Pancreatic pseudocyst-inferior vena cava fistula causing caval stenosis, left renal vein thrombosis, subcutaneous fat necrosis, arthritis and dysfibrinogemia

Ann. Ital. Chir., 2010; 81: 215-220

Alberto Porcu, Pier Luigi Tilocca, Luca Pilo, Francesca Ruiu, Giuseppe Dettori

Department of General Surgery, University of Sassari Faculty of Medicine, Sassari, Italy

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AIM: *We describe the case of a 38 year old man, with a story of alcohol abuse, who developed a very painful nodular subcutaneous fat necrosis, fever and polyarthritis, denying any abdominal symptoms due to a pancreatic pseudocyst-inferior vena cava fistula.*
MATERIAL OF STUDY: *The authors discuss the unusual and protracted course with intermittent hyperamylasemia and hyperlipasemia related to clinical manifestations such as subcutaneous fat necrosis, polyarthritis, pleural effusion and dysfibrinogenemia, and vascular complications as inferior vena cava stenosis and left renal vein thrombosis without abdominal symptomatology.*
RESULTS: *After ultrasonograms and CT Scans showing a 3-4 cm cyst at the pancreatic head with a solid bud protruding into the pseudocystic cavity, and an ERCP showing a communication between the pancreatic duct and the pseudocyst but failing in demonstrating the vascular fistula, the patient underwent a Roux-en-y pseudocyst-jejunostomy and suture of the caval communication leading to complete recovery with normalization* of laboratory findings.
DISCUSSION: *In our case, the locally sclerosing activity of the enzymes in the endothelium led to a communication between the inferior vena cava and the pseudocyst and to a complete thrombosis of the left renal vein and to a stenosis of the inferior vena cava itself. The fluctuance of the symptomatology severity was probably due to an intermittent opening of the passage between pseudocyst and vena cava. Such a clinical case, to the author knowledge, has never been reported.*
CONCLUSION: *When in presence of very high levels of amylasemia and lipasemia in spite of the paucity of abdominal symptomatology, and the onset of unusual complications such as panniculitis, pleural effusion, arthritis and coagulative disorders, a pancreatic pseudocyst-inferior vena cava fistula should be kept in consideration during diagnosis.*

Key words: Pleural effusion, Pseudocyst-inferior vena cava fistula, Subcutaneous fat necrosis.

Introduction

Vascular complications are described in acute and chronic pancreatitis. To the author's knowledge, a pancreatic pseudocyst-inferior vena cava fistula has never been reported. We discuss the uncommon clinical course of a patient with pancreatic pseudocyst-inferior vena cava fistula whose manifestations such as arthritis, subcutaneous fat necrosis, pleural effusion and dysfibrinogenemia, are well known when considered individually but extremely rare when presenting together. Surgical correction by a Roux-en-Y pseudocyst-jejunostomy and direct suture of the caval opening led to a complete recovery with normalization of serological findings.

Pervenuto in Redazione Dicembre 2009. Accettato per la pubblicazione Febbraio 2010
Correspondence to: Dr. Alberto Porcu,Via Barzini 4, 07100 Sassari (e-mail: albporcu@hotmail.com; alberto@uniss.it).

ABBREVIATIONS

CT Scan: Computed Tomography Scan
TPN: Total Parenteral Nutrition
ICU: Intensive Care Unit
INR: International Normalized Ratio
ERCP: Endoscopic Retrograde Cholangio Pancreatography
DIC: Disseminated Intravascular Coagulation

Case report

After drinking a litre of beer, a 38 year old man, with a history of alcohol abuse, had a 24 hour episode of epigastric pain radiating through to his back, which he attributed to gastritis and treated by himself with non-steroid analgesics. He remained well until a month later, when he developed a very painful nodular subcutaneous fat necrosis in the legs and the trunk, fever (39-40 CC) and polyarthritis with involvement of the right knee, left ankle, left wrist and small joints of the right foot. He was admitted to a medical center where he denied any abdominal symptoms. The examination demonstrated neither epigastric tenderness nor mass. The palpation of the subcutaneous fat necrosis caused extreme pain. The joints involved were tender and painful on motion. The right knee was warm and swollen with fluctuance. The cultures of the yellow-brown fluid obtained by the arthrocentesis were negative. The CT Scan of the upper abdomen showed a focal hypodense lesion at the pancreatic head, as expression of a probable focal pancreatitis.
There were no stones in the gallbladder and in the bile duct. Neither pancreatic
calcification, nor peripancreatic stranding or fluid were noted.

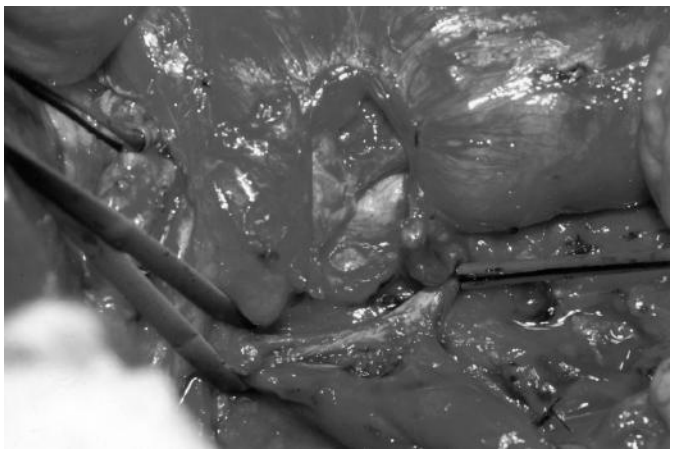

Fig. 1: Intraoperative picture of the pseudocyst of the inferior edge of the pancreatic head, with a strong adhesion to the inferior vena cava at the confluence with the left renal vein. The cava is stenotic between the previous site and the retrohepatic portion, with a thickening of its' wall. The left renal vein appear to be obstructed and there is a collateral vein circulation.

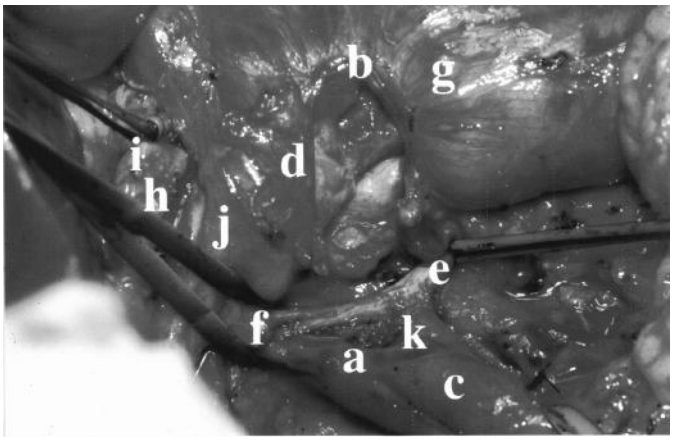

Fig. 2: Intraoperative picture of the pseudocyst of the inferior edge of the pancreatic head, with a strong adhesion to the inferior vena cava at the confluence with the left renal vein. The cava is stenotic between the previous site and the retrohepatic portion, with a thickening of its' wall. The left renal vein appear to be obstructed and there is a collateral vein circulation.
a) inferior vena cava opening; b) passage to the pancreatic duct; c) inferior vena cava; d) cut wall of the pancreatic pseudocyst; e) obstructed left renal vein; f) inferior vena cava stenosis; g) duodenum; h) hepatic artery; i) gastroduodenal artery; j) bile duct; k) area of strongest adhesion between inferior vena cava and pancreatic pseudocyst.

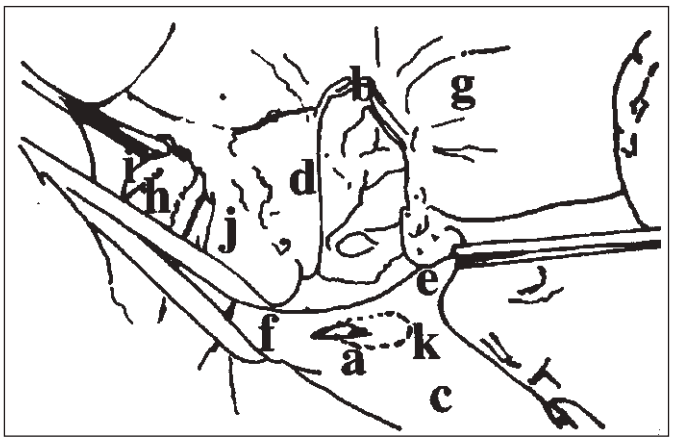

Fig. 3: Schematic representation of the pseudocyst of the inferior edge of the pancreatic head, with a strong adhesion to the inferior vena cava at the confluence with the left renal vein. The cava is stenotic between the previous site and the retrohepatic portion, with a thickening of its' wall. The left renal vein appear to be obstructed and there is a collateral vein circulation.
a) inferior vena cava opening; b) passage to the pancreatic duct; c) inferior vena cava; d) cut wall of the pancreatic pseudocyst; e) obstructed left renal vein; f) inferior vena cava stenosis; g) duodenum; h) hepatic artery; i) gastroduodenal artery; j) bile duct; k) (interrupted line) area of strongest adhesion between inferior vena cava and pancreatic pseudocyst.

No lymphadenopathy or intraperitoneal free fluid was observed. Laboratory findings revealed WBC 16 000 mm3; serum amylase 6300 U/l (N 30-110), serum lipase 14200 U/l (N 23-300); there were no other pathological data. Skin lesions and joint manifestations settled over the next two weeks with TPN. During the l0 months fol1owing dismissal, he was hospitalised many times in different centers. The serum amylase and lipase levels fluctuated between slightly increased (320 U/l and 550 U/l) and very high values (16500 U/l and 145000 U/l,

respectively), without correlation with TPN or oral diet. During the course of the disease the skin and joint lesions relapsed many times, correlating with the highest level of pancreatic enzymes, although they sometimes increased even when the simptomatology was silent. The patient lost 20 kg and spent several days in a medical ICU with a conspicuous bilateral pleural effusion. There was a temporal relation between the highest amylase and lipase levels and the worsening of the coagulation tests: Prothrombine time INR 1.16 (N 0.8- 1.2); Activated partial thromboplastine time 28.40 sec (N 18-30 sec) with a ratio of 0.97 (N 0.8-1.2); Thrombine time: no clotting (N 18-22 sec); Antithrombine III 92% (N 70-120%); D Dimero (Vidas-Elfa) 830 ng/ml (N 0-200); Optical fibrinogen 170 mg/dl (N 200-400); Clauss fibrinogen 67 mg/dl (N 150-400); Antigen fibrinogen 300 mg/dl (N 200-400). The patient, however, never had bleeding problems. Further ultrasonograms and CT Scans showed a 3-4 cm cyst at the site of the previous focal hypodense lesion of the pancreatic head, which resolved and relapsed several times. An ERCP showed a communication between the pancreatic duct and the pseudocyst, but failed to visualize a vascular fistula. The patient was referred to our department for surgical treatment of a suspected pancreatic neoplasia arising from a CT Scan image of a solid bud protruding into the pseudocystic cavity. Surgical exploration (Figg. 1, 2, 3) showed a 4 cm pseudocyst of the inferior edge of the pancreatic head, with a strong adhesion to the inferior vena cava at the confluence with the left renal vein. The cava was stenotic between the previous site and the retrohepatic portion, with a thickening of its' wall. The left renal vein appeared obstructed and there was a collateral vein circulation. The remaining part of the pancreas was normal without signs of peripancreatic inflammation. The pseudocyst revealed a hemorrhagic content, without signs of infection, which increased when the pressure within the cavity was lost by opening it. The source of the haemorrhage was a few mm communication with the vena cava, which was immediately oversewn. There was another communication (1.5 mm) with the pancreatic duct. A Roux-en-y pseudocyst - jejunostomy was performed (Figg. 4,5,6).The clinical manifestations, inclusive of the laboratory findings, resolved completely in a few days, with the exception of the right knee which remained painful on motion for 3 weeks.

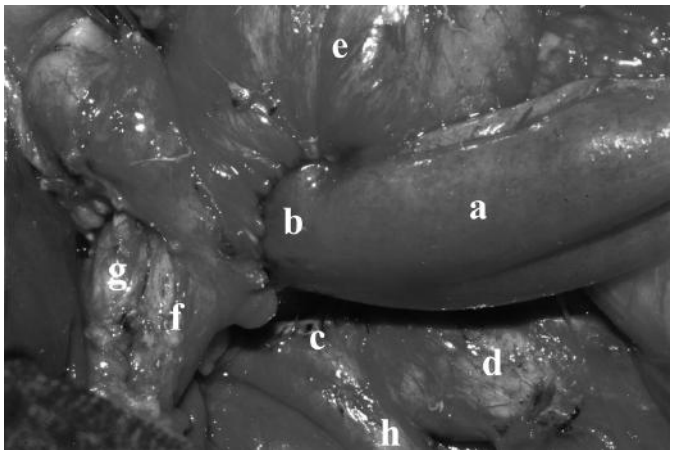

Fig. 5: Intraoperative picture of Roux-en-y pseudocyst – jejunostomy and suture of the inferior vena cava opening.
a) Roux-en-Y jejunal loop; b) Roux-en-Y pseudocyst - jejunostomy; c) suture of the inferior vena cava opening; d) inferior vena cava; e) duodenum; f) bile duct; g) hepatic artery; h) right renal vein.

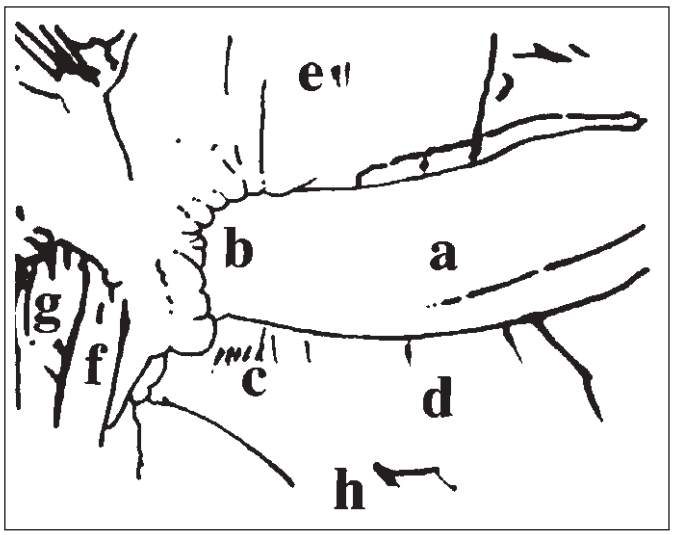

Fig. 6: Schematic representation of the Roux-en-y pseudocyst - jejunostomy and suture of the inferior vena cava opening.
a) Roux-en-Y jejunal loop; b) Roux-en-Y pseudocyst - jejunostomy; c) suture of the inferior vena cava opening; d) inferior vena cava; e) duodenum; f) bile duct; g) hepatic artery; h) right renal vein.

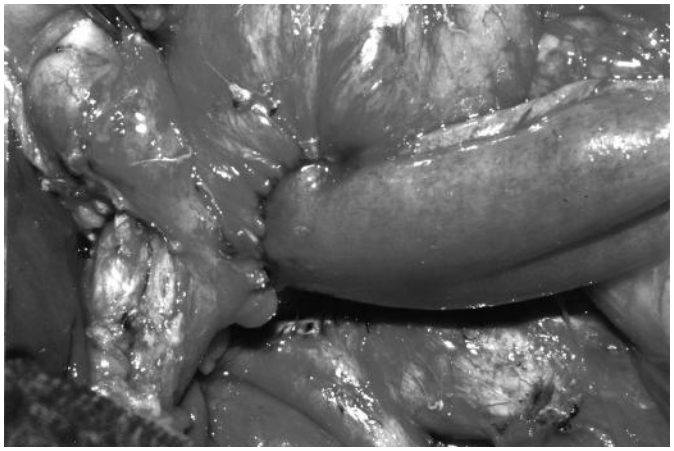

Fig. 4: Intraoperative picture of Roux-en-y pseudocyst – jejunostomy and suture of the inferior vena cava opening.

Discussion

Few cases of communication between a pancreatic pseudocyst or pancreatic duct and the portal venous system have been described [1-3] and almost all of them, as

our case, reported a metastatic subcutaneous fat necrosis without an important history of pancreatic and peripancreatic symptomatology. The probable explanation of this phenomenon is given, after the first episode of pancreatitis, by the reduction of the stasis in the pancreatic duct that can easily discharge its' secretions in a low pressure district, thus avoiding pancreatic edema, pancreatic necrosis and peripancreatic compression and inflammation. In our case, the locally sclerosing activity of the enzymes in the endothelium led to a stenosis of the inferior vena cava (only the second case ever reported) [4] and to a complete thrombosis of the left renal vein (only other two cases have been described) [5,6], bringing about a swelling of the legs and causing the formation of well developed collateral vessels. Fluctuance of the symptomatology severity, which was proportional to the levels of hyperamylasemia and hyperlipasemia, was probably due to an intermittent opening of the passage between pseudocyst and vena cava, which would explain the ERCP failure in demonstrating the communication with the vena cava, likely closed during the exam. It is not the aim of this document to discuss if the multisystem involvement with severe tissue injury in acute pancreatitis and during exacerbation of chronic pancreatitis is related to the high circulating concentration of pancreatic enzymes or to the effect of inflammatory mediators such as cytokines, complement, some endotelial activated adhesion molecules, etc. It is not even our intention to debate about what mechanism could explain the activation of the pancreatic enzymes released in the systemic circulation. We could only observe that the very high levels of the pancreatic enzymes, probably reached during the opening phase as a result of a massive release in the venous circulation, presented at the same time of the complex clinical manifestations, which will be considered separately:

PANNICULITIS - Disseminated subcutaneous fat necrosis is associated with 2% of pancreatic diseases, mainly pancreatitis and pancreatic carcinoma [7-10]. In half the cases it can precede the diagnosis of pancreatic disorders from a few weeks up to 13 weeks [7,11], since the pancreatic disorder is sometimes clinically silent for the entire course of the disease [7,12]. Pathognomonic histologic features of the acute pancreatitis should be a focal fat necrosis with "ghost cells", while granulomatous and lipophagic panniculitis are present in the chronic lesions [11].

Histopathologic findings tend to evolve in a few days from an initial septal inflammatory infiltrate to a fully developed lobular panniculitis [13]. The role of the circulating pancreatic lipase in generating fat necrosis remains doubtful; many authors report a very high lipasemia (as our case), while others report normal levels throughout the patient's pancreatic disease course [3]. However, the pathogenic action appears to be confirmed by a positive intracellular staining of adipocytes with a monoclonal antibody against pancreatic lipase in a nodular pancreatic panniculitis [14].

Pleural effusion

Pancreatitis is the cause of a pleural effusion in on1y 1-2% of the patients admitted to a medical ICU [15]. Pleural effusion during the course of an acute pancreatitis or an acute exacerbation of chronic pancreatitis, can be the expression of a fistulous tract between either the pancreatic duct or pancreatic pseudocyst and the pleural cavity or the manifestation, as in our case, of the severe remote tissue damage by the direct lytic activity of the pancreatic enzymes [16-18] or the sequela of multiple inflammatory agents triggered by the formers. The fistulous tract as a cause of pleural effusion is more common in chronic alcoholic pancreatitis (99%), and chest symptoms are complained about more frequently (68%) than abdominal symptoms (24%) [16]. Pleural effusion without a fistulous tract is a sign of severity in the pancreatic process. It's seen in 84.2 % of cases with severe pancreatitis and only in 8.6 % of patients with mild pancreatitis; however, it is an independent predictor of severity in only a minority of cases [19].

Arthritis

Although polyarthritis is a rare manifestation of pancreatitis, it was
already reported in the late 19th century by Hansemann [20]. This combination
typically presents in male patients with a history of alcohol abuse. The joints commonly involved are ankles, elbows, knees, wrists and the small ones of the hands and feet; the involvement may be either symmetrical or asymmetrical (21,22,10). The arthrocentesis yields a viscous yellow-brown fluid, similar in appearance to a purulent exudate, but bacterial cultures are negative (as in our case) and there is no proof of other infections [21-23]. Polyarthritis can precede or follow the abdominal symptoms but in some cases the underlying pancreatitic process may be clinically silent, adding difficulties to the diagnosis and sometimes leading to a misinterpretation.

Dysfibrinogenemia

It is well known that disseminated intravascular coagulation (DIC) and consequent fibrinolitic activity, with fibrinogen-fibrin degradation products, are increased in case of acute pancreatitis, leading to coagulation abnormalities. This is insufficient to explain, in our case, the combination of almost normal coagulation tests with only the alteration of the thrombine time, that in our patient did not clot at all. Therefore, although the patient had no evidence of previous haemorrhage, a condition of dysfibrinogenemia was suspected and, because of risk of severe haemorrhagic accident, an investigation of coagulation profile was undertaken. This acquired dysfibrinogenemia is only the second case ever reported [24]. It was clearly demonstrated by the great discrepancy [25] between the levels of the antigen fibrinogen (300, N

200-400) and the functional (optical and Clauss) fibrinogen concentration (170 and 67 respectively). As in the other case described, the dysfibrinogenemia was not associated with a bleeding problem and the normal platelet count and the almost normal prothrombine time would imply that the DIC was not severe (D dimero 830, N 0-200). No high performance liquid chromatography was performed to analyze the fibrinopeptide release from fibrinogen but it is likely that an aspecific degradation occurred, as the previous case described (the lysis of the C terminal end of the A-alpha chains), by the protheolytic activity of the pancreatic enzymes (trypsin). The immediate restoration of the thrombine time and the disappearance of the discordant results between the functional and antigen fibrinogen values immediately after the operation support this hypothesis.

Conclusion

The incidence reported in the literature of vascular complications during the course of acute pancreatitis is very low, probably because they remain undiscovered due to their asymptomatic presentation, like the cavaI stenosis and the left renal thrombosis of our case. The other vascular complication of our patient, the fistula between the pancreatic pseudocyst and the inferior vena cava, was probably the determinant factor of the systemic manifestations. Unfortunately the paucity of the abdominal symptomatology, in spite of the very high levels of amylasemia and lipasemia, such as occurs in the case where there is a direct release of the pancreatic lytic enzymes in the vascular bed, may delay the diagnosis and treatment and lead to unexpected operatory findings. Therefore, the onset of unusual complications such as panniculitis, pleural effusion, arthritis and coagulative disorders, should be kept in consideration during diagnosis; once the correct diagnosis is determined, a Roux-en-Y pancreatic-pseudocyst-jejunostomy, with the repair of the vascular opening, should be considered immediately to prevent the possible threatening course of this disease.

Riassunto

Fistola tra pseudocisti pancreatica e vena cava inferiore determinante stenosi cavale, trombosi della vena renale sinistra, liponecrosi sottocutanea, artrite e disfibrinogemia.

OBIETTIVO: Col presente lavoro descriviamo il caso di un uomo di 38 anni, con una storia clinica di abuso di bevande alcooliche, che ha sviluppato, in assenza di sintomatologia addominale, un quadro clinico caratterizzato dalla comparsa di noduli sottocutanei di liponecrosi estremamente dolenti, febbre e poliartrite. Tale quadro è risultato essere determinato da una fistola tra una pseudocisti pancreatica e la vena cava inferiore.

MATERIALI E METODI: L'inusuale e prolungato decorso clinico è stato caratterizzato da innalzamenti intermittenti della amilasemia e della lipasemia correlati a manifestazioni cliniche quali liponecrosi sottocutanea, poliartrite, versamento pleurico e disfibrinogemia e a complicanze vascolari rappresentate dalla stenosi della vena cava inferiore e dalla trombosi della vena renale sinistra. Il Paziente non ha mai lamentato dolore addominale. L'ecografia e la TC addominali hanno mostrato una cisti in rapporto con la testa del pancreas di 3-4 cm con una immagine protrudente al suo interno mentre l'ERCP pur mostrando la comunicazione tra la pseudocisti e il dotto pancreatico, non ha evidenziato la fistola tra la pseudocisti stessa e la vena cava. Il Paziente è stato sottoposto all'intervento chirurgico di pseudocisti-digiunostomia su ansa a Y e sutura della breccia cavale con la successiva risoluzione della sintomatologia e la normalizzazione delle alterazioni ematochimiche.

DISCUSSIONE: Nel caso descritto, l'attività sclerosante sull'endotelio da parte degli enzimi pancreatici ha determinato una comunicazione tra la vena cava inferiore e la pseudocisti portando inoltre alla trombosi della vena renale sinistra e alla stenosi della vena cava inferiore stessa. L'incostanza della severità della sintomatologia può essere probabilmente ascritta a un'apertura intermittente del passaggio determinatosi tra la pseudo cisti e la vena cava. Una tale situazione clinica, per quanto a conoscenza degli autori, non sarebbe mai stata descritta precedentemente.

CONCLUSIONI: In presenza di elevati valori di lipasemia e amilasemia pur in assenza di alcuna sintomatologia addominale e di fronte a inusuali manifestazioni quali panniculite, versamento pleurico, artriti e disordini della coagulazione, si dovrebbe tenere in considerazione tra le ipotesi diagnostiche la possibilità di una fistola tra pseudocisti pancreatica e vena cava inferiore.

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