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Case Report

Hypertriglyceridemia Induced Acute Pancreatitis: A Case Series

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Abstract

Hypertriglyceridemia (HTG) is a rare but a noted cause for acute pancreatitis (AP). Elevated levels of triglyceride above 700 mg/dl have been correlated as a causative factor for AP. Several cases have been reported in the last with varying level of severity. Among them, HTG due to pregnancy leading to AP has been documented as a life-threatening complication for both the mother and the child. Several modalities for treatment have been tried, but the mainstay remains conservative management as in any AP and dietary modification and fibrates during time of discharge. Here is a case series of HTG-induced pancreatitis which includes two pregnant ladies, with course in the hospital and outcome. The literature of the same has been reviewed.

Keywords: Female, Hypertriglyceridemia, Pancreatitis, Pregnancy

INTRODUCTION

Acute pancreatitis (AP) is one of the most common causes for hospitalization in the United States, accounting for around 220,000 cases per year.[1] Among the new cases, 80% are interstitial, and 20% are necrotizing. AP carries an overall mortality of around 5% and as high as 47% in patients with multi-organ failure.[2] Necrotizing pancreatitis is responsible for almost all mortalities attributed to AP. Alcohol use, gallstones, hypertriglyceridemia (HTG), hypercalcemia, medications, endoscopic retrograde cholangiopancreatography, and trauma account for most cases of AP; however, approximately 20% remain idiopathic.[3] The role of pancreas divisum and sphincter of oddi dysfunction is controversial. Clinical manifestations range from mild epigastric discomfort to critical illness and death. Occasional cases are only diagnosed at autopsy. Diagnosis is based on clinical features, biochemical tests, and imaging studies. Guidelines by the American College of Gastroenterology state that the diagnosis of AP requires the presence of the two of the following three criteria: (1) Characteristic abdominal pain, (2) serum amylase and/or lipase >3 times the upper limit of normal, and (3) computed tomography (CT) scan findings compatible with AP.[4] HTG-induced AP is still considered a rare entity, although the reported incidence varies between 1-4% and 12-38%.[5-7] South Asians have an increased prevalence of diabetes and dyslipidemia characterized by high triglyceride (TG) and low high-density lipoprotein (HDL) cholesterol concentrations, which, regardless of their geographical location, place them at higher risk for coronary artery disease.[8,9] Although several reports from around the world have highlighted this exaggerated risk of coronary heart disease, there are few reports of hyperlipidemia-induced pancreatitis in this ethnic group. Here is a case series of 4 females presenting with pancreatitis caused by HTG with reviewing the literature of the same.

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CASE REPORT

Case 1

A 44-years-old female presenting with 1 day history of pain abdomen, more in the upper abdomen that was radiating to the back to the emergency department with associated symptoms of vomiting and anorexia. No previous history of similar complaints. No history of fever. No history of trauma. She is not a case of diabetes mellitus. She is nonsmoker, nonalcoholic. On examination, patient is moderately built and nourished with body mass index of 21.

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Pulse rate on admission was 104 beats/min. Respiratory rate was 20 breaths/min. Saturation maintaining with room air. Blood pressure was 140/90 mmHg. There were no signs of severe dehydration. She was conscious and appeared anxious. Per abdomen examination revealed tenderness in the epigastrium and hypochondriac region with guarding. There was no free fluid clinically. Bowel sounds were sluggish. Respiratory system examination showed decreased breath sounds in left lower lung fields with dullness on percussion. The patient was worked up with routine blood and radiological investigations.

Total count was 12,230 cells/cumm with neutrophilic predominance. Serum amylase was 350 mg/dl and serum lipase 840 mg/dl. Her erect abdominal X-ray showed no air under the diaphragm and no dilated bowel loops. Chest X-ray showed obliteration of costophrenic angle on the left side. Ultrasound showed no common bile duct calculi and gallbladder was normal. Liver function tests (LFTs) and serum calcium levels turned out normal. Blood sugar was slightly elevated. Lipid profile showed HTG of 1129 mg/dl. Total cholesterol was 366 mg/dL.

The patient was managed conservatively with fluid resuscitation. Prophylactic antibiotics were started. Contrast-enhanced CT (CECT) showed AP with CT severity index (CTSI) of 6. Adequate analgesia was given. Patient was started on fenofibrate once she could tolerate orally. She improved symptomatically and was discharge with enzymes and asked to follow-up regularly. Diet modification advised. Time duration of hospitalization - 8 days.

Case 2

A 26-years-old female with 33 weeks of pregnancy was admitted with sudden onset of generalized pain abdomen since 1 day. She had 2 episodes of vomiting. Pain was more on the upper abdomen. She was not a diabetic and until this episode, she was on regular follow-up for her pregnancy and had no issues regarding that. On admission, patient appeared conscious. Pulse rate was 110 beats/min. Respiratory rate was 26 breaths/min. She was not maintaining saturation in room air and had 100% saturation with 4 L/min of oxygen by mask. Her blood pressure was 110/60 mmHg at the time of admission. Per abdomen examination showed diffuse tenderness with guarding. Her obstetric examination showed normal fetal heart rate. She had bilateral decreased breath sounds in lower lung fields.

The patient was admitted under intensive care, and fluid correction was started. Investigations revealed serum amylase of 620 mg/dL, serum lipase 1690 mg/dL. She had elevated total count of 16,100 cells/cumm with neutrophilia. Her LFTs and serum calcium were normal. Lipid profile showed TG of 5766 mg/dL. Total cholesterol was 506 mg/dL. Her arterial blood gas revealed decompensated metabolic acidosis of 7.248. Ultrasound showed features of AP with a large amount of fluid collection. Blood sugars on admission were 263 mg/dL.

Patient was treated aggressively with fluids and analgesics. Correction of acidosis was started and she was also started on insulin. Induction of labor was done, and she delivered a single live born baby of 1.9 kg with respiratory distress and was shifted to Neonatal Intensive Care Unit. The patient deteriorated and was later intubated as she was not maintaining saturation. She developed Multi-organ dysfunction with decreased urine output and hypotension. Her creatinine became 2.4 mg/dL. She developed deranged coagulation profile with raised prothrombin time, activated partial thromboplastin time international normalized ratio. She went into cardiac arrest and was revived. Trop T and CK-MB sent showed elevation (1.24 and 10.30, respectively) patient succumbed to the condition with multi-organ failure. Time duration of hospitalization - 2 days.

Case 3

A 34-years-old female patient presented in the emergency department with pain abdomen radiating to the back since 2 days. The patient had 4 episodes of vomiting and had fever at the time she came to the hospital. She had no similar history in the last. On examination, patient was conscious. Her pulse rate was 96 beats/min, and respiratory rate was 16 breaths/min. Her blood pressure was 130/90 mmHg. She was maintaining saturation in room air. On examination, there was tenderness in the upper abdomen and umbilicus. No free fluid per abdomen clinically. Bowel sounds were sluggish.

On investigating, erect X-ray abdomen was normal. Ultrasonography showed peripancreatic edema. Serum amylase was 380 mg/dL, lipase 902 mg/dL. Total counts were 20,540 cells/cumm with neutrophilia. LFT and serum calcium were normal. She had HTG of 755 mg/dL. CECT abdomen showed Pancreatitis with CTSI 6.

The patient was admitted and managed conservatively with adequate fluid resuscitation and analgesia. She was improving symptomatically and was started orally. However, patient was not affordable for further treatment and was discharged against medical advice. Time duration of hospitalization - 3 days.

Case 4

A 20-years-old female with 30 weeks gestation presented to the obstetrics and gynecology department with complaints of pain abdomen in the epigastrium radiating to the back and vomiting with anorexia. On examination, her pulse rate was 110 beats/min and blood pressure 120/70 mmHg. She was not having any respiratory

distress. Abdomen had tenderness in epigastrium and voluntary guarding.

Ultrasound revealed single live gestation along with features of pancreatitis with peripancreatic fluid and signs of inflammation. Total count was 12,010 cells/cumm with neutrophilia. Amylase and lipase were 586 and 422 mg/dL, respectively. LFT and serum calcium were normal. Lipid profile revealed gross elevation of TG levels of 960 mg/dL. CT scan was not done in view of pregnancy.

The patient was managed conservatively with intravenous fluids, analgesics. Obstetric monitoring was done rigorously. Patient improved symptomatically. She was discharged with advice for regular follow-up and dietary modifications.

DISCUSSION

HTG amounts for approximately 3% of all the causes for AP, main causes being gallstones and alcohol. AP is a well-recognized complication of elevated TG levels. Although the exact mechanism is unknown, there is the view that an elevated cholesterol level alone may not lead to pancreatitis.[6] When serum TGs are elevated above 800 mg/dL, there is invariably chylomicronemia, which may impair circulation in the capillary beds, exposing the chylomicrons to pancreatic lipase, thus damaging the pancreatic acini and microvasculature. Typically HTG-induced pancreatitis occurs in a patient with a pre-existing lipid abnormality, along with the presence of a secondary precipitating factor (e.g., poorly controlled diabetes, alcohol or medication). The TG levels of > 1000 to 2000 mg/dL in patients with Type I, III, IV, and V hyperlipoproteinemia (Fredrickson's classification) is the identifiable risk factor.[10] Genetic factors determine over 60% of the variability in serum lipids.[6] HTG can be primary in <5% of the cases, due to genetic causes and more often secondary to other causes such as diabetes, obesity, pregnancy, excess carbohydrate intake, hypothyroidism, alcohol, hepatitis, sepsis, renal failure, and drugs such as estrogen, glucocorticoids, β-blocker, bile acid binding resins, thiazide, tamoxifen cyclosporine protease inhibitors, and isotretinoin.[11]

The first and third case did not have any predisposing factors that were identified for the cause of HTG. In the second and fourth case, however, the patient was pregnant, which has been a cause for HTG.

Plasma lipid concentrations become altered within the hormonal milieu of pregnancy, but these rarely have clinical consequences.[12] A rare exception is pregnancy-related HTG, whose complications, namely AP, hyperviscosity syndrome, and possibly preeclampsia,[13] are life-threatening. Plasma TG concentration normally increases 2- to 4-fold in uncomplicated late gestation,[14] but for most women with normal baseline TG levels and no compromise in metabolic pathways, such increases are well tolerated. Increased estrogen levels of pregnancy also lead to increased synthesis of TGs and very low-density lipoproteins (VLDL) by liver. However, in rare instances, sometimes associated with genomic alterations that affect key metabolic entities, pregnant women can develop HTG, defined as plasma TG above the 95th percentile for age. In particular, the very rare subgroup of pregnant women that develops severe HTG, defined as plasma TG > 11.4 mmol/L (1000 mg/dL), show an increased risk of acute complications and are at risk of expressing hyperlipidemia in the future.[12] To date, a few rare mutations of lipoprotein lipase, APOE, and, APOC2 genes have been described in the context of gestational chylomicronemia.[15-19]

The incidence of AP in pregnancy varies and is approximately 1 in 1000 to 1 in 10,000 births.[20] Older reviews of AP in pregnancy reported maternal and fetal mortality rates as high as 20% and 50%, respectively.[21-26] The risk of developing AP increases progressively when TG levels exceed 500mg/dL. It also increases as pregnancy advances, with 19% risk in 1st trimester, 26% in 2nd trimester, 53% in 3rd trimester, and 2% in postpartum period.[21]

The mainstay of the management of a case of HTG-induced AP remains the same as in any other case of AP. Fibrates are the mainstay of therapy, they reduce plasma TG levels by up to 50% and raise the HDL cholesterol by 20%.[27] They modulate peroxisome proliferator-activated receptors-α in the liver, with decreased hepatic secretion of VLDL and increased lipolysis of the plasma TG.[28] They also reduce small dense LDL particles and increase HDL.[29] Heparin and insulin infusion are low-cost alternatives to plasmapheresis, but the first modality of choice for treatment of HTG still remains conservative approach with nutritional and pharmacological methods.[30]

All our patients were managed conservatively for the pancreatitis. The first and the third patient received diet modifications and were started on fibrates before discharge. The patient with pregnancy manifested with severe pancreatitis for whom, insulin with glucose infusion was started. Treatment in lines of multiple organ dysfunction syndrome was given promptly. However, patient's response was poor, and both the mother and the baby succumbed to the disease.

CONCLUSION

HTG-induced AP still remains a Pandora's box with surprising types of patients. It has proven to cause severe disease in pregnancy, which happened so in the patient in this study. Factors that help in knowing the

predictability of pancreatitis in patients with HTG has to be explored.

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