

## CASE REPORT

# Primary Pancreatic T-cell Lymphoma - a case report and literature review

Franz R. A. Torrez\*

Department of Surgery, São Paulo Hospital, Federal University of São Paulo, SP, Brazil

### 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 an 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 [5,6] but the histopathological diagnosis is essential as current evidence favours chemotherapy and radiotherapy as the main treatment [7,8]. Pancreatic T-cell lymphoma 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 62 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 8kg.

His previous medical records revealed a previous history of smoking (ceased 15 years ago) and a current alcohol intake of about 45g/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 37mg/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).

Due to tumour resectability and unsettled radiological diagnosis we chose to perform a pancreatoduodenectomy (image 4). Intraoperatively we found a bulky mass with a strong adhesion to the superior mesenteric vein, that needed to be resected 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 mature T-cell Lymphoma (image 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 an autologous stem-cell transplantation by the oncohematology service. In the 8<sup>th</sup> 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%<sup>[9]</sup>. 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<sup>[1,2]</sup>. Diagnostic criteria for PPL include: lack of peripheral lymphadenopathy; lack of involvement of mediastinal lymph node; normal peripheral white

Received September 14<sup>th</sup>, 2020 - Accepted March 18<sup>th</sup>, 2021

**Keywords** Normal lipase pancreatitis Gabapentin induced bullous pemphigoid Azathioprine induced pancreatitis

**Correspondence:** Arun Muthukumar Department of Anaesthesia and Critical Care Calcutta National Medical College and Hospital, Kolkata, West Bengal, India

**Tel** +919445544089

**E-mail** arunmuthukumar27@gmail.com

blood cells count; pancreatic mass with the involvement of lymph nodes confined to the pancreas; lack of involvement of liver or spleen [16].

The most frequent subtype of PPL is diffuse large B-cell lymphoma accounting for 59 to 80% of the cases[4,7,10]. 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[2,19]. 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  $\beta$ 2-microglobulin are helpful for diagnosis and prognosis - although they're not specific markers[1,6], 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]. 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]. 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].

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[21]. 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.

### ACKNOWLEDGEMENTS

The authors thank Drs. Julia de Castro Vieira Veloso and Glaucio Rodrigo Silva de Siqueira from Radiology Department for image assistance. We also thank the patient for his consent to this publication.

### REFERENCES

1. Flamm A, Sachdev S, Dufresne F. Gabapentin-Induced Bullous Pemphigoid. J Am Osteopath Assoc 2017; 117: 191-193. PMID: 28241331.
2. Zachariae CO. Gabapentin-induced bullous pemphigoid. Acta Derm Venereol 2002; 82: 396-397. PMID: 12430752.
3. Weissman S, Aziz M, Perumpail RB, Mehta TI, Patel R, Tabibian JH. Ever-increasing diversity of drug-induced pancreatitis. World J Gastroenterol 2020; 26: 2902-2915. PMID: 32587438.