Chylomicronemia syndrome, the common link between hyponatremia and pancreatitis

Síndrome de quilomicronemia, el vínculo común entre hiponatremia y pancreatitis

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Resumen

La hipertrigliceridemia es responsable hasta el 10% de los casos de pancreatitis, apareciendo como la tercera etiología más común. Este artículo describe el caso de una mujer de 29 años, admitida en el internamiento de medicina interna para investigación de hiponatremia grave asintomática. Posteriormente fue diagnosticada con pancreatitis, con presencia concomitante de pequeños cálculos biliares y síndrome de quilomicronemia, comprobando que se trataba de un caso de pseudo-hiponatremia. Después de la alta, la paciente mantuvo episodios de pancreatitis, incluso después de la colecistectomía, en probable relación con mala adhesión médica a la terapia hipolipidémica.

Palabras-clave: Pancreatitis, hiponatremia, hipertrigliceridemia, amilasa, lipasa.

Abstract

Hypertriglyderidemia is responsible for up to 10% of cases of pancreatitis, appearing as the third most common etiology. This article describes the case of a 29-year-old woman admitted to the internal medicine department in order to investigate an asymptomatic severe hyponatremia. Later, she was diagnosed with pancreatitis, and with the concomitant presence of small gallstones and chylomicronemia syndrome, so the hyponatremia was proved to be a pseudohyponatremia. After discharge, the patient maintained episodes of pancreatitis, even after cholecystectomy, in probable relation with bad medical compliance to hypolipidemic therapy.

Keywords: Pancreatitis, hyponatremia, hypertriglyceridemia, amylase, lipase.

Introduction

Pancreatitis consists in an inflammation of the pancreas that can be triggered by multiple causes, the most frequent being gallstones and alcohol.[1,2,3,4] Hypertriglyceridemia (HTG) appears as the third most common cause of pancreatitis, responsible for up to 10% of the cases.[2,4,5,6] Although theories have been proposed, the mechanism by which high triglycerides levels (TG) can trigger pancreatitis is unknown.[7]

Case description

A 29-year-old woman with a history of type 2 diabetes, class 2 obesity (BMI 37.3Kg/m^2) and cholelithiasis was admitted to the emergency department due to abdominal pain and a 3-day constipation. She was chronically medicated with metformin + vildagliptin 850/50mg twice daily. The patient denied alcohol, tobacco or drugs consumption. Upon physical examination, she presented tenderness of the upper abdominal quadrants and multiple xanthomas of the face, arms and legs (Figure 1).

Relevant laboratory results at admission were haemoglobin of 12.5g/dL, WBC 15700/µL, platelets 330000/µL, glucose 85mg/dL, sodium 111mmol/L, potassium 4,1mmol/L, Amylase 128U/L, Lipase 192U/L, AST 65U/L, ALT 5U/L, LDH 138U/L, alkaline phosphatase 47U/L, total bilirubin 5.8 µmol/L, c-reactive protein (CRP) 19,2mg/L (Table1).

Abdominal ultrasound exposed hepatomegaly, with hepatic steatosis, otherwise unremarkable. Abdominal x-ray showed mild Intestinal distention without hydro-aerial levels.

After pain medication and laxatives, the pain resolved and the patient was admitted to the internal medicine ward to investigate the hyponatremia.

The clinical condition deteriorated with recrudescence and exacerbation of the abdominal pain. Blood analysis showed a pronounced elevation of CRP 418mg/L, amylase 108U/L, lipase 242 U/L, maintaining the hyponatremia, with normal TSH (Table1).

It is relevant to refer that the blood sample was lipemic, with the standing plasma containing a cream layer over a turbid layer. Blood cultures were collected and empiric antibiotic therapy with Piperacillin-Tazobactam started. Further study included abdominal computed tomography (Fig. 2), relating signs of acute pancreatitis as well as small size gallstones. The patient received treatment with intravenous fluids, fasting and pain control, obtaining clinical improvement. Later we acknowledged the lipid profile results: total cholesterol 1282mg/dl, HDL 40mg/dl, TG 6221mg/dl. Medical therapy with rosuvastatin 40mg and fenofibrate 267mg was started.

During the hospital stay the patient evolved with no complications and no organic dysfunction and after three weeks she was discharged, with TG 994mg/dl. With the diagnosis of type V hyperlipoproteinemia in Fredrickson classification (based on the examination of standing plasma and Total cholesterol/TG ratio)[8,9], she was referred to genetic testing, but no abnormalities were found.

After discharge, the patient presented wavering TG in relation with inappropriate compliance, TG varying from 299 to 5825mg/dl. She had another admission with the diagnosis of pancreatitis and after 6 months she was submitted to cholecystectomy. Two months after surgery the patient had another recurrence of pancreatitis, with TG 5444mg/dl. A magnetic resonance was performed and the possibility of residual choledocholithiasis was discarded.

Discussion

The association between severe HTG and pancreatitis was first described by Speck in 1865.[6,10] Individuals with

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Fig 1. Xanthomas dispersed by both patient´s Knees.

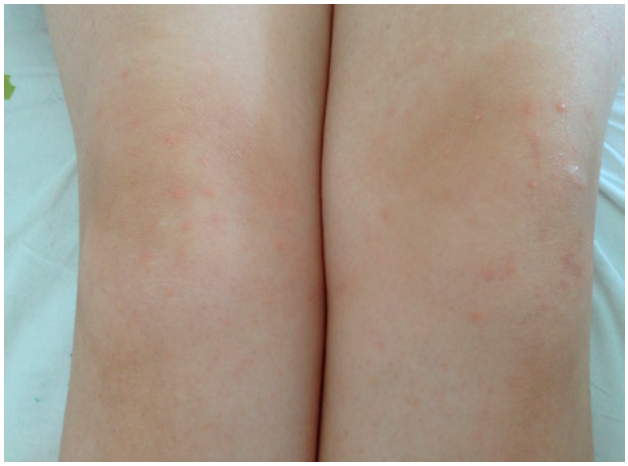

Fig 2. Computed tomography displaying peri-pancreatic densification and oedema as a sign of pancreatitis.

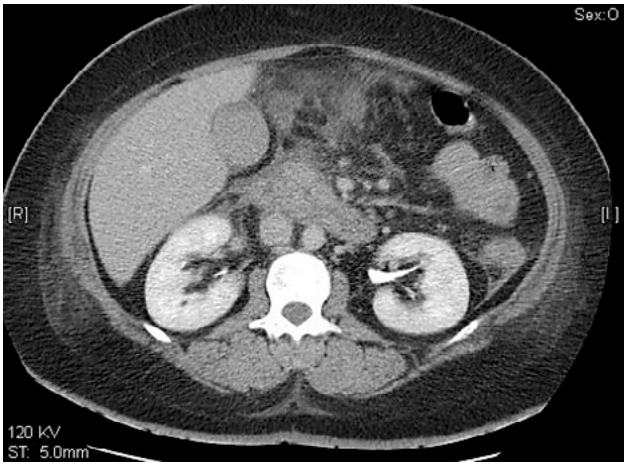

Table 1. Relevant laboratory results on emergency department (ER) and on internal medicine department (IMD) when the clinical condition deteriorated.

Parameters	ER	IMD	Normal Range
Haemoglobin (g/dL)	12.5	12.0	11.5-16.0
WBC (10^3/µL)	15.7	10.3	4.0-10.0
Platelets (10^3/µL)	330	292	150-500
Glucose (mg/dL)	85	211	74-106
BUN (mmol/L)	4.9	2.4	2.1-7.1
Creatinine (mg/dL)	0.14	0.48	0.6-1.1
Sodium (mmol/L)	111	128	136-146
Potassium (mmol/L)	4,1	3.3	3.5-5.1
Amylase (U/L)	128	108	28-100
Lipase (U/L)	192	242	22-67
AST (U/L)	65	9	15-35
ALT (U/L)	5	15	3-34
Lactate dehidrogenase (U/L)	138	138	100-190
Alkaline phosphatase (U/L)	47	47	42-98
Total bilirubin (µmol/L)	5.8	5.9	5.0-21.0
Conjugated bilirubin (µmol/L)		0.5	<3.4
Unconjugated bilirubin (µmol/L)		5.3	1.7-17.1
C-reactive protein (mg/L)	19.2	418	<5
Total cholesterol (mg/dL)		1282	<201
HDL (mg/dL)		40	40-60
TG (mg/dL)		6221	<150
Hb A1c (%)		7.7	4.0-6.0
TSH (µUI/L)		1.8	0.34-5.60

TG>1000mg/dl have an increased risk to develop pancreatitis.[2,4,6,10]

HTG can be caused by genetics or by secondary factors, such as uncontrolled diabetes, alcohol or medication.[11] Chylomicronemia syndrome is characterized by the presence of chylomicronemia (TG>1000mg/dL), as well as the presence of eruptive xanthomas, lipemia retinalis or abdominal pain, and it is frequently related with recurrent pancreatitis.[7,11,12]

The diagnosis of pancreatitis requires at least two of the three criteria: typical abdominal pain, lipase or amylase serum levels raised more than three times the normal upper limit, and detection by CT.[10] However, serum lipase and specially amylase are less reliable when the pancreatitis is caused by HTG as its concentrations can be in normal range or only mildly elevated.[1,2,10]

In our case the diagnosis of pancreatitis was first obscured by the mild elevation of serum levels of amylase and lipase, not superior to three times the normal range on the first evaluation; only on reassessment did the lipase attain diagnostic values, with amylase remaining merely slightly raised. As the patient referred constipation and the abdominal pain subsided after laxatives, the pain was attributed to constipation.

Against this backdrop the hyponatremia was the most valued anomaly and only after the relapse and exacerbation of the abdominal pain, the possibility of an abdominal malady was weighted.

The knowledge of the TG made obvious that we were before a pseudo-hyponatremia. The whole scenery was an important reminder that before hyponatremia, the first step is to confirm that it is real and not a pseudo-hyponatremia.

Another important singularity was the presence of two potential trigger factors. The presence of gallstones is the most common cause to pancreatitis so it was difficult to assume that they had no contribution to the clinical condition. However, it was also not wise to ignore the HTG and the fulfilment of the diagnostic criteria of chylomicronemia syndrome. The relapse of pancreatitis even after cholecystectomy, supported the HTG as the trigger to pancreatitis. The presence of a lipemic blood sample is also an important factor as it should always raise the suspicion of HTG induced pancreatitis.[4]

There are no guidelines for the treatment of pancreatitis associated with HTG.[6] The initial management is similar to any other cause, relying on intravenous fluids, pain management and dietary restriction.[1] Nevertheless, besides supportive care a crucial goal is to reduce TG in order to decrease or eliminate the trigger. Fibrates with or without statins are the first line treatment to lower TG, but they need time to be effective.[2,10] In acute settings the celerity in obtaining the target results can be fundamental in the patients´ outcome, therefore other strategies have been reported and proven its efficacy in some studies. Apheresis has been successfully tested and is capable of a quick reduction of TG, sometimes in only one session. Its limitations lie in the high cost, the inaccessibility in some centres and in the fact that the technique is not totally innocuous. A more commonly used measure is intravenous insulin perfusion, with or without heparin, also proven to be effective in reducing TG in several studies although the results are not as fast as apheresis.[1,2,3,6,11]

Our patient was effectively treated with only supportive care. Some authors defend that this approach may be sufficient,[11] and the clinical improvement should be the guide to choose the treatment options. The more severe cases, with multiorganic dysfunction and instability, as well as the absence of improvements signs should prompt a more aggressive treatment.[1,2,10]

References

1. Khan R, Jehangir W, Regeti K, Yousif A. Hypertriglyceridemia-Induced Pancreatitis: Choice of Treatment. Gastroenterol Res. 2015;8(3-4):234-236
2. Chaudharya A, Iqbala U, Anwarb H, Siddiquic HU, Alvi M. Acute Pancreatitis Secondary to Severe Hypertriglyceridemia: Management of Severe Hypertriglyceridemia in Emergency Setting. Gastroenterol Res. 2017;10(3):190-192
3. Lu MLRY, Agito MD. Triglyeride-induced Pancreatitis: Diagnostic and Therapeutic Approach. Gastroenterol Hepatol Endosc. 2016; 1(1): 1-5
4. Minhas J, Thakkar D, Dargin J. Hypertriglyceridemia-induced acute pancreatitis. The Journal of Emergency Medicine. 2017; 52(3): e89-e90
5. Wang S, Chou Y, Shangkuan W, Wei K, Pan Y, Lin H. Relationship between Plasma Triglyceride Level and Severity of Hypertriglyceridemic Pancreatitis. PLoS One. 2016; 11(10): e0163984
6. Ewald N, Hardt PD, Kloer HU. Severe hypertriglyceridemia and pancreatitis: presentation and management. Curr Opin Lipidol. 2009;20(6):497-504.
7. Tannock L, Bhat A. Risk Assessment and Guidelines for the Management of High Triglycerides. 2015. (Available from: www.ncbi.nlm.nih.gov/books/NBK326745/)
8. Beaumont JL, Carlson LA, Cooper GR, Fejfar Z, Fredrickson DS, Strasser T. Classification of hyperlipidaemias and hyperlipoproteinaemias. Bull World Health Organ. 1970; 43:891–915
9. Fredrickson DS, Levy RI, Lees RS. Fat transport in lipoproteins-an integrated approach to mechanisms and disorders. N Engl J Med. 1967; 276(5):273-81
10. Campos A, Santos J, Freitas C, Castro A, Santos S, Pimentel JP et al. Plasmapheresis in the Management of Acute Pancreatitis due to Severe Hypertriglyceridemia—Reporting New Cases. Journal of Renal and Hepatic Disorders. 2017; 1(1):29-34
11. Uysal E, Acar YA, Gökmen E, Kutur A, Dogan H. Hypertriglyceridemia Induced Pancreatitis (Chylomicronemia Syndrome) Treated with Supportive Care. Case Reports in Critical Care. 2014: DOI 10.1155/2014/767831
12. Leaf DA. Chylomicronemia and the chylomicronemia syndrome: a practical approach to management. Am J Med. 2008; 121(1):10-2.