

Hypertriglyceridemic Pancreatitis and Pregnancy: A Case Report

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ARTICLE INFO	ABSTRACT
<i>Article type:</i> Case Report	Background & aim: Elevated triglyceride levels in women with hereditary forms of hypertriglyceridemia may involve the risk of pancreatic attacks during pregnancy.
<i>Article History:</i> Received: 25-Jan-2015 Accepted: 11-July-2015	Case report: In this study, we present the clinical course of a 42-year-old pregnant woman with two vaginal deliveries and one cesarean section (gravidity: 4, parity: 3, live: 2, death: 1) admitted to our hospital. Gestational age was 33-34 weeks based on the last menstrual period and ultrasound results. Although hypertriglyceridemia and pancreatitis were controlled by pancreatitis treatment, intrauterine fetal death occurred in the patient. In addition, fish oil, gemfibrozil and antum were administered to decrease serum triglyceride (TG) levels. Finally, the patient was discharged with good general conditions and a TG level of ≤ 200 mg/dl four weeks after the onset of the disease.
<i>Key words:</i> Acute pancreatitis Hyperlipidemia Hypertriglyceridemia Pregnancy	Conclusion: Hyperlipidemic pancreatitis is associated with maternal and fetal mortality and morbidity. Therefore, treatments should be initiated immediately after the diagnosis of this disease during pregnancy. Complications caused by elevated TG levels could be prevented with appropriate and timely interventions.

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Introduction

Hyperlipidemia involves abnormally elevated levels of any lipids and is the most common form of dyslipidemia. Hyperlipidemia is normally detected in individuals with decreased lipoprotein lipase activity and is divided into two subtypes of primary and secondary (1). Genetic susceptibility is the major contributing factor to primary hyperlipidemia, whereas secondary hyperlipidemia is mainly caused by alterations in plasma lipid profile and lipoprotein metabolism; such example is diabetes-associated changes in the metabolism. Hyperlipidemia could also be of idiopathic origin (2).

Acute pancreatitis (AP) is a life-threatening complication associated with hypertriglyceridemia (hyper-TG) (3). Hyper-TG is the third most common cause of AP after gallstones and alcohol consumption. The incidence rate of AP in adults ranges from 4.8 to 38 per 100,000 cases (4).

According to the literature, pregnancy is associated with increased plasma levels of

triglyceride (TG) and total cholesterol. Furthermore, pregnancy may result in increased TG levels in women with hereditary forms of elevated TG, involving a higher risk of pancreatic attacks. Maternal and fetal morbidity and mortality are the most significant complications caused by hyper-TG (5). On the other hand, diabetes, alcohol consumption and increased weight gain are among the main risk factors for severe hyper-TG during the third trimester of pregnancy (6).

In this study, we presented a case of pancreatitis and hyperlipidemia in a 42-year-old pregnant woman referring to our health care center.

Case report

A 42-year-old pregnant woman with a history of two vaginal deliveries and one cesarean section (gravidity: 4, parity: 3, live: 2, death: 1) was admitted to Imam Reza Hospital

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on December 9, 2013. Gestational age was estimated at 33-34 weeks based on the last menstrual period and ultrasound results, and the fetal heart rate (FHR) was calculated at 148 beat/min.

The patient presented with hypertension and hyperlipidemia; her blood pressure was reported to be 120-140/80-90 mmHg since October 2013 (about two months before admission), while it was 120/80 mmHg upon admission. In addition, hyperlipidemia had been controlled within the past two years, and the patient was treated by gemfibrozil 300mg capsules (three times per day) for hyperlipidemia prior to hospitalization. The initial laboratory results obtained before admission are shown in Table 1.

Following hospitalization due to hyper-TG, the patient was regularly examined by an endocrinologist, who discontinued the gemfibrozil treatment, and prescribed fish oil (500 mg, three times daily) instead in order to manage the uncontrolled hyper-TG.

On the second day of hospitalization, the patient was referred to a cardiologist due to excessive sweating and tachycardia (heart rate: 105 bpm). Echocardiographic results were normal, with the exception of aortic valve calcification, and 24-hour urine protein level was reported to be 130 mg on December 11. Laboratory results of the patient after hospitalization are shown in Table 2.

The patient underwent obstetric ultrasound on December 12 and non-stress test on

December 14, and the results were normal and reactive, respectively. At day six of admission (December 15, 7 a.m.), the patient had complaints of epigastric pain; therefore, she was prescribed antacid medication.

The endocrinologist re-examined the patient on December 15 (9 a.m.). Moreover, a cardiologist evaluated the patient for tachycardia, and the heart rate was reported to be 100 bpm. Afterwards, the patient received hydration, and echocardiography and electrocardiography were repeated indicating normal results. In the evening of the same day, tachycardia was recorded with the heart rate of 118-122 bpm.

The tachycardia and epigastric pain gradually became more severe on December 15 (12 p.m.), and the general condition of the patient deteriorated as well. FHR monitoring had been carried out continuously since the onset of this condition, and only mild tachycardia was detected.

Additionally, plasma levels of lipase and amylase were recorded at 795 and 1575 mg/dl, respectively. In the abdominal ultrasound performed on December 15 (4 p.m.), there was a prominence of the head of the pancreas, and the swelling was considered as a symptom of AP.

The patient was administered with ceftriaxone (1g/intravenous/twice daily) and clindamycin (900mg/intravenous/three times daily) at 8 p.m. Moreover, arterial blood gas (ABG) test and foley catheterization were carried out in order to monitor the input and

Table 1. Laboratory Indices of the Studied Patient before Hospitalization

	Laboratory Indices			
	July 18 (2013)	August 4 (2013)	October 13 (2013)	October 18 (2013)
Cholesterol (mg/dL)	280	210	656	650
Triglyceride (TG) (mg/dL)	1680	611	2,700	3,200
High-density Lipoprotein (HDL) (mg/dL)	N/A	41	38	37
Low-density Lipoprotein (LDL) (mg/dL)	N/A	56	110	320

Table 2. Laboratory Indices of the Studied Patient after Hospitalization

Date of Test	Laboratory Indices					
	Cholesterol (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	Amylase (mg/dl)	Lipase (mg/dl)
December 10 (2013)	102	5,885	45	109	35	45
December 15 (2013)	N/A	47,771	40	55	795	1575

output of the patient. At this stage, the heart rate was equal to 135 bpm, respiratory rate was 30, and the ABG test was indicative of metabolic acidosis and respiratory alkalosis.

On December 16, there was a sudden occurrence of decelerations and bradycardia. However, due to the severe sepsis of the mother, cesarean section could not be performed and intrauterine fetal death occurred 24 hours after the onset of pancreatitis.

The patient was transferred to the intensive care unit (ICU), and due to the decreased hematocrit levels, abdominal and pelvic ultrasounds were conducted in order to detect possible internal bleeding; however, the results of both examinations were normal. In addition, the patient underwent plasmapheresis.

On the third day after the presentation of pancreatitis (December 17, 1:30 p.m.), labor initiated naturally, and the patient had a vaginal delivery resulting in a stillborn male fetus with a birth weight of 3400 g. During hospitalization, three units of packed cells were transfused due to the decreased hematocrit (one unit on December 19, two units on December 20).

The treatment process continued as to control and manage hyper-TG and pancreatitis. Moreover, computerized tomography (CT-scan) was performed on December 19, which was indicative of bilateral pleural effusion, pulmonary lobar collapse, enlarged pancreatic head with heterogeneous enhancement, peripancreatic fat stranding and ascites.

There were no signs of pancreatic necrosis or abscess formation in the CT-scan results; however, ascites was detected around the enlarged pancreatic head. Due to the reduced hemoglobin level (12 to 7), ascites tapping was performed, indicating non-hemorrhagic ascites or exudative ascites. Consequently, fish oil, gemfibrozil and antum were prescribed in order to decrease the serum TG levels. Finally, the patient was discharged with good general conditions and a TG level of ≤ 200 mg/dl about four weeks after the onset of the disease.

Discussion

By blocking the clearance of triglyceride-rich lipoproteins from the plasma, severe hyper-TG may cause disorders in the lipid metabolism. In this condition, TG levels increase due to the

excessive hepatic production of very-low-density lipoproteins (VLDL) or heterozygous lipoprotein lipase deficiency (15).

Among the major risk factors of high TG levels are obesity, diabetes, estrogen therapy, thyroid diseases, alcohol consumption and use of certain medications (7). Hyper-TG could be a life-threatening condition in patients with genetic susceptibilities. For instance, in familial hypertriglyceridemia, which is an autosomal dominant disease, serum TG levels tend to increase. This condition occurs in 1:500 individuals (8).

Elevation of triglyceride-rich lipoproteins in the plasma could be accompanied by severe clinical manifestations, such as AP, in which the TG levels become higher than 1,000 mg/dL (9). AP is defined as an acute inflammation of the pancreas, with variable involvement of other surrounding tissues or remote organs. This disorder leads to severe complications including necrosis, abscess and pseudocyst formation (10).

The main clinical manifestations of pancreatitis are the rapid onset of moderate-to-severe pain in the upper abdomen, insufficient pain relief with changing body position, and band-like pain radiating to the back (11). The patient presented in this study experienced similar pains.

Due to the decreased VLDL clearance during pregnancy, lipid abnormalities could be associated with severe TG level elevations, predisposing pregnant women to pancreatitis. In a normal pregnancy, plasma lipid levels usually return to normal following delivery (4). In our patient, the laboratory results including high cholesterol, low-density lipoprotein, high-density lipoprotein and TG levels led us to the diagnosis of hyper-TG.

In general, pancreatitis has a low incidence rate during pregnancy, and the prevalence of AP during pregnancy is 3 in 10,000 cases; however, AP might cause maternal and fetal mortality and morbidity in some cases. The rate of maternal mortality associated with AP is estimated at 20% in complicated pregnancies, while the fetal mortality rate is relatively low. Therefore, early and prompt treatment is of paramount importance in order to obtain successful outcomes in AP patients (12). Regarding the

described case, FHR was not detectable 24 hours after the onset of pancreatitis, and the patient underwent vaginal delivery resulting in a stillbirth.

Use of lipid-lowering medications, fat restriction and intravenous heparin and insulin therapy, together with glucose infusion, are considered as the main treatment options for hypertriglyceridemia-induced pancreatitis (4).

Furthermore, serum TG levels of >1,000 mg/dL are considered as a major risk factor for this disease. In order to avoid pancreatitis, TG levels need to be lowered to <200 mg/dL by controlling the dietary plan, lifestyle and fasting blood sugar of the patients. Additionally, use of medications and substances such as fibrates, fish oil and niacin could noticeably lower serum TG levels.

Fibrate is the most effective medication to reduce TG levels (13) and is normally administered to patients diagnosed with hyper-TG. In addition, fibrates have been found to be practical in the long-term treatment of hyperlipidemia. However, medical experts have suggested that the use of fibrates and statins should be discontinued during pregnancy and breastfeeding since they may cause teratogenicity (14).

In high-risk cases, dietary counseling, exercise and weight management are necessary before pregnancy, and these patients need to be monitored closely during this period; it is also noteworthy that TG monitoring is required in all pregnancies. Most of the medications used for hyper-TG treatment are contraindicated during pregnancy since they have not been thoroughly investigated.

In the present case, we prescribed gemfibrozil in order to reduce the serum cholesterol and TG levels. On the other hand, administration of omega-3 fatty acid seems to be a more viable intervention, as well as the only safe medical treatment during pregnancy with moderate TG-lowering effects. It should be noted that these acids are rarely effective if used as triglyceride-lowering agents only.

Combination therapy is required for refractory hyper-TG (15, 16). The patient presented in this study was treated by combined omega-3 fatty acids (3-4 g/day), gemfibrozil and antum. Other prescribed medications were

imipenem, metronidazole, heparin, octreotide and pantoprazole.

For extremely high TG levels, therapeutic plasmapheresis could be used to prevent hypertriglyceridemia-induced complications during pregnancy. Furthermore, plasma exchange could be an effective option for gestational hypertriglyceridemia-induced pancreatitis. Novel modalities in this regard include insulin and heparin treatment, use of medium-chain triglycerides, plasmapheresis and gene therapy for lipoprotein lipase deficiency (4). In the present case, the patient underwent plasmapheresis.

Since pregnancy may dysregulate controlled lipid levels in women with familial hyper-TG and lead to AP, all pregnant women presented with non-obstetric abdominal pains need to be examined for hypertriglyceridemia-induced pancreatitis. Thorough evaluation of these conditions and proper management of possible AP lead to a good patient prognosis.

Conclusion

According to the findings of this study, severe hyper-TG could lead to pancreatitis. Although pregnancy-induced hyper-TG is a rare condition, it might appear as a life-threatening disorder in some patients. In this regard, general and specific therapies have been proposed for the reduction of TG levels during pregnancy. Controlled diet, pharmacological therapies and avoiding the risk factors are essential in order to prevent further pancreatic attacks. Pancreas-related complications could be managed and controlled with appropriate and early interventions.

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