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Case Report

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Acute pancreatitis in pregnancy and familial chylomicronemia syndrome: case report and literature review

Batoul Jaafar, Jessica Abou Chaaya, Shahed Ammar, Ibrahim Salti

Division of Endocrinology and Metabolism, Department of Internal Medicine, American University of Beirut Medical Center, Beirut 1107 2020, Lebanon.

Correspondence to: Dr. Jessica Abou Chaaya, Department of Internal Medicine, American University of Beirut, Cairo St., Beirut 1107 2020, Lebanon. E-mail: Jessica.abouchaaya@hotmail.com

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Abstract

Acute pancreatitis rarely occurs in pregnancy, with hypertriglyceridemia being the fourth leading cause during pregnancy. Hypertriglyceridemia, of which Familial Chylomicronemia Syndrome is the most severe form, ranks among the four principal causes of pancreatitis in pregnancy. Total Plasma exchange (TPE) has been found to be an effective and safe intervention both as a therapeutic and a prophylactic act. A 22-year-old female with FCS presented at the 21st week of gestation with acute hypertriglyceridemia pancreatitis. Despite medical management, she was then started on TPE at the two-week follow-up after serum triglyceride level was out of control. The triglyceride dropped from 55.0 % to 77.5 % during these sessions. Despite these interventions, pancreatitis recurred in week 34. An emergency C-section was carried out after a drop in the fetal heart rate. Postpartum triglycerides dropped by 57 % but remained above 1,000 mg/dl. FCS is difficult to manage during pregnancy, and it frequently fails to respond to various pharmacologic lines. TPE can help prolong a pregnancy, but it is not a definite treatment. Novel therapies for hypertriglyceridemia in pregnancy await additional safety testing.

Keywords: Familial chylomicronemia syndrome, hypertriglyceridemia, pancreatitis, pregnancy, total plasma exchange

INTRODUCTION

Acute pancreatitis rarely occurs in pregnancy, with an estimated incidence rate of 1 per 1,000 to 10,000 pregnancies[1-3]. Delay in recognition and/or proper management is associated with high maternal and fetal mortality rates. Due to the rarity of the disease and the wide range of different medical and obstetric etiologies of epigastric pain, the diagnosis is frequently missed. Acute pancreatitis in pregnancy can be secondary to different etiologies, with gallstones being the most common cause[3-5] [Table 1]. The risk of pancreatitis associated with hypertriglyceridemia (HTG) rises with duration of pregnancy: 19% in the first trimester, 26% in the second trimester, 53% in the third trimester, and 2% in the postpartum period[5,6].

Women with hereditary anomalies in lipoprotein metabolism, such as Familial Chylomicronemia Syndrome (FCS), are more likely to develop severe HTG later in pregnancy. In addition, according to Fredrickson classification, familial HTG (type 4), familial combined hyperlipidemia (type 2B), familial dysbetalipoproteinemia (type 3), and inherited lipodystrophy syndromes are all known primary genetic disorders that cause hypertriglyceridemia. FCS (OMIM 238600), commonly known as type 1 hyperlipoproteinemia and previously as lipoprotein lipase deficiency (LPLD), is a rare autosomal recessive disorder with an incidence of 1-2 per million. It is the most severe form, with serum chylomicron accumulation, severe HTG (> 1,000 mg/dL), and recurrent pancreatitis occurring in childhood[7]. Patients can have hepatosplenomegaly, lipemia retinalis, and eruptive xanthomas[8-10]. Bi-allelic mutations in the LPL gene are the most common cause of this disorder, followed by mutations in other genes that contribute to the function of LPL, such as Apolipoprotein C2 (APOC2), Apolipoprotein A5 (APOA5), Lipase Mutation Factor 1 (LMF1), and glycosylphosphatidylinositol-anchored high-density lipoprotein-binding protein 1 (GPIHBP1). Genetic testing can be helpful in establishing the diagnosis when clinical or biochemical data are inconclusive.

Based on small case series and case reports[5,11], the mainstream therapy for FCS has consisted of a very low-fat diet (10% to 15% of daily caloric intake) to lower plasma triglyceride (TG) levels below 750-880 mg/dL and abort the attacks of pancreatitis[12]. Due to the absence of a standard prophylactic regimen, additional therapies have included fibrates, marine omega-3 fatty acids, eicosapentaenoic acid, nicotinic acid, and therapeutic plasma exchange (TPE)[11]. Nil per Os (NPO or nothing by mouth) and hydration with or without artificial feeding, heparin, insulin, and TPE have all been described as treatments for acute bouts of pancreatitis[11]. TPE has become more widely adopted due to promising results, with the first case described in the literature being that of Swoboda *et al.* in 1993[4,7,13-15].

Here, we describe a pregnant patient with uncontrolled FCS who experienced two episodes of pancreatitis during the second and third trimesters and delivered a healthy premature baby at week 33. The aim of reporting this case is to emphasize the challenges faced upon treatment of acute pancreatitis secondary to FCS-induced HTG. Multiple therapies have been used, including a very low-fat diet, fibrates, icosapent ethyl, intravenous insulin, and frequent elective TPE sessions.

CASE REPORT

We present the case of a 22-year-old primigravid woman with a medical history of poorly managed FCS diagnosed at the age of three months. Her family background reveals a history of severe HTG (800-1,000 mg/dL) among her mother and siblings, along with HTGP in her maternal uncle. Nevertheless, obtaining a detailed family history and confirming diagnoses in relatives proved challenging due to inconsistent follow-up and economic constraints. At the age of 3 years old, she presented with severe hypertriglyceridemia-induced pancreatitis (HTGP). The diagnosis was made based on additional clinical findings of hepatosplenomegaly and eruptive xanthomas in addition to biological findings of a creamy

Table 1. Most common causes of acute pancreatitis in pregnancy

Causes of pancreatitis in pregnancy	Percentage %
Gallstones	66
Alcohol	12
Idiopathic	17
Hypertriglyceridemia	5

supernatant and clear infranatant on a refrigerated plasma sample. Genetic testing was not done at that time due to the poor socioeconomic status of the patient, who was also an infant of consanguine parents. She did not follow a very low-fat diet throughout her adolescence. The patient had poor metabolic control prior to pregnancy when she had recurrent HTGP (peak TG 2,500 mg/dL) almost twice a year. She denied alcohol intake or smoking. Prior to pregnancy, she was taking fenofibrate 160 mg daily but failed to have an adequate response since her TG levels ranged between 1,300 and 1,500 mg/dL.

The initial presentation to our Emergency Department was at 21 weeks of gestation with acute epigastric pain radiating to the back that was relieved by leaning forward, as well as frequent episodes of vomiting. Two weeks prior to her Emergency department (ED) presentation, she visited the Endocrinology Clinic for tighter control of her TG (TG 4,707 mg/dL), (Total Cholesterol 376 mg/dL, HDL 13 mg/dL). She was only taking Icosapent ethyl 2 g twice daily because her physician had discontinued her fenofibrate due to its potential teratogenic adverse effect. During this visit, Niacin (500 mg/day) was added, and she was referred to a registered dietitian for diet counseling. Given the risk of gestational diabetes in this high-risk patient and the low level of shortage, niacin was stopped a few days later. Her vital signs were stable at the time of presentation, with a blood pressure of 90/54 mmHg, a heart rate of 85 bpm, a temperature of 36.7 °C, a respiratory rate of 20 bpm, and a SO2 level of 99%. On physical examination, a gravid soft abdomen and epigastric discomfort were noted. She did not have any eruptive xanthomas, and her slit lamp eye exam came back normal. Venous blood was extremely lipemic. Blood studies showed elevated TG 4,273 mg/dL (< 150 mg/dl), amylase 175 IU/L (10-120 IU/L), lipase 105 U/L (13-60 U/L), HCO3 18 mmol/L (24-30 mmol/L), lactic acid 1.7 mmol/L (0.55-2.2 mmol/L), Calcium 9.2 mg/dL, blood glucose 188, and HbA1C 4.3%. Complete blood count, renal function tests, and liver tests were all normal. Mild splenomegaly, acute pancreatitis changes, and bilateral pleural effusions were all evident on abdominal ultrasonography with no signs of gallbladder stones. A fetal ultrasound was negative. Based on the clinical picture and the radiological findings, the diagnosis of HTGP was established since pancreatic enzyme levels can be interfered with by elevated TG[16].

Upon this diagnosis, the patient began adhering to NPO instructions and started on a regimen of continuous IV Insulin Glulisine (0-3 U/hr), daily 40 mg subcutaneous molecular weight heparin, and continuous aggressive intravenous (IV) fluid r (D10W 120 ml/h) with the aim to keep blood sugar levels between 100 mg/dl and 200 mg/dl. Her blood glucose ranged from 76 to 282 mg/dL; thus, she did not experience any episodes of hypoglycemia (75 mg/dL or below). Thromboprophylaxis was indicated in a high coagulable state with HTGP and bed rest. She had significant symptomatic hypocalcemia (Calcium 6.3 mg/dL) five h after presentation, indicated by carpopedal spasm, tetany, and a moderate prolongation of the QT segment on ECG. During this event, an ultrasound scanning showed a positive fetal heart rate and active flexion and extension of the fetus. Over the course of 36 hours, aggressive IV calcium gluconate replenishment was necessary to normalize serum calcium. On day 6, the serum TG level declined dramatically to 585 mg/dL, prompting the introduction of a very low-fat diet (15 percent fat of total daily calories) while maintaining IV insulin to prevent rebound HTG. With clinical improvement, the patient was started on a very low-fat diet with good tolerance. After one week, we decided to discontinue the insulin,

given the stable serum TG level, clinical improvement, and discharge plans [Figure 1]. We discharged her home with a prescription for Icosapent ethyl 2 g twice daily, Fenofibrate 200 mg daily, and a very low-fat diet after her serum TG level was 1,596 mg/dL on day 15, but thromboprophylaxis was stopped at home due to the fear of injections and patient noncompliance. We started TPE upon a repeat serum TG level of 3,899 mg/dl two weeks after discharge.

TPE was selected to possibly decrease the serum level of TG and eventually decrease the risk of acute pancreatitis. All TPE sessions were done using 5% albumin as a replacement fluid and heparin as an anticoagulant through a right femoral Central venous catheter. Before and after each session, a Nonstress test was performed. From week 26 to week 33, she received a total of 12 TPE treatments, with 2 sessions during each admission every 7-13 days, resulting in a serum TG reduction of 55.0 percent to 77.5 percent after each visit [Figure 2 and Table 2]. Note that the patient did not undergo screening for gestational diabetes by oral glucose tolerance test because, despite the decrease in TG level after each session, the patient presented on week 34 of pregnancy with recurrent pancreatitis.

On week 34, she presented to the Emergency room with a second episode of HTGP with early contractions. Studies revealed serum TG 4,719 mg/dl, calcium 6.6 mg/dl, amylase 704 IU/L, and lipase 519 U/L. Oral intake was suspended, and TPE was started according to the same protocol as before. An emergency C-section was performed a few hours later for fetal distress. A yellowish milky intra-abdominal fluid (approximately 500 cc) was discovered intra-operatively. She delivered a healthy female baby weighing 2,165 grams, with an Apgar score of 4 at 1 min and 9 at 5 min. The neonate was admitted to the neonatal ICU for 2 days because of prematurity. TG level dropped by 29% just after delivery, and by 57% (2,029 mg/dl) on the second day from the initial serum level on presentation. A very low-fat diet was initiated along with IV insulin, aiming to reduce TG below 1,000 mg/dL. Insulin was stopped after 4 days at a TG level of 753 mg/dL, and she was discharged home 2 days later with a TG level of 808 mg/dL. She was once again advised to follow a very low-fat diet and given Icosapent ethyl 2 g twice daily.

DISCUSSION

We presented the case of a 22-year-old female patient with poorly controlled FCS presenting with acute pancreatitis secondary to FCS-induced HTG. This case revealed the challenges faced during the treatment of pancreatitis caused by severe HTG. Acute pancreatitis in pregnancy is an uncommon complication that affects 1 in 1,000 to 1 in 10,000 women[1-3,5]. Its fetal and maternal morbidity burden was traditionally significant until recently, owing to early diagnosis and better management[1]. The considerable fall in maternal and fetal mortality rates in current reports (approximately 0% to 3%, respectively) compared to what was previously recorded (37% and 60%, respectively) demonstrates this[5]. Maternal adverse outcomes include pancreatic pseudocyst formation, pancreatic necrosis, shock, hypocalcemia, preeclampsia, eclampsia, chylous ascites, pleural effusion, and chronic pericarditis[2]. The fetal risks arise from preterm labor, which may result in prematurity and, in severe cases, lead to fetal death in utero[5,17]. On the other hand, there is evidence supporting the association between mild to moderate HTG, low-grade inflammation, and risk of acute pancreatitis. This correlation has been substantiated in multiple studies, including the work of Hansen *et al.*, which involved a sample size of approximately 118,000 individuals with HTG[18]. The incidence of primary HTGP in pregnancy is estimated to be 1 in 25,000 individuals[5]. It is still uncertain at what exact serum TG level pregnant women might develop pancreatitis. However, women with serum TG levels above 1,000 mg/dL are at an increased risk of developing severe pancreatitis (4%), and at a median TG level of 2,600 mg/dL, the risk has been observed to rise to 14%[2,4,7,9].

Table 2. Changes in TG levels pre- and post-TPE after each admission (2 sessions per admission), TG level and percentage decrease; mean and standard deviation for pre- and post-TPE TG levels, for TG level and percentage decrease

Admission	Pre-TPE TG (mg/dl)	Post-TPE TG (mg/dl)	Amount TG decrease (mg/dl)	Percentage decrease (%)
1	4,000.00	1,800.00	2,200.00	55.00
2	1,800.00	800.00	1,000.00	55.56
3	3,800.00	1,200.00	2,600.00	68.42
4	4,000.00	900.00	3,100.00	77.50
5	5,000.00	900.00	4,100.00	82.00
6	4,800.00	1,500.00	3,300.00	68.75
Mean	3,900.00	1,183.33	2,716.67	67.87
SD	1,136.66	397.07	1,060.97	11.05

TG: triglycerides; TPE: therapeutic plasma exchange; SD: Standard Deviation.

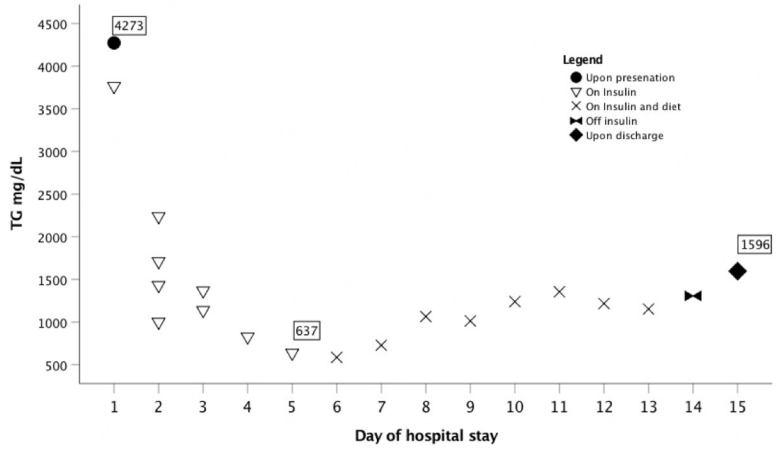

Figure 1. Changes in serum triglyceride level during the first hospitalization for pancreatitis. TG: triglycerides.

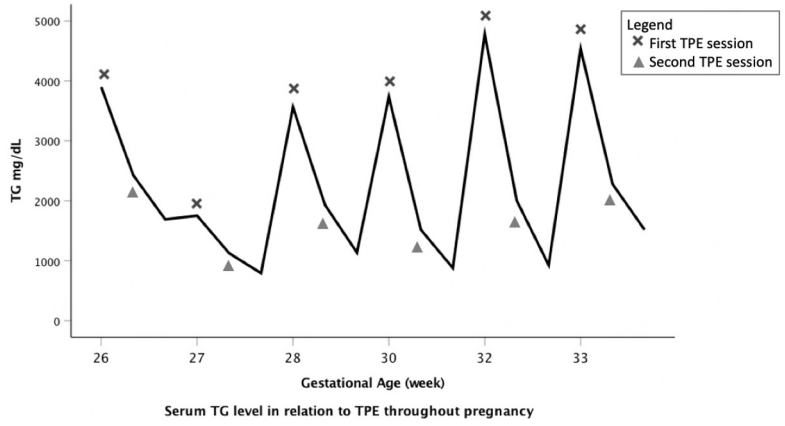

Figure 2. Changes in serum triglycerides level during elective TPE over 12 sessions.

Primary HTG-induced pancreatitis was shown to be more severe than other etiologies, and patients had worse outcomes[2,3,5,7]. In women with primary HTG, the risk of developing pancreatitis increases during pregnancy and becomes more pronounced as the pregnancy advances[2,3]. This is due to physiologic hormonal changes that occur in the last two-thirds of pregnancy, which are principally manifested by a rise

in serum estrogen levels and an insulin-resistant state. This is attributed to the downregulation of the LPL gene expression, which reduces LPL function and, as a result, the clearance of both VLDL and TG. The placental lactogen, on the other hand, increases TG substrates, free fatty acids (FFA), and adipose tissue lipolysis. Despite a 2.5-fold increase in TG levels, pregnant women without primary HTG seldom develop pancreatitis because TG levels rarely exceed 300 mg/dL by the third trimester; this is of minimal clinical consequence[2,3,5].

FCS (OMIM 238600) is an extremely rare autosomal recessive disorder caused by biallelic mutations of either the LPL or apo C-II, which induce lipoprotein lipase (LPL) and apo C-II deficiencies, resulting in defective TG hydrolysis. It is characterized by severe HTG that begins in childhood and manifests as hepatosplenomegaly, lipemia retinalis and eruptive xanthomas, and recurrent pancreatitis[7-10]. In fact, many cases of FCS syndrome in women are discovered in the third trimester of pregnancy as there are marked changes in the lipid profile, often resulting in a 2- to 4-fold increase in triglyceride level; therefore, pregnancy is an exacerbating factor for uncontrolled FCS[9]. In addition, according to the "reset hypothesis", weaning, rather than delivery, will terminate the maternal metabolic effects of pregnancy[19]. Throughout literature, few cases are reported of pregnant women presenting with acute pancreatitis secondary to FCS-induced HTG[9,17,19,20-24] [Table 3]. Acute pancreatitis is hypothesized to be caused by the lipolysis of TG by pancreatic lipase. This process results in the generation of free fatty acids, which, in turn, have a direct cytotoxic effect on the acinar cells[4,7,11]. FCS is a severe form of primary genetic HTG that manifests during infancy and is characterized by extremely high blood TG levels (>1,000 mg/dl), resulting in recurrent HTGP[3,10]. The majority of HTGP cases occur when TG levels exceed 3,000 mg/dl, and most guidelines recommend commencing therapy at a TG level of 2,000 mg/dl[10].

So far, there are no established guidelines for managing HTG during pregnancy[2,5,11]. The primary objective of treatment is to lower serum TG levels and prevent HTGP. Most pharmacological agents used in pregnancy are classified as pregnancy class C and should only be used when other conservative approaches have failed[11]. Furthermore, most TG-lowering drugs are ineffective in FCS as compared to other primary HTG disorders, which is also related to LPL deficiency. The safe TG limit for pregnant women with HTGP is clear: less than 1,000 mg/dl. TG levels of less than 500 mg/dl may be safer[4,7,11]. However, the safe limit for patients without pancreatitis is debatable. Safe limits should be based on patient characteristics, attainable TG levels without significant side effects by therapeutic apheresis, duration of pregnancy, and presence of symptoms[25].

In our patient, we had limited treatment options due to the scarcity of studies in the literature regarding the management of FCS during pregnancy. While various novel therapies were studied in the general population, they are rarely investigated in pregnant women. Given the failure of our patient to respond to nutritional recommendations, we were restricted to conventional therapy options. In addressing her acute pancreatitis and recognizing the imperative of preventing recurrence, we decided to employ TPE. Throughout literature, different treatment techniques were studied and used in such cases, but on the other hand, novel therapies required further testing. The basic lifestyle approach is a very low-fat diet and medium-chain fatty acids. The core therapy is to limit saturated and unsaturated fat intake to 10%-15% of total daily calories, or 20-40 g[2,5,9-12]. To promote compliance, patients are advised to seek the instructions of a registered dietitian. It is necessary to take fat-soluble vitamin supplements. It is also critical to limit alcohol consumption and avoid certain medications that might exacerbate HTG[9]. In addition, the patient was advised to use medium-chain fatty acids since they decrease postprandial rise in TG level by decreasing the synthesis of chylomicrons[26]. Our patient's TG level was not controlled despite following a very low-fat diet as directed by a registered dietician and documented by a food frequency questionnaire, and additional

Table 3. Cases of pregnant women with acute pancreatitis secondary to FCR-induced HTG and treatment modalities used

Author	Age	Peak TG (mg/dl)	Pancreatitis episodes	Time onset of pancreatitis	Treatment	Number of TPE sessions
Shi *et al.*[20] (2020)	26	1,777	2 (1 in each pregnancy)	40 + 1 37 + 2	Emergent C-section, NPO	0
Kim *et al.*[21] (2020)	19	3,667	1	25	Insulin SC Heparin Marine Oil TPE	13
Gupta *et al.*[17] (2014)	32	12,570	1	38 + 4	Emergent C-section TPE	1
Tsai *et al.*[22] (2004)	23	6,000	1	28	Gemfibrozil	0
Lennertz *et al.*[23] (1999)	34	9,410	1	31	TPE	1
Sanderson *et al.*[24] (1991)	33	12,000	2 (1 in each pregnancy)*	33 32 + 5	Low-fat diet and Hydration	0
Our case	22	5,000	2 (same pregnancy)	21 & 34	NPO Low-fat diet TPE	12

TG: triglycerides; TPE: therapeutic plasma exchange; NPO: Nil Per Os; Time Onset of Pancreatitis: gestational age in weeks and days at the time of pancreatitis; *: Sanderson *et al.* reported the patient had a third pregnancy with no acute pancreatitis, prophylactic hospitalization[24].

therapy was indicated.

Some conventional and novel therapy options include: (1) Fibric acid derivatives: They have a limited role in FCS because they promote TG-rich particle clearance by acting on the peroxisome proliferator-activated receptor alpha (PPAR-), increasing LPL activity, and reducing apoC3 levels[7,10]. Because they are classified as category C by the Food and Drug Administration, there is minimal information about their usage during pregnancy (FDA). According to certain case studies, they can be used after the second trimester with no documented side effects, including teratogenicity[27-29]. Similarly, our patient was prescribed fenofibrate but did not respond, and no teratogenic effects were observed; (2) Niacin: Because it is designated as pregnancy class C, there is limited data on its utilization in FCS and its safety during pregnancy. It reduces TG through lowering VLDL secretion, peripheral lipolysis, and apoC-3 levels[10]. With dosages of 2 to 3 grams per day, it can lower plasma TG levels by around 20%, which is normally seen in 6 weeks[10,12]. We were not able to assess its potency in our patient because she had to stop using it after only a few days due to a shortage of supply. It is also worth mentioning that niacin is associated with an increased risk of thrombocytopenia, and therefore, its use is questionable and its safety during pregnancy is now well established[30-33]; (3) Volanesorsen: It is a second-generation antisense oligonucleotide (ASO) to apoC3. As a novel licensed therapy, it was proven to be effective in patients with FCS, with a 50% decrease in TG and no episodes of pancreatitis[34]. It was not tested in pregnant women; however, animal trials revealed no maternal-fetal harm[34]. Furtherly, this drug was inaccessible due to its high cost in our case.

On the other hand, some treatment techniques require hospitalization, including: (1) Insulin: It is effective at lowering serum TG levels by increasing the activity of the LPL enzyme[7]. It can be given intravenously or subcutaneously, with identical outcomes; however, the IV method is more practical and easier to titrate. It acts synergistically with fasting, leading to an 87% reduction in TG when employed in combination, compared to 40% when used alone[11]. When IV insulin was combined with TPE in a study, it resulted in a 92.6% decrease in 24 h at the expense of adverse effects such as respiratory distress and acute kidney injury. Shaka *et al.* described its use in FCS in a non-diabetic patient, where it was an effective therapy, but the result was transient, and the patient eventually needed elective TPE[35]. Similarly, IV insulin proved a temporary therapy in our patient since once it was withdrawn and feeding resumed, TG went up again;

(2) Therapeutic plasma exchange / plasmapheresis / apheresis: It is being utilized more frequently in patients with HTG-induced pancreatitis because of its rapid action and the additive benefit of reducing inflammatory cytokines[4,7,14]. TPE has been shown to be efficacious and safe in the acute setting during pregnancy, as well as a prevention for acute or recurrent pancreatitis[11,14]. Therapeutic apheresis can be considered the first-line treatment for pregnant women with HTGP, and it has been used electively to prevent pancreatitis[4,11]. In one study, the first session resulted in a TG decrease of more than 60%[14]. Among patients with severe HTGP, TPE therapy resulted in a considerable reduction in clinical symptoms, according to many case studies. It was also observed in another study that it hastens the recovery process[11,13]. Based on these observations, TPE is considered a superior therapeutic option for individuals with severe HTG (> 2,000 mg/dl), and it was also proven to be useful for the treatment of severe HTGP according to the Revised Atlanta Classification[13]. However, there was no clear relation between apheresis usage and improved APACHE II scores, duration of stay in the ICU or, overall, in the hospital, or prevention of sequelae from severe pancreatitis[4]. TPE is classified as Category 3 (Grade 2C) when used during HTGP[4]. Djelmis *et al.* reported successful use of TPE as a preventive modality in a pregnant patient with FCS[36]. They performed TPE twice weekly and the patient delivered at full term without any complications. Unlike our patient, theirs had a lower baseline blood TG level (2,000 mg/dl), which was subsequently reduced to 1,000 mg/dl after each treatment.

Our patient's post-treatment TG level was virtually always over 1,000 mg/dl, even though the sessions were done practically every week. Furthermore, pharmaceutical therapy for decreasing TG throughout her pregnancy was ineffective. Despite regular TPE treatments, she developed a second HTGP in her third trimester, and the TPE attempt failed due to premature contractions and abnormalities in fetal heart rate, necessitating an urgent C-section. TPE's use as a conventional therapy is hampered by the high cost of treatment, its temporary nature, and its lack of availability in all healthcare settings[7,9]. Compared to TPE, double filtration lipid apheresis was shown to be less successful in reducing TG and have greater side effects, including higher infection rates, hemorrhage, hemolysis, anemia, and technical issues owing to tube blockage[25]. This case is of importance to be reported since only rare subjects are reported in the literature and the challenge of managing acute pancreatitis in patients with FCS-induced HTG. In addition, our patient is the first to develop pancreatitis twice during a single pregnancy, even after prophylactic TPE. The limitation is the lack of genetic testing due to the low socioeconomic status of the patient, and the unavailability of novel drugs in the region.

CONCLUSION

In conclusion, FCS is a very rare primary hypertriglyceridemia disorder that can manifest itself in pregnancy as severe hypertriglyceridemia and acute pancreatitis. A metabolic disease that is manifested by disruption of chemical reactions leading to accumulation of excessive metabolites[37]. Our patient, diagnosed in infancy, was uncontrolled throughout adolescence, and upon pregnancy, the complications started to occur. Acute pancreatitis develops in uncontrolled FCS patients, but in pregnancy, this remains a challenging approach with limited studies. Pharmacological agents are often ineffective, and a very low-fat diet may not be enough to keep HTG under control. To prevent HTGP and unfavorable maternal-fetal outcomes, affected women should be followed closely and frequent TPE is advised. Safety studies on novel therapies for hypertriglyceridemia due to FCS in pregnancy are required.

DECLARATIONS

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Authors' contributions

Participated in literature review, collecting data, and writing the manuscript: Jaafar B, Abou Chaaya J, Ammar S
Reviewed the manuscript: Salti I

Availability of data and materials

The data that support the findings of this study are available from the corresponding author, [B.J], upon reasonable request.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

An oral informed consent was taken from the patient to participate since it is an anonymous case report.

Consent for publication

An oral informed consent was taken from the patient to publish since it is an anonymous case report.

REFERENCES

1. Igbinosa O, Poddar S, Pitchumoni C. Pregnancy associated pancreatitis revisited. *Clin Res Hepatol Gastroenterol* 2013;37:177-81. DOI PubMed
2. Pitchumoni CS, Yegneswaran B. Acute pancreatitis in pregnancy. *World J Gastroenterol* 2009;15:5641-6. DOI PubMed PMC
3. Eddy JJ, Gideonsen MD, Song JY, Grobman WA, O'Halloran P. Pancreatitis in pregnancy. *Obstet Gynecol* 2008;112:1075-81. DOI PubMed PMC
4. Syed H, Bilusic M, Rhondla C, Tavaria A. Plasmapheresis in the treatment of hypertriglyceridemia-induced pancreatitis: a community hospital's experience. *J Clin Apher* 2010;25:229-34. DOI PubMed
5. Ducarme G, Maire F, Chatel P, Luton D, Hammel P. Acute pancreatitis during pregnancy: a review. *J Perinatol* 2014;34:87-94. DOI PubMed
6. Chen CP, Wang KG, Su TH, Yang YC. Acute pancreatitis in pregnancy. *Acta Obstet Gynecol Scand* 1995;74:607-10. DOI PubMed
7. Ewald N, Hardt PD, Kloer HU. Severe hypertriglyceridemia and pancreatitis: presentation and management. *Curr Opin Lipidol* 2009;20:497-504. DOI PubMed
8. Musambil M, Al-Rubeaan K, Al-Qasim S, Al Naqeb D, Al-Soghayer A. Primary hypertriglyceridemia: a look back on the clinical classification and genetics of the disease. *Curr Diabetes Rev* 2020;16:521-31. DOI PubMed
9. Falko JM. Familial chylomicronemia syndrome: a clinical guide for endocrinologists. *Endocr Pract* 2018;24:756-63. DOI PubMed
10. Chaudhry R, Viljoen A, Wierzbicki AS. Pharmacological treatment options for severe hypertriglyceridemia and familial chylomicronemia syndrome. *Expert Rev Clin Pharmacol* 2018;11:589-98. DOI PubMed
11. Rawla P, Sunkara T, Thandra KC, Gaduputi V. Hypertriglyceridemia-induced pancreatitis: updated review of current treatment and preventive strategies. *Clin J Gastroenterol* 2018;11:441-8. DOI PubMed
12. Santamarina-Fojo S. The familial chylomicronemia syndrome. *Endocrinol Metab Clin North Am* 1998;27:551-67, viii. DOI PubMed
13. Gavva C, Sarode R, Agrawal D, Burner J. Therapeutic plasma exchange for hypertriglyceridemia induced pancreatitis: a rapid and practical approach. *Transfus Apher Sci* 2016;54:99-102. DOI PubMed
14. 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. DOI PubMed
15. Swoboda K, Derfler K, Koppensteiner R, et al. Extracorporeal lipid elimination for treatment of gestational hyperlipidemic pancreatitis. *Gastroenterology* 1993;104:1527-31. DOI

16. Tariq H, Gaduputi V, Peralta R, et al. Serum triglyceride level: a predictor of complications and outcomes in acute pancreatitis? *Can J Gastroenterol Hepatol* 2016;2016:8198047. DOI PubMed PMC
17. Gupta N, Ahmed S, Shaffer L, Cavens P, Blankstein J. Severe hypertriglyceridemia induced pancreatitis in pregnancy. *Case Rep Obstet Gynecol* 2014;2014:485493. DOI PubMed PMC
18. Hansen SEJ, Madsen CM, Varbo A, Nordestgaard BG. Low-grade inflammation in the association between mild-to-moderate hypertriglyceridemia and risk of acute pancreatitis: a study of more than 115000 individuals from the general population. *Clin Chem* 2019;65:321-32. DOI PubMed
19. Lonardo A, Suzuki A. Concise review: breastfeeding, lactation, and NAFLD. An updated view of cross-generational disease transmission and prevention. *Metab Target Organ Damage* 2023;3:16. DOI
20. Shi XL, Yang Q, Pu N, et al. Identification and functional characterization of a novel heterozygous missense variant in the LPL associated with recurrent hypertriglyceridemia-induced acute pancreatitis in pregnancy. *Mol Genet Genomic Med* 2020;8:e1048. DOI
21. Kim AS, Hakeem R, Abdullah A, et al. Therapeutic plasma exchange for the management of severe gestational hypertriglyceridaemic pancreatitis due to lipoprotein lipase mutation. *Endocrinol Diabetes Metab Case Rep* 2020;2020:19-0165. DOI PubMed PMC
22. Tsai EC, Brown JA, Veldee MY, Anderson GJ, Chait A, Brunzell JD. Potential of essential fatty acid deficiency with extremely low fat diet in lipoprotein lipase deficiency during pregnancy: a case report. *BMC Pregnancy Childbirth* 2004;4:27. DOI PubMed PMC
23. Lennertz A, Parhofer KG, Samtleben W, Bosch T. Therapeutic plasma exchange in patients with chylomicronemia syndrome complicated by acute pancreatitis. *Ther Apher* 1999;3:227-33. DOI PubMed
24. Sanderson SL, Iverius PH, Wilson DE. Successful hyperlipemic pregnancy. *JAMA* 1991;265:1858-60. PubMed
25. Basar R, Uzum AK, Canbaz B, et al. Therapeutic apheresis for severe hypertriglyceridemia in pregnancy. *Arch Gynecol Obstet* 2013;287:839-43. DOI
26. Hauenschild A, Bretzel RG, Schnell-Kretschmer H, Kloer HU, Hardt PD, Ewald N. Successful treatment of severe hypertriglyceridemia with a formula diet rich in omega-3 fatty acids and medium-chain triglycerides. *Ann Nutr Metab* 2010;56:170-5. DOI PubMed
27. Cruciat G, Nemeti G, Goidescu I, Anitan S, Florian A. Hypertriglyceridemia triggered acute pancreatitis in pregnancy - diagnostic approach, management and follow-up care. *Lipids Health Dis* 2020;19:2. DOI PubMed PMC
28. Carpentier AC, Frisch F, Labbé SM, et al. Effect of alipogene tiparvovec (AAV1-LPL(S447X)) on postprandial chylomicron metabolism in lipoprotein lipase-deficient patients. *J Clin Endocrinol Metab* 2012;97:1635-44. DOI PubMed
29. Gaudet D, Stroes ES, Méthot J, et al. Long-term retrospective analysis of gene therapy with alipogene tiparvovec and its effect on lipoprotein lipase deficiency-induced pancreatitis. *Hum Gene Ther* 2016;27:916-25. DOI
30. Salmon F, Grosios K, Petry H. Safety profile of recombinant adeno-associated viral vectors: focus on alipogene tiparvovec (Glybera®). *Expert Rev Clin Pharmacol* 2014;7:53-65. DOI PubMed
31. Gaudet D, Digenio A, Alexander V, et al. The approach study: a randomized, double-blind, placebo-controlled, phase 3 study of volanesorsen administered subcutaneously to patients with familial chylomicronemia syndrome (FCS). *Atherosclerosis* 2017;263:e10. DOI
32. Royer DJ, George JN, Terrell DR. Thrombocytopenia as an adverse effect of complementary and alternative medicines, herbal remedies, nutritional supplements, foods, and beverages. *Eur J Haematol* 2010;84:421-9. DOI PubMed
33. Blumer I, Hadar E, Hadden DR, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2013;98:4227-49. DOI PubMed PMC
34. Ross CJ, Twisk J, Meulenberg JM, et al. Long-term correction of murine lipoprotein lipase deficiency with AAV1-mediated gene transfer of the naturally occurring LPL(S447X) beneficial mutation. *Hum Gene Ther* 2004;15:906-19. DOI PubMed
35. Shaka H, Edigin E, Yap SE, Asemota I. SAT-565 familial homozygous lipoprotein lipase defect presenting with recurrent chylomicronemia syndrome: making a case for elective plasmapheresis as an adjuvant treatment modality. *J Endocr Soc* 2020;4:SAT-565. DOI PMC
36. Djelmis J, Ivanisevic M, Kosi N. Plasmapheresis in pregnant patient with familial hypertriglyceridemia. *Eur J Obstet Gynecol Reprod Biol* 2016;201:226-7. DOI PubMed
37. Lonardo A. Editorial: metabolism and target organ damage. *Metab Target Organ Damage* 2021;1:1. DOI