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CASE REPORT

Primary follicular lymphoma of the pancreas: A rare tumour mimicking pancreatic carcinoma

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Abstract

Introduction: Primary pancreatic lymphomas are extremely rare. Clinically, primary pancreatic lymphoma mimics symptoms of carcinoma of the pancreatic head. Clinical and radiological features may overlap with other pancreatic conditions such as carcinoma, neuroendocrine tumours and autoimmune pancreatitis. *Case Report:* We report a case of a 75-year-old man who presented with symptoms of obstructive jaundice. Ultrasonography and computed tomography (CT) showed an ill-defined lobulated soft tissue lesion at the head/uncinate process of the pancreas measuring 4.5 x 4.9 x 5.8 cm. The patient underwent pancreaticoduodenectomy for suspected pancreatic head/uncinate process carcinoma. Histopathology and immunohistochemical assessment of the pancreatic lesion established the diagnosis of a low-grade follicular lymphoma. *Discussion:* Clinical and imaging features of primary pancreatic lymphoma may often overlap with pancreatic carcinoma. There is a value of obtaining preoperative tissue diagnosis such as tissue biopsy and fine needle aspiration (FNA) cytology with or without flow cytometry to make an accurate diagnosis of non-Hodgkin lymphoma and alleviate the need of more radical surgery in pancreatic lymphoma.

Keywords: Non-Hodgkin lymphoma, primary pancreatic lymphoma (PPL), follicular lymphoma, pancreas, obstructive jaundice

INTRODUCTION

Gastrointestinal lymphomas constitute 10-15% of all non-Hodgkin lymphomas and 30-40% of all extranodal lymphomas.[1,2] Gastrointestinal non-Hodgkin lymphoma (NHL) usually involves the stomach and the small bowel. Rarely, it can also present as a pancreatic mass. Most cases of pancreatic non-Hodgkin lymphoma are part of a disseminated disease. Primary pancreatic lymphoma is rare and accounts for less than 1% of all primary pancreatic tumours.[3]

Diagnosis of primary pancreatic lymphoma requires the absence of palpable superficial lymphadenopathy or mediastinal nodes enlargement, and normal leukocyte count. Furthermore during laparotomy pancreatic mass predominates and if grossly-involved lymph nodes are seen they are usually confined to the peripancreatic region with no hepatic or splenic involvement.[4] Clinical presentation of primary pancreatic lymphoma mimics pancreatic carcinoma, for example patient presents with abdominal pain, weight loss, vomiting, jaundice, night sweats and fever.[5] However, CA 19.9 level is usually normal unless biliary obstruction is present.[6] Clinical and imaging features of primary pancreatic lymphoma may overlap with other pancreatic conditions such as carcinoma, neuroendocrine tumours and autoimmune pancreatitis. Therefore, histological diagnosis is mandatory because of different prognosis and therapeutic approaches of these conditions. We report a case of primary pancreatic lymphoma in an elderly man presented with symptoms of obstructed jaundice mimicking pancreatic carcinoma.

CASE REPORT

A 75-year-old man presented with jaundice for two weeks. He denied having fever, abdominal pain, and loss of appetite or weight. His bowel and urine output were otherwise normal. He

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had hypertension and bilateral glaucoma. Initial ultrasound of hepatobiliary system as a workup for jaundice showed an ill-defined, hypoechoic lesion at the head of pancreas measuring 4.0 x 4.5 cm with both intrahepatic and extrahepatic ducts dilatation. Subsequent abdominal computed tomography (CT) scan revealed an ill-defined lobulated soft tissue lesion at the head/uncinate process of the pancreas measuring 4.5 cm x 4.9 cm x 5.8 cm causing biliary tree obstruction suggestive of pancreatic head/uncinate process carcinoma (Fig. 1). Subcentimeter porta hepatis lymph nodes measuring 0.9 cm in largest diameter were also seen. The liver and spleen were unremarkable. Chest radiograph showed no evidence of lung or mediastinal mass. His liver function test showed mild to moderate derangement with obstructive pattern (Total Bilirubin and Direct Bilirubin: 172 μmol/L and 132.6 μmol/L respectively [Normal Total Bilirubin: <20.5 μmol/L, Direct Bilirubin: <5 μmol/L]), Alkaline Phosphatase (ALP): 276 U/L [Normal ALP: 45-115 U/L] and Alanine Transaminase (ALT): 151 U/L [Normal ALT: 7-55 U/L]) while his white blood cells count, serum CA 19.9 marker and amylase were within normal limits. Based on the clinical and radiological findings which support the diagnosis of pancreatic carcinoma, the patient underwent pancreaticoduodenectomy (Whipple procedure). Intraoperative finding showed a mobile head of pancreas tumour, a large mesenteric node measuring 4 x 5 cm and multiple subcentimeter peripancreatic and portal nodes. The common bile duct and common hepatic duct were dilated. The mesenteric lymph node was removed en bloc together with the resected specimen.

The resected pancreas and duodenum revealed a 5 cm, irregular yellowish-to-tan mass within the pancreatic head (Fig. 2). The tumour surrounded the main pancreatic duct, distal common bile duct but did not appear to obliterate the duct. Enlarged peripancreatic and mesenteric lymph nodes were readily identified: the largest measured 4.5 cm in greatest dimension.

Microscopically, the pancreatic mass showed infiltration by neoplastic lymphoid cells forming follicular pattern with no reactive lymphoid tissue seen. The neoplastic follicles are composed of predominantly centrocytes characterised by small to medium sized cells with hyperchromatic nuclei, inconspicuous cleaved nucleoli, and scanty cytoplasm. Few scattered centroblasts characterised by large cells with vesicular nuclei and prominent peripheral nucleoli are seen with a count of 4 centroblasts per high power field. The mesenteric lymph node showed diffuse effacement of the normal lymph node architecture with infiltration by similar neoplastic lymphoid follicles as the pancreas. The remaining lymph nodes showed reactive hyperplasia. Immunohistochemical studies revealed that the tumour cells express CD20, CD10, and BCL2. CD23 highlights the follicular dendritic meshwork. They were negative for CD3, CD5, and Cyclin D1. Ki-67 showed a proliferative index of 20% in the neoplastic follicles (Fig. 3).

The overall findings were consistent with low-grade follicular lymphoma, WHO grade I with involvement of mesenteric lymph node. Radiologic imaging showed no evidence of extra-abdominal disease.

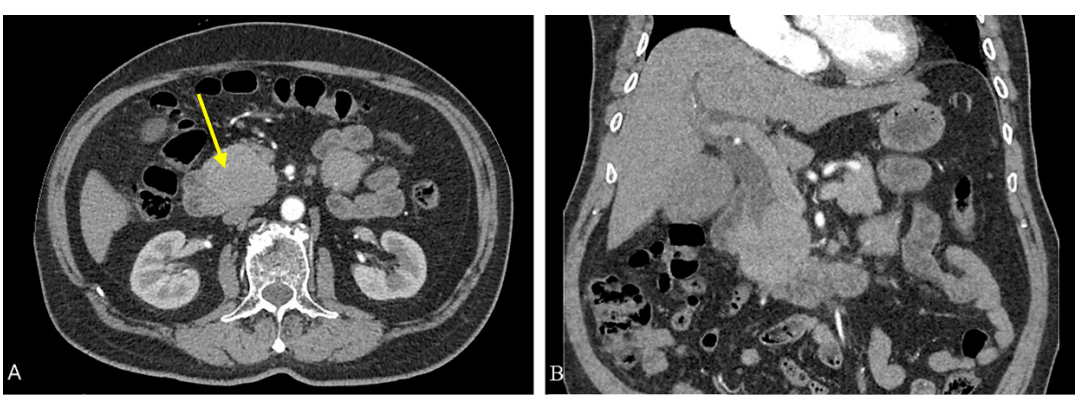

FIG. 1: (A) Computed tomography (CT) scan revealed an ill-defined lobulated soft tissue lesion at the head/uncinate process of the pancreas measuring 4.5 cm x 4.9 cm x 5.8 cm. The mass is isodense to the rest of the pancreas in the portovenous phase. There is no clear fat plane with the D2 of the duodenum laterally (arrow). (B) Dilatation of common bile duct and intrahepatic ducts are evident.

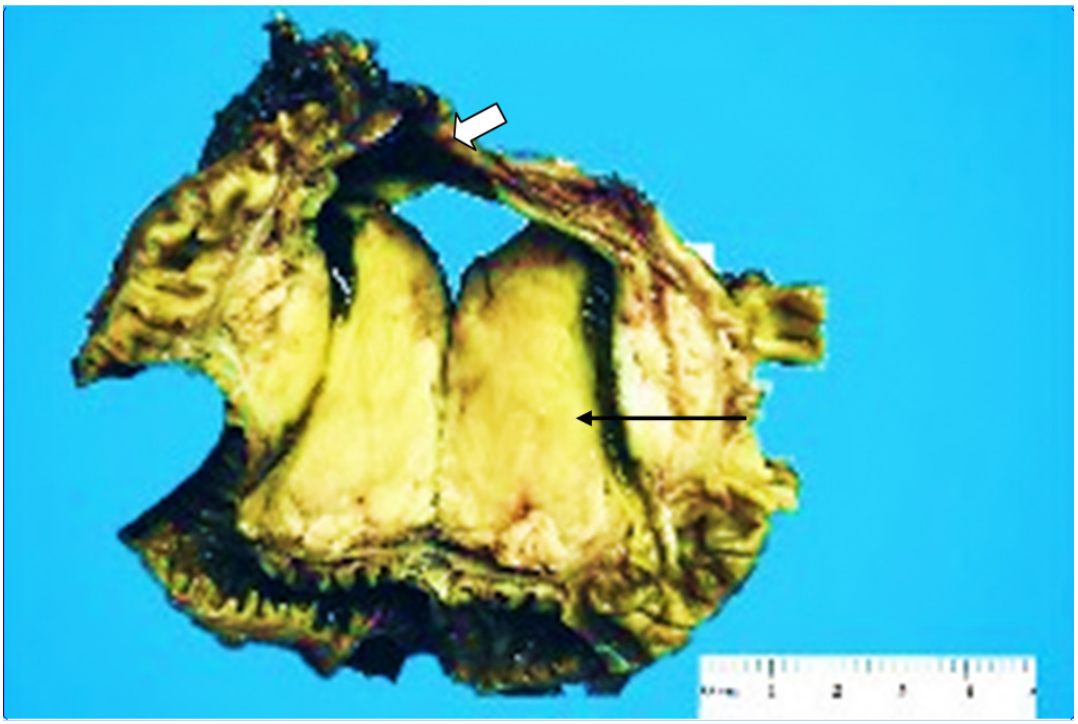

FIG. 2: Grossly, a firm, yellowish-to-tan tumour was seen at the head of pancreas (arrow). The common bile duct was dilated (arrowhead).

DISCUSSION

Lymphoma originating from pancreas comprises only 0.6% of total cases of extranodal malignant lymphoma.[7] The most common histologic type of the pancreatic lymphoma is diffuse large B-cell lymphoma, while follicular lymphoma is rare.[8] An extensive review of the international literature has revealed a total of 102 patients with Non-Hodgkin lymphoma primarily involving the pancreas with majority of cases being diffuse large B-cell lymphoma (Table 1).[4,9-38] Only 9 cases were follicular lymphoma.[18,19,37]

The accurate diagnosis of primary pancreatic lymphoma may be missed when the tumour is confined to the pancreas and surrounding peripancreatic lymph nodes. A study attempted to elaborate the distinguishing features between pancreatic carcinoma and pancreatic haematologic malignancy. The study found that features more often seen in patients with haematologic malignancies includes young age at presentation, large tumour size, low preoperative CA19.9 level, history of a pre-existing haematological malignancy, presence of B symptoms, absence of jaundice or diabetes mellitus.[39] In this case however, the patient is elderly, presented with obstructive jaundice and a large mass in the head of pancreas. This led to high suspicion of pancreatic adenocarcinoma instead of primary pancreatic lymphoma. Primary pancreatic lymphoma is less likely to present with jaundice and mass at head of the pancreas thus reducing the suspicion of primary pancreatic lymphoma.[40]

Albeit gastrointestinal lymphoma has a wide variety of imaging appearances, one study have shown that certain findings such as bulky mass or diffuse infiltration with preservation of fat planes and no obstruction, multiple site involvement, and associated bulky lymphadenopathy can strongly suggest the diagnosis.[41] According to two other studies, there were radiological findings that may favour primary pancreatic lymphoma instead of pancreatic adenocarcinoma such as bulky localised pancreatic head tumour, no significant pancreatic duct dilatation, lack of calcification or necrosis, no enlarged lymph nodes below the level of the renal veins, and no retroperitoneal, hepatic, or splenic involvement.[42,43] In contrary, two studies have shown that abdominal CT is not a definitive method in distinguishing pancreatic carcinoma from pancreatic haematologic malignancy.[44,45] This further implies the difficulty in preoperative diagnosis of primary pancreatic lymphoma. In our patient, the clinical and imaging features are

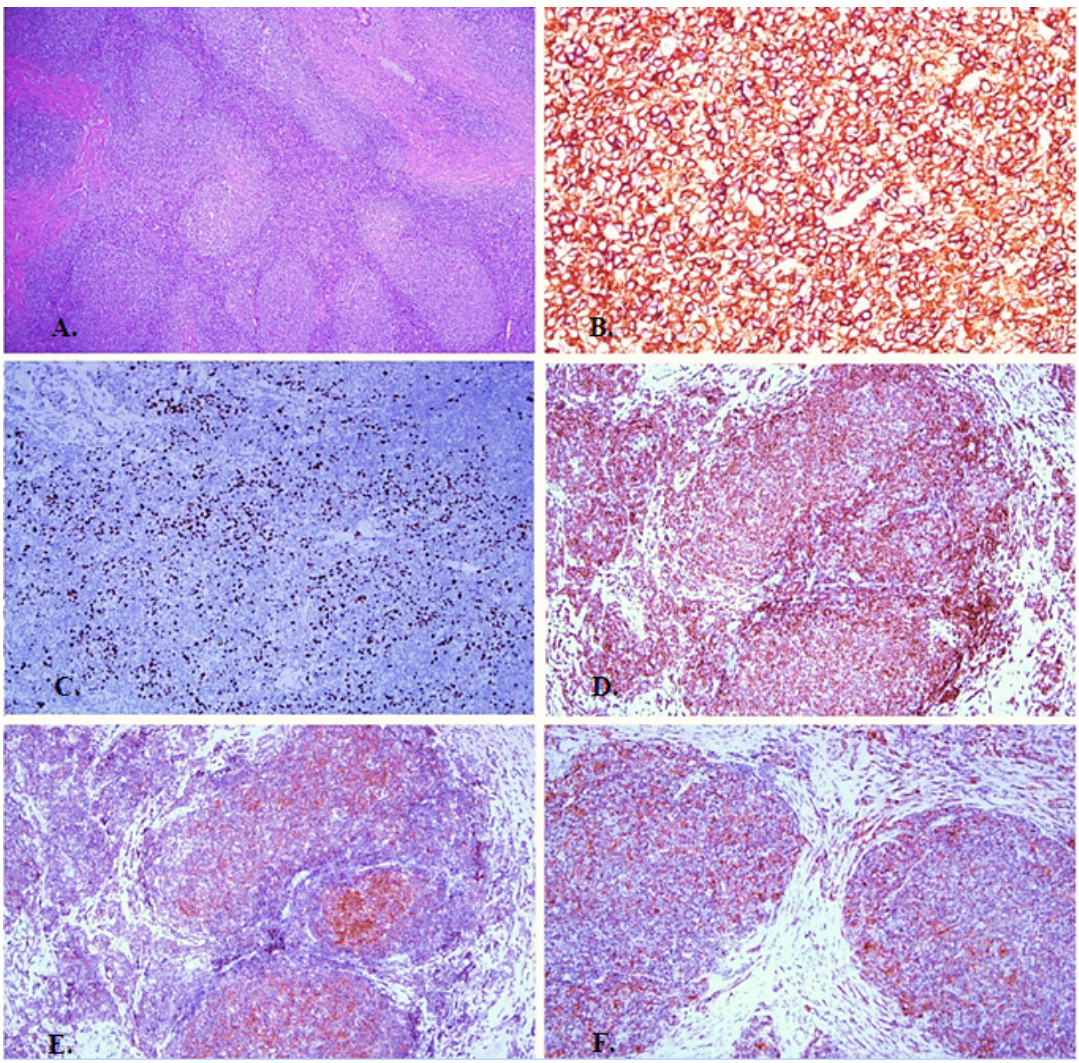

FIG. 3: (A) Microscopic examination: Haematoxylin & eosin staining showing pancreatic infiltration by poorly defined neoplastic lymphoid follicles (H&E, x4). (B) Medium sized neoplastic lymphoid cells expressing CD20 (x10). (C) The Ki-67 proliferative index is 20% (x10). (D, E, & F) The neoplastic lymphoid cells express CD23, CD10, and BCL2 (x10).

rather inconclusive for preoperative diagnosis of pancreatic lymphoma as he presented with symptoms of obstructive jaundice and bulky lesion in pancreatic head/uncinate process causing biliary tree obstruction. There were no pancreatic duct dilatation, calcification, or hepatic and splenic involvement seen. Only subcentimeter porta hepatis lymph nodes were found. These findings within his age group are more suggestive of pancreatic carcinoma leading the primary team to proceed with surgical resection.

Haematological malignancies are generally treated medically, with surgical management limited to cases necessitating secondary symptom control. Therefore, preoperative tissue diagnosis would be useful to prevent unwarranted radical surgery in suspected cases involving haematological malignancies. It has been reported that endoscopic ultrasound-assisted fine needle aspiration (EUS-FNA) may be utilised in the diagnosis of pancreatic carcinoma and pancreatic haematologic malignancy.[46] A retrospective study showed that the diagnostic accuracy of fine needle aspiration (FNA) with cytology for primary pancreatic lymphoma is improved greatly with the addition of flow cytometry and immunohistochemistry.[40] This study shows that cytology alone made the final diagnosis of lymphoma in only 28% of the patients versus

TABLE 1: Summaries of literature reviews on primary pancreatic lymphoma

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Shtamler *et al.*[9]	1988	Female/31	Diarrhoea, vomitting, upper abdominal pain, and weight loss	Head	Diffuse histiocytic lymphoma	CT: Enlarged liver with severe dilatation of the intrahepatic bile ducts. Space occupying lesion in head of the pancreas measuring 50 x 80 mm in size. No enlarged retroperitoneal lymph nodes.	CT – guided needle biopsy was performed with inconclusive diagnosis.	PD + CMT	CR + Second surgery 5 months later for ruptured pancreatic pseudocyst
Webb *et al.*[10]	1989	4 males and 5 female/49-76	Weight loss, jaundice, abdominal pain, gastric outlet obstruction (3)	Not specified	Diffuse histiocytic lymphoma (6), Mixed lymphocytic histioctic cell lymphoma (2), Diffuse lymphocytic lymphoma (1)	CT: Panreatic mass ranging 5 – 10 cm, periaortic lymph nodes enlargement (6), and CBD and/or intrahepatic dilatation (5)	Radiologically guided tissue biopsy (4), peripheral lymph node biopsy (1), and laparotomy (4)	PD (1) + CMT (9)	CR(6) + Deaths (3)
Hirabayashi *et al.*[11]	1991	Male/74	Epigastric pain,weight loss	Body and tail	Diffuse non-Hodgkin's lymphoma	CT: Pancreatic mass with involvement of peripancreatic fat. The peripancreatic lymph nodes and spleen were intact.	NA	Partial pancreatectomy + splenectomy	AWD
Joly *et al.*[12]	1992	Female/23	Jaundice, fever	Head	Non-Hodgkin lymphoma, composed of cleaved, large, B-cells	CT: Low-density tumour of the head of the pancreas with necrotic center.	Not done	PD + CMT	Developed multiple mesenteric and mediastinal lymphadenopathies, and pulmonary metastasis. Died of disease.
Van Beers *et al.*[13]	1993	5 males and 3 females/ 26 – 77	Epigastric pain (8), jaundice (4), fatigue (2)	Head (5), body and tail (3)	Non-Hodgkin B lymphomas of low grade (2), intermediate grade (2), high grade (4)	CT: Two patterns were observed; large infiltrating lesion with poorly defined contour and well delineated masses. The pancreatic tumours were isodense and homogenous on precontrast CT. They appear heterogenous in dynamic CT (6). Retroperitoneal, mesenteric, and peripancreatic lymphadenopathies were observed (5)	Non-surgical biopsy of the pancreatic area (4), peripheral lymph node biopsy (2), bone marrow biopsy (1), surgical biopsy of pancreas (1)	NA	NA

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Behrns *et al.*[4]	1994	8 males and 4 females/NR	Abdominal pain, weight loss, palpable mass	Head (6), body (3), tail (2), whole of pancreas (1)	DLBCL (7), mixed (2), small cleaved lymphoma (2)	NA	Preoperative tissue biopsy (6)	RT (5), CMT (2), RT+CMT (3), PD (2)	Died of disease (10)
Borrowdale *et al.*[14]	1994	Male/35	Epigastric discomfort, mild back pain, nausea and lethargy Acute onset of jaundice, with pale stools and dark urine	Not specified	Malignant lymphoma of the B cell type	CT: Mass in the head of the pancreas measuring 6 cm, with inhomogeneous appearance and poorly defined margins. Compression and displacement of the distal CBD and proximal pancreatic duct with dilatation.	Not done	CMT	NA
Ezzat *et al.*[15]	1996	4 males and 1 female/38–51	NA	Head (4), body and tail (1)	DLBCL (5)	NA	CT guided biopsy (2)	CMT (3), CMT+RT (2), PD (2)	CR (4), AWD (1)
Salvatore *et al.*[16]	2000	Male/59	Left sided abdominal pain, early satiety	Whole pancreas (diffuse involvement)	DLBCL	CT: Splenomegaly with multiple lesions and left upper abdominal peri-aortic lymphadenopathy. The pancreas appeared normal	Tissue biopsy during exploratory laparotomy	CMT	NA
Forootan *et al.*[17]	2001	Female/55	Epigastric pain, recent anorexia, early satiety, weight loss, palpable mass	Not specified	Diffuse mixed cellularity non-cleaved type non-Hodgkin's lymphoma	CT: Large para-aortic mass with heterogenous, mixed enhancement and encasement of great vessels.	Not done	Surgical tumour debulking + CMT	CR
Nayer *et al.*[18]	2004	7 males and 1 female/35-75	Abdominal pain (6), jaundice, acute pancreatitis, obstruction, diarrhoea	Head (7), body and tail (1)	LBCL (4), High-grade B-cell lymphoma (1), FCL (1), small lymphocytic lymphoma (1), suspicious (1)	CT: The tumours varied in size from 2-15 cm in greatest dimension.	Radiologic (USG/ CT) guidance FNA cytology with flow cytometric analysis	RT+CMT (3), CMT (4), NA	CR (5) AWD (1) No information (2)

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Volmar *et al.*[19]	2004	7 males and 3 females/46-86	NA	Head (8), body (1), tail (1)	LBCL (6), FCL (3), and unclassified B-cell lymphoma (1)	NA	FNA biopsies with flow cytometry analysis under ultrasound (3), CT (4), endoscopic ultrasound (7) guidance	CMT	Died (1) PR (2) CR (7)
Ji *et al.*[20]	2005	Male/46	Abdominal pain, jaundice	Head	DLBCL	CT: Hypodense pancreatic mass compressing CBD with dilatation of the gallbladder	Not done but intraoperative frozen section was performed suspicious of anaplastic carcinoma	PD	CR
Arcari *et al.*[21]	2005	4 males and 1 female/58-71	Pain and weight loss	Head (5)	LBCL (3) lymphoplas-macytic lymphoma (2)	CT: Hypodense/hypoechoic pancreatic head mass ranging from 3 to 6.5cm	FNA cytology with tissue core biopsy (3)	PD+CMT (2), CMT+RT (2), CMT (1)	CR (4) Relapse (1) Died due recurrent cholangitis post surgery (1) and liver cirrhosis (1)
Lee *et al.*[22]	2006	Female/61	Abdominal pain	Head	DLBCL	CT: Well defined mass located at the head of the pancreas which was slightly enhanced during the arterial phase	Intraoperative frozen section confirmed as lymhoma	Partial excision of mass + CMT	CR
Wang *et al.*[23]	2006	Male/49	Abdominal pain, jaundice with tea coloured urine	Head	Burkitt lymphoma	CT: Suspicious periampullary tumour with mild CBD dilatation. MRI: Relatively clearly defined and homogeneous signal mass in the pancreatic head with biliary dilatation on enhanced study.	Endoscopic guided biopsy reported as chronic inflammation	PD	Died 2 days due to post operative complication
Lin *et al.*[24]	2006	5 males and 1 female/16-65	Pain, mass, weight loss, jaundice, nausea, vomiting	Head (3), body and tail (2), whole of pancreas (1)	B-cell lymphoma (3) and Non-Hodgkin B lymphoma (3)	CT: The tumours were larger than 6 cm (4), with almost homogeneous density and unclear edges. Enhanced CT scan only enhanced the edges slightly.	EUS-guided fine-needle aspiration (2)	PD+CMT (4), CMT+RT (2)	Died (3) Lost to follow up (2) CR and on follow up (1)

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Basu *et al.*[25]	2007	Male/42	Abdominal pain, Jaundice	Body	DLBCL	CT: Large, lobulated, heterogeneously enhancing, soft tissue mass arising from body of pancreas with compression of CBD.	Trucut biopsy	CMT+RT	CR
Liakakos *et al.*[26]	2008	Male/65	Abdominal pain, jaundice, anorexia	Head	DLBCL	CT: Large heterogeneous enhancement of a large tumour of the head of the pancreas, in contact with the superior mesenteric vein (SMV), without signs of infiltration or encasement of the vein, or the superior mesenteric artery. Limited lymphadenopathy was also detected in the peripancreatic and the para-aortic regions.	CT-guided fine needle aspiration (FNA) biopsy was not diagnostic	PD+CMT	Alive
Hashimoto *et al.*[27]	2008	Male/50	Jaundice	Head	DLBCL	CT: Low-density mass, 10 cm in diameter, in the retroperitoneal space behind the pancreas head, distal bile duct and the PV were obstructed	Not done	CMT+PD	CR
Saglam *et al.*[28]	2009	Male/20	Weight loss, back pain, mandible numbness, night sweats, and poor exercise tolerance	Not specified	Burkitt lymphoma	CT: Nodular, homogeneous, and hypodense mass that showed minimal contrast enhancement MRI: T1 weighted nodular, partially well-circumscribed, homogeneous, hypointense lesion in the body of the pancreas. T2 weighted homogeneous, hyperintense pancreatic lesion. Post-gadolinium T1-weighted, areas of linear and punctate contrast enhancement were observed along the septations inside the lesion.	US guided fine needle aspiration cytology	CMT	Died of sepsis after 2nd month of chemotherapy

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Bautist *et al.*[29]	2009	Male/13	Pain	Tail	Non-Hodgkin B lymphoma	CT and MRI showed a well defined 5 cm solid mass with necrohaemorrhagic center located in pancreas tail, without compromising neighbour structures.	CT guided biopsy	CMT	CR
Haji *et al.*[30]	2009	1 male and 2 females/ 52 – 65	Vague abdominal pain, low grade fever, loss of appetite and weight, melena (1)	Head (2), tail (1)	DLBCL (5)	CT: Hypodense mass in body of pancreas, head and tail (1) encasing the vessels, peri-pancreatic lymph node enlargement with no bile or pancreatic duct dilatation.	CT-guided core biopsy or fine needle aspiration procedure (2)	CMT+RT (2), PD+CMT (1)	CR
Sugishita *et al.*[31]	2010	Male/16	Abdominal pain, jaundice	Head	DBCL	CT: 3.0 × 4.5 cm homogeneously enhancing mass localised between the inferior vena cava and pancreatic head. The common pancreatic duct was dilated and the common bile duct was stenosed. MRI: Pancreatic head with low signal intensity on T1W images and high intensity on T2W images, which enhanced inhomogeneously	Not done	PD+CMT	CR
Abe *et al.*[32]	2010	Male/56	Asympto-matic	Head	B-cell lymphoma	CT: A 5 cm tumour located in the head of pancreas, while an enhanced CT scan showed a slight increase in the tumour without encasement of arteries or veins. MRI: Pancreatic mass with homogeneously high signal intensity on T2-weighted images and low signal intensity on T1-weighted images with gadolinium enhancement PET/CT: Unique intense uptake of FDG in the pancreas.	Laparoscopic assisted biopsy	PD-CMT	NA

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Alexander *et al.*[33]	2011	Male/61	Fatigue, weight loss, and jaundice	Head	DLBCL in association with low-grade follicular lymphoma in the surrounding lymph nodes	CT: A 5-cm enhancing mass that effaced the pancreatic parenchyma and closely apposed the superior mesenteric vein near the portal vein confluence. There was no upstream dilatation of the pancreatic duct or intrahepatic bile duct. Several borderline to mildly enlarged peripancreatic and mesenteric lymph nodes were noted.	Fine-needle aspiration was not attempted due to intervening blood vessels between the mass and the ultrasound probe.	PD-CMT	CR
Anderloni *et al.*[34]	2015	Female/33	Jaundice, fever, abdominal pain	Head	Non-Hodgkin B lymphoma	CT: Common bile duct dilation (diameter 10 mm) with a pancreatic hypodense mass (4.5 x 4 x 5 cm) involving the head of the pancreas with diffuse enlarged "sausage-shaped" pancreatic gland and irregular narrow pancreatic duct suggestive for autoimmune pancreatitis MRI: Hypovascular enlargement of the whole pancreas with homogeneous enhancement in the tardive phases and multiple bilateral hypovascular renal lesions	Upper gastrointestinal endoscopy (UGIE) guided biopsy	CMT	CR
Fukuba *et al.*[35]	2016	Female/60	Epigastric pain, fever, weight loss, drenching night sweats	Head	DLBCL	CT: Lesion measuring 9.5 cm in diameter that was surrounded by part of the hepatic portal, head of the pancreas, and posterior wall of duodenum. The mass had a smooth edge and uniform density, and was of lower contrast. MRI: Low intensity area in T1-weighted images and a slightly high intensity area in T2-weighted images. There were no findings of necrosis or fluid storage in the mass. PET/CT: Accumulation of FDG in the mass.	Initial cytology of pancreatic juice is negative Endoscopic ultrasound-guided tissue biopsy	CMT	CR

Authors	Year	No of Cases/ Gender/Age	Clinical presentation	Location of tumour in pancreas	Histopathology diagnosis	Imaging findings	Preoperative cytology/tissue biopsy	Treatment	Outcome at ime of review
Lili *et al.*[36]	2017	2 males/ 32-62	Pain, jaundice	Head (1), tail (1)	DLBCL	CT: Heterogeneous enhanced mass arising from the pancreatic head and tail. Multiple enlarged lymph nodes in the abdominal cavity (1)	CT guided biopsy	PD + CMT (1)	CR
Boninsegna *et al.*[37]	2017	6 males 8 females/ 41 – 85	Abdominal pain or discomfort, jaundice, palpable mass, systemic symptoms	Head (6), body-tail (7), whole pancreas (1)	FCL (5), DLBCL (6), high grade B-cell lymphoma (3)	CT: Tumour encasement of coeliac axis, superior mesenteric artery and superior mesenteric vein (5); splenic vein and artery encasement (2). There were no signs of infiltration, with no vessel wall irregularity or stenoses. There were presence of necrosis (2), enlarged lymph nodes (11), peri-pancreatic fat stranding (14), enlarged common hepatic duct (6) and enlarged main pancreatic duct (5).	US-guided percutaneous biopsy (6), US-guided endoscopic biopsy (7), endoscopic biopsy of the neoplasm involving the duodenum wall (1)	CMT	NA
Konjeti *et al.*[38]	2018	Female/68	Belching, abdominal bloating, weight loss	Head	Burkitt lymphoma	CT: Periportal solid 7.5 × 4.9 × 12.7 cm mass which obstructed the central hepatic ducts and encased the main portal vein; difficult to separate the lesion from liver and pancreatic parenchyma.	CBD brushing cytology showed atypical lymphocytes suspicious for malignant lymphoma. FNA cytology and tissue biopsy of pancreatic head	CMT	Died of sepsis and bacteriaemia

Abbreviations: AWD, alive with disease; CBD, common bile duct; CMT, chemotherapy; CR, complete remission; CT, computed tomography; DHL, diffuse histiocytic lymphoma; DLBCL, diffuse large B cell lymphoma; DP, distal pancreatectomy; FNA, fine needle aspiration; FCL, follicular cell lymphoma; LBCL, large B cell lymphoma; MRI, magnetic resonance imaging; NA, not available; NHBL, non-Hodgkin B lymphomas; PD, pancreaticoduodenectomy; PET/CT, positron emission tomography/computed tomography; PR, partial remission; RT, radiotherapy.

91% of patients with pancreatic adenocarcinoma. Nonetheless the use of FNA with or without flow cytometry to diagnose lymphomas, including primary pancreatic lymphoma, has its own limitations.[47] Rare cases presenting as T-cell lymphoma and Hodgkin lymphoma are often difficult to quantify on fine needle aspirate subjected to flow cytometry. Moreover, Hodgkin lymphoma often requires the identification of the characteristic Reed-Sternberg cells which may be difficult to find. In addition, the yield of endoscopic ultrasound guided FNA with flow cytometry also depends on the adequacy of material obtained during the sampling and could be missed if the endoscopist does not keep a high index of suspicion. Endoscopic ultrasound-assisted fine needle aspiration (EUS-FNA) is a valuable tool to diagnose primary pancreatic lymphoma. Flow cytometry analysis can be used as a complementary tool with conventional cytology. Pre-operative tissue biopsy or cytological diagnosis would be necessary to prevent unwarranted surgery in suspected cases involving primary pancreatic lymphoma.

CONCLUSION

It is important to differentiate between primary pancreatic lymphoma and the more common adenocarcinoma of the pancreas, as its treatment and prognosis differ significantly. Primary pancreatic lymphoma should be considered in the differential diagnosis of pancreatic tumours and an attempt to obtain preoperative tissue diagnosis such as fine needle aspiration (FNA) cytology with or without flow cytometry and/or tissue biopsy may be necessary before proceeding to radical surgery.

Conflicts of Interest: The authors declared no conflict of interest.

REFERENCES

1. Wu XC, Andrews P, Chen VW, Groves FD. Incidence of extranodal non-Hodgkin lymphomas among whites, blacks, and Asians/Pacific Islanders in the United States: Anatomic site and histology differences. Cancer Epidemiol. 2009; 33: 337-46
2. d'Amore F, Brincker H, Gronbaek K, *et al*. Non-Hodgkin's lymphoma of the gastrointestinal tract: A population-based analysis of incidence, geographic distribution, clinicopathologic presentation features, and prognosis. Danish Lymphoma Study Group. J Clin Oncol. 1994; 12: 1673-84
3. Mishra MV, Keith SW, Shen X, Bar Ad V, Champ CE, Biswas T. Primary pancreatic lymphoma: A population-based analysis using the seer program. Am J Clin Oncol. 2013; 36(1): 38-43.
4. Behrns, KE, Sarr, MG, Strickler, JG. Pancreatic lymphoma: Is it a surgical disease? Pancreas. 1994; 9(5): 662-7.
5. Dawson, IM, Cornes, JS, Morson BC. Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis. Br J Surg. 1961; 49: 80-89.
6. Sandrasegaran K, Tomasian A, Elsayes KM, Nageswaran H, Shaaban A, Shanbhogue A, Menias CO. Hematologic malignancies of the pancreas. Abdominal Imaging. 2015; 40(2): 411-23.
7. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer. 1972; 29(1): 252-60.
8. Shirai Y, Okamoto T, Kanehira M. Pancreatic follicular lymphoma presenting as acute pancreatitis: Report of a case. Int Surg. 2015; 100(6): 1078-83.
9. Shtamler B, Bickel A, Manor E, Shahar MB, Kuten A, Suprun H. Primary lymphoma of the head of the pancreas. J Surg Oncol. 1988; 38(1): 48-51.
10. Webb TH, Lillemoe KD, Pitt HA, Jones RJ, Cameron JL. Pancreatic lymphoma. Is surgery mandatory for diagnosis or treatment? Annals of surgery. 1989; 209(1): 25-30.
11. Hirabayashi K, Kawakami H, Aizawa T, *et al*. A case of the primary pancreatic lymphoma. Rinsho Ketsueki. 1991; 32(4): 414-8.
12. Joly I, David A, Payan, MJ, Sahel J, Sarles H. A case of primary non-Hodgkin lymphoma of the pancreas. Pancreas. 1992; 7(1): 118-20.
13. Beers BV, Lalonde L, Soyer P, *et al*. Dynamic CT in pancreatic lymphoma. J Comput *Assist* Tomogr. 1993; 17(1): 94-7.
14. Borrowdale R, Strong RW. Primary lymphoma of the pancreas. ANZ J Surg. 1994; 64(6): 444-6.
15. Ezzat A, Jamshed A, Khafaga Y, *et al*. Primary pancreatic non-Hodgkin's lymphomas. J Clin Gastroenterol. 1996; 23(2): 109-12.
16. Salvatore J, Cooper B, Shah I, Kummet T. Primary pancreatic lymphoma: A case report, literature review, and proposal for nomenclature. Medical Oncology. 2000. 17(3): 237-47.
17. Forootan H, Mansour Ghanaie F, Ghofrani H. Primary pancreatic lymphoma: A case report and literature review. Med J Islam Repub Iran. 2001; 15 (2): 117-21
18. Nayer H, Weir EG, Sheth S, Ali SZ. Primary pancreatic lymphomas: A cytopathologic analysis of a rare malignancy. Cancer. 2004; 102: 315–321
19. Volmar KE, Routbort MJ, Jones CK, Xie HB. Primary pancreatic lymphoma evaluated by fine-needle aspiration: Findings in 14 cases. Am J Clin Pathol. 2004; 121: 898-903.
20. Ji Y, Kuang TT, Tan YS, Chen Y, Zeng HY, Jin DY. Pancreatic primary lymphoma: A case report and review of the literature. Hepatobiliary Pancreat Dis Int. 2005; 4: 622-6.
21. Arcari A, Anselmi E, Bernuzzi P, *et al*. Primary pancreatic lymphoma. Report of five cases. Haematologica. 2005; 90: ECR09.
22. Lee MK, Jeon SW, Lee YD, *et al*. A case of primary pancreatic non-Hodgkin's lymphoma. Korean J Intern Med. 2006; 21: 123-6.

23. Wang YJ, Jeng CM, Wang YC, Chang PP, Wang TH. Primary pancreatic Burkitt's lymphoma mimicking carcinoma with obstructive jaundice and very high CA19-9. Eur J Gastroenterol Hepatol. 2006; 18(5): 537-40.
24. Lin H, Li SD, Hu XG, Li ZS. Primary pancreatic lymphoma: Report of six cases. World J Gastroenterol. 2006; 12: 5064-7.
25. Basu A, Patil N, Mohindra P, *et al*. Isolated non-Hodgkin's lymphoma of the pancreas: Case report and review of literature. J Can Res Ther. 2007; 3: 236-9.
26. Liakakos T, Misiakos EP, Tsapralis D, Nikolaou I, Karatzas G, Macheras A. A role for surgery in primary pancreatic B-cell lymphoma: A case report. J Med Case Rep. 2008; 2: 167.
27. Hashimoto M, Umekita N, Noda K. Non-Hodgkin lymphoma as a cause of obstructive jaundice with simultaneous extrahepatic portal vein obstruction: A case report. World J Gastroenterol. 2008; 14: 4093-5.
28. Sağlam M, Yilmaz MI, Mas MR, *et al*. A case of pancreatic Burkitt lymphoma: Radiological findings. Diagn Interv Radiol. 2009; 15: 39-42.
29. Francisco B, Lucas M, Del Mar AM, Maria F-NJ, Manuel F-S, Amparo V. Abdominal pain as the first manifestation of primary pancreatic lymphoma. J Pediatr Hematol Oncol. 2009; 31(3): 222-3.
30. Haji AG, Sharma S, Majeed KA, Vijaykumar DK, Pavithran K, Dinesh M. Primary pancreatic lymphoma: report of three cases with review of literature. Indian J Med Paediatr Oncol. 2009; 30: 20-3.
31. Sugishita H, Watanabe Y, Yamamoto Y, *et al*. Primary pancreatic lymphoma: The role of surgical treatment. Case Rep Gastroenterol. 2010; 4: 104-10.
32. Abe Y, Tamura K, Sakata I, *et al*. Unique intense uptake demonstrated by (18) F-FDG positron emission tomography/computed tomography in primary pancreatic lymphoma: A case report. Oncol Lett. 2010; 1: 605-7.
33. Alexander RE, Nakeeb A, Sandrasegaran K, *et al*. Primary pancreatic follicle center-derived lymphoma masquerading as carcinoma. Gastroenterol Hepatol (NY). 2011; 7: 834-8.
34. Anderloni A, Genco C, Ballarè M, Carmagnola S, Battista S, Repici A. A case of primary pancreatic non-Hodgkin B-cell lymphoma mimicking autoimmune pancreatitis. J Gastrointestin Liver Dis. 2015; 24: 245-8.
35. Fukuba N, Moriyama I, Ishihara S, *et al*. Primary pancreatic malignant lymphoma diagnosed from endoscopic ultrasound-guided fine-needle aspiration findings. Internal Medicine. 2016; 55(1): 31-5.
36. Yu L, Chen Y, Xing L. Primary pancreatic lymphoma: Two case reports and a literature review. OncoTargets and therapy. 2017; 10: 1687-94.
37. Boninsegna E, Zamboni GA, Facchinelli D, *et al*. CT imaging of primary pancreatic lymphoma: Experience from three referral centres for pancreatic diseases. Insights Imaging. 2018; 9: 17-24.
38. Konjeti VR, Hefferman GM, Paluri S, Ganjoo P. Primary pancreatic Burkitt's lymphoma: A case report and review of the literature. Case Rep Gastrointest Med, 2018; vol 2018, 4 pages.
39. Rock J, Bloomston M, Lozanski G, Frankel WL. The spectrum of hematologic malignancies involving the pancreas: Potential clinical mimics of pancreatic adenocarcinoma. Am J Clin Pathol. 2012; 137(3): 414-22.
40. Johnson EA, Benson ME, Guda N, Pfau PR. Differentiating primary pancreatic lymphoma from adenocarcinoma using endoscopic ultrasound characteristics and flow cytometry: A case-control study. Endoscopic Ultrasound. 2014; 3(4): 221-5.
41. Ghai S, Pattison J, Ghai S, O'Malley ME, Khalili K, Stephens M. Primary gastrointestinal lymphoma: Spectrum of imaging findings with pathologic correlation. Radiographics. 2007; 27: 1371-88
42. Saif MW. Primary Pancreatic Lymphomas. JOP. 2006; 7(3): 262-73.
43. Merkle EM, Bender GN, Brambs HJ. Imaging findings in pancreatic lymphoma: Differential aspects. AJR Am J Roentgenol. 2000; 174(3): 671-5.
44. Lawler LP, Horton, KM, Fishman EK. Peripancreatic masses that simulate pancreatic disease: spectrum of disease and role of CT. Radiographics. 2003; 23(5): 1117-31.
45. Teefey SA, Stephens DH, Sheedy PF 2nd. CT Appearance of primary pancreatic lymphoma. Gastrointest Radiol. 1986; 11(1): 41-43.
46. Alomari AK, Ustun B, Aslanian HR, Ge X, Chhieng D, Cai G. Endoscopic ultrasound-guided fine-needle aspiration diagnosis of secondary tumors involving the pancreas: An institution's experience. CytoJournal. 2016; 13:1.
47. Khashab M, Mokadem M, Dewit J. Endoscopic ultrasound-guided fine-needle aspiration with or without flow cytometry for the diagnosis of primary pancreatic lymphoma - A case series. Endoscopy. 2010; 42(3): 228-31.