Hypertriglyceridemic pancreatitis in pregnancy: case reports and review of the literature

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We report two cases of acute pancreatitis in pregnancy due to hypertriglyceridemia, and review the literature discussing how this clinical issue can be managed.

Case 1

A 32-year-old Bangladeshi woman was seen urgently in outpatient clinic with an unplanned pregnancy of approximately six weeks' gestation.

She had a past history of polycystic ovarian syndrome, non-alcoholic fatty liver disease, obesity and developed type 2 diabetes six years previously. She had been noted at diagnosis of diabetes to have mild hypertriglyceridemia (Table 1), which was thought to be due to uncontrolled diabetes. Over the preceding four years, she had suffered three bouts of acute pancreatitis. On the first admission, she was noted to have marked hypertriglyceridemia. Despite high doses of insulin, statin, fibrate, omega-3 fish oils, metformin and sitagliptin, her glycaemic control remained poor (glycated haemoglobin ranging from 9.4% [79 mmol/mol] to 11.8% [105 mmol/mol]) as did her lipid control, despite input from diabetes nurses, dietitian and an inpatient admission for stabilization of glucose levels. She admitted her dietary concordance was poor. She had two previous uneventful pregnancies prior to her diagnosis of diabetes, neither of which was complicated by gestational diabetes.

She was counselled about the high risk of pancreatitis in pregnancy, but remained keen to continue the pregnancy. Fibrate, insulin, metformin and fish oil therapy was continued as the risk of hypertriglyceridemia-induced pancreatitis was deemed significant. She was seen by a dietitian and booked into the diabetic pregnancy service for weekly review. Glycaemic control and lipid control remained suboptimal despite rapid titration in insulin doses.

At 12 weeks' gestation, she was admitted with acute abdominal pain and vomiting. Abdominal examination showed peritonism. She was dehydrated, blood pressure 110/80 mmHg and pulse 120 regular. Serum amylase was elevated at 1464 (normal range <90 U/L). Arterial blood gases were normal. She was admitted to the High Dependency Unit and received supportive therapy with intravenous fluids, starvation and antibiotics, and made a rapid recovery within five days. Careful counselling of her risk of recurrent pancreatitis was discussed. The option to have frequent plasma exchange during pregnancy was offered, but after discussion with her family she opted for a medical termination of pregnancy, which she underwent at 14 weeks' gestation. Contraceptive advice was given to eliminate the risk of unplanned pregnancy in the future.

Case 2

A 24-year-old woman was admitted with acute abdominal pain. She had been diagnosed with hypertriglyceridemia during an admission with pancreatitis two years previously (Table 2), and treated with a statin and fibrate, achieving reasonable control of her hypertriglyceridemia. On examination, she had signs of peritonism, blood pressure 88/42 mmHg and pulse 130 regular. Serum amylase was 8962 (normal range <90 U/L). Pregnancy test was positive, and ultrasound confirmed a gravid uterus of approximately eight weeks' gestation, and oedema of the pancreatic head. She was admitted to intensive care, treated with antibiotics, intravenous fluids and starvation. Her

Table 1.
Case 1 blood results.

	At diagnosis of diabetes	*At admission with first bout of pancreatitis*	*At admission with pancreatitis in pregnancy*	*On glucose/ insulin and starvation*	*Post discharge*
Total cholesterol (mmol/L)	5.7	23.4	26.7	2.3	5.2
Triglycerides (mmol/L)	6.3	67.1	78.9	2.1	6.2

Table 2.
Case 2 blood results.

	At admission with first bout of pancreatitis	*At admission with pancreatitis in pregnancy*	*On parenteral nutrition*	*Post discharge*
Total cholesterol (mmol/L)	12.4	16.7	2.3	4.3
Triglycerides (mmol/L)	34.2	46.6	5.3	3.2

condition deteriorated, developing adult respiratory distress syndrome, requiring respiratory and inotropic support. She suffered foetal loss at day 4, but slowly recovered, without the need for laparotomy. Computerized tomography of the abdomen showed necrotizing pancreatitis, but no fluid collection or pseudocyst formation. She was discharged at day 17, back on her lipid lowering medication. She was given advice to avoid pregnancy in the near future.

Discussion

Pancreatitis due to hypertriglyceridemia is uncommon in pregnancy, with a quoted incidence of between 1 in 1500 to 1 in 4500 pregnancies.[1] It is, however, an important cause of pancreatitis in pregnancy, accounting for around 30% of all cases, second only to gallstone disease.[2]

Hypertriglyceridemia is a well-recognized cause of pancreatitis.[3] The exact mechanism by which triglycerides induce pancreatitis is unclear, but it is thought that high levels of triglycerides are hydrolysed in the pancreatic vascular bed, leading to high free fatty acid levels, which induce inflammatory changes and ischaemia. In pregnancy, the risk of pancreatitis is increased in women with significant hypertriglyceridemia. Oestrogenic effects during pregnancy lead to a 2- to 4-fold increase in the prevailing level of triglyceride due to increased synthesis of triglyceride and very low-density lipoprotein (VLDL) by the liver, and down-regulation of lipoprotein lipase (LPL) gene expression.[4] In women with normal lipid metabolism, fasting serum triglycerides rarely exceed 3.4 mmol/L in pregnancy. In women with abnormal lipid metabolism, levels of serum triglycerides much above 10 mmol/L increase risk of acute pancreatitis substantially. Levels as high as this may occur in patients with defective lipoprotein lipase (LPL) activity (usually due to LPL gene mutations) or defective apolipoprotein E (isoform E2).[5] Secondary causes of hypertriglyceridemia, such as diabetes, hypothyroidism and excess alcohol should always be considered. Drugs such as steroids, atypical antipsychotics and retinoic acid can also elevate triglycerides.

Risk of acute pancreatitis from hypertriglyceridemia in pregnancy appears to be highest in the third trimester, and tends to be a more severe form of pancreatitis than that due to gall stone disease.[1]

Pancreatitis in pregnancy may be associated with haemolysis, elevated liver enzymes, low platelets (HELLP) syndrome or pre-eclampsia/eclampsia leading to a high foetal mortality or preterm delivery. The experience of a major surgical intensive care unit in managing such cases over 11 years in Nanjing, China, reports an outcome of 38.9% preterm delivery and 33% foetal loss.[2] Maternal morbidity and mortality can also be significant, and two-organ involvement is associated with increased mortality and morbidity.

Acute management of pancreatitis in pregnancy is not dissimilar to that of non-gestational acute pancreatitis, including starvation, nasogastric decompression, antibiotics and careful monitoring. Severe hypertriglyceridemia can be acutely treated with glucose insulin infusion,[6] or intravenous heparin infusion[7] as both insulin and heparin stimulate LPL activity. Whilst fibrates are not licensed for use during pregnancy, there are case reports of successful use of fenofibrate[8] or omega 3 fatty acids[9] during pregnancy resulting in favourable pregnancy outcome.

Management of massive hypertriglyceridemia in pregnancy can be a therapeutic challenge. Patients who are uncontrolled on fibrate and fish oil therapy are at high risk of pancreatitis, particularly in the final trimester. Therefore, other modalities to clear triglyceride rich particles such as plasmapheresis, lipid apheresis and extracorporeal lipid elimination techniques have been used in a small number of case reports.[10] These techniques are useful in reducing the triglyceride concentration in serum rapidly, thereby reducing the risk of recurrence of pancreatitis. Multiple treatments may be required during pregnancy to maintain the low level of triglyceride throughout gestation. Frequency of monitoring triglycerides during pregnancy is unclear, but is dependent upon level of triglycerides and response to therapy. In addition, there is not a clear consensus on threshold for intervention in pregnancy, although 5.6 mmol/L has been suggested. One theoretical concern is that a very low fat diet might lead to a deficiency in essential fatty acids, hence having an adverse effect on foetal development, but this is not confirmed.

In summary, we report two cases of severe pancreatitis due to hypertriglyceridemia in pregnancy. The condition needs to be considered in all pregnant women presenting with pancreatitis. Women with pre-existing hypertriglyceridemia need careful counselling regarding the risks of pregnancy-induced pancreatitis.

References

1. Eddy JJ, Gideonsen MD, Song JY, Grobman WA, O'Halloran P. Pancreatitis in pregnancy. *Obstet Gynecol* 2008;112:1075–81
2. Geng Y, Li W, Sun L, Tong Z, Li N, Li J. Severe acute pancreatitis during pregnancy: eleven years experience from a surgical intensive care unit. *Dig Dis Sci* 2011;56:3672–7
3. Ewald N, Hardt PD, Kloer H-U, Giessen M. Severe hypertriglyceridemia and pancreatitis: presentation and management. *Curr Opin Lipidol* 2009;20:497–504
4. Potter JM, Nestel PJ. The hyperlipidemia of pregnancy in normal and complicated pregnancies. *Am J Obstet Gynecol* 1979;133:165–70
5. Hiéronimus S, Benlian P, Bayer P, Bongain A, Fredenrich A. Combination of apolipoprotein E2 and lipoprotein lipase heterozygosity causes severe hypertriglyceridemia during pregnancy. *Diabetes Metab* 2005;31:295–7
6. Jabbar MA, Zuhri-Yag MI, Larrea J. Insulin therapy for a non-diabetic patient with severe hypertriglyceridemia. *J Am Coll Nutr* 1998;17:458–61
7. Sleth JC, Lafforgue E, Servais R, *et al*. A case of hypertriglycideremia-induced pancreatitis in pregnancy: value of heparin. *Ann Fr Anesth Reanim* 2004;23:835–7
8. Whitten AE, Lorenz RP, Smith JM. Hyperlipidaemia associated pancreatitis in pregnancy managed with fenofibrate. *Obstet Gynecol* 2011;117:517–19
9. Takaishi K, Miyoshi J, Matsumura T, Honda R, Ohba T, Katabuchi H. Hypertriglyceridemic acute pancreatitis during pregnancy: prevention with diet therapy and omega-3 fatty acids in the following pregnancy. *Nutrition* 2009;25:1094–7
10. Sivakumaran P, Tabak SW, Gregory K, Pepkowitz SH, Klapper EB. Management of familial hypertriglyceridemia during pregnancy with plasma exchange. *J Clin Apher* 2009;24:42–6