Presentation and management of acute hypertriglyceridemic pancreatitis in pregnancy: A case report

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Abstract

Pancreatitis related to hypertriglyceridemia can occasionally occur during pregnancy, particularly if there are underlying genetic abnormalities in lipid metabolism. We report the case of a 27-year-old female with hypertriglyceridemic pancreatitis in pregnancy that was treated initially with lipid lowering medications, followed by plasma exchange for persistently elevated triglyceride levels. Despite multiple interventions, she developed recurrent pancreatitis and simultaneously had a preterm birth. In this case report, we highlight the various therapies and the use of plasmapheresis in secondary prevention of hypertriglyceridemic pancreatitis in pregnancy.

Keywords

Pregnancy, pancreatitis, hypertriglyceridemia, plasmapheresis, hyperlipidemia

Introduction

Pancreatitis is a potential complication of hypertriglyceridemia when the serum triglyceride (TG) level exceeds 11.3 mmol/L.¹ Serum TG concentrations can increase 2- to 4-fold during pregnancy, usually peaking in the third trimester.¹ Despite this fact, hypertriglyceridemic pancreatitis in pregnancy almost solely occurs in women with underlying genetic abnormalities in lipid metabolism. At present, there are no guidelines for the management of hypertriglyceridemic pancreatitis in pregnancy, but plasmapheresis has been increasingly reported.^{2–7} We report the management of recurrent hypertriglyceridemic pancreatitis in a pregnant female with familial hypertriglyceridemia.

Case report

A 27-year-old gravida 1 para 0 of Asian descent at 23 weeks' gestational age (GA) presented with severe epigastric pain, vomiting and decreased fetal movements. Her medical history was significant for familial hypertriglyceridemia previously treated with rosuvastatin, and she denied any alcohol use. There was no known family history of hereditary lipid disorders. Prior to her presentation the pregnancy had been uneventful and she was not on any regular medications. At triage, her heart rate was 118 beats per minute, blood pressure 109/61 mmHg, respiration rate 24 breaths per minute and oxygen saturation 96% on 2 L per minute of supplemental oxygen. Her weight was 57.3 kg with body mass index 21. She did not exhibit any stigmata of hyperlipidemia. Abnormal laboratory findings included a white blood cell count of $21.5 \times 10^9/L$ (normal range $4\text{--}12 \times 10^9/L$), lipase of 515 U/L (0–60 U/L) and serum TG level of 30.6 mmol/L (0.60–2.30 mmol/L); calcium was normal. Total cholesterol was 5.02 mmol/L, *high-density lipoprotein* (HDL) 0.36 mmol/L, total cholesterol to HDL ratio 13.9. Abdominal ultrasound revealed pancreatic inflammation with no signs of gallstones or biliary duct dilation.

She was treated with an infusion of insulin regular starting at 0.1 units per kilogram per hour with a concomitant infusion of dextrose 5% in water. Her insulin infusion was titrated to maintain the blood glucose between 4 and 6 mmol/L requiring insulin rates between 0.1 and 0.3 U/kg/h. This reduced her TG level to 5.7 mmol/L by day five. By discharge at 25 weeks' GA she was asymptomatic with a TG level of 7.0 mmol/L, and was prescribed fenofibrate 200 mg once daily, omega-3 fatty acids 3 g once daily, and a diet low in fat (<30% of daily calorie intake) and simple carbohydrates (<40 g/day), and encouraged to consume complex rather than simple carbohydrates.

Three weeks after discharge, our patient's TG level had increased to 16 mmol/L. However, as the patient had also been recently diagnosed with gestational diabetes (GDM) at 28 weeks' GA (75 g oral glucose tolerance test, plasma glucose was 9.2 mmol/L at 2 h), it was thought that dietary management of her blood glucose might improve her TG level and no changes to her medications were made. At 29 weeks' GA, she was still asymptomatic, but her TG level had risen further to 22.2 mmol/L despite having optimal glycemic control. She was admitted for prophylactic management with an insulin infusion, but insulin was not considered a viable outpatient option due to persistent hypoglycemia even with low-dose subcutaneous basal insulin (glargine 3 units once daily), requiring ongoing 10% dextrose in water infusions.

After consulting with nephrology, she underwent plasmapheresis at 30 weeks' GA, which she tolerated well. Two liters of 5% albumin was used as the 1:1 replacement fluid over 2 h. Her TG level dropped from 18 mmol/L pre-treatment to 8.4 mmol/L the following day, and she was discharged with intensive outpatient monitoring. Four days following discharge, her TG level rose to 21.8 mmol/L. She had weekly plasmapheresis for the next two weeks using the same procedure. She eventually agreed to commence atorvastatin, 40 mg once daily.

At 33 weeks' GA, our patient presented to labor and delivery with nausea, vomiting and back pain. Her TG level was 40 mmol/L, lipase was 504 U/L and an ultrasound confirmed pancreatitis. Unfortunately, she developed fever, tachycardia, and new vaginal bleeding. Betamethasone was administered to promote fetal lung maturity. A placental abruption was identified, and she proceeded to have a vaginal delivery. The infant spent time in the neonatal intensive care unit, but fortunately did well. She underwent further plasmapheresis shortly after her delivery. At post-partum day 1, her TG level plummeted to 2.3 mmol/L. The patient was discharged on fenofibrate and omega-3 fatty acids, along with lifestyle measures. Repeat TG level at six weeks

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Table 1. Treatment modalities for hypertriglyceridemia.

Treatment	Dose	Expected response	Reproductive safety	Lactation data
Fibric acid derivatives	Micronized fenofibrate 200 mg PO daily	LDL-C ↓16–27% HDL-C ↑9% TG ↓46–54% ^{12a}	No teratogenic effects seen in animal reproductive studies. ¹³	No published data to date.
Omega-3 fatty acids (DHA)	Gemfibrozil 600 mg PO twice daily 3–4 g PO daily	HDL-C ↑5–9% TG ↓25–30% ^{14a,15a}	An RCT did not identify any serious safety concerns related to DHA supplementation for mother or newborn. ¹⁶ An observational study did not find any association with PTD, or adverse effect on birthweight. ¹⁷	Compatible.
HMG CoA reductase inhibitors	Atorvastatin 5–80 mg PO daily Rosuvastatin 5–20 mg PO daily Pravastatin 10–80 mg PO daily Simvastatin 5–40 mg PO daily	LDL-C ↓20–60% HDL-C ↑5–10% TG ↓10–33% ^{18a,19a}	Large cohort study did not find a significant teratogenic effect from maternal use of statins in the first trimester. ²⁰	Transferred into breast milk, ²¹ limited published data to date.
Insulin	Intravenous infusion titrated to serum blood glucose of 5–10 mmol/L ^{22a}	TG ↓32–48% ^{22a}	Safe in pregnancy.	Compatible.
Heparin	Intravenous infusion (therapeutic anticoagulation) ²³	TG ↓76% after 18 h ²³	No placental transfer due to high molecular weight. ²⁴	Compatible.
Plasmapheresis	Frequency not defined, titrate to desired clinical effect	TG ↓94%, LDL ↓64% and HDL ↑850% after 3 sessions ^{25a}	Multiple case reports have not demonstrated any safety concerns. ^{2–7}	No published data to date.
Niacin	Extended release: 500 mg qhs, titrated to 1–2 g qhs	LDL-C ↓18% HDL-C ↑29% TG ↓21–24% ^{26a}	No human studies in pregnancy.	No published data to date.

LDL-C: low-density lipoprotein cholesterol; HDL: high-density lipoprotein; PTD: preterm delivery; TG: triglycerides; RCT: randomized controlled trial.

^aData are from non-pregnancy studies.

Figure 1. Serum triglyceride levels and timing of therapeutic interventions.

*Admission 1: 22 April–6 May, 2014. Insulin R and glucose infusions 22–26 April; resumed 29 April–3 May. Insulin glargine subcutaneous injections 3–6 May, required simultaneous D10W infusion. Fenofibrate and omega-3 fatty acids started 24 April.

**Admission 2: 3–14 June. Insulin R and glucose infusions 3–10 June. Insulin glargine 10–14 June, glucose infusion still required.

***Admission 3: 30 June–7 July. IV insulin from admission 30 June to delivery 1 July at 33 weeks' GA.

+Gestational diabetes mellitus (GDM) diagnosed.

++Plasma Exchange (PLEX) 13, 20, 26 June, 2 July.

post-partum was 3.4 mmol/L, and both a fasting glucose and a 75 g 2 h oral glucose tolerance test were normal.

Discussion

While hypertriglyceridemic pancreatitis in pregnancy is a rare occurrence, it is associated with serious complications for both mother and fetus.⁸ A retrospective study by Tang et al. found a 12% rate of preterm delivery (PTD) among 103 cases of acute pancreatitis.⁹ Mortality rates in pancreatitis have been reported as high as 20% for mother and 50% for fetus, although these estimates have likely declined over the last few decades due to both earlier detection and reduced preterm births.^{6,8}

Various treatments have been reported in pregnancy (outlined in Table 1), including fibrates, statins, heparin, insulin and plasmapheresis, but to date there are no randomized controlled trials (RCTs) comparing these modalities. Our patient was unable to maintain safe TG levels despite lifestyle measures, fenofibrate therapy and high-dose omega-3 fatty acids. Unfortunately, our patient was unwilling to try statin therapy until we had exhausted all other options. An insulin regimen was not deemed safe or practical since her GDM was well controlled with diet alone, and she became hypoglycemic with low-dose insulin therapy. Heparin was not trialled as although it may initially increase lipoprotein lipase, which helps to remove triglycerides from plasma, there is growing evidence of secondary paradoxical hypertriglyceridemia, making its use controversial.¹⁰

Anecdotal reports have shown that plasmapheresis can dramatically reduce lipid levels via filtration of plasma in hypertriglyceridemic pancreatitis in pregnancy.^{2–7} Piolot et al. achieved a mean decrease of 70% in serum TG levels following a single session of plasmapheresis, slightly higher than that achieved in our patient.¹¹ Our patient

responded to conservative measures during her first episode of hypertriglyceridemic pancreatitis in pregnancy, but required plasmapheresis when her TG approached dangerous levels following her hospitalization (Figure 1). Her levels rebounded within four days of treatment, and she was later readmitted to hospital for pancreatitis and PTD, which may reflect the need for more aggressive plasmapheresis in cases of difficult-to-control TG levels in pregnancy. Sivakumaran et al.³ reported the use of a prophylactic plasmapheresis protocol to maintain TG concentrations less than 11.3 mmol/L in one patient, which prevented pancreatitis and ended with the delivery of a healthy full-term infant. A total of 12 sessions of plasmapheresis were required in that case, which implies the transient nature of its effect. Further studies into the use of plasmapheresis for prevention of hypertriglyceridemic pancreatitis in pregnancy are needed, including the optimal time to begin plasmapheresis, frequency and duration and any adverse effects. In this case, plasmapheresis was only used after the patient became refractory to various medical treatments. Previous literature suggests that a target TG level of less than 11.3 mmol/L reduces the risk of pancreatitis, regardless of the treatment utilized.¹

Given that this is a rare and difficult to treat disease, development of a registry to further study this condition could be beneficial.

Authors' contribution

RL and SJR contributed equally to the preparation of this manuscript.

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Guarantor

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Contributorship

Rodger and Lim co-wrote the manuscript under the supervision of Hawkins. All three authors were directly involved in the care of the patient described in the case report. All above authors meet the conditions of authorship and each author participated sufficiently in the work to take public responsibility for appropriate portions of the content.

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