Ketoacidosis with Hypertriglyceridemia-Induced Pancreatitis in a Patient with Gestational Diabetes: A Case Report

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Hypertriglyceridemia-induced acute pancreatitis in pregnancy is not a common complication. Moreover, ketoacidosis in gestational diabetes occurs rarely. Here we report a case of ketoacidosis with hypertriglyceridemia-induced pancreatitis in a patient with gestational diabetes that was successfully treated with insulin and supportive care. In this case, a 36-year-old woman (at 32 weeks' gestation) was diagnosed with gestational diabetes 4 weeks prior, but did not have well controlled blood sugar. She complained of severe epigastric pain concomitant with nausea and vomiting. Radiology and laboratory tests found hypertriglyceridemia (1,996 mg/dL), acute pancreatitis, and ketoacidosis with absence of fetal deceleration on a non-stress test. The patient's condition improved with insulin therapy and fluid replacement. To our knowledge, this is the first report of a case of ketoacidosis with hypertriglyceridemia-induced pancreatitis in a patient with gestational diabetes. (Endocrinol Metab 27:89-92, 2012)

Key Words: Acute pancreatitis, Gestational diabetes, Hypertriglyceridemia

INTRODUCTION

Hypertriglyceridemia is an uncommon but well recognized cause of acute pancreatitis; other recognized causes are next alcohol abuse and gallstone-induced disorders [1,2]. Chang et al. [3] reported that hypertriglyceridemia causes 56% of all gestational pancreatitis. During pregnancy there is a physiologic rise in plasma lipid levels, however these increases are usually not enough to cause pancreatitis. In a diabetic pregnancy, hypertriglyceridemia has been found to be more exaggerated compared to the rise in plasma lipid levels during normal pregnancy, this may be the root cause of a higher prevalence of hypertriglyceridemia in acute pancreatitis. Diabetic ketoacidosis (DKA) is a serious metabolic complication especially in pregnancy. Its occurrence is not common, moreover in gestational diabetes. As in any other disease associated with pregnancy, acute pancreatitis and ketoacidosis lead to greater concerns as they pose instant serious threat to the life of mother, fetus, or both. There are some reports of hypertriglyceridemia-induced acute pancreatitis in pregnancy [4-7] and DKA in gestational diabetes [8-10]. However, the case described here is ketoacidosis with hypertriglyceridemia-induced pancreatitis in patient with gestational diabetes.

CASE REPORT

A 36-year-old multigravida (gravida 7, spontaneous abortion 1, and induced abortion 5) was at 32 weeks of gestation when she visited an outpatient clinic to control her blood glucose. She had been diagnosed with gestational diabetes by an oral glucose tolerance test (50 g) showing 438 mg/dL 4 weeks prior. However, the patient had not undergone further evaluation or treatment. The patient did not have a history of alcohol drinking, drug abuse, gallstones, signs of infection, or a family history of diabetes. However, she stated that she had been eating a high carbohydrate and caloric diet, which included instant noodles and had no diet control even after having received her diagnosis of gestational diabetes. Upon hospitalization to control her blood glucose, her vital signs were stable and there was no abdominal pain or tenderness on examination. Furthermore, there were no stigmas of hyperlipidemia, such as xanthelasma, xanthoma, or eruptive xanthoma. A random blood glucose test was 294 mg/dL and HbA1c was 8.6%. Initial biochemical analysis revealed WBC 6,100 K/µL (PMN 74.1%), hemoglobin 14.3 g/dL, hematocrit 30.4%, sodium 120 mEq/L, potassium 3.5 mEq/L, chloride 91 mEq/L, BUN 5.2 mg/dL, total bilirubin 1.77 mg/dL.
direct bilirubin 0.88 mg/dL, and urine glucose (+++). Urine and serum ketone bodies were negative. The fetal condition was satisfactory on a fetal non-stress test. While the patient was receiving multiple subcutaneous insulin injections with human insulin for blood sugar control, severe epigastric pain with nausea and vomiting was developed on the 2nd hospital day. The nature of the pain was deep, continuous, and was improved by knee-chest position.

At that time, the vital signs were stable, but there were epigastric tenderness and decreased bowel sounds. Laboratory tests showed a blood glucose of 277 mg/dL, pH 7.236, PCO₂ 25.8 mmHg, HCO₃⁻ 10.6 mmol/L, base excess -15.4 mmol/L, sodium 124 mEq/L, total bilirubin 2.04 mg/dL, direct bilirubin 0.33 mg/dL, hs-CRP 27.054 mg/dL, amylase 385 IU/L, lipase 395 IU/L, and serum ketone bodies 3.6 mmol/L. On hepatobiliary ultrasonography, the pancreas showed edematous changes with fatty infiltration, which suggested acute pancreatitis (Fig. 1A); there was no evidence of a biliary problem. In order to determine the cause of acute pancreatitis, we analyzed the patient’s lipid profile, which revealed total cholesterol (TC) level of 700 mg/dL, triglyceride (TG) 1,996 mg/dL, and low density lipoprotein cholesterol (LDL-C) 117 mg/dL. The fetal status was monitored via non-stress testing, which demonstrated no variability at that time. We could diagnose ketoacidosis associated with hypertriglyceridemia-induced acute pancreatitis with fetal distress state.

The patient fasted and was administered insulin therapy along with fluid therapy. Her symptoms and laboratory findings improved gradually (Table 1, Fig. 1B) with recovering of fetal stress status. On the 12th hospital day, the patient was discharged and provided with self-injection insulin (MSII regimen) without fibrates. At 38 weeks of gestation, the patient delivered a healthy baby (birth weight 3,125 g) by cesarean section. After 4 weeks of delivery, laboratory test showed that fasting / 2 hour postprandial blood glucose 219/531 mg/dL and C-peptide 2.07/8.20 ng/mL, TC 322 mg/dL, TG 322 mg/dL and LDL-C 147 mg/dL. Based on these levels, the patient’s medications were switched to glimepiride/metformin, fibrate, and a statin medi-

Table 1. Patient’s laboratory result

<table>
<thead>
<tr>
<th></th>
<th>2nd HD</th>
<th>3rd HD</th>
<th>4th HD</th>
<th>5th HD</th>
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<tr>
<td>pH</td>
<td>7.236</td>
<td>7.272</td>
<td>7.345</td>
<td>7.344</td>
<td>7.367</td>
<td>7.374</td>
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<td>Base excess (mmol/L)</td>
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<td>-13.8</td>
<td>-12.7</td>
<td>-11</td>
<td>-10.5</td>
<td>-8</td>
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<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>10.6</td>
<td>11.6</td>
<td>11.5</td>
<td>13.4</td>
<td>13.4</td>
<td>15.8</td>
</tr>
<tr>
<td>Ketone body (mmol/L)</td>
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<td>1.1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Amylase (IU/L)</td>
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<td>328</td>
<td>65</td>
<td>39</td>
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<tr>
<td>Lipase (IU/L)</td>
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<td>108</td>
<td>68</td>
<td>43</td>
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<td>-</td>
</tr>
<tr>
<td>ESR (mm/H)</td>
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<td>-</td>
<td>120</td>
<td>120</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
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<td>-</td>
<td>15,718</td>
<td>9.36</td>
<td>-</td>
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</tr>
<tr>
<td>TC (mg/dL)</td>
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<td>572</td>
<td>551</td>
<td>-</td>
<td>504</td>
<td>-</td>
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<tr>
<td>TG (mg/dL)</td>
<td>1996</td>
<td>896</td>
<td>578</td>
<td>334</td>
<td>391</td>
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<tr>
<td>HDL-C (mg/dL)</td>
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<td>57.8</td>
<td>53</td>
<td>-</td>
<td>33.9</td>
<td>-</td>
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<tr>
<td>LDL-C (mg/dL)</td>
<td>117</td>
<td>308</td>
<td>382</td>
<td>-</td>
<td>384</td>
<td>-</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HD, hospital day; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

![Fig. 1. A. Ultrasoundographic finding in abdomen. Visible pancreas showed edematous change with surrounding fat infiltration; this is suggestive of acute pancreatitis. B. This shows a mildly improved state of acute pancreatitis.](http://www.enm-kes.org)

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Ketoadiotosis with Hypertriglyceridemia-induced Pancreatititis in a Patient with GDM

During pregnancy, there is a physiologic increase in cholesterol and triglyceride plasma levels. In the diabetic pregnancy, hypertriglyceridemia has been found to be more exaggerated compared to the rise in TGs observed during normal pregnancy; however, there are contradictory studies showing no additional increase in plasma TG levels for diabetic pregnant women [11,12]. Several mechanisms have been suggested; all are related to augmentation of the insulin-resistant state and adipose tissue lipoprotein lipase (LPL) activity, and in an increase in plasma estrogen concentrations [13]. However, it has been suggested that this increase is not sufficient to cause pancreatitis, and preexisting genetic abnormalities in the lipid metabolism are required. In this case, all of above factors except genetic abnormalities, which we were not able to evaluate, were considered causes of hypertriglyceridemia with additional dietary factors, such as the excessive intake of a high carbohydrate and high caloric diet.

Hypertriglyceridemia can alter sodium levels leading to pseudohyponatremia, since excess TG in serum can displace water-containing sodium [14]. On initial observation, our patient’s case showed hyponatremia, which had recovered spontaneously with the lowering of the TG level without additional treatments for the sodium level. Therefore, in the case of hyponatremia with severe hypertriglyceridemia, clinicians should consider the possibility of pseudohyponatremia and avoid overtreatment with hypertonic saline.

Acute pancreatitis is uncommon in pregnancy. Its incidence has been reported 1/1,000-1/10,000 births [15], and pancreatitis secondary to hyperlipidemia has an estimated incidence of 1 in 25,000 births. However, it has been reported that hypertriglyceridemia caused 50% of gestational pancreatitis [3]. The mechanism of how hypertriglyceridemia precipitates acute pancreatitis remains unknown. One possible theory is that pancreatic lipase hydrolyses excess TG by releasing free fatty acids into the vascular bed of the pancreas, thereby causing pancreatic acinar cell and capillary injury, with resulting ischemia. Another possible theory is that hyperviscosity, due to elevated levels of chylomicrons in these pancreatic capillaries, leads to ischemia and acidosis in the pancreas [16]. It has been postulated that genetic abnormalities in lipid metabolism may be exacerbated during pregnancy and may cause gestational hyperlipidemic pancreatitis [17].

The incidence of DKA in pregnancy has been reported as 1-3%, with fetal loss rate of 9%. Although DKA occurs more common in patients with type 1 diabetes, it has been recognized in patients with type 2 diabetes, as well as in patients with gestational diabetes [8-10]. The majority (78-90%) occur in the second and third trimesters of pregnancy due to increased insulin resistance contributed by insulin antagonistic hormones like human placental lactogen, prolactin, and cortisol. Other ordinary contributing factors may be cessation of insulin therapy (40%) and infection (20%), pregnancy-related factors may be relative state of starvation by itself, lowered buffering capacity and the effect of emesis.

In addition, the fetus may suffer from acidosis that crosses the placenta, resulting from academia that decreases uterine blood flow, tissue perfusion, and oxygenation. Because the fetus is not directly accessible, external fetal heart rate tracings may be useful in showing decreased or absent variability, absent accelerations, and late decelerations. In this case, the fetal status was also monitored with non-stress test that did not experience variability based on maternal DKA, and any negative signs were reversed after treatment of maternal DKA. Several retrospective studies have reported a perinatal mortality rate of 9-35% in cases of maternal DKA. Early recognition and proper treatment of maternal DKA may avoid adverse fetal outcomes.

Formal treatment guidelines for hypertriglyceridemia in pregnancy do not exist, nor are there guidelines for treatment of hyperlipidemic pancreatitis, which consists primarily of supportive care. Several reports of effective management have included a low fat diet,
detailed fluid administration, insulin injection to increase LPL activity, antihyperlipidemia therapy (e.g., fenofibrate), heparin injection to increase LPL activity, and plasmapheresis [16]. In our present case, hypertriglyceridemia was controlled simply with insulin and fluid without lipid lowering agents.

To our knowledge, the present case is the first published case of ketoacidosis with hypertriglyceridemia-induced pancreatitis in a patient with gestational diabetes. By increasing awareness of hypertriglyceridemia as a cause of acute pancreatitis especially in gestational diabetes, pregnant women with any type of diabetes require follow-up for lipid abnormalities, in cases of screening or during an acute pancreatitis episode.

요 약

고중성지방혈성 채장염은 매우 드물어 급성 채장염의 1-4% 정도이자, 임신 중 발생률은 54% 정도로 보고되고 있다. 임신 중 발생하는 채토산증은 연간 임산부 1,000명당 4.6-8건 발생하는 것으로 알려져 있으며, 임신성 당뇨병에서는 드물고, 기저 당뇨병을 가진 산모의 감염이 아닌 산모의 오작동 등에 의해 발생하는 경우가 대부분이다. 저자 등은 임신성 당뇨병 환자에서 고중성지방혈성 채장염에 병발한 당뇨병성 채토산증 1례를 경험하였기에 보고하는 바이다.

증례: 36세 산모(임신 32주)가 내원 후 시행한 50 g 포도당 단 병검에서 438 mg/dL로 임신성 당뇨병을 진단 받았으나, 치료 없이 자녀가 내과에서 시행한 수측검사 무작위 혈당검사 294 mg/dL, 당화혈소포 8.6%로 혈당조절을 위해 입원하였다. 다혈 혈중 인슐린 주사로 혈당을 조절하던 중 입원 2일째 오심, 구토를 동반한 심한 상복부 통증을 호소하여 시행한 동맥혈검사 pH 7.213, PCO₂ 179 mmHg, PO₂ 53 mmHg, BE -19.6 mmol/L, HCO₃ 7 mmol/L, 음이온차 17.6 meq/L, 혈중 채토산 3.6 mmol/L, 혈당 277 mg/dL, 아밀라체 385 U/L, 리파아제 395 IU/L이었으며 임신 38주에 재발시 간헐적 속부 통증, 급성 채장염 소견을 보이고, triglyceride (TG)/total cholesterol (TC) low density lipoprotein cholesterol (LDL-C) 1996/700/117 mg/dL로 측정되었다. 비타민검사로 태아 상태 판찰하여 gabexate mesylate, 인슐린 정맥 투여로 임상증상 및 혈액검사 상호를 보였다. 임신 38주에 재발방 경술 시행하여 3,125 gm 남아를 출산하였고, 4주 후 공복 및 식후 2시간 혈당 219/531 mg/dL, TC/TG/LDL-C 227/322/147 mg/dL로 측정되어 glimepiride/ metformin, fibrate, statin 복용하면서 외래 경과 관찰 중이다.

REFERENCES


http://www.enm-kes.org

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