

CASE REPORT

Primary Pancreatic T-Cell Lymphoma - A Case Report and Literature Review

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ABSTRACT

Primary pancreatic lymphoma is a rare form of extranodal malignant lymphoma. Most cases show a diffuse large B-cell immunophenotype. Hereby we describe the case of a 62-year-old man that was admitted in the emergency department of São Paulo Hospital with abdominal pain, weight loss and jaundice. Imaging exams showed a bulky resectable tumour in the pancreatic head. The patient underwent pancreatoduodenectomy and the histopathological analysis showed a primary pancreatic T-cell lymphoma. He received chemotherapy and subsequent autologous stem-cell transplantation. He presented a complete remission with no evidence of disease in the 8-months follow up. Literature review on this disease recommends the diagnostic to be done with endoscopic or percutaneous biopsy and the best treatment choice is systemic therapy, but evidence is scarce. There are few cases of T-cell primary pancreatic lymphoma described in the literature, with a worse prognosis compared to other immunophenotypes.

INTRODUCTION

Primary pancreatic lymphomas (PPL) are a rare group of tumours that represent 0.5% of pancreatic tumours [1, 2]. The most frequent subtype is diffuse large B-cell lymphoma [3]. In imaging exams they can be misdiagnosed as adenocarcinomas [4, 5, 6] but the histopathological diagnosis is essential as current evidence favours chemotherapy and radiotherapy as the main treatment [7, 8]. Pancreatic T-cell lymphomas are extremely rare with less than ten cases published - the majority in eastern countries - and have a poor prognosis [4]. We hereby report a case of a primary pancreatic T-cell lymphoma recently treated in our service in Brazil.

CASE REPORT

A sixty-two-year-old caucasian man presented at the emergency department of São Paulo Hospital (Federal University of São Paulo) in July/2020 with cholestatic symptoms initiated 40 days before admission. His complaints also were progressive epigastric pain, itchy

skin and gynecomastia. He denied fever or night sweat, but had a weight loss of about 8 kg. His previous medical records revealed a previous history of smoking (ceased 15 years ago) and a current alcohol intake of about 45 g/day for the last 50 years. He also had a hiatus hernia but denied any medication use or allergies. He was born in São Paulo and there was no family history of malignancy in first-degree relatives. Physical examination revealed jaundice and right upper quadrant pain on abdominal palpation. The vital signs were normal, he was eutrophic and had no abdominal mass, peripheral lymphadenopathy or nasal/oropharyngeal lesions.

The laboratory tests revealed a normal blood count, renal function, albumin and coagulation tests. Total bilirubin was 18 mg/dL (normal <1), direct bilirubin was 15.5 mg/dL (normal <0.6). Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 88 and 66 U/L respectively (both normal <40). Alkaline phosphatase (ALP) was 644 U/L (normal <105) and gamma glutamyl transferase (GGT) was 260 U/L (normal <60). The high-sensitivity C - reactive protein (hsCRP) was 37 mg/L (normal <1). Anti-hepatitis C virus antibody (anti HCV-Ab) and hepatitis B virus surface antigen (HBs-Ag) were in normal levels and HIV serology was negative. Serum CA-125 was 12.5 U/ml (normal <35), Carcinoembryonic antigen (CEA) was 6.5 ng/mL (normal <5.5) and CA 19-9 was >10.000 U/mL (normal <34).

A computed tomography (CT) scan and a magnetic resonance imaging (MRI) were performed and revealed a large tumour centered in the pancreatic head involving the gastroduodenal artery and was close to the superior

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Abbreviations ALP alkaline phosphatase; CEA carcinoembryonic antigen; PPL primary pancreatic lymphomas vein
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mesenteric vein (**Figure 1**) and inferior vena cava (**Figure 2**). It's size was 7.3 cm in the largest axis and had prominent mesenteric and hepatic hilum lymph nodes. The magnetic resonance cholangiopancreatography (MRCP) showed main bile duct and pancreatic duct enlargement. Esophagogastroduodenoscopy showed an extrinsic compression involving the second and third part of duodenum, with a normal mucosa (**Figure 3**).

Due to tumour resectability and unsettled radiological diagnosis we chose to perform a pancreatoduodenectomy (**Figure 4**). Intraoperatively we found a bulky mass with a strong adhesion to the superior mesenteric vein, that needed to be respected and a portomesenteric vascular anastomosis was performed. The patient had a good surgical recovery and was discharged from hospital 15 days after the procedure. The pathology report revealed a non-Hodgkin matures T-cell Lymphoma (**Figure 5**). The Epstein-Barr virus (EBV)-RNA in situ hybridization study was negative.

The patient received adjuvant chemotherapy with 6 cycles of CHOP (cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone) regimen and underwent

autologous stem-cell transplantation by the oncohematology service. In the 8th postoperative month, the patient was asymptomatic with no sign of disease recurrence in the imaging follow up.

DISCUSSION

The most frequent histological type of pancreatic tumours is adenocarcinoma with about 85% of all cases, followed by neuroendocrine tumours with an incidence of about 5% [9]. In the bottom of the list are less frequent types such as sarcomas, metastasis and squamous cells carcinomas. Primary pancreatic lymphomas are rare, comprising about 0.5% of pancreatic cancers and less than 2% of extranodal lymphomas [1, 2]. Diagnostic criteria for PPL include: lack of peripheral lymphadenopathy; lack of involvement of mediastinal lymph node; normal peripheral white blood cells count; pancreatic mass with the involvement of lymph nodes confined to the pancreas; lack of involvement of liver or spleen.

The most frequent subtype of PPL is diffuse large B-cell lymphoma accounting for 59 to 80% of the cases [4, 7, 10].

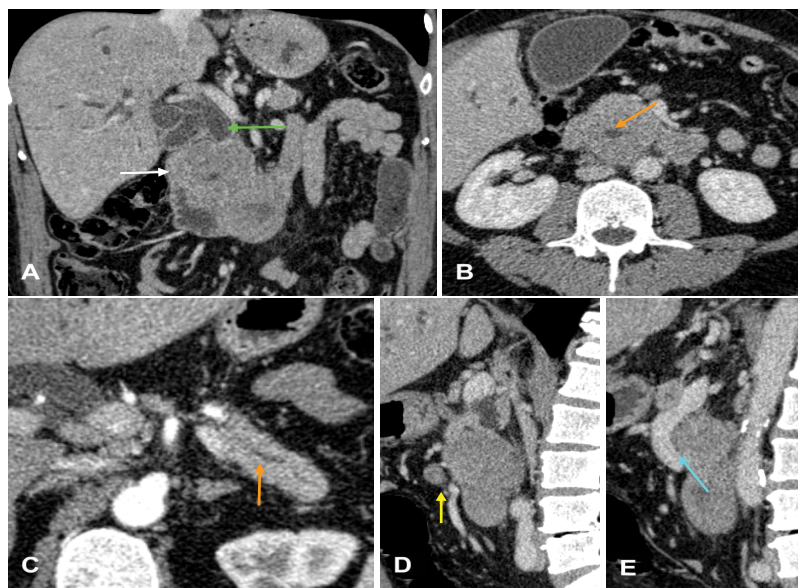


Figure 1. Upper abdomen CT scan with venous contrast enhancement. **(a)**. In the coronal view, white arrow shows bulky tumour in the pancreatic head, green arrow shows bile ducts enlargement. **(b, c)**. In the axial view, orange arrows show pancreatic duct enlargement. **(d, e)**. In the sagittal view, yellow arrow show lymph node enlargement inferior to renal hilum and blue arrow show no invasion of inferior mesenteric vein.

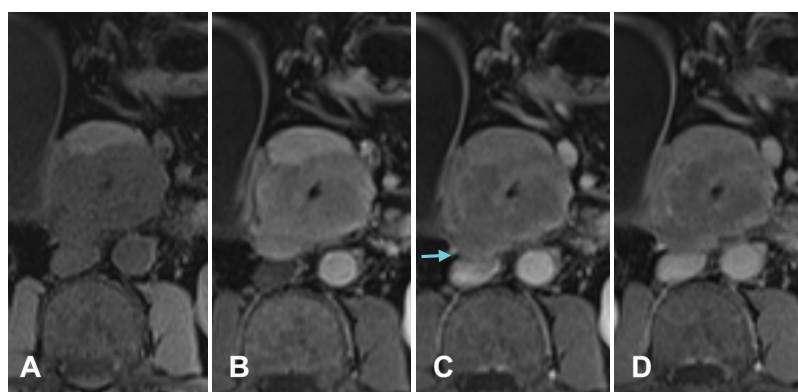


Figure 2. Upper abdomen MRI in axial view. **(a)**. no contrast enhancement, **(b)**. arterial phase, **(c)**. portal venous phase, **(d)**. equilibrium phase. Blue arrow shows close contact with inferior vena cava.

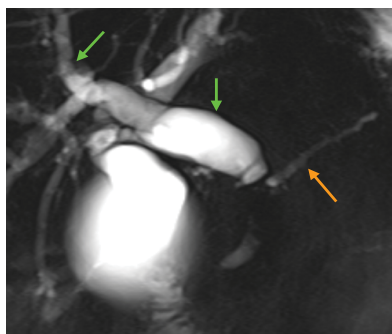


Figure 3. MRCP shows intra and extrahepatic bile duct enlargement (green arrow) and pancreatic duct enlargement (orange arrow).

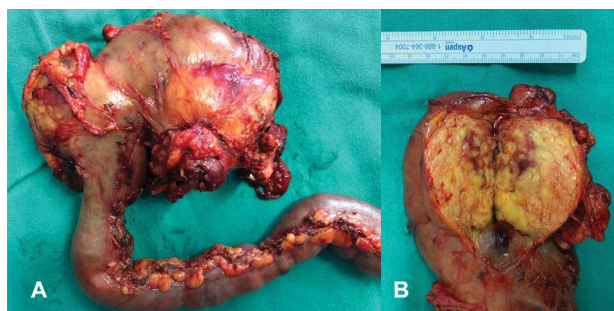


Figure 4. Pancreatoduodenectomy surgical (a). specimen in anatomic position and (b). cut in tumour site (B).

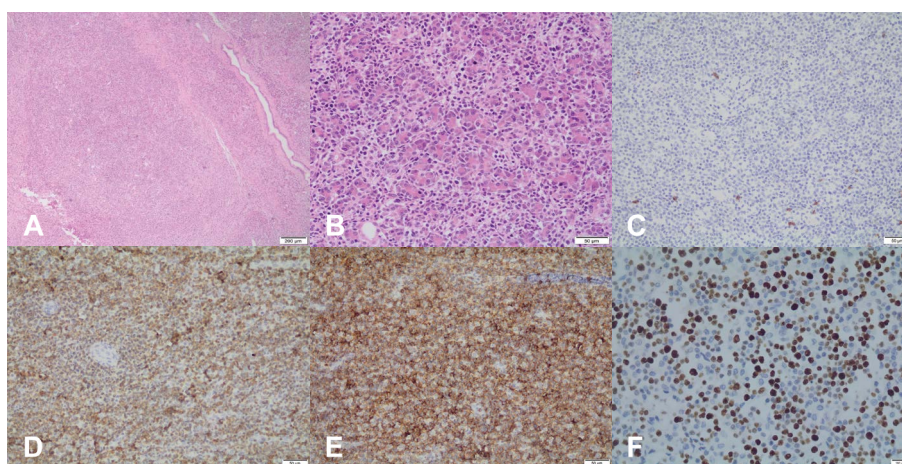


Figure 5. Histopathological analysis showing atypical lymphoid cells in hematoxylin and eosin staining ((a). 250 µm and (b). 50 µm). Immunohistochemical analysis showed CD20 negative cells ((c). 50 µm); CD3/CD8 positive cells ((d, e). 50 µm) and KI-67 expression in 60-80% neoplastic cells ((f). 50 µm).

Table 1. Publication information, patient characteristics, treatment and outcome.

Author	Country	Year	Age	Sex	Disease treatment	Follow up
Satake <i>et al.</i> [11]	Japan	1991	52	M	ChT	DOD 6m
			48	M	None	DOD 8m
Nishimura <i>et al.</i> [4]	Japan	2001	54	M	ChT	DOD 2m
			46	F	ChT + S	NED 4m
Matsubayashi <i>et al.</i> [12]	Japan	2002	82	M	None	DOD 2m
Aloui-Kasbi <i>et al.</i> [13]	Tunisia	2005	11	M	None	DOD 0m PMD
Galarreta <i>et al.</i> [14]	Peru	2012	22	F	None	DOD 0m PMD
Liu <i>et al.</i> [2]	China	2013	62	M	S	DOD 6m
Facchinelli <i>et al.</i> [22]	Italy	2018	NI	NI	None	DP, 31m
Chon <i>et al.</i> [15]	Republic of Korea	2020	80	F	ChT + RT	DOD 1m
Current study	Brazil	2021	62	M	S + ChT	NED 8m

ChT Chemotherapy; DOD Died of disease; DP Disease progression; NED No evidence of disease; NI Not informed; PMD post-mortem diagnosis; RT Radiotherapy; S Surgery

T-cell pancreatic lymphoma is a very rare entity, with 10 cases reported in the literature, most of them in eastern countries. **Table 1** presents data available about these case reports.

The most common clinical presentation of PPL is with nonspecific symptoms such as abdominal pain, nausea, vomiting, weight loss and abdominal mass in the physical examination [2, 11]. Patients can also develop cholestatic symptoms, duodenal obstruction or acute pancreatitis. B-symptoms like night sweats, fever and chills can also be present, however it's uncommon [2, 5].

Laboratory exams usually show an elevation of ALP, GGT, AST, ALT and bilirubins [2]. High levels of CA 19-9 are not common [1, 2]. Lactate Dehydrogenase (LDH) and β 2-microglobulin are helpful for diagnosis and prognosis - although they're not specific markers [1, 6, 12], high levels indicate a worse evolution of the disease [1].

CT-scan and MRI often show a large, well-defined bulky mass centered on the pancreatic head, with homogeneous contrast enhancement [5, 6, 13, 14, 15]. Pancreatic duct dilatation and vascular infiltration are rare in PPL and can help to distinguish it from adenocarcinoma. Lymphadenopathy below the renal veins is also suggestive of lymphoma [5, 6]. Some cases may present with a poorly-defined infiltrative mass or diffuse pancreatic enlargement - the differential diagnosis of auto-immune pancreatitis should be done dosing serum IgG4 [5, 16]. Fluoro-deoxy-glucose positron emission tomography (FDG-PET/CT) can be useful in diagnosis and staging, as the reported maximal standardized uptake values (SUVmax) range from 7.4 to 26.5 - much higher values when compared to adenocarcinoma (SUVmax ranging from 2 to 12)[5, 17].

The biopsy is essential for choosing the best treatment. In suspicion of a pancreatic lymphoma an endoscopic ultrasonography (EUS) with fine needle aspiration (FNA) is required to confirm the diagnosis and the immunophenotype, which should be done by experienced endoscopists [18]. Percutaneous FNA guided by CT or ultrasonography (US) is an alternative and, in case of insufficient material for diagnosis, a surgical biopsy by laparoscopy or laparotomy should be considered [8, 17] - especially when flow cytometry is not available [17].

The treatment of choice in PPL is chemotherapy - similar to the treatment applied to extranodal non-Hodgkin lymphoma - and it consists in six to eight cycles of CHOP (cyclophosphamide, doxorubicin and vincristine + prednisolone) [1, 3]. Rituximab can be added (R-CHOP) to B-cell lymphomas [3] and some authors describe good response to stem cell transplantation when completed chemotherapy [8] or in case of relapsed/refractory disease [19, 20, 21, 22]. Some papers also advocate the use of radiotherapy combined with chemotherapy [8, 20].

The role of surgical interventions remains controversial. Most institutions save it for symptomatic interventions - like biliary and/or gastric bypass due to tumor obstructions - or in cases that require an incisional

biopsy [1, 3, 8]. However some authors describe better outcomes when the resection was performed, probably due to debulking, allowing better chemotherapy penetration [6]. Surgery may also be proposed as a rescue treatment for patients that failed systemic treatment [6, 8]. Pancreatoduodenectomy in PPL is technically challenging due to large tumours and a normal pancreatic parenchyma which leads to great morbidity and it should not be routinely indicated as the upfront treatment [8]. In case of postoperative diagnosis, chemotherapy should be initiated for long term remission [3].

Literature shows an overall survival of about 2-6.5 years for patients with PPL [19] with a cure rate up to 30% in 5 years [1]. However, in our study the T-cell-PPL showed a much worse prognosis: most of the patients deceased within 8 months or less. The only two patients who survived received a combined treatment with chemotherapy and surgery. More research is necessary for proposing a standard treatment although the rarity of this disease makes it difficult to find quality evidence.

CONCLUSION

Primary pancreatic lymphoma is a rare disease with a challenging diagnosis by conventional imaging. The biopsy is essential and endoscopic ultrasonography with fine-needle aspiration is a valuable tool to perform it. Most cases show B-cell immunophenotype and have good results with chemoradiotherapy. Surgical intervention is reserved to diagnostic and palliative procedures and may be considered as a rescue treatment in selected cases. T-cell PPL is even rarer with a paucity of cases reported in literature. The prognosis is worse and the best therapeutic choice is not established due to scarce evidence.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Dunphy L, Abbas SH, Al Shoek I, Al-Salti W. Primary Pancreatic lymphoma: a rare clinical entity. *BMJ Case Rep* 2020; 13:e231292. [PMID: 31907215]
2. Liu W, Hua R, Zhang JF, Huo YM, Liu DJ, Sun YW. First report of primary pancreatic natural killer/T-cell nasal type lymphoma. *Eur Rev Med Pharmacol Sci* 2013; 17:318-22. [PMID: 23426534]
3. Zheng SM, Zhou DJ, Chen YH, Jiang R, Wang YX, Zhang Y, et al. Pancreatic T/histiocyte-rich large B-cell lymphoma: A case report and review of literature. *World J Gastroenterol* 2017; 23: 4467-4472. [PMID: 28706431]
4. Nishimura R, Takakuwa T, Hoshida Y, Tsujimoto M, Aozasa K. Primary Pancreatic Lymphoma: Clinicopathological Analysis of 19 Cases from Japan and Review of the Literature. *Oncology* 2001; 60:322-329. [PMID: 11408800]

5. Anand D, Lall C, Bhosale P, Ganeshan D, Qayyum A. Current update on primary pancreatic lymphoma. *Abdom Radiol (NY)* 2016; 41:347-55. [PMID: 26830418]
6. Battula N, Srinivasan P, Prachalias A, Rela M, Heaton N. Primary pancreatic lymphoma: diagnostic and therapeutic dilemma. *Pancreas* 2006; 33:192-4. [PMID: 16868486]
7. Sadot E, Yahalom J, Do RK, Teruya-Feldstein J, Allen PJ, Gönen M, et al. Clinical features and outcome of primary pancreatic lymphoma. *Ann Surg Oncol* 2015; 22:1176-84. [PMID: 25341750]
8. Grimison PS, Chin MT, Harrison ML, Goldstein D. Primary pancreatic lymphoma--pancreatic tumours that are potentially curable without resection, a retrospective review of four cases. *BMC Cancer* 2006; 6:117. [PMID: 16674812]
9. Ilic M, Ilic I. Epidemiology of pancreatic cancer. *World J Gastroenterol* 2016; 22:9694-9705. [PMID: 27956793]
10. Lin H, Li SD, Hu XG, Li ZS. Primary pancreatic lymphoma: report of six cases. *World J Gastroenterol* 2006; 12:5064-7. [PMID: 16937508]
11. Satake K, Arimoto Y, Fujimoto Y, Nishiwaki H, Nishino H, Umeyama K, et al. Malignant T-cell lymphoma of the pancreas. *Pancreas* 1991; 6:120-4. [PMID: 1994376]
12. Matsubayashi H, Takagaki S, Otsubo T, Iiri T, Kobayashi Y, Yokota T, et al. Pancreatic T-cell lymphoma with high level of soluble interleukin-2 receptor. *J Gastroenterol* 2002; 37:863-7. [PMID: 12424573]
13. Aloui-Kasbi N, Mbarek S, Bellagha I, Hammou A. Primary T-cell lymphoma of the pancreas in children. *Tunis Med* 2005; 83:114-6. [PMID: 15969235]
14. Galarreta CI, Yopez E, Velez C, Aita G. Primary T cell lymphoma of the pancreas: clinical case report. *Rev Gastroenterol Peru* 2012; 32:423-8. [PMID: 23307095]
15. Chon HK, Choi KH, Kim TH. Primary Pancreatic Natural Killer/T-Cell Lymphoma. *Pancreas* 2020; 49:e21-e23. [PMID: 32168254]
16. 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; 49:80-9. [PMID: 13884035]
17. Nayer H, Weir EG, Sheth S, Ali SZ. Primary pancreatic lymphomas: a cytopathologic analysis of a rare malignancy. *Cancer* 2004; 102:315-21. [PMID: 15386314]
18. Sadaf S, Loya A, Akhtar N, Yusuf MA. Role of endoscopic ultrasound-guided-fine needle aspiration biopsy in the diagnosis of lymphoma of the pancreas: A clinicopathological study of nine cases. *Cytopathology* 2017; 28:536-541. [PMID: 28737285]
19. Islam S, Callery MP. Primary pancreatic lymphoma--a diagnosis to remember. *Surgery* 2001; 129:380-3. [PMID: 11231470]
20. Behrns KE, Sarr MG, Strickler JG. Pancreatic lymphoma: is it a surgical disease? *Pancreas* 1994; 9:662-7. [PMID: 7809023]
21. Zahid U, Akbar F, Amaraneni A, Husnain M, Chan O, Riaz IB, et al. A Review of Autologous Stem Cell Transplantation in Lymphoma. *Curr Hematol Malig Rep* 2017; 12:217-226. [PMID: 28478586]
22. Facchinelli D, Sina S, Boninsegna E, Borin A, Tisi M, Piazza F, et al. Primary Pancreatic Lymphoma: Clinical Presentation, Diagnosis, Treatment and Outcome. *Eur J Haematol* 2020; 105:468-475. [PMID: 32542880]