Hyperglyceridaemia-induced acute pancreatitis in pregnancy: Experience from a tertiary hospital in Singapore

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SUMMARY

Acute pancreatitis (AP) is a serious condition that can occur suddenly in pregnancy. We present a case of sudden onset of epigastric pain with severely deranged serum triglyceride levels in a 32-year-old Vietnamese primigravida with no significant past medical history in the Singapore General Hospital. The patient was managed in the intensive care unit, with plasmapheres and intravenous insulin and was eventually a healthy term foetus was delievered via ceasarian section. This case showcased multidisciplinary co operation between the obstetrics, anaesthetic, endocrinology and intensive care team and serves as a reminder to consider this rare condition for future similar presentations.

INTRODUCTION

Acute pancreatitis (AP) in pregnancy is rare but it is a serious condition with a low incidence of less than 1 in 10000.[1] It usually presents with sudden severe abdominal pain and depending on the severity of the disease and can endanger a pregnancy.[2] AP presents most commonly during the third and post-partum period. AP in pregnancy is usually secondary to biliary obstruction by gallstones. Hypertriglyceridaemia-induced pancreatitis (HLP) which is an extremely rare but important cause of AP and is the main focus of this case report. HLP carries a much higher likelihood of severe AP and is strongly associated with poor fetal outcomes such as fetal distress and stillbirth. We present a case of a woman with this rare entity.

CASE REPORT

The patient, Mdm N is a 32-year-old Vietnamese primigravida with no significant past medical history. The course of her pregnancy was uneventful until 31 weeks of gestation when she presented with constant epigastric pain and dyspnoea. Blood investigations done in the emergency department revealed significantly elevated serum lipase of above 600 U/L and serum amylase of 837 U/L (Table I). An arterial blood gas sample confirmed a compensated metabolic acidosis. The blood samples appeared chylous (Figure 1) and showed a serum triglyceride level of above 50 mmol/L and total cholesterol of 37.36 mmol/L. A provisional diagnosis of hypertriglyceridaemia-induced acute pancreatitis in pregnancy was made and the patient was admitted for further management.

The foetus was appropriately grown on ultrasound with an estimated foetal weight of 2041g and cardiotocography (CTG) was normal. Intramuscular steroid injections in the form of betamethasone were administered to accelerate fetal lung maturity in anticipation of the possible necessity for preterm delivery. She was also started on subcutaneous enoxaparin, a low molecular weight heparin (LMWH) for prophylaxis against venous thromboembolism and also to lower triglyceride levels.

The patient was admitted to the intensive care unit (ICU) for further monitoring. She was started on intravenous insulin with a 10% dextrose infusion to correct her metabolic acidosis.

Despite intravenous insulin, repeat arterial blood gas revealed worsening of the metabolic acidosis. In view of worsening acidosis and extremely high triglyceride levels, she underwent urgent plasmapheresis via a vascular catheter (Figure 2).

The patient's triglyceride levels reduced steadily after 1 cycle of plasmapheresis intravenous insulin, hydration and LMWH.

Subsequently, administration of insulin was converted to daily subcutaneous form and she placed on a low-fat diet. MRI cholangiography was also performed to rule out biliary causes and demonstrated absence of biliary tract stones. the patient was eventually discharged after 10 days of hospitalisation with subcutaneous insulin and oral omega 3 supplements. Her serum triglyceride level at the time of discharge was 8.41mmol/L.

She was followed 2-weekly in our high-risk pregnancy clinic and serial serum triglyceride levels remained stable as shown in table II. Foetal growth parameters were followed up closely with regular ultrasound scans and were deemed within normal range.

In recognition of the risk of relapse, she was electively admitted at 37 weeks of gestation for induction of labour. Despite multiple prostaglandin pessaries, she failed induction of labour and subsequently underwent an uneventful cesarean section. A healthy term foetus was delievered. Mdm N was reviewed by endocrine post operatively and her serum triglycerides remained stable. She was discharged well 3 days' post operation as per routine protocol and started on oral fibrates for long-term control of her hypertriglyceridaemia.

This article was accepted: 26 May 2021
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Table I: Summary of bloods done at admission

Blood results			
Haemoglobin (g/dL)	10.5	Potassium (mmol/L)	3.2
White blood count (x10^9/L)	13.04	Glucose (mmol/L)	5.6
Platelet (x10^9/L)	274	Creatinine (umol/L)	62
Neutrophils absolute (x10^9/L)	11.4	Bicarbonate (mmol/L)	14.1
		Amylase (units/L)	867
pH	7.405	Lipase (units/L)	>600
pCO2 (mmHg)	26.0	Ketones (mmol/L)	3.5
PO2 (mmHg)	98.0	C-reactive protein (mg/L)	128
Base excess (mmol/L)	-8.0	Calcium, serum (mmol/L)	1.87
		Amylase (units/L)	867
Heart rate (bpm)	125	Blood cultures (aerobic)	No bacterial growth
Temperature	38.3 degrees	Blood cultures (anaerobic)	No bacterial growth
Blood pressure	98/59	Cholesterol, total (mmol/L)	37.36
		Cholesterol, HDL (mmol/L)	>6
Urea (mmol/L)	1.5	Triglyceride (mmol/L)	>50.00
Sodium (mmol/L)	117	Cholesterol, total (mmol/L)	37.36

Table II: Trends of triglyceride level following treatment

Triglyceride trend over the next few days after starting treatment								
Triglyceride (mmol/L)	31.29	25.21	17.19	14.09	12.39	10.45	9.56	8.83
Triglyceride trend during her outpatient visits								
Triglyceride (mmol/L)	8.41	7.70	9.12	8.73	8.59			
Triglyceride trend post caesarean section								
Triglyceride (mmol/L)	7.19	7.27						

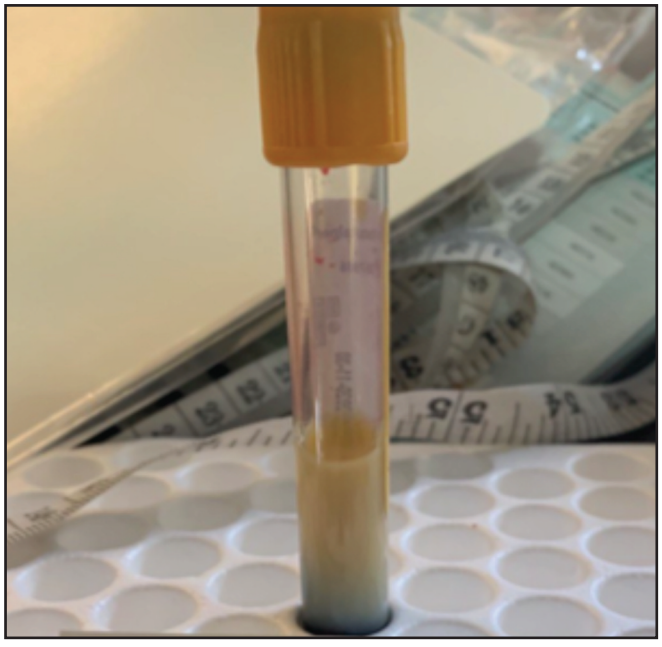

Fig. 1: Lipemic blood sample taken from patient upon admission.

Fig. 2: Plasmapheresis machine demonstrating lipemic plasma extracted from patient.

DISCUSSION

HLP accounts for only 4-6% of cases of AP in pregnancy but is more likely to have severe manifestations and complications as witnessed in our patient. In the third trimester of pregnancy, there is a two to four-fold increase in serum triglycerides level. The significant increase in triglycerides is postulated to be driven by the elevated levels of oestrogen and human placental lactogen (HPL) in the late second to third trimester. HPL stimulate lipolysis in adipocytes while estrogenic state enhances lipogenesis and hepatic VLDL synthesis and decreases hepatic lipase activity, giving rise to increased triglyceride-rich LDL and high-density lipoprotein in the maternal circulation.6 These physiological alterations in lipid metabolism can precipitate an episode of

acute pancreatitis, especially in patients with underlying disorders of lipoprotein metabolism such as those with pre-existing hypertriglyceridaemia.

When evaluating a patient in the secondary or third trimester presenting with abdominal pain, clinicians should maintain a high index of suspicion for HLP and the management requires a multidisciplinary approach. Care of our patient involved obstetricians, neonatologists, endocrinologists, gastroenterologists, nephrologists and radiologists. Initial treatment consists of supportive management with intravenous hydration, bowel rest and a fasting state. This strategy usually results in a drop in serum triglyceride levels after 48 hours. A more aggressive approach was necessary in our patient who was severely ill at presentation. This is especially so since HLP is associated with a maternal mortality rate of up to 9% and a fetal loss rate of 17.5%.[5]

Main treatment modalities are insulin and plasmapheresis, with the aim of lowering triglyceride levels. Insulin lowers serum triglyceride levels by potentiating lipoprotein lipase (LPL) activity and also hormone sensitive lipase in adipocytes. HLP has been proven beneficial in various studies and should ideally be initiated early in cases of severe HLP for rapid removal of plasma lipoproteins and inflammatory cytokines with the aim to reduce serum triglyceride levels and reduce risk of pancreatic necrosis.[6,7] Our patient was also started on heparin in the form of LMWH. Heparin stimulates the release of LPL into the circulation to further reduce triglyceride levels, though the effects are transient as chronic use results in a depletion of LPL. We also used supplementation with omega-3 fatty acids in our patient which is safe in pregnancy and is known to increase LPL activity. Fibrates, the mainstay of pharmacological therapy for hypertriglyceridaemia in non-pregnant individuals, has been used in pregnancy though its safety has not been proven. We decided not to use this drug as our patient remained stable with the other modalities.

Apart from maternal complications such as acute renal failure, sepsis and acute respiratory distress syndrome, there are also potential foetal complications with HLP. Foetal risks from AP in pregnancy include pre-term labour, prematurity, and in-utero foetal death.[6] In a retrospective review between 1996 and 2006, describing 43 pregnant women with acute pancreatitis, there were 6 pre-term delivery and only 2 of these infants survived. An observational study of 54 pregnant women with AP showed that HLP is associated with more intrauterine foetal distress and worse foetal outcomes compared to AP from other aetiologies. Close foetal monitoring with cardiotocography and growth scans should be performed.

We attribute the good obstetric outcome in our patient to the initial aggressive medical treatment to correct maternal acidosis and reduce serum triglyceride levels. This and subsequent close antenatal surveillance allowed our patient to carry her pregnancy to term. The decision to induce labour at 37 weeks, albeit unsuccessful, can be justified on risk-benefit considerations. The physiological changes in pregnancy continue to predispose these women to a relapse of HLP and delivery of the foetus, once it is mature, is beneficial. Delivery also allows for the subsequent use of lipid-lowering drugs which may be contraindicated in pregnancy.

CONCLUSION

HLP is a rare but potentially lethal cause of abdominal pain in pregnancy associated with and is associated with significant maternal and fetal morbidities. Timely diagnosis and multi-disciplinary management of both AP and hypertriglyceridaemia are crucial in order to minimise complications.

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