Severe Hypertriglyceridemia-Induced Pancreatitis during Pregnancy

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Chylomicronemia syndrome is a rare disorder characterized by the presence of chylomicrons in the fasting state. An acute and potentially life-threatening complication of chylomicronemia syndrome is severe acute pancreatitis. We report a case of a 24-year-old primigravida with severe hypertriglyceridemia-induced pancreatitis. We reviewed the clinical course and treatment of hypertriglyceridemia-induced pancreatitis. She was admitted in the 37th week of gestation with severe abdominal pain, which was radiating to the back, and having uterine contractions. Cesarean delivery was performed under spinal anesthesia, and a healthy male infant was born. Intraoperative findings included milky peritoneal fluid collection. Elevated pancreatic enzymes with significant hypertriglyceridemia (10,092 mg/dL) suggesting acute pancreatitis were also found on chemical analysis. The diagnosis of acute pancreatitis was confirmed by computed tomography scan. Treatment with continuous intravenous insulin—glucose, cessation of oral intake, and nasogastric decompression—dramatically decreased the triglyceride levels to 608 mg/dL within five days. She was discharged as symptom free with strict dietary intervention after 10 days. Intravenous insulin is a low-cost and effective alternative treatment in hypertriglyceridemia-induced pancreatitis during pregnancy. To our knowledge, such a high triglyceride level has not previously been reported in pregnancy.

Key words: pancreatitis ■ pregnancy ■ hypertriglyceridemia ■ women's health

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INTRODUCTION

Lipoprotein lipase (LPL) deficiency, or apoprotein C-II deficiency, are rare disorders of lipid metabolism that cause chylomicronemia syndrome. These abnormalities cause severe hypertriglyceridemia by blocking the clearance of triglyceride-rich lipoproteins from the plasma.[1,2] Massive accumulations of these proteins in the plasma can be accompanied by severe clinical manifestations, including acute pancreatitis, which endangers both the mother and fetus.[3,4] Lipid profile changes in normal pregnancy are characterized by a marked elevation of the total plasma cholesterol and triglyceride levels. Plasma lipid levels usually return to normal levels after term.[5] Pregnancy further exacerbates preexisting lipid abnormalities in chylomicronemia syndrome.[1]

We report a patient with chylomicronemia syndrome. She had very severe hypertriglyceridemia that caused acute pancreatitis during pregnancy and was successfully treated with continuous intravenous insulin-glucose infusion and cessation of oral intake.

CASE REPORT

The patient was admitted in the 37th week of gestation with severe flank abdominal pain, vomiting, fever, general malaise and was found to have uterine contractions. She had no history of gestational diabetes mellitus, alcohol use, oral contraception pills, gallstones, pancreatitis or drug intake. The patient's height and weight were 165 cm and 60 kg, respectively. Blood pressure, pulse and temperature were 120/70 mmHg, 112 beats/min and 38.8°C, respectively. She had epigastric tenderness and minimal hepatomegaly. Fetal heartbeats were present and uterine contractions were noted. Due to signs of fetal distress and advancing preterm labor, a Cesarean delivery was performed under spinal anesthesia, and the patient delivered a healthy 3,230-g male infant. During the operation, an intraabdominal peritoneal fluid sample had a lipemic, milky-pink appearance with triglyceride levels of 1,344 mg/dl. After deliv-

ery, the abdominal pain was not resolved, and acute pancreatitis was suspected.

Initial laboratory evaluation revealed a hematocrit of 37.6% and white blood cell count of 16,400 cells/μL. Lipid profile showed that the triglyceride concentration was 10,092 mg/dL and total cholesterol was 1,159 mg/dL. Investigation of pancreatic enzymes revealed high levels of serum amylase 367 U/L (normal range 30–110 U/L) and pancreatic lipase 797 U/L (normal range 13–60 U/L). Liver, renal and thyroid function tests were normal (Table 1). The patient's plasma was visibly lipemic, demonstrating chylomicrons (type-I pattern) with a cream-like layer on the top and very-low-density lipoprotein cholesterol (VLDL-C) (type-IV pattern) with a turbid plasma infranatant after overnight refrigeration. The patient had an edematous pancreatitis demonstrated by computed tomography scan with no evidence of cholelithiasis. A diagnosis of acute pancreatitis secondary to hypertriglyceridemia was considered. The patient's antenatal history was unremarkable.

Cessation of oral intake and nasogastric decompression together with continuous intravenous glucose-insulin were used. The white blood cell count, erythrocyte sedimentation rate and C-reactive protein decreased in follow-up as did serum amylase and lipase levels. Treatment effectively improved the patient's clinical condition, and triglyceride levels decreased to 608 mg/dL within five days. On the fifth day of her hospitalization, the patient complained of recurrent abdominal pain. Abdominal ultrasonography evaluation revealed a 12-x-8-cm localized fluid collection close to the pancreatic tail. Percutaneous drainage was successfully instituted. Medium-chain triglyceride nutritional support with a low-fat diet as rigid as possible was started on the seventh day of hospitalization. The patient was discharged as symptom free with a triglyceride level of 481 mg/dL after 10 days, and at follow-up at 30 days her triglyceride level was normal (143 mg/dL). The plasma lipid changes, serum amylase and lipase levels during the hospital stay and 30 days after discharge are shown in Table 2.

DISCUSSION

Chylomicronemia syndrome is a rare disorder characterized by the presence of chylomicrons in the fasting state causing a milky appearance of plasma, eruptive xanthomas and hepatosplenomegaly.[1] An acute and potentially life-threatening complication of chylomicronemia syndrome is severe acute pancreatitis. The underlying defects are abnormal lipid metabolisms, such as deficiencies of LPL or apoprotein C-II.[2] Moreover, the clinical picture of disease is not obvious until secondary factors exacerbate the underlying abnormality, e.g., pregnancy, hypothyroidism, diabetes mellitus, estrogen therapy or alcohol ingestion.[6]

Lipid profile changes in normal pregnancy are characterized by marked elevations of total plasma cholesterol and triglyceride levels, occurring predominantly through increased liver synthesis of triglyceride and VLDL-C in response to elevated estrogen levels.[7] Reduction in LPL activity due to the downregulation of LPL gene expression by

Table 1. Patient's laboratory data on admission

	Result	Normal Ranges		Result	Normal Ranges
Triglyceride	10,092	50–160 mg/dL	Creatinine	0.24	0.5–1.3 mg/dL
VLDL	2,018	10–32 mg/dL	Na++	122	135–146 mmol/L
LDL	174	60–130 mg/dL	K+	2.7	3.5–5.2 mmol/L
Amylase	367	30–110 U/L	Leukocyte count	16,400	4.5–11 cells/μL
Lipase	797	13–60 U/L	Hemoglobin	12.9	12–16 g/dL
AST	95	0–40 U/L	TSH	2.0	0.4–4.5 IU/mL
ALT	81	0–41 U/L	Urine amylase	5,466	30–110 IU/L
LDH	609	240–480 U/L	CRP	111	0–10 mg/dL
			Sedimentation rate	68	0–20 mm/h

LDL: Low-density lipoprotein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; TSH: thyroid stimulating hormone; CRP: C reactive protein

Table 2. Serum lipid and pancreatic enzyme levels during hospital stay and 30 days after discharge

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 10	Day 40	Normal Range
Triglyceride (mg/dL)	10092	7412	3644	1793	608	481	143	50–160
Total cholesterol (mg/dL)	1159	987	614	482	380	291	274	130–230
Amylase (U/L)	367	231	155	126	76	65	23	30–110
Lipase (U/L)	797	330	289	251	170	96	41	13–60

estrogen during pregnancy decreases the clearance of VLDL-C.[8,9] These changes further exacerbate pre-existing lipid abnormalities. Such exacerbations can be associated with severe elevations of triglycerides, predisposing pregnant woman at risk for pancreatitis and carry an increased risk of mortality both for the mother and the fetus.[10]

Hypertriglyceridemia-induced pancreatitis during pregnancy has been reported previously.[11,12] The clinical course and treatment of pancreatitis due to hypertriglyceridemia is similar to that of pancreatitis of other causes. Family history of lipid abnormalities should be obtained, and an attempt to identify secondary causes should be made. A serum triglyceride level >1,000 mg/dL is an identifiable risk factor. Reduction of triglyceride levels to well below 1,000 mg/dL effectively prevents further episodes of pancreatitis.[13,14] The main treatment modality of hypertriglyceridemia-induced pancreatitis during pregnancy includes dietary restriction of fat, intravenous heparin and insulin together with glucose infusion, lipid-lowering medications (mainly fibric acid derivatives).[15] The activity of LPL is crucial for clearance of triglycerides from the plasma. Heparin and insulin stimulate LPL activity.[8,9] Plasmapheresis, lipid apheresis and extracorporeal lipid elimination could be therapeutic alternatives.[12] Previous reports suggested an increased maternal mortality rate as high as 20% in pregnancies complicated by acute pancreatitis secondary to hyperlipidemia. The commonest reasons for maternal and fetal mortality are acute pancreatitis itself and, very rarely, acute pancreatitis is associated with preeclampsia-eclampsia or HELLP syndrome.[10,16]

Our patient presented with triglyceridemia-induced pancreatitis in the 37th week of pregnancy. There was no previous history of lipid abnormality, diabetes mellitus or alcohol ingestion. Pregnancy itself was a triggering factor for the aggravation of hypertriglyceridemia and associated pancreatitis. Plasma triglyceride level was 10,092 mg/dL at admission. As far as we know, such a high level of triglyceride level has not been previously reported during pregnancy. A treatment strategy consisting of cessation of oral intake, nasogastric decompression and continuous intravenous glucose-insulin infusion resulted in complete recovery. The patient's clinical condition subsequently improved, and the patient was discharged from hospital on day 10 with a triglyceride level of 481 mg/dL.

Hypertriglyceridemia is a known cause of acute pancreatitis. Hypertriglyceridemia may be primary, such as in chylomicronemia syndrome, or secondary to alcohol abuse, diabetes mellitus, estrogen use as well as pregnancy. The incidence of pancreatitis during pregnancy is low, but related morbidity and mortality is high. Early and prompt treatment is the key factor to successful outcome.

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