Research and Science Today
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DOI: 10.38173/RST.2021.22.2.12:125-130

Title:	*HYPERTRIGLYCERIDAEMIC PANCREATITIS AND DIABETIC KETOACIDOSIS*
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Section: MEDICINE

Issue: 2(22)/2021

Received: 4 July 2021	**Revised:** 19 September 2021
Accepted: 16 Octomber 2021	**Available Online:** 15 November 2021

Paper available online HERE

RST Research and Science Today
WWW.RSTJOURNAL.COM
AUTUMN 2021
No. 2(22)/2021
ISSN-P: 2247-4455 / ISSN-E: 2285-9632

Medicine

HYPERTRIGLYCERIDAEMIC PANCREATITIS AND DIABETIC KETOACIDOSIS

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ABSTRACT:
ACUTE PANCREATITIS IS AN INFLAMMATORY CONDITION OF THE PANCREAS WITH MULTIPLE ETIOLOGIES. HYPERTRIGLYCERIDAEMIC PANCREATITIS (HTG-AP) IS NOT A COMMON CAUSE OF AP BUT IS ASOCIATED WITH A INCREASED RATE OF COMPLICATIONS. PATIENTS WITH DIABETES MELLITUS ARE AT INCREASED RISK OF AP. THE ASSOCIATIN BETWEEN HYPERTRIGLYCERIDAEMIA, KETOACIDOSIS AND AP IS RARE. THE TREATMENT OF THIS TYPE OF PANCREATITIS IS NOT WELL ESTABLISHED IN CURRENT GUIDELINES, SPECIFIC TERAPEUTIC MEASUREMENTS INCLUDE HEPARIN, INSULIN TREATMENT, PLASMAPHERESIS, COMBINED BLOOD PURIFICATION THERAPY, HIGH-VOLUME HEMOFILTRATION AND HEMOPERFUSION. WE REPORTED TWO CASES OF HYPERTRIGLYCERIDAEMIA (HTG) INDUCED AP, IN PACIENTS WITH UNCONTROLLED TYPE 2 DIABETES MELLITUS AND KETOACIDOSIS ONE TREATED WITH INSULIN INFUSION AND ANOTHER TREATED WITH INSULIN INFUSION AND PLASMAPHERESIS. BOTH CASES WERE SUCCESSFULLY MANAGED WITH SPECIFIC MEASURES AND SUPPORTIVE CARE.

KEYWORDS: ACUTE PANCREATITIS, HYPERTRIGLYCERIDAEMIA, DIABETIC KETOACIDOSIS, PLASMAPHERESIS.

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INTRODUCTION

Acute pancreatitis, diabetes mellitus and hypertryglycerideaemia are diseases with increased incidence in our modern world. Diabetes mellitus is a common metabolic disorder with 102% increasing incidence between 1990 and 2017[8] and the life-threatening complication, diabetic ketoacidosis, had a raported incidence of 0,48/1000 in a japanese study[9] with increased incidence raported in several studies[1011]. Regarding AP the continuous increase in the incidence among both men and women in the last 31 years was reported in a Danish study[12].

HTG-AP is the third cause of AP following alcohol and biliary etiology with a raported incidence between 4% and 9%[1314]. In National Cholesterol Education Program ATP III, triglyceride (TGs) level is normal (<150), borderline high (150-199), high (200-499), and very high (>500 mg/dL)[15]. Hypertriglyceridemia can be primary (inherited) and secondary (acquired) . The conditions associated with HTG include *obesity, metabolic syndrome, diabetes, alcohol, renal disease, pregnancy, medications,* immunological disorders[16]. *TG cut off value asociated with AP is 1000 mg/dl*[17]. The diagnosis of HTG AP is made by the presence of two of three criteria: upper abdominal pain, increase of pancreatic enzymes over three times the upper limit of normal and characteristic radiological finding. The optimal management of HTG-AP is not well established but it is desirable to decrease the TG level quickly[18].

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CASE 1

We report the case of a 47 year old caucasian male who presented to the emergency room for abdominal pain, nausea and vomiting started in the last 48 hours. He had a medical history of type 2 diabetes mellitus terapeutically neglected, former smoker, without history of illicit drug use or alcohol abuse.The clinical examination revealed a restless and anxious pacient, with cold, sweaty skin, Kussmaul breathing, tachycardia (heart rate was 124 beats/min), mean arterial pressure 65 mmHg, distended abdomen and epigastric tenderness.

Laboratory parameters showed severe metabolic acidosis with high anion gap , pH 7.07, bicarbonate 8 mmol/l (normal range 22-28 mmol/l), anion gap 20 mmol/l (normal range 4-12 mmol/l), BE -22 mmol/l hyperglycemia, glucose blood level 727 mg/dl (normal range70-106 mg/dl), lipase 6157 U/l (normal range 73-393 U/l), amylase 822 U/l (normal range 15-115 U/l), severe HTG, TG 4491 mg/dl (normal range 30-150 mg/dl), hypocalcemia 6.1 mg/dl (normal range 8.2-10.7 mg/dl), Na 116 mmol/l (normal range 135-150 mmol/l), K 5.2 mmol/l (normal range 3.5-5.2 mmol/l), LDH 902 U/l (normal range 84-227 U/l), creatinine 1.59 (normal range 0.5-1.5 mg/dl), AST 117 (normal range 2-40 U/l), ALT 88 U/l, creatinine 1.59 mg/dl . Glycated hemoglobin was 11,8 mg/dl (normal range 4.3-6 %). The white blood cell count, hemoglobin and hematocrit values were normal and a high CRP level (>30 mg/l) was found. The serum was lactescent. Urine analysis revealed a urine glucose of 500mg/dL and ketonuria (80mg/dL). The computed tomography (CT) scan showed an oedematous pancreas surrounded by peri-pancreatic, prerenal space and lateroconal fascia fluid colections, a fatty liver, normal gall bladder and bile ducts (Balthazar CT severity index 4).

These data led to the diagnosis of HTG-AP and diabetic ketoacidosis.The treatment was started immediately with insulin bolus 0,1 U/kg followed by insulin 0.1 U/kg/h infusion and volemic resuscitation, in 4 l of normal saline in 24 hours.

After the first 24 hours, the evolution was complicated by the occurrence of hypoxemic respiratory failure and the patient was transferred to intensive care unit (ICU) conscious but very agitated (Richmond Agitation Sedation scale +3) , with severe dyspnea , respiratory rate 36/min , mean arterial pressure 70 mmmHg. The arterial blood gases (ABG) on ICU admission was suggestive for hypoxemia and metabolic acidosis (pH 7.15, CO2 28 mmHg, O2 65mmHg, bicarbonate 8.5 mmol/l, anion gap 18 mmol/l). Glucose blood level was 282 mg/dl, Na 128 mmol/l, K 4.2 mmol/l, ALT 128 U/l, AST 81 U/l, TG level 1250 mg/ml, cholesterol 408 mg/dl, normal values of creatinine and levels. In these conditions we decided on intubation and mechanical ventilation using protective lung strategies. At the ICU admission the APACHE II score was 18 and the SOFA score 4. In the ICU it was continued the fluid resuscitation and insulin infusion. Given the high level of TG and the development of respiratory failure and SIRS (Systemic inflammatory response syndrome) in a patient with HTG-AP we performed a plasmapheresis session using human albumin 5% and heparin anticoagulation.The TG level after plasmapheresis was 345 mg/dl. Blood glucose values were controlled but the patient's condition did not improve, requiring sedation and further mechanical ventilation. The enteral feeding , statine and fibrates terapy were started on the second day of ICU stay via nasogastric tube feeding .On the third day of ICU stay the patient presented fever (39° C) and leukocytosis (WBC 15600/ µL). A CT scan was performed showing bilateral pleural effusion (maximum 3 centimeters), bilateral basal pulmonary infiltrates and slight increase in size of peripancreatic, prerenal and lateroconal fascia fluid. A bacteriological screening was performed and broad spectrum antibiotic was administrated (meropenem). Tracheal aspirate culture was positive for Acinetobacter spp. carbapenem-resistant, colistin-susceptible and the antibiotherapy was escaladated with colistin. During his

ICU stay the patient was hemodynamically stable. After 13 days the pacient was extubated and then transferred to a regular medicine floor. The CT exam performed five weeks later showed the resolution of the pleural effusions and the presence of multiple peripancreatic collections with a tendency to encapsulation and the pacient was was discharged with statine, fibrates terapy and insulin terapy.

CASE 2

A 45 year old woman with history of autoimmune thyroiditis without home treatment, no alcohol consumpton came to the emergency department for severe upper abdominal pain, nausea and vomiting started 4 days earlier when she performed a glucose strip test at home and found a high glucose blood level (345 mg/dl) but she did not go to the hospital.

Clinical examination showed an alert pacient, with decreased skin turgor, respiratory frecvency 22/ min, TA 89/45 mmHg, heart rate 120 beats/min. Laboratory exam pH 7.2, bicarbonat 7.2 mmol/l, BE -20 mmol/l, anion gap 23 mmol/l, hyperglycemia (508 mg/dl), TG 1379 mg/dl , cholesterol 411 mg/dl, creatinine 1,63 mg/dl, urea 29 mg/dl K 5.78 mmol/l, Na 123 mmol/l, total calcium 7 mg/dl, ALT 59 U/l, AST 49 U/l, total bilirubin 0,4 mg/dl, lipase 2329 U/l, amylase 1529 U/l, white blood cell 14400/ µL. Urine analysis revealed a urine glucose of 500mg/dL and ketonuria (30mg/dL), density 1030. The procalcitonin level was > 10 ng/ml and TSH, free T3 and free T4 were in normal range. Glycated hemoglobin was 11,2 mg/dl.

The CT showed pancreatic oedema and peripancreatic, prerenal fluid with a Balthazar CT severity index 4, a fatty liver, no gallstone and normal bile ducts.

The pacient was admitted to ICU with an APACHE score 7 and the treatment was started immediately with volemic resuscitacion and insulin 0.1U/kg bolus followed by continuous infusion with a rate of 0.1 U/h progressively decreased with the decrease in blood glucose. The patient received prophylactic antibiotic treatment, analgesia with Fentanyl. Forty-eight hours after admission, the TG level reached 432 mg/dl. Enteral feeding, statine and fibrate terapy were started on the third day. The patient's evolution was complicated by the occurrence of renal dysfunction framed as AKI stage 2 (AKIN classification/staging system of acute kidney injury) remitted in about 96 hours. The patient's health state improved and five days later she was transferred from the ICU to a diabetes and metabolism clinic.

DISCUSSION

Diabetic ketoacidosis is due to absolute or relative deficiency of insulin that leads to leads to the formation of ketone bodies and the appearance of hyperglycemia, ketoacidosis and ketonuria. Episodes of ketoacidosis are accompanied by hypertriglyceridemia and an increase in the amount of free fatty acids that cause pancreatic injury[19] but acute pancreatitis can lead to diabetic ketoacidosis.

The association between HTG-AP, diabetic ketoacidosis and hyperglycemia is rarely described in the literature and affects both children and adults. This triad is associated with a higher rate of local and systemic complications and higher mortality.[20]

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ISSN-P: 2247-4455 / ISSN-E: 2285-9632

The diagnosis of HTG-AP in patients with diabetic ketoacidosis is difficult due to the fact that ketoacidosis is accompanied by abdominal pain and increased level of amylases and lipases even in the absence of pancreatitis[21], while the amylase level can be normal in pacients with HTG-AP[22].

The cases presented above occurred in patients with uncontrolled diabetes mellitus. The first one evolved as severe acute pancreatitis and the second as moderately severe acute pancreatitis. In the first case, the severity was given by the occurrence of respiratory failure despite insulin terapy and in this context a plasmapheresis session was performed with the decrease of the TG level.The respiratory failure was later maintained by the appearance of ventilator associated pneumonia with multi drog resistant germs. The second case was complicated by AKI stage 2. The two cases had different levels of TG but had the same Balthazar CT severity index and their evolution correlated with triglyceride levels rather than CT score.

The initial treatment in both cases was based on fluid resuscitation and insulin administration. The role of plasmapheresis in the treatment of HTG-AP remains to be established in further studies.

CONCLUSION

The early diagnosis and treatment of HTG-AP associated with ketoacidosis are essential given the lethal potential.They represents a real challenge for clinicians. The control of risk factors is crucial because it leads to a decrease in the incidence of this pathology.

ACKNOWLEDGEMENTS

All authors equally contributed in the research and drafting of this paper
All authors report no pottential conflict of interest.

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