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Erasmo Spaziani*, Annalisa Romina Di Filippo*, Gianluca Caruso*, Martina Spaziani*, Natalia Cenfra°, Luca Pacini*, Marcello Picchio**, Alessandro De Cesare***

**Department of Medico-Surgical Sciences and Biotechnologies, "Sapienza" University of Rome, Polo Pontino, Terracina, Latina, Italy*
°Department of Hematology, "S.M. Goretti" Hospital, Latina, Italy
***Department of Surgery, "P. Colombo" Hospital, Velletri, Rome, Italy*
****Department of Surgery, "Pietro Valdoni", Sapienza University of Rome, Italy*

An uncommon clinical presentation of primary pancreatic lymphoma: Bleeding. Case report and literature review.

BACKGROUND: *Primary pancreatic lymphoma (PPL) represents less than 0.5% of all pancreatic neoplasms. Clinical manifestations are non-specific and diagnosis is delayed in the majority of patients.*
CASE REPORT: *85-year-old woman reporting accidental fall at home 20-days earlier, was admitted with diagnosed of acute abdomen from suspected two-stage rupture of the spleen. The patient complained of pain in the upper abdomen. Blood-chemical tests did not show anemia and leukocytosis, but showed increased CA19.9, CA125, LDH and beta2-microglobulin. Contrast-enhanced CT showed left pleural, perisplenic, perihepatic, and Douglas blood effusion, a neoformation of the body-tail of the pancreas with peri-pancreatic blood layer, splenomegaly due to the presence of a hypodense area as from intraparenchymal hematoma, with an apparently undamaged splenic capsule. The patient underwent emergency exploratory laparotomy, that revealed the presence of modest free serohematic effusion from oozing of the pancreatic neoformation. The local spread of the disease prevented any attempt at surgical resection. Bleeding was checked with the addition of topical hemostats (Tabotamp®) and biopsy sampling of the pancreatic mass was performed. A final histological diagnosis of large cell NHL of centro-follicular origin, double expressor for the CMYC and BCL2 protein, was achieved. The age of the patient, the poor general conditions, the associated pathologies, the locally advanced spread of the disease and the histological aggressiveness, were contraindications to chemo-radiotherapy treatments.*
CONCLUSION: *The initial misdiagnosis was due to the history of recent trauma, the uncommon clinical presentation, the underestimation of the serum increase in markers and the interpretation of the CT.*

KEY WORDS: Acute Abdomen, Hemoperitoneum, Primary Pancreatic Lymphoma

Introduction

Primary pancreatic lymphoma (PPL) is a rare malignant neoplasm, amounting for less than 0.7% of non-Hodgkin's lymphomas (NHL) and less than 0.5% of all pancreatic malignancies [1]. It most frequently affects the elderly and only rarely young patients [1].

Clinical manifestations are non-specific and can mimic adenocarcinoma, endocrine pancreatic tumors, and chronic pancreatitis [1,2]. In one case it was clinically manifested as acute pancreatitis with lung involvement [3]. The most frequently observed clinical manifestations include: pain in the upper abdominal quadrants, rapidly progressive jaundice, acute pancreatitis, intestinal obstruction, diarrhea, weight loss and impaired general status [1].
Diagnosis and staging is based on CT, MRI and PET [4]. Endoscopic-ultrasound guided fine-needle-aspiration cytology (EUS-FNAC) is frequently used for the diagnosis of PPLs without resorting to more invasive diagnostic methods [5].
Lactic dehydrogenase (LDH) and beta-2 microglobulin are considered significant diagnostic and prognostic

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Correspondence to: Annalisa Romina Di Filippo, Via Baldassarre Orero 33, 00159 Roma, Italy (e-mail: annalisa.difilippo@alice.it)

markers [6]. Cases of PPL with elevated serum levels of Ca19-9 have been reported [7].
Surgery is not the first choice for treatment of PPLs and is limited to rare early diagnoses [8].
Incidental identification of early pancreatic lesions, early chemotherapy or radio-chemotherapy, monoclonal antibodies, and stem cell transplantation allow for a significant improvement in prognosis [1,3,9].

Case Report

85-year-old woman was admitted to the UOC of University Surgery "A. Fiorini" hospital in Terracina - Polo Pontino, with diagnosis of acute abdomen from suspected two-stage rupture of the spleen. The patient reported abdominal trauma in the home environment, which occurred 20 days before hospitalization. To the CT scan without contrast medium performed the day before admission, the spleen appeared markedly enlarged with a maximum bipolar diameter of about 15cm, and with the presence of hypodense areas in its context.
The patient had past medical history of heart failure and type II diabetes mellitus in poly-pharmacological treatment. At the time of hospitalization she complained of pain in the upper abdominal quadrants, no anemia (Hb 12.7g/dl) or leukocytosis (GB 9.8x10^3/ul) were present at the blood tests, there was a significant increase in tumor markers CA19.9 (Gica) (196 U/ml; vn<37) and CA125 (138U/ml; vn 0-35), an increase in LDH (1044 U/L; vn 125-220), hypodysprotidemia (4.9 g/dl; vn 6.3-8.3) and hypoalbuminemia (3.2 g/dl; vn 3.5-5.0).
Contrast-enhanced CT scan was suggestive for the presence of a left middle-basal pleural effusion of blood density, with thickness of a about 1.7 cm, and a layer of blood effusion in the perihepatic and perisplenic sites, and Douglas' pouch; it was also suggestive for the presence of a lesion of the body and tail of the pancreas that appeared totally inhomogeneous and surrounded by hypodense blood collection (Fig. 1). The spleen appeared of greatly increased size due to the presence of a hypodense area, as from voluminous intraparenchymal hematoma of 12.5x10.6 cm in diameter, with an apparently undamaged splenic capsule (Fig. 2).
For the suspected CT findings for hemoperitoneum, the patient was subjected to emergency median xypho-pubic laparotomy.
At the opening of the peritoneal cavity, the presence of a modest serum-haematic effusion, a significantly enlarged spleen, and a gross neoformation about 20 cm in diameter of the body and tail of the pancreas were shown. The pancreatic mass appeared to have a hard consistency and a bumpy surface with widespread and persistent dripping of blood. The lesion appeared to infil-

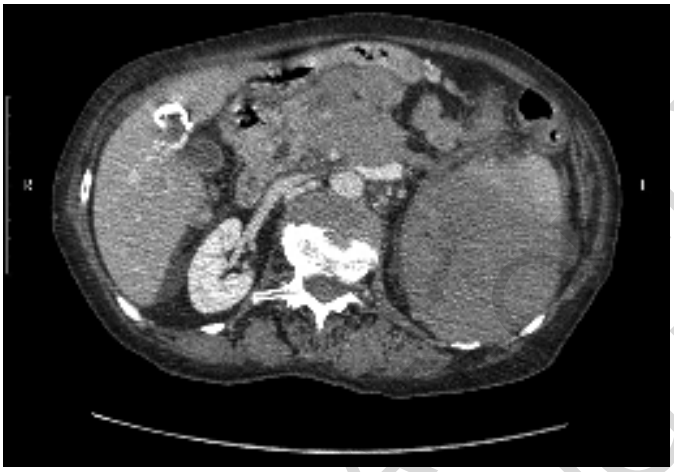

Fig. 1: Contrast-enhanced abdominal CT scan. Portal venous phase: neoformation of the pancreatic body and tail, heterogeneous in appearance, and surrounded by hypodense blood collection.

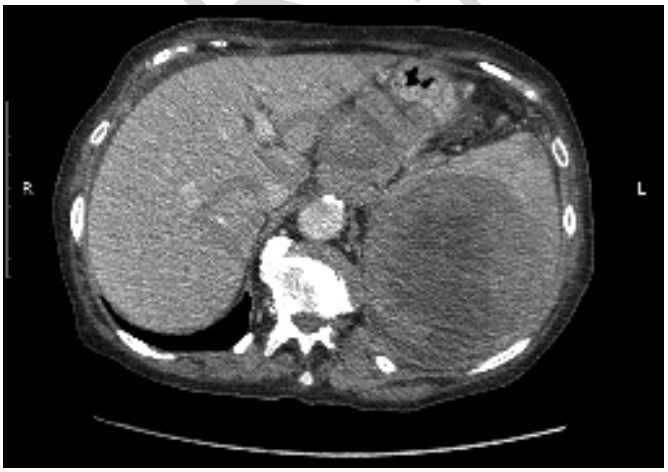

Fig. 2: Contrast-enhanced abdominal CT scan. Portal venous phase: significantly enlarged spleen size, hypodense area from the splenic parenchyma compatible with parenchymal hematoma, and apparently undamaged splenic capsule.

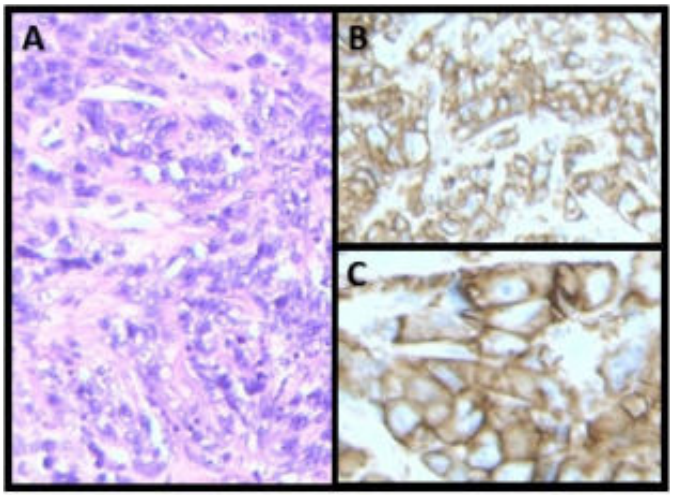

Fig. 3: H&E section shows an incisional biopsy from a solid mass of pancreatic body-tail (A, 20x). The normal glandular tissue is totally replaced by a diffuse population of large B cells CD20 positive (B, 20x and C, 40x).

trate the celiac tripod, the splenic vessels, and the superior mesenteric vessels. A cleavage plane with the stomach and spleen was not identifiable.
We proceeded to biopsy, and control the bleeding of the neoformation with affixing of topical hemostats (Tabotamp®)
On histopathological examination the lesion showed a diffuse proliferation of cellular elements with lymphoid habitus, of large size, with irregularly contoured nuclei and evident central and peripheral nucleoli. The immunophenotypic pattern of the lesion was found BCL2 positive (90% of the cells), CMYC positive (40% of the cells), MUM1 positive, Ki-67 80%. Non-Hodgkin Lynphoma (NHL) was diagnosed, with large B-cell subtype of centro-follicular origin (GCB subtype according to Hans's algorithm) double expression for the MYC and BCL2 protein (Fig. 3).
The advanced age of the patient, the poor general conditions, the associated pathologies in poly-pharmacological treatment, the absence of a cleavage plane with the stomach, spleen and large vascular trunks, contraindicated the surgical approach and chemo-radiotherapy treatment. Patient's condition rapidly deteriorated due to disease progression, with exitus letalis after 6 weeks from PPL diagnosis.

Discussion

Diagnosis of PPL is usually very difficult due to the lack of a specific symptomatology.
As reported in the Literature it is not possible to diagnose reliably, on the basis of only clinical, laboratory and radiological findings this rare disease [5,10].
In our case, previous accidental trauma, referred pain in the upper abdominal quadrants, and CT images led to the diagnostic suspicion of hemoperitoneum from two-stage rupture of the spleen. For this reason, the patient was hospitalized with the diagnosis of acute abdomen, confirming what is reported in the literature in which the initial diagnosis proves to be incorrect in 82% of the cases observed [9].
Because of this diagnostic suspicion, the patient was urgently subjected to exploratory laparotomy with xiphopubic incision. The exploration of the peritoneal cavity and the retroperitoneal space excluded the presence of a serious hemoperitoneum from traumatic spleen injury. The presence of free serum-haematic fluid between the intestinal loops and in the peritoneal recesses proves to be of modest magnitude, due to the blood oozing from necrotic disintegration of the pancreatic neoplastic mass, as already reported in the literature [11].
Because of the lack of a cleavage plane between pancreatic mass, stomach, duodenum and vascular structures, due to local spread of the disease, any resective surgical approach was contraindicated [8,12]. Therefore, only biopsy sampling for histological examination and control of bleeding by applying oxidized and regenerated absorbable cellulose (Tabotamp®) were carried out.
In our case, the initial misdiagnosis was due to the uncommon clinical presentation of the PPL, the history of recent trauma, the underestimation of the serum markers increase and the interpretation of the CT findings.
At the evaluation of contrast-enhanced CT images, had been erroneously overestimated the extent of peritoneal and retroperitoneal blood effusion, described as acute hemoperitoneum from trauma of the spleen and body-tail pancreas. While, on the other hand, the typical features of extra-nodal lymphomatous lesions were not appreciated [4].
In agreement with other authors, the malignant pancreatic lymphoma we reported showed an increase in the serum level of Ca 19-9 and CA 125 which, together with the increase in LDH and beta2-microglobulin, if correctly evaluated, would have supported the diagnostic suspicion of an extranodal lymphomatous neoformation, avoiding the use of inappropriate exploratory laparotomy [7,13].
Exitus letails after 6 weeks from the diagnosis of PPL was due to locally advanced disease progression, whose high aggressiveness correlated with the double expression for the CMYC and BCL2 protein.

Riassunto

Il linfoma pancreatico primitivo (PPL) rappresenta meno dello 0.5% di tutte le neoplasie pancreatiche. Le manifestazioni cliniche di esordio non sono specifiche e la diagnosi è tardiva nella maggioranza dei pazienti.
Osservazione Personale: Donna di 85 anni, ricoverata presso l'Ospedale Universitario "A. Fiorini" di Terracina-Polo Pontino, con diagnosi di addome acuto da sospetta rottura in due tempi della milza. Al ricovero la pz lamentava dolore a carico dei quadranti addominali superiori e riferiva caduta accidentale in casa avvenuta 20 giorni prima. Presentava esami ematochimici negativi per anemia e leucocitosi (Hb12.7g/dl; GB9.8x10/UL), significativo incremento del CA19.9 (196 U/ml), del CA125 (138 U/ml), delle LDH (1044 U/L) e della beta2-microglobulina.
La CT torace-addome-pelvi con mdc mostrava versamento a densità ematica in sede pleurica sinistra, perisplenica, periepatica e nel Douglas e una neoformazione del corpo-coda pancreas con falda ematica peripancreatica. La milza appariva di dimensioni notevolmente aumentate, con presenza di area ipodensa di 12.5x10.6 cm di diametro come da ematoma intraparenchimale, con capsula splenica apparentemente indenne.
La pz veniva sottoposta a laparotomia esplorativa urgente per sospetto emoperitoneo. All'apertura della cavità peritoneale si dimostrava la presenza di modesto versamen-

to libero sieroematico da stillicidio della neoformazione pancreatica. La diffusione locale della malattia impediva ogni tentativo di resezione chirurgica. Si procedeva a controllo del sanguinamento con apposizione di emostatici topici (Tabotamp®) e a prelievo bioptico dalla neoformazione pancreatica. Si poneva diagnosi istologica finale di Linfoma Non-Hodgkin a grandi cellule di origine centro-follicolare, doppio espressore per la proteina CMYC e BCL2 all'immunoistochimica.

L'età della pz, le scadenti condizioni generali, le patologie associate in trattamento poli-farmacologico, la diffusione localmente avanzata della malattia e l'aggressività istologica controindicavano il trattamento chemio-radioterapico.

Conclusione: La diagnosi di PPL è molto difficile e tardiva nella maggioranza dei pz, poichè le manifestazioni cliniche di esordio sono di solito aspecifiche; così come nel caso da noi riportato in cui il sanguinamento intra-retro-peritoneale era difficilmente riconducibile ad una malattia pancreatica.

I riferito trauma addominale, la sintomatologia clinica aspecifica, la CT in cui non erano state evidenziate le alterazioni caratteristiche dei linfomi extranodali, la sottovalutazione dell'aumento dei livelli plasmatici dei marcatori CA19-9 e CA125, delle LDH e della beta2-microglobulina, sono state nel nostro caso la causa di errata diagnosi e indicazione al trattamento chirurgico in urgenza.

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