Management of a Patient With Chylomicronemia Syndrome During Pregnancy With Medical Nutrition Therapy: a Case Report

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Abstract

Background: Hypertriglyceridemia (HTG) during pregnancy may be accompanied by acute pancreatitis, hyperviscosity syndrome, and preeclampsia. HTG during pregnancy should be managed by a multidisciplinary team, however, no clinical guidelines exist for severe gestational HTG.

Case presentation: We herein present a case of 36-year-old G1P0Ab0, with a history of severe HTG-induced necrotizing pancreatitis 9 years ago. There was no family history of HTG. During these years, she did not follow any appropriate diet or medical therapy for HTG. She became pregnant in May 2019, without preconception counseling. Eruptive and tuberoeruptive xanthomas appeared in 27^{th} week of pregnancy. Serum triglycerides (TGs) and fasting blood sugar (FBS) were 6620 and 124 mg/dL, respectively. Showing HTG and gestational diabetes (GDM). After admission for management of severe HTG; she was put on parenteral nutrition with dextrose water 5% and infusion insulin therapy without receiving any enteral carbohydrate for two days. Following that, very low fat diet and omega-3 fatty acids (1200 mg/day) were stated. After 4 weeks, TG levels reached 1000 mg/dL and her self-monitoring blood glucose levels showed appropriate blood glucose for pregnancy. She underwent a successful elective cesarean section in 39^{th} of pregnancy.

Conclusion: This case report demonstrates that HTG during pregnancy could be well managed by medical nutrition therapy (MNT).

Background

Hypertriglyceridemia (HTG) can arise from hepatic overproduction, decreased clearance of chylomicrons and very low density lipoprotein (VLDL) remnant, ineffective lipolysis, or a combination of these factors [1]. HTG has been defined as fasting TG concentrations ≥150 mg/dL [2]. Severe HTG is defined as TG concentration >885mg/dL, which is almost accompanied by the pathological presence of chylomicrons; this affects 0.1–0.2% of the population[3]. Chylomicronemia manifested by eruptive xanthomas, lipemia retinalis, hepatosplenomegaly, and episodes of pancreatitis called as chylomicronemia syndrome [1].

According to World Health Organization International Classification of Diseases (WHO ICD), chylomicronemia is seen in type I and type V with elevated chylomicron and VLDL in type V and isolated elevation of chylomicron in type I of hyperlipoproteinaemia [4].

Severe hypertriglyceridemia is most often due to polygenic susceptibility interacting with secondary non-genetic factors [5], including consumption of high-fat foods, alcohol, estrogen-containing medication, pregnancy, obesity, insulin resistance, diabetes, hypothyroidism, nephrotic syndrome or medications that increase VLDL secretion (e.g., steroids, and beta-blockers) [6, 7].

During pregnancy, significant alterations to lipid homeostasis occur [7] include an increase in TG and total cholesterol levels which are mediated by estrogen, progesterone, and human placental lactogen

(HPL) [8].The presence of HTG in pregnancy has many risks including acute pancreatitis, hyperviscosity syndrome, and preeclampsia [1].

There are no strict clinical guidelines for the treatment of HTG during pregnancy. Generally, during the prenatal period, a low-fat and low-glycemic diet with adequate nutrients to avoid essential fatty acid deficiency are advised. In refractory cases, hospitalization for parenteral nutrition or intravenous insulin therapy, fibrate use after the first trimester, and plasmapheresis are considered [1, 8]. Unfortunately, there are only a few studies addressing the management of HTG during pregnancy.

Case Presentation

We herein present a case of 36-year-old G1P0Ab0, with sever HTG presented in second trimester of pregnancy.

She gave a history of hospital admission 9 years ago with acute abdominal pain and severe HTG >6000 mg/dl. HTG-related acute necrotizing pancreatitis was diagnosed by laparoscopic excision of necrotic tissues and by ruling out other causes of pancreatitis. Since then, she did not follow specific diets for HTG. During her irregular medical visits, occasional fibrates were prescribed by her physician. She did not reported severe HTG in her first and second degree family. Pre-pregnancy weight and body mass index (BMI) were 52 kg and 19.5 kg/m^2 respectively. She became pregnant without preconception counseling.

At the beginning of pregnancy, her serum TG level was 619 mg/dl with normal fasting blood sugar (FBS). She still did not have a specific diet and did not consult an endocrinologist or nutritionist for HTG because she had a low socioeconomic status. Eruptive xanthomas in forearms, legs, back, and tuberoeruptive xanthomas on her elbows (figure 1) occurred in 27^{th} week of pregnancy and she was admitted hospital in November 2019. Her serum lipoprotein profile was as following: fasting triglycerides: 6620 mg/dL, total cholesterol: 459 mg/dL, high density lipoprotein cholesterol (HDL-C): 76 mg/dL, and serum amylase and lipase levels were within normal limits. Except pregnancy, no other aggravating factors for HTG were found. After admission, TG level reached 8683 mg/dl (figure 2). FBS was normal in early pregnancy. However the glucose tolerance test (GTT) with 75 g anhydrase glucose showed: FBS: 124 mg/dl, 1-hour glucose: 168 mg/dl, 2-hour glucose: 130 mg/dl indicating presence of gestational diabetes. There were no thyroid, liver, and renal function abnormalities. Abdominal ultrasound imaging was unremarkable with no evidence of pancreatitis, and hepatosplenomegaly.

To reduce TGs rapidly, patient was put on dextrose 5% in water (D5W, 2500 ml per day) and insulin regular (5-7 unit/hour) infusion, without any enteral intake, and with close monitoring for blood sugar and serum electrolytes including sodium and potassium levels. After two days, TG level was 5560 mg/dl. Insulin infusion was discontinued. A low-fat diet consisting of 10%, 25%, and 65% of energy from fat, protein, and carbohydrate, respectively was prescribed by the dietician. The diet consisted of 4 servings of skim-fat milk or yoghurt, 4 servings of vegetables, 6 servings of fruits, 1 serving of simple carbohydrate such as sugar or honey, 11 servings of grains, 8 servings of meat and/or protein alternatives. She was

educated on food labeling in order not to consume any processed food items, which often have added fat. Three servings of meat and its substitutes were prescribed; including plant-based proteins such as legumes, one serving from egg white and other servings from white meat including chicken and turkey. Concurrently, 7 capsules daily of omega-3 fatty acids containing 360 mg eicosapentaenoic acid (EPA) and 240 mg docosahexaenoic acid (DHA) per capsule (equal to 4200 mg) were started in divided doses. But, due to the problem of cost and availabilitythe patient received omega-3 at a dose of 5 capsules daily (equal to 3000 mg) for 10 days and then 2 capsules daily (equal to 1200 mg) for the rest of the pregnancy.

She was followed by a multidisciplinary team consisting of endocrinologist, obstetrician, and registered dietitian. In the first week after administration of medical nutrition therapy (MNT) and omega-3 fatty acids, TG levels dropped to 2700 mg/dL. Self-monitoring of blood glucose revealed mean level of FBS and 2-h plasma glucose equal to 74 mg/dl and 96mg/dl, respectively. She was discharged with a 10% fat-restricted diet with medium-chain TGs (MCT) 15 g daily. Continuing MNT for 4 weeks, TG levels reached to 1000 mg/dl and all SMBGs were in the recommended ranges for the pregnancy. From the time of admission to the specialists and up to labor, she had regular weekly contacts with her endocrinologist and dietician. Due to concerns about the fetal growth and TG levels, the patient's diet was carefully and weekly adjusted until the end of pregnancy. During pregnancy, her blood pressure was not higher than 110/80 mmHg and preeclampsia did not occur. At the end of pregnancy her body weight was 58 kg (equal to 6 kg weight gain).

Although we planned to terminate pregnancy at 36^{th} weeks; in view of low fetal growth for the gestational age, we decided to delay this for a few weeks. It was vital to carry out close monitoring of fetal wellbeing along with maternal surveillance for sign and symptoms of pancreatitis; fortunately they did not occur and so she underwent elective cesarean section at 39^{th} week of pregnancy with TG level of 1700 mg/dL. She delivered a healthy baby girl weighting 2750 g. Patient had an uncomplicated postoperative course and was discharged, and recommended to continue her diet. A few days after delivery, her TG level dropped to 1200 mg/dL. She was advised to safety breastfeed her baby. At the second month of postpartum no complication or health problems related to HTG.

Discussion

Our patient was a 36-year-old pregnant woman with presentation of chylomicronemia syndrome during pregnancy, who was managed successfully with MNT.

The widely used term familial chylomicronemia syndrome is synonymous with monogenic chylomicronemia [5].The absence of secondary factors, and HTG diagnosis at young adulthood are suggestive of monogenic chylomicronemia,particularly if hypertriglyceridemia is severe and associated with pancreatitis[3].

Considering past history of necrotizing pancreatitis at 27 years accompanied with severe HTG, and a lack of family history of HTG and because we do not have access to conduct genetic testing, our differential diagnosis based on clinical evidence is rare monogenic HTG.

Guidelines advise a combination of restricting dietary fat intake with drug treatment (e.g. fibrates, niacin, or omega-3 fatty acids) to manage severe HTG in the non-pregnant patients. However, no clear clinical guidelines exist for severe gestational HTG to maintain the balance between maternal and fetal needs. We suggest that women with gestational HTG should be managed by multidisciplinary team [9, 10], as it is associated with many clinical challenges [7].

The HTG perimeters for admission depends on may factors and presenting symptoms [8]. The patient was admitted due to rapid TG increase, poor dietary compliance, previous pancreatitis due to HTG despite the absence of present pancreatitis and presence of GDM [8]. Short-term hospitalizations can be used proactively to rapidly reduce TG levels through parenteral nutrition (PN), or intravenous insulin therapy if GTT is also impaired, and plasmapheresis [7, 9, 10].

PN is effective because systemic delivery of lipids bypasses the portal system, allowing for peripheral metabolism and trans-placental passage of fats [1]. Moreover, insulin is a rapid and potent activator of LPL. It can be used to treat severe HTG because it increases removal of TGs from the plasma. Given the risks of hypoglycemia, it is usually co-administrated with glucose infusion [7]. Therefore, after the patient was hospitalized, we prescribed D5W and regular insulin infusion through two separate veins. But no significant drop in TG levels was observed after two days (Figure 2).

Use of fibrates and niacin in gestational HTG is much more controversial. Although it has been documented that their use after the first trimester has no obvious adverse effects [7], their safety during pregnancy has not been established [8]. Moreover, in monogenic causes of hyperchylomicronemia syndrome, lipid-lowering agents such as fibrates seem to be ineffective[11]. The definitive diagnosis in our patient was not established, however, as it was possible that she had a monogenic cause of HTG; we decided to avoid prescribing fibrates and niacin.

In non-pregnant individuals, higher doses of omega-3 fatty acids which contain EPA and DHA (4 g/day total EPA+DHA) have been shown to reduce ongoing metabolic control, concentration of VLDL and possible chylomicron secretion [2, 3]. Omega-3 fatty acids are the cornerstone of safe therapy for mother and child in long-term [6,7]. As previously mentioned, due to cost and limited availability our patient received only 1200mg of omega-3 daily.Therefore, the triglyceride drop does not appear to be related to omega-3.

Dietary counseling should be initiated immediately. The diet should be low in fat, less than 20% [7], ideally there should be less than 10% of calories from fat [6]. However, adherence to such a regimen is extremely challenging for most patients [6]. In addition, restricted fat intake can lead to maternal and more importantly fetal deficiency of omega-3 and omega-6 essential fatty acids (EFA) (including alpha-linolenic acid (ALA) and linoleic acid (LA)) as well as the vital long-chain omega-3 polyunsaturated fatty

acids (including EPA and DHA). Although symptoms of EFA deficiency are relatively mild for the mother (typically skin dryness and desquamation) [7], fetal EFA and long-chain polyunsaturated fatty acids deficiency may end in impaired fetal brain and visual development [7]. The diet should include a minimum of 300 mg of EPA and DHA [7]. The use of omega-3- fatty acids, and medium-chain triglycerides (MCTs) will provide calories, while preventing plasma TGs increase [6, 7]. Although the safety of MCTs has not been specifically evaluated in the fetus [12], in a randomized double-blind intervention by Rayyan et al. MCT- containing emulsion were safe and well tolerated by preterm infants[12]. The patient was discharged with a low fat diet, containing mostly medium-chain triglyceride foods.

Although metabolic control is ongoing, TG concentrations may rapidly rebound at any time [3]. The risk of pancreatitis is always present and more effective therapies are required [13].

Close surveillance of plasma TG concentrations during pregnancy is essential and should be followed up at least on a monthly basis. As pregnancy progresses, TG levels may need to be monitored every 1 to 2 weeks [7]; we carried this out with our patient.

Strong consideration should be given towards induction once fetal maturity is established (i.e. at 36^{th} weeks), especially in women whom TG levels show a steep upward trend in the third trimester [7]. However, as previously discussed due to the low fetal growth for her gestational age, she underwent elective cesarean section with meticulous fetal and maternal monitoring at 39^{th} week of pregnancy.

In the postpartum period, the decision to resume these medications will depend on the latest blood results and trend of the serum TGs as well as maternal breastfeeding plans [7]. In the postpartum period, considering the relative reduction of TGs, our patient continued to receive individualized MNT.

Conclusion

As far as we know, this is the first case reporting gestational severe HTG, who was high risk for pancreatitis, and was treated with MNT successfully. The management led to the termination of a safe pregnancy and the birth of a healthy baby girl. Hopefully we will see more case studies and in the future, so we can begin to provide recommendations on MNTs that are acceptable for pregnant women.

Abbreviations

HTG: Hypertriglyceridemia, TGs: Serum triglycerides, FBS: Fasting blood sugar, GDM: Gestational diabetes, MNT: Medical nutrition, VLDL: Very low density lipoprotein, WHO ICD: World Health Organization International Classification of Diseases, HPL: Human placental lactogen, BMI: Body mass index, HDL-C: High density lipoprotein cholesterol, GTT: Glucose tolerance test, D5W: Dextrose 5% in water, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid, EFA: Essential fatty acids, ALA: Alpha-linolenic acid, LA: linoleic acid, MCTs: Medium-chain triglycerides.

Declarations

Ethics approval and consent to participate

The ethics committee of the Research Institute for Endocrine Sciences (RIES) of Shahid Beheshti University of Medical Sciences approved the study protocol and informed consent form was obtained from the patient.

Consent for publication statement

Consent for publication was obtained from that patient for her medical nutrition therapy data.

Availability of data and materials

All patient laboratory data's and documents are available from the corresponding author on reasonable request at any stage (including after publication).

Conflict of Interests

None of the authors had any financial and non-financial competing interests**.**

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Authors' contributions

M. Z. and F. H. interpreted in diagnosis of disease, medical treatment and follow-up of the patient and G. A., and P. M. contributed in MNT. All authors read and approved the final manuscript.

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Statement of Informed Consent

Informed consent was obtained from the patient.

Declaration of interests

The authors declare that they have no known competing financialinterestsor personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Figures

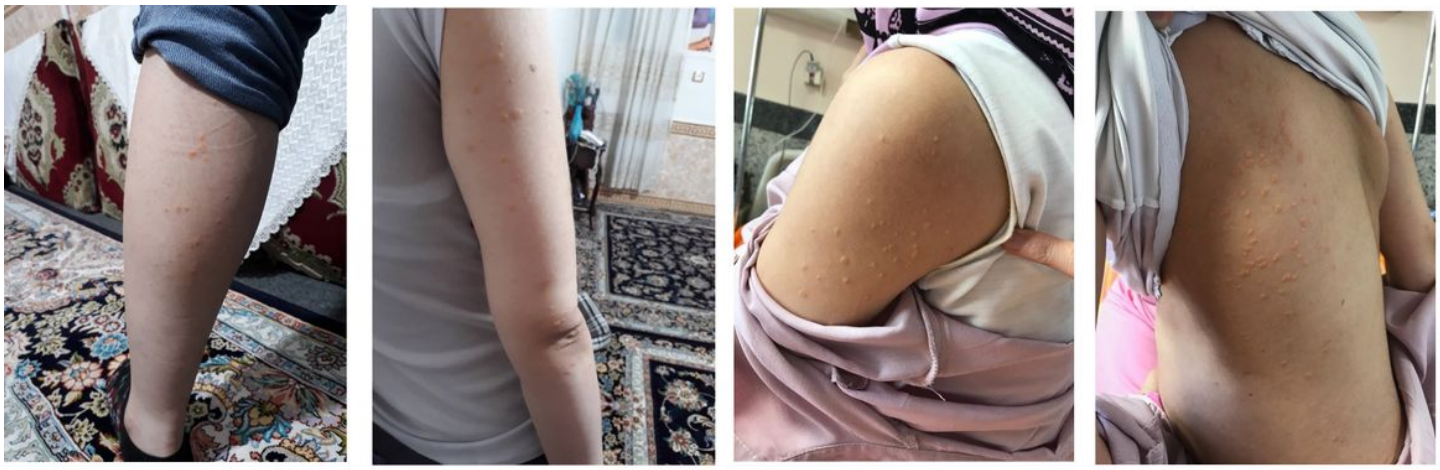

Figure 1

Eruptive and tuberoeruptive xanthomas

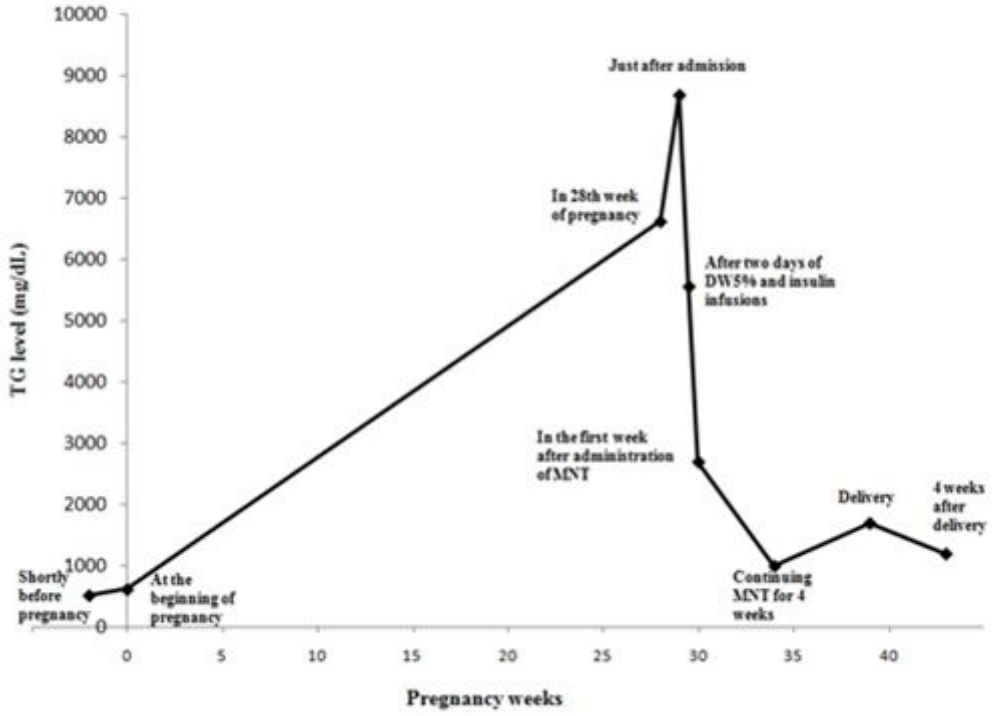

Figure 2

Serum triglyceride (TGs) concentration during pregnancy and postpartum