CASE REPORT

Acute pancreatitis as an unusual presentation of primary splenic lymphoma

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Accepted 28 September 2017

SUMMARY

A 51-year-old man with no relevant medical history presents to the emergency department complaining of a recent worsening of few months upper abdominal pain with back radiation and postprandial fullness, without B symptoms. Laboratory analysis showed hyperamylasaemia, elevated lactate dehydrogenase and inflammatory parameters. Abdominal ultrasonography revealed a heterogeneous solid mass in the spleen/splenic hilum with pancreatic parenchyma continuity and no biliary tract dilation or gallstones. A mild acalculous acute pancreatitis diagnosis was made. Abdominopelvic CT revealed a large heterogeneous mass infiltrating the spleen and pancreas and obstructing the common bile duct at the pancreatic level with upstream dilation of biliary and pancreatic ducts, with splenic vein invasion. Several necrotic, peripancreatic and hepatic hilar adenopathies were also observed. Ultrasound-guided biopsy showed a primary splenic diffuse large B-cell non-Hodgkin's lymphoma. Chemotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) was performed with lack of response and the patient died within 10 months of diagnosis onset.

BACKGROUND

Acute pancreatitis represents one of the most common gastrointestinal conditions in clinical practice. In the absence of gallstones or significant alcohol use, which together account for about 80% of all causes, the aetiological work-up of acute pancreatitis can be challenging.¹⁻³ Malignant aetiology of acute pancreatitis is very rare. Despite secondary involvement of the spleen in 30%–40% of non-Hodgkin's lymphoma, primary splenic diffuse large B-cell lymphoma (DLBCL) represents an uncommon subtype (less than 1%).²⁻⁵ Pancreatic parenchyma infiltration by DLBCL is an unusual aetiology of acute pancreatitis.

We report an uncommon presentation of a primary splenic DLBCL in a young patient. Few reports of acute pancreatitis due to secondary lymphomatous involvement of the pancreas have been reported, being as far as we know the third reported case in the literature of acute pancreatitis caused by a primary splenic lymphoma. Primary splenic lymphoma should be considered in the differential aetiological work-up of unexplained acute pancreatitis, since the chemotherapy is usually effective. Additionally, we also reviewed the reported literature.

CASE PRESENTATION

A 51-year-old man with a medical history of controlled epilepsy and dyslipidaemia presented to the emergency department with a recent worsening of few months' upper abdominal pain with back radiation, postprandial fullness and no B symptoms (fever, weight loss or night sweats). There was no abdominal trauma, falls, history of smoking or alcohol abuse. His physical examination was unremarkable except for a low body mass index (17.5 kg/m²), and a painful and palpable abdominal mass, without peritoneal irritation signs.

INVESTIGATIONS AND DIFFERENTIAL DIAGNOSIS

Laboratory analysis showed normocytic normochromic anaemia (haemoglobin 11.6 g/dL), hyperamylasaemia (583 U/L; upper limit of normal (ULN):100), elevated lactate dehydrogenase (408 U/L; ULN:220) and C-reactive protein (10.7 mg/dL; ULN:0.5). Abdominal ultrasonography showed a heterogeneous solid mass of approximately 11 cm × 10 cm in dimension, without internal vascularisation, located in the upper pole of the spleen/splenic hilum with apparent pancreatic parenchyma continuity, and no biliary tract dilation or gallstones (figure 1). Thus, a diagnosis of a mild acalculous acute pancreatitis (Ranson's criteria upon admission 1; Bedside Index for Severity in Acute Pancreatitis (BISAP) score 0) was made, providing a supportive care with fluid therapy and analgesics, without improvement. An abdominopelvic CT was performed showing a large heterogeneous lobulated mass, with 9.5 cm × 13 cm × 13 cm in dimension, infiltrating the spleen and pancreas, and splenic vein invasion. Several necrotic, peripancreatic and hepatic hilar adenopathies were also observed, obstructing the common bile duct at the pancreatic level with upstream dilation of biliary and pancreatic ducts, as well as collateral venous circulation and mild peritoneal effusion (figure 2A,B). Carcinoembryonic antigen (CEA), Carbohydrate antigen (CA) 19.9 and CA 125 serum tumour markers were normal. It was decided to perform an ultrasound-guided percutaneous biopsy of the splenic mass which revealed a monotonous population of intermediate-to-large in size cells, with rare necrosis or apoptosis. On immunohistochemical study, the tumour cells were positive for CD20, Bcl6, MUM1 and Ki67, and compatible with a primary splenic DLBCL (figure 3A–C). The patient developed progressive cholestasis with

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To cite: Gravito-Soares E, Gravito-Soares M, Pina-Cabral JE, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222643

Figure 1 Abdominal ultrasonography showed a heterogeneous solid mass of approximately 11 cm×10 cm in dimension, without internal vascularisation, located in the upper pole of the spleen/splenic hilum with apparent pancreatic parenchyma continuity, and no biliary tract dilation, gallstones or peritoneal effusion.

acute cholangitis because of biliary tract obstruction, with good response to empirical antimicrobial therapy using piperacillin-tazobactam. A complementary staging study was performed including a bone marrow biopsy with no involvement by lymphoproliferative disease (Ann Arbor stage II, low-intermediate international prognostic index risk).

TREATMENT, OUTCOME AND FOLLOW-UP

The patient underwent chemotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone). 18F-FDG (fluorodeoxyglucose) positron emission tomography surveillance at 3–6 months showed a debulking of the splenic mass (figure 4A,B), in relation with partial response, having been proposed for splenectomy. However, a progression of lymphoma

occurred with leptomeningeal (confirmed by lumbar puncture) and left arm soft tissue (confirmed by ultrasound-guided percutaneous biopsy (figure 5)) metastasis. He died within 10 months of diagnosis onset.

DISCUSSION

Acute pancreatitis represents one of the most common gastrointestinal conditions, being a frequent cause of hospitalisation. Alcohol use (25%–35%) and gallstones (40%–70%) are the most common causes of acute pancreatitis. In the absence of gallstones or significant alcohol use, the aetiological work-up can be challenging and includes several causes, such as medications/toxins, infectious agents, autoimmunity, trauma/ischaemia and metabolic causes.^{1–3} However, despite an exhaustive diagnostic study,

Figure 2 Abdominopelvic CT (A: axial view, B: coronal view) showing a large heterogeneous lobulated mass, with 9.5 cm×13 cm×13 cm in dimension, infiltrating the spleen and pancreas, splenic vein invasion, multiple necrotic, peripancreatic and hepatic hilar adenopathies (10–32 mm) conditioning dilation of the Wirsung and intrahepatic and extrahepatic bile ducts with abrupt ending at the pancreatic level of the common bile duct, collateral venous circulation and mild peritoneal effusion.

Figure 3 Ultrasound-guided percutaneous biopsy of the splenic mass revealed a monotonous population of intermediate-to-large in size cells, with rare necrosis or apoptosis (A, H&E 100 $\times$). Immunohistochemical study was positive for CD20 (B, H&E 40 $\times$; C, H&E 100 $\times$), Bcl6, MUM1 and Ki67 (>80%), and negative for BCL2, CD10 and CD3, compatible with a primary splenic diffuse large B-cell non-Hodgkin's lymphoma.

10% of acute pancreatitis remains idiopathic.^{2,3} The malignant aetiology of acute pancreatitis is a rare aetiology that may trigger this condition by obstruction of the main pancreatic duct or less frequent by tumour infiltration into the pancreatic parenchyma.¹ Idiopathic acute pancreatitis is misdiagnosed in 5%–14% of benign or malignant pancreatobiliary tumours.¹

Non-Hodgkin's lymphoma often arises from lymph nodes, although it may also occur in extranodal sites, including the spleen.⁵ Secondary involvement of the spleen occurs in 30%–40% of non-Hodgkin's lymphoma and has been well described. However, a primary splenic DLBCL is an uncommon entity (less than 1%).^{2–5} Early diagnosis of primary splenic DLBCL is difficult because of unspecific symptoms, including abdominal pain, fever, weight loss and fatigue.^{2,5,6} Other symptoms can result from direct invasion of the perisplenic organs such as pancreas, stomach, diaphragm and omentum.⁵ Extranodal DLBCL sites had lower proportion of advanced disease at diagnosis than lymph node disease.⁷ Within extranodal DLBCL sites, the haematological system has been associated with better prognosis than liver/pancreas.⁷ Compared with DLBCL of other

locations, primary splenic DLBCL showed more frequency of bone marrow infiltration, B symptoms and progression-free survival despite no difference in overall survival.⁴ Low-intermediate risk in the international prognostic index had a 5-year survival of 51%.⁵ Treatment can include splenectomy, chemotherapy and radiotherapy.^{5,8} Due to relatively favourable clinical course, even in cases of difficult surgical removal tumours, chemotherapy is often effective.^{2,6,8}

Secondary involvement of the pancreas by DLBCL has rarely been described in the literature,^{2,6,9–11} and represents an uncommon aetiology of acute pancreatitis. Contrast-enhanced CT scan is required in an unexplained acute pancreatitis, even in young patients (more than 40 years).¹⁶ Histopathology is crucial to exclude primary pancreatic tumours or autoimmune pancreatitis.^{2,5}

Several cases of malignancy-related acute pancreatitis have been reported previously. However, as far as we know, only two cases of acute pancreatitis induced by primary splenic lymphoma have been reported before. Wu *et al*² described a case of a 68-year-old woman with pancreatic tail infiltration by

Figure 4 18F-FDG (fluorodeoxyglucose) positron emission tomography surveillance at 3 months (A) and 6 months (B) showed a hypermetabolic splenic lesion with dimension reduction (Deauville score 5).

Figure 5 Left arm soft tissue ultrasonography showed a 7.2 cm heterogeneous mass with multiple hypoechoic nodules and marked internal vascularity.

primary splenic DLBCL. This patient presented with abdominal pain and B symptoms (weight loss), without increased lactate dehydrogenase. She died without having started chemotherapy by urosepsis within 12 days of diagnosis. Peralta Vargas *et al*³ reported the other case of 84-year-old woman with pancreatic infiltration by a primary splenic marginal zone B-cell lymphoma. Presenting symptoms include vomiting, abdominal pain and B symptoms (nocturnal diaphoresis and weight loss), and also no elevation of lactate dehydrogenase. The patient underwent splenectomy without recurrence of lymphoproliferative disease after 5 months of follow-up.

In our case report and contrarily to reported literature, B symptoms were absent at presentation, elevated lactate dehydrogenase was observed, and the patient developed a fatal disease progression despite initial partial response to chemotherapy.

In conclusion, we report a case of primary splenic DLBCL with an unusual presentation in a young patient. As far as we know, this is the third reported case in the literature of acute pancreatitis due to secondary lymphomatous infiltration of the pancreas by a primary splenic lymphoma. This case highlights a very unusual aetiology of acute pancreatitis. Primary splenic

lymphoma should be considered in the differential aetiological work-up of unexplained acute pancreatitis, even in a young patient, especially in presence of abdominal mass and elevated lactate dehydrogenase. In this case, the prognosis was dismal despite early-stage diagnosis and initial partial response to chemotherapy.

Contributors EGS and MGS contributed equally in writing the manuscript and reviewing the literature. EGS is the article guarantor. JEPC and LT reviewed the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Acute pancreatitis is one of the most frequent causes of hospitalisation with a challenging aetiological work-up.
- ▶ Alcohol use (25%–35%) and gallstones (40%–70%) are the most common causes of acute pancreatitis.
- ▶ After excluding gallstones and alcohol use, less common causes of acute pancreatitis must be ruled out, including malignancy.
- ▶ Even in young patients, primary splenic lymphoma with secondary pancreatic involvement should be considered in the differential diagnosis of acute pancreatitis, especially in presence of splenic mass and elevated lactate dehydrogenase.
- ▶ Acute pancreatitis represents a very unusual presentation of primary splenic lymphoma.

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