

# Therapeutic Management of Trauma-related Acute Pancreatitis in a Heart Transplant Recipient

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*Acute pancreatitis is a very mortal disease, mortality that increases even more in patients with cardiac transplantation. Medical-surgical management of acute pancreatitis in transplanted patients can make the difference between life and death. The aim of this paper was to highlight the severity of this pathology especially because the patient is immunosuppressed after cardiac transplant. A case of 36-year-old man, known with heart transplant, immunosuppressive treatment and chronic renal failure, who arrived to Emergency Department, with severe abdominal pain and abdominal distention which started after a traumatic accident. Investigations revealed acute pancreatitis that needed three surgeries for acute necrotic hemorrhagic pancreatitis, acute bleeding, left subphrenic abscess and intensive care therapy. With favorable postoperative evolution, patient is discharged 60 days later. His follow up revealed no gastrointestinal or cardiac complication with an improved quality of life.*

*Keywords: pancreatitis, heart transplantation, immunosuppression*

Pancreatitis is associated with high mortality in patients with heart transplantation (HTx) after infections and rejection complications [1]. The mortality rate is very high even if acute necrotizing pancreatitis benefits from suitable treatment [2]. 3% of patients with transplant can develop acute pancreatitis after heart transplant versus 0.1% of patients with other cardiac surgery [3], which means a high risk of death [2]. Several complications like shock, renal failure, sepsis and respiratory dysfunction can be caused by acute pancreatitis [4]. These complications are determined by the activation of the inflammatory pathway that develops a systemic inflammatory response syndrome (SIRS) [5]. Due to the immunosuppression drugs in heart transplantation, patients with acute pancreatitis have a very low survival rate [6]. Two groups of gastrointestinal complications may appear after cardiac surgery: mesenteric ischemia and pancreatitis [7]. More than 50% of patients die during hospitalization for gastrointestinal complications after cardiac surgery [8] and about 40% for pancreatitis if the patient develops this complication much later post cardiac surgery [7]. Hyperamylasemia after open heart surgery is a sign of acute pancreatitis and the percentage of those who develop severe pancreatitis with hemorrhagic pancreatitis or pancreatic abscess in the case of elevated amylases is high [9]. After cardiac surgery, pancreatitis is a serious complication with significant morbidities and mortality, its incidence being even higher in patients with heart transplantation than in those with other cardiac surgeries [9-11]. The evolution of pancreatitis after HTx develops a sterile infection with pancreatic pseudo-cysts followed by systemic sepsis and multiorgan failure [1, 5, 12, 13].

The aim of this paper was to highlight the severity of this pathology especially because the patient is immunosuppressed after cardiac transplant.

Signed informed consent was obtained for publication of scientific data.

## Experimental part

A 32-year old man with end-stage heart failure (ischemic heart disease, left ventricular aneurysm with massive ventricular thrombus, 20% ejection fraction) was evaluated for cardiac transplant. He was treated with loop diuretics (Furosemide 160 mg/day), potassium sparing diuretics (Spironolactone 50 mg/day), beta-blockers drugs (Carvedilol 12.5 mg/day), anticoagulant treatment with Sintrom 1 mg/day. After 1 year on the waiting list an orthotopic transplantation was performed with bicaval technique. After 34 days, the patient was discharged from our service without special problems, with immunosuppressive treatment (Prograf 6 g/day, Cellcept 2g/day, Prednison 20 mg/day), antiviral drug (Valcyte 450 mg/day) antibiotic medication (Sulfamethoxazole-Trimethoprim 800/160 mg/day, loop diuretics (Furosemide 80 mg/day), potassium sparing diuretics (Spironolactone 50 mg/day). The patient is without reject signs at the heart biopsy (ISHLT 0). The patient is in our transplant follow up program and his evolution is without reject signs but with chronic renal failure developed two years after immunosuppression treatment was started (creatinine level 1.87 mg/dL, urea 64 mg/dL), controlled with low doses of loop diuretics Furosemide 20 mg/day with monitoring of electrolytes, renal and hepatic function.

Three years later, he presented to the Emergency Department, with severe abdominal pain and abdominal distention which started after a traumatic accident. The laboratory investigation reveals hemoglobin (Hgb) 8.4g/dL (11-17 g/dL), hematocrit (Htc) 23.3% (34-54%), creatinine 4.23 mg/dL (0.72-1.25 mg/L), serum amylase level > 1263 U/L- (25-125 U/L) Suspicion of acute

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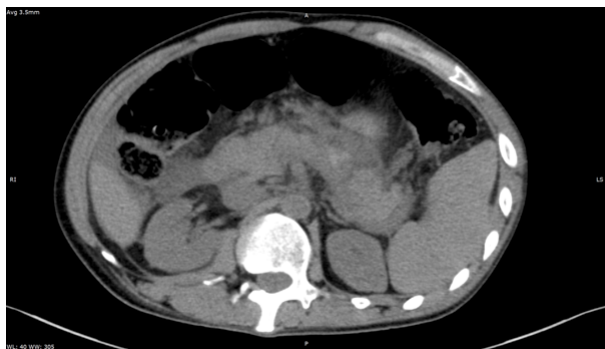


Fig. 1. Peripancreatic and mesenteric abdominal fat with edematous infiltration, fluid collections around the liver and in both paracolic gutters

pancreatitis was done. The computer tomography (fig. 1) revealed peripancreatic and mesenteric abdominal fat with edematous infiltration, fluid collections around the liver and in both paracolic gutters. The CT image is suggestive of acute pancreatitis (Balthasar C). He was treated with intravenous hydration (Glucose 10%, NaCl 9%), antibiotics (Ampicillin 500 mg every 6 h), renal drugs support (Furosemide 20 mg injectable solution two times per day), immunosuppressive drugs (Cellcept 5 mg/day and Prograf 1.5 g/day) and analgic treatment with Tramadol 25 mg/day and Metamizol sodic 1 g/2 mL/day. The patient's status was not improved and after three days he developed surgical acute abdomen. The CT-exam (fig. 2) showed a mildly enlarged pancreas, still moderately edematous and a focal hyperdense lesion in the pancreatic head, presumably hemorrhagic with a large fluid collection (~14/8 cm), reasonably well delimited, with hyperdense margins, dislodging the stomach upwards (pseudocyst). The laboratory investigations revealed serum levels of amylases 1122 U/L, glycemia 94 mg/dL, Leukocytes 10.75

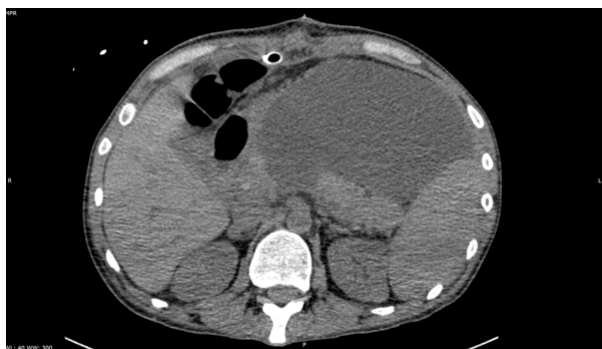


Fig. 2. Mildly enlarged pancreas, moderately edematous and a focal hyperdense lesion in the pancreatic head, presumably hemorrhagic with a large fluid collection (~14/8 cm), reasonably well delimited, with hyperdense margins, dislodging the stomach upwards (pseudocyst)



Fig. 3. 5 cm round lesion, bordering the abdominal wall and maintaining a rather inhomogeneous appearance, with moderate delimited margins

$\times 10^3 \mu\text{L}$ , creatinine level 4.83 mg/dL. Because of the surgical acute abdomen and laboratory investigation the patient has indication of emergent surgical treatment. Emergent surgery consisted on removing all the necrotic peri and intrapancreatic tissue and pancreatogenic exudate in order to avoid the systemic release of toxic and vasoactive substances. Also it was performed a classic cholecystectomy to avoid biliary pancreatitis. A drainage tube was installed and the patient was transferred to ICU. After two weeks of favorable evolution, patient started to have sanguineous drainage and laboratory investigations showed decreased levels of Hgb from 11.2 g/dL to 8.0 g/dL, hematocrit from 33 to 23.2% and increased levels of leukocytes from  $11.2 \times 10^3 \mu\text{L}$  to  $25.6 \times 10^3 \mu\text{L}$ . Surgical re-intervention, for a diffuse pancreatic and peripancreatic hemorrhage was necessary. After long hemostasis, the patient was transferred in the ICU. Two weeks later the laboratory investigations showed increasing serum levels of amylases to 935 U/L. CT-exam (fig. 3) showed a 5 cm round lesion, bordering the abdominal wall and maintaining a rather inhomogeneous appearance, with moderate delimited margins. In the abdominal wall, in the median axis there is a similar lesion, 1.5 cm in diameter which was treated by explorative laparotomy, necrosectomy, lavage and insertion of drains. During hospitalization patient received medical treatment with Targocid 400 mg/day, Colistin 2 mil, Tienam 1g and Metronidazole 500 mg every 8 h, Fluconazole 150 mg/day, Biseptol every two days, immunosuppressive treatment with CellCept and Prograf, intravenous hydration with NaCl 0.9%, Aminoven 10% solution, Glucoses 5%, and parenteral nutrition with Intralipid 20% infusion 250 mL/day. Hospitalization for 60 days was necessary for complete recovery and he was discharged with immunosuppression treatment (Prograf 5 mg and CellCept 500 mg/ twice per day), loop diuretics (Furosemide 80 mg/day), digestive enzymes (Triferment 275 mg/ twice per day), antibiotic (Sulfamethoxazole-Trimethoprim 400/80 mg/day), gastric protection with H2 blocker (Ranitidine 150 mg/ twice per day). He was discharged and follow up revealed no gastrointestinal or cardiac complication (fig. 4).

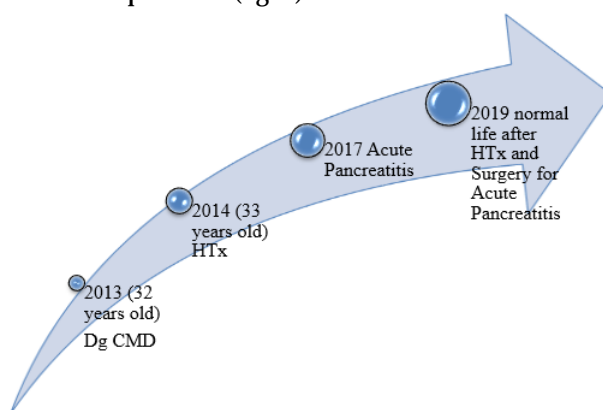


Fig. 4. Major medical events in patient's life

## Results and discussions

Patients with heart, liver, intestinal kidney or bone marrow transplantation have a higher prevalence of developing acute pancreatitis compared to the others patients either by exogenous mechanism or by the drug-induced pancreatitis mechanism [10,11,14]. The pathophysiology is altered by the immunosuppressive treatment, which increases mortality risk in transplanted versus non-transplanted patients [6,11].

For example, even though pancreatitis is not among the clear side effects, it has been reported as a possible rare

and fatal effect of long-term administration of tacrolimus [16]. Due to the absence of specific diagnostic tests, the diagnosis of acute drug-induced pancreatitis is difficult to establish, [10] but in this case we knew that the symptomatology started after an accident, so etiology was clearly post-traumatic.

One of the most serious complications after cardiac surgery is acute pancreatitis and this complication has significant morbidities and mortality [1,2,10]. Severe acute pancreatitis can be associated with systemic inflammation, compensatory immunosuppression, secondary infections, vital organ dysfunction, and death [12]. The diagnosis and treatment can be delayed because transplanted patients are under immunosuppression treatment and they can develop a cryptosymptomatic acute pancreatitis, a fact that increases mortality in orthotopic heart transplant patients [1,11,14,15]. Even with aggressive and appropriate care, the patient can develop acute necrotizing pancreatitis which has a high mortality rate [2].

Orthotopic cardiac transplantation and acute pancreatitis are associated with high mortality, [1-15] appearance of necrotic tissue in acute pancreatitis creating conditions for bacterial infection and development of disorders in the coagulation cascade followed by disseminated intravascular coagulation [17]. Normally, amylase/creatinine clearance rise in acute pancreatitis but because of chronic renal failure induced by immunosuppressive treatment, clearance is decreased and hyperamylasemia can have elevated serum levels above normal [17]. This can cause the rise of clinical manifestations of exocrine pancreatic insufficiency [18].

Even with an optimal management, acute pancreatitis is a disease with a high mortality, regardless of etiology or treatment, due to the complications that can arise [19].

## Conclusions

Less commonly, pancreatitis after cardiac transplantation has a very high mortality, especially since there is no specific protocol to manage this pathology and the risk of rejection of the allograft is increased.

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