiopancreatography are helpful to diagnosis but computed tomography is contraindicated in pregnant patients [7].

Acute pancreatitis can be diagnosed if the symptoms meet at least two of three criteria, as follows: first, severe acute epigastric pain; second, serum amylase or lipase level over 3 times higher than the normal level; and third, manifestation of acute pancreatitis in imaging examinations [8]. Diagnostic criteria for the disease are the same for pregnant women. In this case the patient suffered from severe epigastric pain and the serum amylase and lipase levels increased by over 3 times, thus it was considered acute pancreatitis. For imaging examination, the pancreas could not be identified on ultrasonography, and computed tomography was not performed because the patient was a pregnant woman carrying twins and the symptoms were rapidly exacerbated.

The incidence of acute pancreatitis in pregnancy is as low as about 3:10,000, however it requires rapid diagnosis and treatment because the outcome can be grave [1]. As in non-pregnant cases, gallstone is the most frequent cause in pregnant women, followed by hypertriglyceridemia, hyperthyroidism. Rarely, autoimmune pancreatitis in pregnancy may appear in the form of acute pancreatitis [5]. Approximately 1% to 7% of cases are caused by hypertriglyceridemia, and the incidence of hypertriglyceridemia-induced acute pancreatitis is higher in pregnant women than in non-pregnant ones [9].

Hypertriglyceridemia can occur due to primary causes related to genetic or family history, and secondary causes such as obesity, diabetes, hypothyroidism, pregnancy, alcohol, and the intake of substance such as estrogen.

There are two hypotheses concerning the onset of acute pancreatitis caused by hypertriglyceridemia. One is that increased chylomicron and very low-density lipoprotein raise the viscosity of blood, which induces ischemia in pancreatic capillaries, resulting in inflammation. The other is that increased triglyceride level causes degradation and production of free fatty acid, which damages platelet and vascular endothelium, resulting in inflammation. It is known that through these mechanisms inflammatory mediators exacerbate pancreatic ischemia and acidosis, consequently resulting in acute pancreatitis [10,11].

During pregnancy, synthesis of lipoprotein increases in connection with the rise of estrogen concentration, and increased insulin resistance reduces the activity of lipoprotein lipase and, as a result, the concentration of blood triglyceride increases to approximately 2 to 3 times higher than the normal level. In particular, because insulin resistance increases in the 3rd trimester, hypertriglyceridemia may develop more easily in the 3rd trimester and, accordingly, the incidence of acute pancreatitis is higher.

Early diagnosis and treatment are important. Oral lipid-lowering agent is not used due to the risk of fetal anomaly, and insulin and heparin are used instead. Insulin accelerates degradation of chylomicron, and heparin accelerates secretion of endothelial lipase and, by doing so, lowers blood triglyceride [5]. Pregnancy termination should be considered in cases where the conditions of both a pregnant woman and the fetus worsen.

In Korea, 3 cases of acute pancreatitis in pregnant women were reported during the period from 2008 to 2013. All cases were hypertriglyceridemia-induced acute pancreatitis. One of them maintained pregnancy as the condition was improved, but the other two had premature delivery and one of the neonates died of sepsis. None of the pregnant women died [12-14].

This case demonstrated that acute pancreatitis during pregnancy became worse than that of non-pregnancy. When we meet a 2nd or 3rd trimester pregnant patient who complains of abdominal pain, a greater effort is needed in order to differentiate diseases that could happen in pregnancy. There are many situations like labor, placental abruption, uterine rupture, pregnancy-related liver disease, acute fatty liver, preeclampsia, etc. The approaches to the patient include checking on gestational age, physiologic alterations related to pregnancy, status of fetus, and finding causes of abdominal pain. History taking including family history is important, especially if the possibility of acute pancreatitis is higher. Family history such as dyslipidemia is a risk factor of acute pancreatitis. Early diagnosis and treatment can result in a good prognosis, so active management is necessary. Physical examination, pelvic examination, laboratory test, imaging studies such as ultrasonography and non-contrast magnetic resonance cholangiopancreatography is helpful to differentiate disease and diagnosis with acute pancreatitis in pregnancy.

Lastly, multidisciplinary team approach is needed. Obstetricians, physicians, and radiologists should provide expertise in their area and the best possible medical care for the patient.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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