Acute Pancreatitis Secondary to Hypertriglyceridemia during Pregnancy

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Abstract

Introduction Hypertriglyceridemia (HTG) (triglycerides > 1,000 mg/dL [11.3 mmol/L]) has been associated with a high risk of developing acute pancreatitis (AP) in pregnant women, but this condition is rare. We present the case of a pregnant Saudi with AP secondary to HTG.

Case Report A 27-year-old Saudi female presented at 30 weeks' gestational age with abdominal pain, nausea, and vomiting of 4 days' duration. AP was diagnosed based on clinical presentation, high lipase, and abdominal ultrasound findings. Her triglyceride level was 58 mmol/L. Fenofibrate and intravenous regular insulin infusion with dextrose were started, which decreased triglycerides by the third day from 58.8 to 29 mmol/L (50% reduction) with a further reduction to 11 mmol/L (81%) by day 7 of her admission. Labor was induced at 37 weeks of gestation, and she delivered a healthy neonate.

Conclusion We report successful treatment of AP in pregnancy with intravenous insulin and fenofibrate. Several case reports have discussed the therapeutic option of AP induced by HTG in pregnancy. Lipid-lowering agents are category C in pregnancy. However, few case reports indicate their safety. Insulin, heparin, and apheresis have also been used during pregnancy without any complications.

Keywords
- acute pancreatitis
- hypertriglyceridemia
- pregnancy

Introduction

Acute pancreatitis (AP) is distributed across a range of gestational ages, with significantly more cases presenting later in gestation: 24% in the first trimester, 33% in the second trimester, and 43% in the third trimester. It is associated with preterm delivery and other adverse mother and fetal outcomes.[1] Circulating triglyceride (TG) levels increased two- to fourfold in pregnancy, principally in the third trimester, due to increased TG-rich lipoprotein production and decreased lipoprotein lipase (LPL) activity.[2] AP is conventionally thought to be triggered when TG levels exceed 1,000 mg/dL (11.3 mmol/L).[3,4]

There are reports of fetal death secondary to AP in pregnancy due to hypertriglyceridemia (HTG).[5] Maternal mortality has also been reported as a complication.[6]

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The presentation of AP secondary to HTG is similar to that of AP secondary to other causes, with the primary symptom of abdominal pain, nausea, and vomiting. The International Association of Pancreatology and American Pancreatic Association recommended that two out of three of the following criteria must be met for the diagnosis of AP. These criteria are clinical (upper abdominal pain), laboratory (serum amylase or lipase more than three upper limits of normal), and suggestive imaging.[7,8] Here, we present a case of a pregnant Saudi admitted for AP secondary to HTG.

Case Report

A 27-year-old Saudi female is known to have hyperlipidemia on atorvastatin, which was stopped 3 years before her first uneventful pregnancy. A first-trimester abortion followed her first pregnancy with no records at our institution. She presented to our emergency department at 30 weeks' gestation, complaining of left upper quadrant and epigastric pain for 4 days associated with nausea and vomiting. There were no gallbladder stones or alcohol consumption histories, and the systemic review was unremarkable. She was not using any medication before admission and did not use oral contraceptive pills in the last 4 years. She has a family history of hyperlipidemia (paternal). There was no family history suggestive of AP.

On physical examination, she was conscious, alert, and oriented to time, person, and place. Her pulse rate was 108, oxygen saturation was 97% on room air, blood pressure was 132/78, temperature was 36.9°C, respiratory rate was 22, body mass index was 30, and her glucose level was 5 mmol/L. She had moderate tenderness over the epigastric area, no rebound tenderness, and no organomegaly. There was no eruptive xanthoma or xanthelasmas. The rest of her examinations were unremarkable. Laboratory tests on admission are shown in ►**Table 1**. Abdominal ultrasound showed no gallstones; the pancreas appeared heterogeneous, hypoechoic, and bulky, with minimal peripancreatic fluid suggestive of early pancreatitis changes.

There were no signs of appendicitis, and obstetric ultrasound showed a viable single fetus. The patient was admitted under obstetric care as a case of AP secondary to HTG. Intravenous hydration was started with normal saline and potassium replacement. Antiemetic and analgesics were initiated. Oral fenofibrate 200 mg once daily was administered. Despite conventional treatment, the patient's symptoms persisted, and she had an Acute Physiology and Chronic Health Evaluation II score of 11. She was transferred to the medical intensive care unit on the second day. Insulin infusion was started at a rate of 0.1 U/kg/hour with dextrose 5% and normal saline after adequate potassium replacement. Insulin infusion was titrated based on blood glucose and monitored every hour. The lipid profile was monitored daily. Triglycerides went down by 50% in the first 3 days after the above infusion (58.8–29 mmol/L) and dropped by 81% by the seventh day to 11 mmol/L (►**Table 2**).

Regular insulin infusion was stopped after triglycerides dropped below 7 mmol/L (day 12). Her symptoms improved, and she was transferred to the general ward. Total hospital stay was 48 days on a restricted fat diet, fenofibrate, and insulin infusion with dextrose based on TG level target below 7 mmol/L. She had a total of 14 days of insulin infusion overall. She had an uncomplicated vaginal delivery with

Table 1 Patient's laboratory data on admission

Parameters	Patient's results	Reference values
White blood cell count	12	4–11 × 10^9
Hemoglobin	93	120–160
Hematocrit	0.27	0.360–0.540
Platelets	303	150–400 × 10^9
Aspartate aminotransferase (u/L)	7	5–34
Alanine aminotransferase (u/L)	5	5–55
Total bilirubin (μmol/L)	5.1	3.4–20.5
Lactic acid (mmol/l)	2.6	0.5–2.20
Thyroid-stimulating hormone (mIU/L)	1.05	0.35–4.94
Sodium (mmol/L)	130	136–145
Potassium (mmol/L)	2.6	3.5–5.1
Urea (mmol/L)	1.3	2.5–6.7
Creatinine (μmol/L)	45	50–98
Amylase (u/L)	93	25–125
Urine amylase	> 3,010	24–400 U/L
Lipase (u/L)	515	8–78
Triglycerides (mmol/L)	58	< 1.7
Total cholesterol (mmol/L)	24.9	< 5.18
LDL-cholesterol (mmol/L)	0.58	< 2.6
HDL-cholesterol (mmol/L)	0.29	> 1.55

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2 Lipid profile series after starting insulin infusion

Lipid profile	Baseline	Day 3	Day 7	Day 9	Day 12
Triglycerides (mmol/L)	58.8	29	11	8	7
Total cholesterol (mmol/L)	24.9	23	13	11	9
LDL-cholesterol (mmol/L)	1.68	2.7	4.55	5.38	4.8
HDL-cholesterol (mmol/L)	0.27	0.38	0.60	0.62	0.65

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein.

labor induction at 37 weeks. She did not require any insulin infusion after delivery as her TG level remained between 4 and 5 mmol/L. Her TG level was 1.47 mmol/L at discharge.

Discussion

The pathophysiological mechanism of AP secondary to HTG has not yet been fully elucidated. A popular theory suggests that markedly TG-rich environments promote lipolysis by pancreatic lipase. This results in increased liberation of high concentrations of free fatty acids, which, in turn, inflict damage to the vascular endothelium and the pancreatic acinar cells.[9] In vitro studies also suggested a role for fatty acid-induced mitochondrial toxicity in the pathogenesis of HTG-induced pancreatitis.[10]

Lipid-lowering agents such as fenofibrate and gemfibrozil are category C during pregnancy. However, some case reports reported that these medications were used in pregnancy without complications. Doses used were in the form of fenofibrate 145 to 200 mg once daily or gemfibrozil 600 mg twice daily.[11,12] These agents reduce plasma TG levels by 50% and raise HDL cholesterol by 20%. They also decrease very-low-density lipoprotein secretion and increase lipolysis of plasma triglycerides.[12] LPL is an enzyme produced by capillary endothelial cells of muscles and adipose tissues, which hydrolyzes triglycerides to glycerol and fatty acids.[13] The activity of LPL is crucial for the clearance of triglycerides from the plasma. Heparin and insulin stimulate LPL activity.[14]

Neutral protamine Hagedorn insulin has been reported to decrease TG from 3,616 to 1,246 mg/dL (65%) with a single dose of 10 units (0.15 U/kg).[15] Intravenous heparin was reported to be safe in several case reports at a dose of 10,000 to 15,000 U per day to decrease TG by 80 to 90% in 24 to 48 hours.[16] Apheresis was reported to decrease TG, with many case reports suggesting its safety in pregnancy.[17] One study found that two consecutive plasma exchanges led to a remarkable reduction in TG levels by 73 and 82%, respectively.[18]

Conclusion

AP in pregnancy carries considerable risks of preterm delivery, fetal loss, and maternal mortality. TG-lowering agents, heparin, insulin, and apheresis appear to be effective therapies in managing HTG-induced AP.[11] Their exact mechanism of action, effects, and safety need to be addressed more in pregnancy. No clinical guidelines for HTG-induced AP exist to date. There is a great need to establish these guidelines to properly guide health care practitioners in managing this serious disease.

Consent

The patient consented prior to reporting the case.

Authors' Contributions

All named authors contributed to the conduct of the work, drafting, and finalization of the manuscript and approved its final version.

Compliance with Ethical Principles

No prior ethical approval is required for single case reports or small case series.

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Conflict of Interest

None declared.

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