



CASE REPORT

Therapeutic Plasma Exchange for Acute Pancreatitis Secondary to Hypertriglyceridemia: Case Report and Review of the Literature

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Abstract

A patient with acute pancreatitis was admitted to our Intensive Care Unit due to arterial hypotension and hypoxemia that responded to fluid resuscitation and supplemental oxygen; the blood chemistries revealed extremely elevated triglycerides and cholesterol levels. A therapeutic plasma exchange was performed on an emergency basis and determined their sharp decrease. The patient was transferred to a regular ward 6 days later, and a CT-scan obtained after one more week at demonstrated a large pseudocyst even if the patient remained asymptomatic and was discharged home to be followed in an outpatient clinic.

Keywords

Hypertriglyceridemia, Hypercholesterolemia, Acute pancreatitis, Plasma exchange

Introduction

Although Acute Pancreatitis (AP) in most cases is an auto-limiting process that usually subsides in few days, in roughly 20% of patients it can progress to a life-threatening Multiple Organ Dysfunction Syndrome [1]. In these cases, the main clinical challenge consists in the early identification of patient at risk of deterioration needing the admission to the intensive care unit (ICU) [2]. Independently from its severity, the treatment of AP is mainly supportive except when specific therapeutic measures can be used against the triggering causes, such as (a) Biliary obstruction

or cholangitis that require an urgent endoscopic retrograde cholangiopancreatography; and (b) High concentrations of triglycerides (TG) [2]. Actually, after biliary obstruction and ethanol consumption, this latter represents the third cause of AP, accounting for 30% of cases. Although hypertriglyceridemia (HTG) is a feature of different hyperlipoproteinemia types, including I, III, IV and V, only elevated values of chylomicrons (CM) have been associated with AP [3]. It is not clear yet the clinical course and the outcome if HTG-associated AP differs from the more common forms of AP: actually, some authors demonstrated an increased incidence of organ failures and a worse outcome but these findings have not been confirmed by other investigations [3-5]; it is possible that likewise other clinical conditions characterized by a hyperinflammation such as septic shock, the presence of coexisting diseases and frailties accounts for these contrasting results. Anyway, besides the other measures of organ support, the lowering of the TG is warranted in order to reduce the inflammatory response.

Here we report the case of a patient with AP due to exceedingly high levels of TG treated with a therapeutic plasma exchange (TPE) performed on an emergency basis.

Case Description

As the data presented are anonymous the local ethical committee deemed unnecessary any informed

consent; moreover, at admission, all patients are requested to give their consent to use their data for study purpose, provided that their privacy is respected.

A 49-year-old woman without any relevant clinical history was admitted to our ICU due hypotension and dyspnea associated with severe abdominal pain and vomit. The symptoms began 6 hours before and rapidly worsened alongside with dyspnea. At the clinical examination the patient was overweight (Body Mass Index = 29); the mean arterial pressure (MAP) was 55 mmHg; the heart rate (HR) was 125 bpm and the respiratory rate was 28 with a SpO₂ = 92% while breathing at a FiO₂ = 50%; oliguria was also present; the intraabdominal pressure (IAP) was 12 mmHg and remained stable throughout the clinical course. The

CT of the abdomen revealed a diffusely edematous pancreas with a moderate amount of ascites. The MAP, the HR and the urinary output improved after the i.v. administration of 3000 ml of crystalloids; the urine appeared milky (Figure 1A).

The blood samples had to be resent twice because the clogging of the analyzer prevented their processing. When the blood chemistries became available, it appeared that this circumstance could be ascribed to a severe HTG associated with hypercholesterolemia (Table 1).

Aiming to reduce the overall lipid burden, a filter-based TPE was performed on an emergency basis aiming to remove and substitute 1.5 times the total

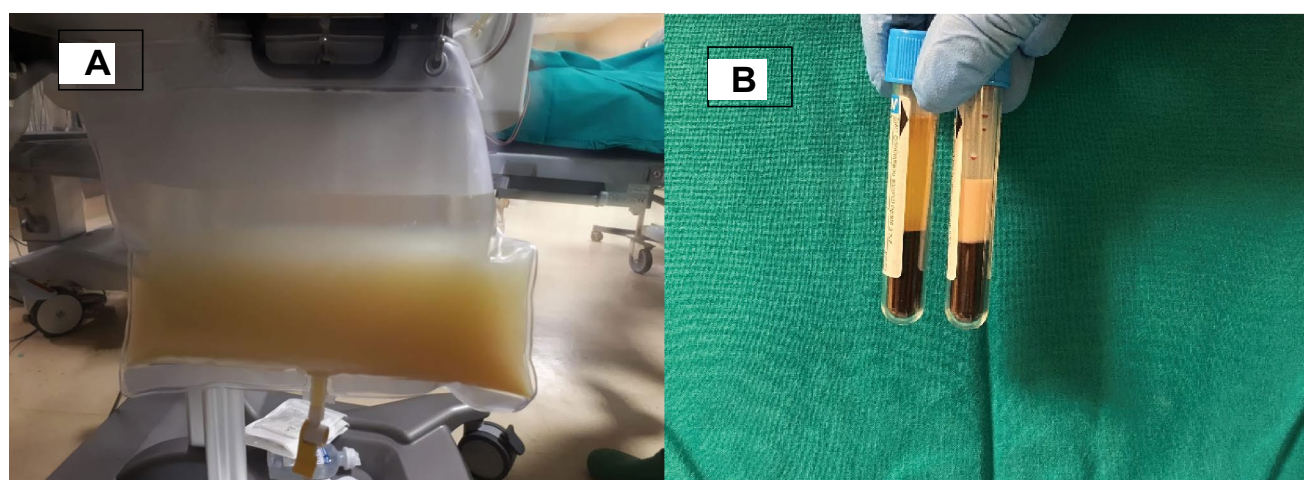


Figure 1: Urine collection bag (A) and plasma (B) before (left) and after (right) the plasma exchange.

Table 1: Blood chemistries.

Variable	Range	Admission*	D2**	D3	D4	D5
Hb (g/dl)	12-16	18.9	10.0	8.7	8.4	7.7
RBC ($\cdot 10^6$)	4.2-5.0	5400	3260	2820	2640	2550
WBC ($\cdot 10^3$)	4-11	15.19	10.06	8.12	12.40	16.02
Platelets ($\cdot 10^3$)	150-450	276	184	209	238	295
C - Reactive Protein (mg/dl)	< 5	187.5	315.3	376.2	385.5	355.1
BUN (mg/dl)	15-50	30	41	21	22	23
Creatinine (mg/dl)	0.5-1.1	0.81	0.56	0.38	0.39	0.4
Blood Glucose (mg/dl)	65-110	200	170	135	124	166
Amilase (U/L)	8-53	337	45	11	14	12
LDH /U/L)	< 250	822	532	n.a.	n.a.	n.a.
Total Bilirubine (mg/dl)	0.3-1.2	0.26	0.75	n.a.	0.4	0.33
Tryglycerides (mg/dl)	< 170	6561	602	422	321	338
Total Cholesterol (mg/dl)	< 200	852	218	173	142	121
HDL Cholesterol (mg/dl)	< 40	201	38	32	24	19
Apolipoprotein A1 (mg/dl)	105-205	95	Not Repeated			
Apolipoprotein B (mg/dl)	55-130	89				
Lipoprotein A (mg/dl)	< 30	4				

*: Before the plasma exchange; **: 18 hours after the plasma exchange; Hb: Hemoglobin; RBC: Red Blood Cells; WBC: White Blood Cells; BUN: Blood Urea Nitrogen; LDH: Lactate Dehydrogenase; n.a.: not available

plasma volume (TPV). This variable was calculated with the formula.

$$TPV = Total\ Blood\ Volume(TBV) * (1 - Hematocrit) [6];$$

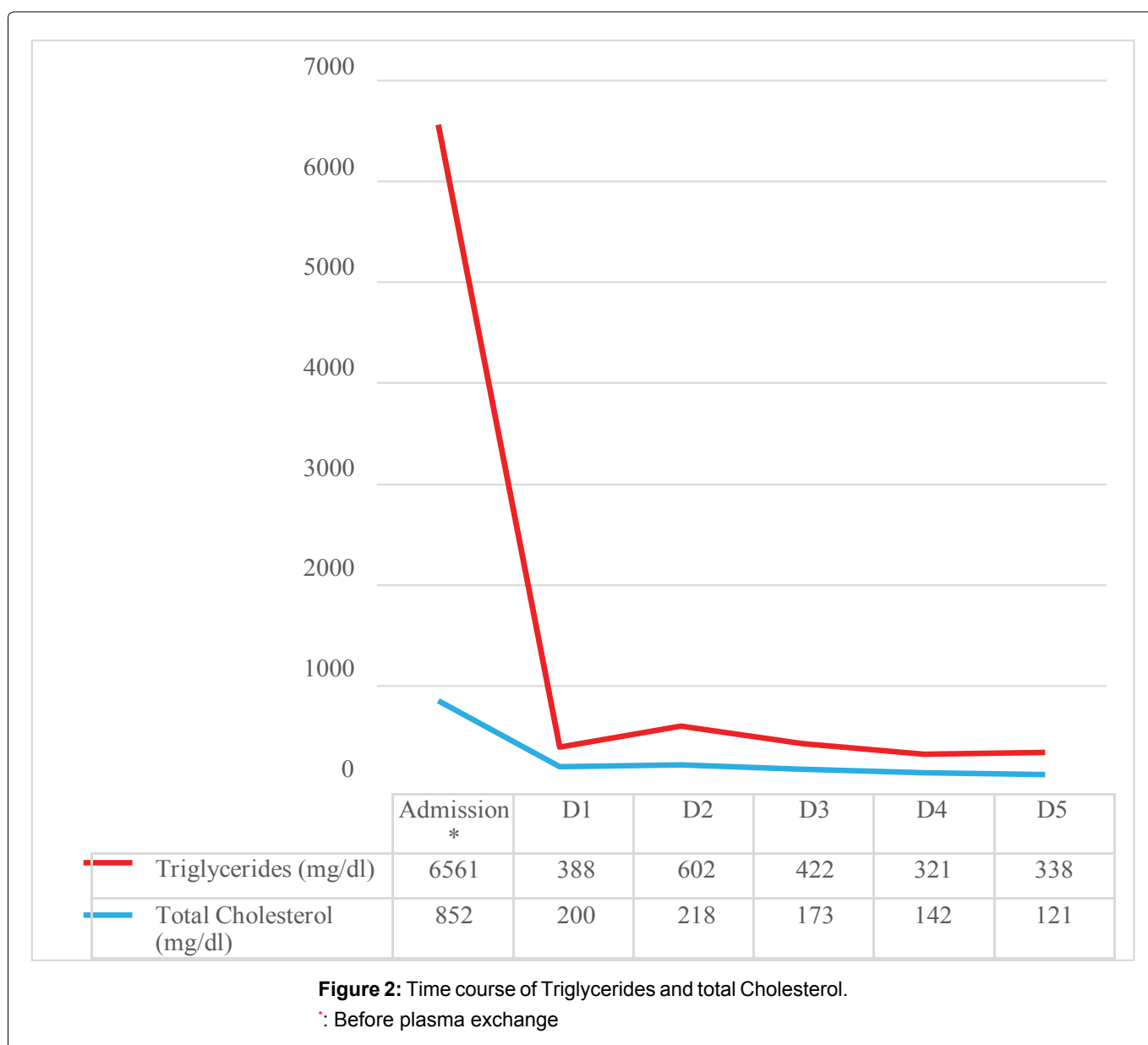
Overall, 3000 ml of plasma were removed and replaced with 5% albumin [7]; at the end of the procedure, both the TG and the cholesterol sharply decreased (by 94% and 77% respectively) and the plasma did not appear lipemic any longer (Figure 1B). In the following days, the TG and the cholesterol remained only moderately elevated (Figure 2), the amylase diminished but the C-reactive protein (CRP) increased likely indicating an ongoing inflammatory process.

An enteral nutrition supplemented with ω -3 fatty acids was initiated after 48 hours. The patient was discharged to the surgical ward 6 days after the ICU admission. Two weeks later, at the CT scan the pancreas appeared almost completely substituted by a large pseudocyst but the patient was asymptomatic and was discharged home a few days later to be followed on an outpatient basis.

Discussion

The treatment of severe AP basically consists in a prudent fluid resuscitation possibly associated to the administration of vasopressors, the support of failing organs and the nutrition preferably via the enteral route; moreover, a close monitoring is recommended aiming to the early detection of harmful complications including the increase of the IAP and the occurrence of pancreatic infections, hemorrhage and necrosis [1,2]. The severity of the AP can be assessed either by imaging and by monitoring the related systemic effects [2,8].

The HTG-associated AP does not represent an exception both in the pathogenesis and in the subsequent clinical course. Actually, as the concentration of CM increases almost linearly with that of TG [9], these latter can be considered as a proxy of either the risk of direct cellular damage exerted by the release of free fatty acids (FFA) and of the microvascular obstruction caused by the former. Even if the underlying biologic mechanism is not fully understood, the release of FFA



from the TG under the action of the pancreatic lipase is the most likely primer; following their detachment, they self-aggregate in micellar particles exerting a detergent action on the acinar and endothelial cells causing an ischemic injury that is further aggravated by the impairment of the microvascular blood flow caused by the CM; the subsequent release of damage-associated molecular patterns (DAMPS) trigger the inflammatory response whose spillover from the pancreas determines ultimately and accounts for the occurrence of organ failures [3-5]. Although the risk of AP increases with TG levels > mg 1000/dl (> 11.3 mmol/L), a “safe” concentration has not been identified yet [4] and its occurrence has been reported even at TG levels well below this value [3,4]; then, it appears that “the higher the levels of TG, the higher the probability to suffer from AP” [3]. Consequently, it is conceivable that a rapid abatement of the blood lipids could represent a high value target. To this aim, the American Society of Clinical Apheresis recommend the use of TPE despite the low quality of the published investigation [10] and other authors consider an urgent TPE as a first-line treatment of HTG-associated AP due to its strong FFA and CM clearance capabilities [4,5], even if a recent metanalysis failed to demonstrate any effect on the mortality as compared to a more conservative approach [11].

Although in our patient the HTG-AP could be classified as moderately severe on the basis of the initial clinical and imaging findings [9], other variables indicated a more severe condition as demonstrated by the late development of a large pseudocyst. First, although it appears that there is not a direct relationship between the levels of the TG and the severity of the AP, their concentrations stranded among the highest values reported in different metanalyses [3,4]. Second, the elevated values of the CPR in the absence of any identified infection that were present since the admission and that increased later on suggest that the inflammatory process was not influenced by the reduction of the TG; actually, Szatmary, et al. [12] demonstrated that a CRP > 150 mg/dl measured after 48 hours from the admission indicated a severe systemic inflammatory response; moreover, as the TPE significantly reduces the levels of CRP, its concentration indicates a “de novo” production under a persisting inflammatory stimulus as that exerted by DAMPS released after the TPE [13]; aiming at their removal, it is conceivable the use of a blood purification technique able to remove the inflammatory mediators and DAMPS once the HTG has subsided as demonstrated by some investigators in patients with AP [14,15].

Conclusions

The HTG-associated AP is an uncommon and life-threatening occurrence that requires a prompt diagnosis and treatment. In this circumstance, the TPE is valuable to abate the HTG possibly in association with of another

blood purification technique in order to decrease the inflammatory mediators.

Conflict of Interests

None.

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