Case Report

Abruptio Placentae Caused by Hypertriglyceridemia-Induced Acute Pancreatitis during Pregnancy: Case Report and Literature Review

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Background. Hormonal effects during pregnancy can compromise otherwise controlled lipid levels in women with hypertriglyceridemia and predispose to pancreatitis leading to increased morbidity for mother and fetus. Elevation of triglyceride levels is a risk factor for development of pancreatitis if it exceeds 1000 mg/dL. Pancreatitis should be considered in emergency cases of abdominal pain and uterine contractions in Emergency Department at any stage of pregnancy. We report a case of abruptio placentae caused by hypertriglyceridemia-induced acute pancreatitis. Also, literature review of cases of acute pancreatitis induced by hypertriglyceridemia in pregnancy has been made. Case. A 22-year-old woman presented to our Emergency Department, at 35 weeks of gestation, for acute onset of abdominal pain and uterine contraction. Blood tests showed a high rate of triglyceride. The patient was diagnosed with abruptio placentae caused by hypertriglyceridemia-induced acute pancreatitis. Immediate cesarean section was performed and it was observed that blood sample revealed a milky turbid serum. Insulin, heparin, and supportive treatment were started. She was discharged on the 10th day. Conclusion. Consequently, patients with known hypertriglyceridemia or family history should be followed up more closely because any delay can cause disastrous conclusions for mother and fetus. Acute pancreatitis should be considered in pregnant women who have sudden onset, severe, persistent epigastric pain and who have a risk factor for acute pancreatitis.

1. Introduction

Acute pancreatitis (AP) is a rare complication in pregnancy, occurring in approximately three in 10000 pregnancies [1, 2]. Hypertriglyceridemia is recognized as the third most common cause of gestational acute pancreatitis after gallstones and alcohol and occurs in about 4% of all cases [2]. An increase in plasma lipid level during pregnancy has been well documented. It is thought to represent a physiologic response to the hormonal changes; however, it is not sufficient to cause acute pancreatitis. Gestational pancreatitis due to hypertriglyceridemia usually occurs in pregnant women with preexisting abnormalities of the lipid metabolism. There are effective treatment choices during pregnancy such as dietary restriction of fat, intravenous heparin, and insulin and plasmapheresis. We report a case of abruptio placentae caused by hypertriglyceridemia-induced acute pancreatitis.

2. Case Report

A 22-year-old patient, Para 1, Gravida 2, presented to our Emergency Department of Gynecology and Obstetrics, at 35 weeks of gestation for acute onset of abdominal pain and uterine contraction. It was learned that the patient's history had no follow-up hypertriglyceridemia. On physical exam, her heart rate was at 100 pulses per minute, and her blood pressure was at 110/70 mm-Hg, respiratory rate 18 /min. Her abdomen was defensive. Her cervical os was dilated to 1-2 cm and minimal bleeding. The patient had mild epigastric tenderness. Decelerations were seen in pregnant cardiotocography follow-ups with abnormal abdominal pain and uterine contractions continued and simultaneous wide bleeding area (like abruptio placenta) was seen on the posterior part of placenta in ultrasound. Immediate cesarean section was performed under general anesthesia because of contraction of
the tetanic type in the manual contraception. She gave birth to a healthy infant of 2980 g. Amylase, lipase, triglyceride, HDL, and LDL were studied in the patient’s blood after emulsion of chylous fluid from abdomen during the cesarean section. Liver enzymes were high: ast: 241, sub. 147. It was observed that blood sample revealed a milky turbid serum. Laboratory finding included a triglyceride at 3297 mg/dl and amylase 827 U/L, lipase 1576 U/L. Abdominal ultrasound showed thickened pancreas without necrosis; acute pancreatitis compatible with diffuse edema was observed on pancreas. Biliary tract was naturally observed. Other causes of cholestasis of pregnancy, such as cholangitis, acute hepatitis, and hemophagocytic syndrome, were ruled out. Oral intake of the patient was stopped; intravenous fluid replacement therapy, antibiotherapy, proton pump inhibitor, insulin, and heparin therapy were started. She was discharged on the 10th day of treatment. Even though the patient did not have previous history of diabetes or gestational diabetes, the baby was born 4 to 3 weeks earlier. It was thought that this condition might be related to maternal hyperlipidemia for newborn’s doctors.

3. Discussion

Acute pancreatitis (AP) is a rare complication in pregnancy. Diagnosis becomes difficult because it can interfere with the physiological findings in pregnancy. Acute pancreatitis should be considered in pregnancies with nausea, vomiting, and epigastric pain. Gallstones, hypertriglyceridemia, and alcohol especially play a role in the etiology of acute pancreatitis.

Hypertriglyceridemia is the second most common cause of acute pancreatitis in pregnancy. Diagnosis is made when the serum triglyceride is > 1000 mg/dl. Hypertriglyceridemia in pregnant patients can occur with preexisting dyslipidemia, associated with others diseases (hypertension, diabetes mellitus, and alcoholism), or without any predisposing factor. Triglycerides concentration rises gradually, 2.5-fold over prepregnancy levels, reaching a peak during the third trimester to almost twice as high value of nonpregnant value. This is thought to be due to estrogen-induced increases in triglyceride synthesis and very low-density lipoprotein secretion [29]. Therefore, AP is more common in the third trimester of pregnancy. Lipids decrease gradually postpartum to reach prepregnancy level in 6 weeks [30, 31]. Epigastric pain, spreading pain, nausea, vomiting, and distension can be seen at the beginning of the symptoms in acute pancreatitis cases. Findings of peritoneal irritation are not seen in general, especially when there is epigastric pain in mild cases as indicated by physical examination findings. In severe cases, epigastric tenderness and peritoneal irritation findings may be accompanied by ileus, fever, and tachycardia. The increase in serum amylase reaches peak values 6-12 hours after the onset of the event. The exact diagnosis of pancreatitis is based on the amylase/creatinine clearance rate. Serum lipase values also increase. Imaging methods can be used in the diagnosis of acute pancreatitis from ultrasonography, computed tomography, and magnetic resonance imaging. Ultrasound is the most appropriate method for pregnancy.

Acute pancreatitis treatment in pregnancy is similar to nonpregnant treatment of hyperlipidemia. Pregnancy pancreatitis treatment is primarily medicinal and approximately 90% of patients respond to medical treatment. Medical treatment of AP is mostly supportive. These treatments include low fat diet [32, 33], antihyperlipidemic therapy [32, 33], insulin [32, 34] (to increase lipoprotein lipase activity), heparin [33, 35] (to increase lipoprotein lipase activity), and even plasmapheresis [32, 35].

Our patient was admitted with acute onset of abdominal pain and uterine contraction to our clinics in the 35th week of gestation. She had lipid abnormality in her history, but her history had no follow-up hypertriglyceridemia. Pregnancy had induced aggravation of hypertriglyceridemia and associated pancreatitis. In addition, acute pancreatitis induced by the pregnancy was accompanied by abruptio placenta and delivery was performed with an emergency cesarean section. It was observed that blood sample revealed a milky turbid serum. We managed our patient conservatively in postoperative period. Oral intake of the patient was stopped; intravenous fluid replacement therapy, antibiotherapy, proton pump inhibitor, insulin, and heparin therapy were started. The patient's clinical condition subsequently improved.

Cases of acute pancreatitis induced by hypertriglyceridemia during pregnancy published in the literature are listed in Table 1. In the majority of published case, medical treatment was first tired. Oral intake was closed, supportive treatment started. However, pregnancy-induced pancreatitis has been mortal in some cases and has gone as far as maternal death.

Ihuang et al. performed a retrospective study on 21 pregnant women diagnosed with acute pancreatitis (AP). Patients were divided into acute biliary pancreatitis (ABP), hypertriglyceridemia-induced acute pancreatitis (HTGP), and idiopathic groups according to etiology. 95% of the patients were in the third trimester of gestation. The percentage of patients with HTGP was higher than that of ABP (48% versus 14%). The percentage of severe acute pancreatitis (SAP) in the HTGP group was higher than that in the ABP group (40.0% versus 0%). In the HTGP group, five patients given were plasma exchange therapy and five were not. According to the results of this study it was found that plasma exchange may be safe and effectively administered for HTGP patients during pregnancy with SIRS or multiple organ dysfunction syndrome (MODS) [36].

In a study by Lingyu Luo et al., they retrospectively reviewed 121 acute pancreatitis in pregnancy (AIP) cases. The correlation between AIP types, severity, biochemical parameters, and mortality was analyzed. The most common causes of AIP were gallstone and hypertriglyceridemia. Lower level of serum calcium could be used as an indicator for the severity of the AIP. According to the result s of this study it was found that the severity of AIP was associated with higher risk for neonate asphyxia and maternal and fetal death [37].

In a prospective study performed by Athyros VG et al., 17 cases of acute pancreatitis induced by hypertriglyceridemia were included in the study. These patients were followed for 42 months. In the content of the study causative conditions
Table 1: Case literature of acute pancreatitis induced by hypertriglyceridemia during pregnancy.

| First Author | Year | Age | G/P | Birth | Medication | Other | Mode | BW | Indication | Laboratory | After Treatment |
|--------------|------|-----|-----|-------|------------|-------|------|----|------------|-------------|----------------|
| Billion JM [3] | 1991 | 32  | 35  | 35    | TPN        |       |      |    |            |             |                |
| Achard JM [4] | 1991 |     |     |       |            |       |      |    |            |             |                |
| Perrone G [5] | 1996 | 37  | 35  |       | Diet, Gemfibrozil |   |      |    |            |             |                |
| Ibrahim Bildirici [6] | 2002 | 26  | G2P2 | 24   | Insulin, Plasmapheresis | C/S  |      |    | Fetal Distress (750 g) | Serum Amylase: 487 | TGP: 2316 |
| Chee-Chuen Loo [7] | 2002 | 37  | G3P2 | 37   | Ranitidine, Heparin, Insulin | SV D |      |    |            | Serum Amylase: 956 | TGP: 2066 |
| J.C. Sleth [8] | 2004 | 28  | G2P1 | 37   | Heparin    | C/S  |      |    | Unstable Condition of the Mother | Serum Amylase: 2316 | TGP: 100 |
| A. Abu Musa [9] | 2006 | 39  | G2P1 | 28   | Plasmapheresis | C/S  |      |    | A Repeat C/S Delivery | Serum Amylase: 596 | TGP: 492 |
| Shih-Chang Chuang [10] | 2006 | 28  | G1P0 | 34   | Antibiotics, TPN | Pancreatic Necrosectomy, Right Hemicolectomy, Ileostomy, Cholecystostomy, Gastrostomy, Feeding Jejunostomy |      |    |    | Unstable Condition of the Mother | Serum Amylase: 1365 | TGP: 319 |
Table 1: Continued.

| First Author | Year | Age | G/P | Birth | Medication | Other | Mode BW | Indication | Laboratory * | After Treatment ** |
|--------------|------|-----|-----|-------|------------|-------|--------|------------|--------------|-------------------|
| Alptekin Gürsoy [11] | 2006 | 24  | G1P0 | 37    |            |        | C/S    | Fetal Distress | TG: 10092     | Cholesterol: 1159  |
|               |      |     |      |       |            |       |        |             | Panc. Amylase: 367 | Panc. Lipase: 797 |
|               |      |     |      |       |            |       |        |             | TG: 143        | Cholesterol: 274  |
|               |      |     |      |       |            |       |        |             | Panc Amylase: 23  | Panc Lipase: 41   |
| V. Exbrayat [12] | 2007 | 31  | 33   |       | Plasmapheresis, Heparin |       | C/S    | Fetal Distress | TG: 11300      | Cholesterol: 2500  |
|               |      |     |      |       |            |       |        |             | Panc Amylase: 334 | Panc Lipase: 168 |
|               |      |     |      |       |            |       |        |             | TG: 1000       |                   |
| Luminita S. Crisan [13] - 1 | 2008 | 27  | G2P0 | 35    | TPN, Analgesics, Bowel Rest | ARDS | C/S    | Fetal Distress |               |                   |
| Luminita S. Crisan [13] - 2 | 2008 | 29  | G3P1 | 30    | TPN, Analgesics, Bowel Rest | Acute Myocardial Infarction | Forceps-Assisted Vaginal Delivery (1854 g) |               |                   |
| Luminita S. Crisan [13] - 3 | 2008 | 34  | G3P0 | 33    | TPN, Analgesics, Bowel Rest | ARDS | SVD    | Low BPP     |               |                   |
| Luminita S. Crisan [13] - 4 | 2008 | 23  | G1P0 | 35    | TPN, Analgesics, Bowel Rest |       | C/S    | Fetal Distress | TG: 8447       | Cholesterol: 240  |
| L. Vandembroucke [14] | 2009 | 34  | 37   |       | Heparin, A Low-Fat Diet |       | C/S    | Fetal Distress | TG: 2225       | Cholesterol: 278  |
|               |      |     |      |       |            |       |        |             | Panc. Amylase: 959 | Panc. Lipase: 181 |
| Dilek Altun [15] - 1 | 2012 | 27  | G1P0 | 5     | Plasmapheresis, Heparin |       | Termination |             | TG: 2699       | Cholesterol: 230  |
|               |      |     |      |       |            |       |        |             | Panc. Amylase: 956 | Panc. Lipase: 2580 |
|               |      |     |      |       |            |       |        |             | TG: 570        | Cholesterol: 2500 |
|               |      |     |      |       |            |       |        |             | Panc. Amylase: 208 | Panc. Lipase: 208 |
| Mindaugas Serpytis [16] | 2012 | 31  | G2P0 | 33    | Heparin, Insulin, Plasmapheresis |       | C/S    | (3100 g)    | TG: 1576       | Cholesterol: 183  |
| First Author            | Year | Age | G/P | Birth | Medication                          | Other                                   | Mode | BW     | Indication                        | Laboratory * | After Treatment ** |
|------------------------|------|-----|-----|-------|-------------------------------------|-----------------------------------------|------|--------|-----------------------------------|---------------|---------------------|
| **Kumar Thulasi-dass** [17] - 1 | 2013 | 37  | G3P0| 14    | Insulin, Metformin, Fish Oil Therapy | Termination                             |      |         | Termination                       | TG: 1421      | TG: 111             |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 481                  |               | Cholesterol: 93      |
|                        |      |     |     |       |                                     |                                         |      |         | Serum Amylase: 1464               |               |                     |
| **Kumar Thulasi-dass** [17] - 2 | 2013 | 24  | G1P0| 8     | ARDS                                | Spontaneous Abortion                    |      |         |                                   | TG: 839       | TG: 57              |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 300                  |               | Cholesterol: 77      |
|                        |      |     |     |       |                                     |                                         |      |         | Serum Amylase: 8962               |               |                     |
| **Rafet Basar** [18] - 1 | 2013 | 32  | G3P0| 37    | Heparin, Fatty Acids, DF            |                                         | C/S  |        | Spontaneous Abortion              | TG: 1400      | TG: 380             |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | TG: 12000                         |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | TG: 758                           |               |                     |
| **Rafet Basar** [18] - 2 | 2013 | 30  | G2P1| 36    | Heparin, Fatty Acids, DF, Plasmapheresis |                                         | C/S  |        | Elective                          | TG: 523       |                     |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               | Normal              |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 325                  |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Panc. Amylase: 178                |               |                     |
| **Ying Hang** [19]     | 2013 | 31  | G2P0| 27    | Noninvasive Positive Pressure Ventilation (NPPV), Drainage of Chylous Ascites, Peritoneal Lavage, ARDS | C/S (1180 g) |        | Fetal Distress                    | TG: 523       |                     |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: Normal               |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Panc. Amylase: Normal             |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Panc. Lipase: 161                 |               |                     |
| **Bahiyyah Abdullah** [20] | 2014 | 25  | G4P3| 8     | Diagnostic Laparoscopy, Acute Hemorrhagic Pancreatitis | Spontaneous Abortion                  |      |         |                                    | Serum Amylase: 1273 |                     |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               | Serum Amylase: 147  |
| **Tejal Amin** [21]    | 2014 | 40  | G5P4| 18    | Insulin                              | IU/MF                                  |      |         |                                    | TG: 836       | TG: 90              |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 300                  |               |                     |
| **Natasha Gupta** [22] | 2014 | 32  | G5P4| 38    | Plasmapheresis                       | Preeclampsia, Pleural Effusion, Chronic Pericarditis, Retinal Detachment | C/S  |        | Unstable Condition of the Mother   | TG: 12,570    |                     |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 1067                 |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Panc. Amylase: 161                |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Panc. Lipase: 1330                |               |                     |
| **Fadi Safi** [23]     | 2014 | 24  | G9P8| 35    | Plasmapheresis                       | C/S (1720 gr) |        | Unresponsiveness to Treatment     | TG: 2661      |                     |
|                        |      |     |     |       |                                     |                                         |      |         |                                    |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Cholesterol: 683                  |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | Serum Amylase: 802                |               |                     |
|                        |      |     |     |       |                                     |                                         |      |         | TG: 425                           |               |                     |
| First Author | Year | Age | G/P | Birth | Medication | Other | Mode BW | BW | Indication | Laboratory * | After Treatment ** |
|--------------|------|-----|-----|-------|------------|-------|---------|----|------------|--------------|------------------|
| Rachel Lim [24] | 2015 | 27  | G1P0 | 33    | Insulin, Plasmapheresis | Placental Abruption | SVD | TG: 720 | Cholesterol: 90 | Panc. Lipase: 504 | TG: 41 |
| Ying Liu [24] | 2015 | 30  | G1P0 | 32    | Plasmapheresis | Compound Heterozygosity (Glu242lys and Lef252Val) | C/S | Fetal Distress | TG: 2160 | Cholesterol: 670 | Panc. Amylase: 132 | TG: 420 |
| Funda Gok [25] | 2015 | 37  | 31   | Insulin, | IUMF | SVD | TG: 9742 | Cholesterol: 705 | Panc. Amylase: 570 | Panc. Lipase: 39 | TG: 556 | Panc. Lipase: 77 |
| Hae Rin Jeon [26] | 2016 | 28  | G1P0 | 23 | IUMF, Pancreatic Cells Necrotized, Diabetic Ketoacidosis, Metabolic Acidosis, Cardiac Arrest, EX | | | | | | |
| Ioanna Poly-pathelli [27] | 2017 | 38  | G2P1 | 30 | Heparin, Fatty Acids, Antibiotics | C/S | Resistant Exaggerated Thrombocytosis | TG: 14440 | Cholesterol: 1600 | Serum Amylase: 540 | TG: 521 |
| Tamanna Chibber [28] | 2017 | 38  | 11   | Cardiac Arrest, EX | | | TG: >1254 | Cholesterol: 648 | Panc. Lipase: 1079 |

BW: birth weight, G: gravida, P: parity, SVD: spontaneous vaginal delivery, BPP: biophysical profile, TPN: total parenteral nutrition, DF: double filtration apheresis, C/S: cesarean section, TG: triglyceride, ARDS: Adult Respiratory Distress Syndrome, and IUMF: Intra-Uterine Mort Fetus.

Triglyceride and total cholesterol units are calculated in mg/dL. Other units are converted to mg/dL.

Serum Amylase: normal range is between 30 and 110 (U/L) [11].
Pancreatic Amylase: normal range is between 17 and 115 (U/L) [11].
Pancreatic Lipase: normal range is between 13 and 60 U/L (U/L) [11].
TG: normal range is between 50 and 160 mg/dL (mg/dL) [11].
Cholesterol: normal range is between 130 and 230 (mg/dL) [11].

* Highest values.
** Lowest values.
of HTG-induced AP were familial HTG in eight patients, HTG caused by uncontrolled diabetes mellitus in five, HTG aggravated by drugs in two (one by tamoxifen and one by fluvastatin), familial hyperchylomicronemia (HCM) in one, and lipemia of pregnancy in one. During the acute phase of pancreatitis, patients underwent standard treatment. After that, HTG was efficiently controlled with high dosages of fibrates or a fibrate plus acipimox, except for the patient with HCM, who was on a specific diet (the only source of fat was fibrates or afibricate plus acipimox, except for the patient with HCM). One of the patients died of pancreatitis, patients underwent standard treatment. After that, the acute phase of pancreatitis with acute respiratory distress syndrome. According to the results of the study it was found that appropriate diet and drug treatment, including dose titration, of severe HTG are very effective in preventing relapses of HTG-induced AP [38].

As a result, pancreatitis can be seen in pregnancy in cases with uncontrolled hypertriglyceridemia. Patients with known hypertriglyceridemia or family history should be followed up more closely. Acute pancreatitis should be considered in pregnant women who have sudden onset, severe, persistent epigastric pain and who have a risk factor for acute pancreatitis.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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