

# Pancreatic Masses: Not All of Them are Pancreatic Adenocarcinoma: Differential Diagnosis

## Pankreatik Kitleler: Hepsi Adenokarsinom Değildir

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**ABSTRACT** Primary pancreatic lymphoma (PPL) is a very rare tumor of the pancreas and can mimic pancreatic adenocarcinoma (PAC) clinically and radiographically. The rarity of PPL and its similarity to PAC can potentially lead to misdiagnosis of a minority of potentially curable patients. However, the management of PPL differs greatly from that of PAC. The most appropriate way of diagnosis in these patients is fine-needle aspiration biopsy before surgery. We report two cases with PPL presenting with a mass in the pancreas. One the patients was diagnosed after major open surgery and the other one was diagnosed by fine-needle aspiration biopsy.

**Key Words:** Pancreas; lymphoma; adenocarcinoma

**ÖZET** Primer pankreatik lenfoma (PPL), pankreasın nadir tümörlerinden biri olup, klinik ve radyolojik olarak pankreas adenokarsinomunu (PAK) taklit edebilmektedir. PPL' nin seyrekliği ve PAK'a olan benzerliği, iyileşebilir hastaların küçük bir kısmında yanlış tanı almasına neden olabilmektedir. PPL tedavisinin PAK'tan farklı olması, bu hastaların tedavisi açısından önem arz etmektedir. Bu hastalarda PPL tanısı koymamanın en kolay yolu, cerrahi öncesi yapılan iğne aspirasyon biyopsisidir. Pankreasta kitle ile ortaya çıkan iki PPL vakasını sunmaktayız. Bu hastalardan birine iğne aspirasyon biyopsisi ile tanı konurken, diğerine tanı büyük batın cerrahisi sonrası konmuştur.

**Anahtar Kelimeler:** Pankreas; lenfoma; adenokarsinom

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**P**Primary pancreatic lymphoma (PPL) is an uncommon form of extranodal non-Hodgkin's lymphoma (NHL) and potentially curable without surgical resection.

The incidence of PPL is estimated to be less than 1% of all NHL and 0.2-4.9% of all pancreatic malignancies.<sup>1,2</sup> However, involvement of the pancreas by NHL has been frequently reported.<sup>3,4</sup> PPL is defined as involvement of only pancreatic tissue or additional involvement of pancreatic lymph nodes without any organ or lymph node.<sup>5</sup> PPL can mimic pancreatic adenocarcinoma (PAC) clinically and radiographically. Treatment and prognosis of these tumors are utterly different. Therefore, PPL and PAC must be diagnosed accurately. PPL has a high cure rate with chemotherapy and/or radiotherapy. However, the diagnosis of PPL is very difficult before surgery.<sup>6-8</sup>

We report two cases of PPL presenting with a mass in the pancreas. One of the patients was diagnosed after major open surgery and the other one was diagnosed by fine-needle aspiration biopsy.

## CASE REPORTS

### CASE 1

A 58-year-old female was admitted to our hospital due to abdominal pain in September 2007. She had seven kilograms of weight loss in 15 days. Physical examination revealed a palpable non-tender epigastric mass and icteric sclera. The patient had a normal blood count. Biochemical investigation revealed the following values: total bilirubin 7.84 mg/dl; alanine aminotransferase (ALT) 471 U/l; aspartate aminotransferase (AST) 269 U/l; gamma glutamyltranspeptidase (GGT) 434 U/l and alkaline phosphatase (ALP) 445 U/l. A tumor marker, serum carbohydrate antigen 19-9 (CA 19-9), was found increased as 83,71 U/ml (Normal range 0-31 U/ml). Abdominal ultrasound (US) revealed a mass in the head of the pancreas and abdominal computerized tomography (ACT) confirmed a 5 x 6.5 cm mass with dilatation of bile duct and normal gallbladder image. ACT with angiography revealed the mass that invaded the superior mesenteric vein with multiple lymphadenopathies in the peripancreatic region that were measured as 2.5 cm.

Percutaneous transhepatic cholangiography (PTC) confirmed the dilatation of the proximal bile duct and stenosis of the distal bile duct due to external compression characterized by shoulder sign (Figure 1). Percutaneous transhepatic drainage was performed. The patient underwent surgical resection of the tumor by means of a modified Whipple's procedure and Roux-n-Y reconstruction of the gastrointestinal tract. Pathologic examination of the surgical specimen revealed malignant lymphoma. Tumor cells consisted of large and atypical lymphocytes (Figure 2a) and possessed positivity for CD 20, a B cell marker protein, (Figure 2b), CD 79 alpha and also for Ki-67 index (82%). Tumor cells were negative for the T cell marker protein CD 3. The diagnosis was diffuse large B-cell lymphoma stage II E according to Ann Arbor Classification (Figure 2c).

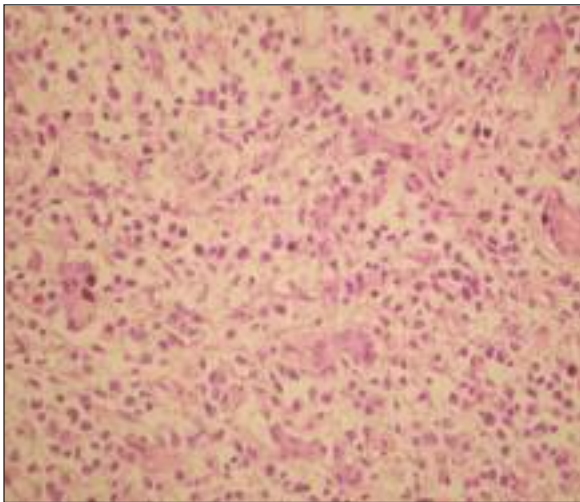


**FIGURE 1:** PTC image showed dilatation of the proximal bile duct and stenosis of the distal bile duct due to external compression.

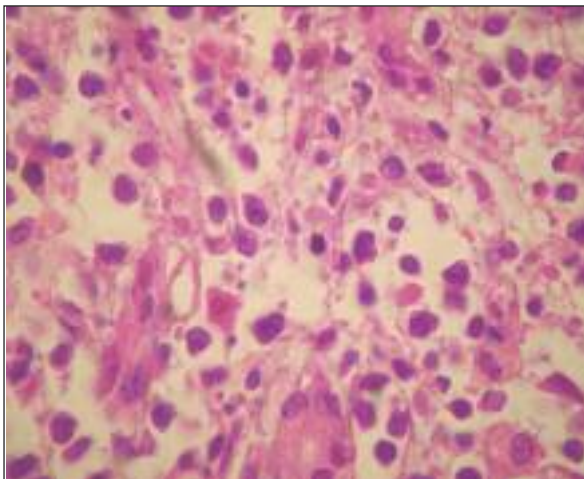
Chemotherapy protocol was implemented as six cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) and eight cycles of rituximab. In the follow-up period, the patient was in complete remission.

### CASE 2

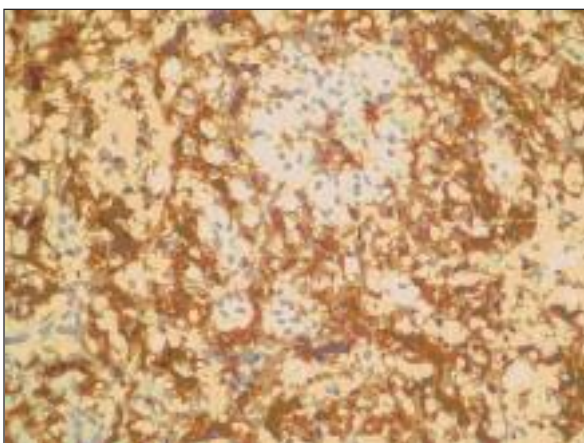
A 61-year-old female was admitted to hospital with the complaints of abdominal pain and jaundice in September 2008. Physical examination revealed a palpable non-tender mass in the epigastric region and icteric sclera and skin. Sedimentation was 130 mm/h and blood count was normal. Biochemical investigation revealed the following values: total bilirubin, 11,25 mg/dl; ALT, 626 U/l; AST, 360 U/l; GGT, 495 U/l and ALP, 158 U/l. US and CT imaginations of the abdomen revealed the mass (Figure 3a). PTC revealed dilatation of the proximal bile duct and stenosis of the distal bile duct by external compression of mass characterized by shoulder sign (Figure 3b). CT-guided fine-needle aspiration biopsy (FNAB) was performed. Pathologic examination revealed a malignant lymphoma. Tumor cells



a (Hematoxylin-eosin x100)

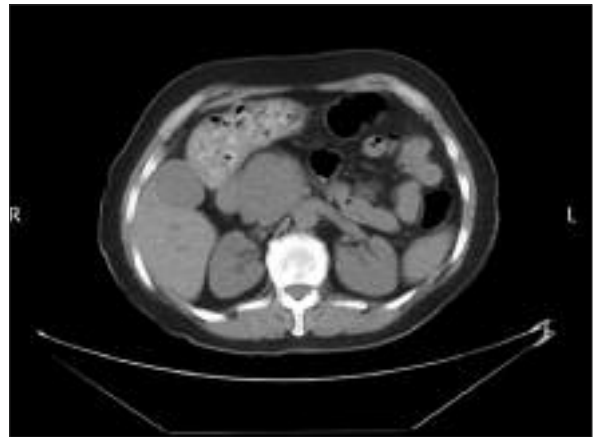


b (Hematoxylin-eosin x400)



c (Immunoperoxidase x200)

**FIGURE 2:** Hematoxylin-eosin staining of the tumor: infiltration of atypical lymphocytes, surrounding the pancreatic ductus (a, b), These lymphoma cells were positive for CD20 (c)



a



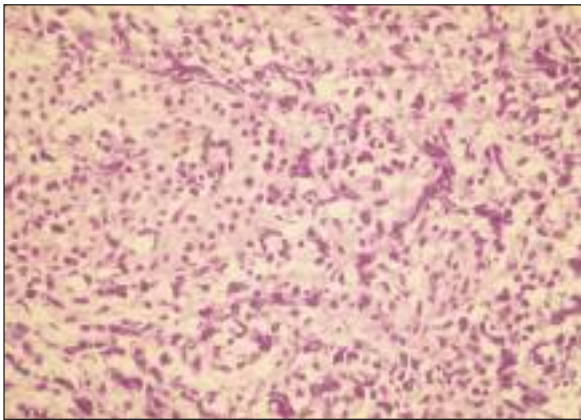
b

**FIGURE 3:** CT image of the abdomen showing a 7x5 cm pancreatic mass at the head of pancreas and dilatation of choledoch and bile ducts (a) and PTC image reveals extrinsic dilatation of the proximal bile duct and stenosis of the distal bile duct by external compression (b).

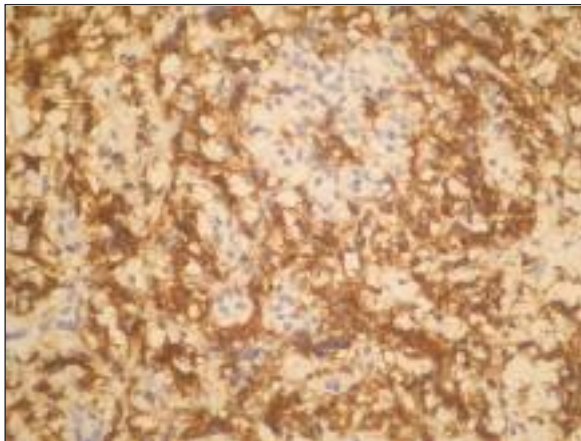
had membrane staining with CD 20, CD 10 and LCA (Figure 4). Ki-67 index was positive as 80%. She was diagnosed as diffuse large B-cell lymphoma stage I E according to Ann Arbor classification. Percutaneous transhepatic drainage was performed and a biliary stent was inserted. Six cycles of CHOP and eight cycles rituximab chemotherapy were administered. After the treatment, she is still followed up with complete remission.

## DISCUSSION

NHL frequently occurs at primary extranodal sites, most commonly in the gastrointestinal tract



a (Hematoxylin-eosin x100)



b (Immunoperoxidase x200)

**FIGURE 4:** Hematoxylin-eosin staining of the tumor: infiltration of lymphocytes, with the island of Langerhans (a) and positive staining for CD20 (b)

and rarely in the pancreas.<sup>9</sup> Clinically, PPL usually presents with the symptoms of the pancreatic head carcinoma. Abdominal pain, weight loss, jaundice, acute pancreatitis and small bowel obstruction are clinical manifestations. Elevation of transaminases, ALP and direct bilirubin are common findings of both pancreatic malignancies.<sup>10</sup> Tian et al suggested that CA 19-9 level essentially remained normal throughout the course of PAC tumors smaller than 5 cm in diameter, and CA 19-9 may be a useful indicator of treatment in patients with resectable tumors.<sup>11</sup> It may also increase in other malignancies including PPL invading particularly the upper gastrointestinal tract as described in the first case.<sup>12</sup> CA 19-9 level was mildly high in our first case at the beginning, but it was not measured in the second case. Therefore,

re, PPL can not be differentiated from PAC either clinically or laboratory investigations unless the diagnosis is based on the histopathological examination.

Imaging techniques, such as US and CT scan, are very important in the diagnosis and staging of pancreatic masses. Merkle et al. reported that the presence of a bulky localized tumor in the pancreas without any significant dilation of the main pancreatic duct supports a diagnosis of pancreatic lymphoma over adenocarcinoma. They described imaging findings in pancreatic lymphoma and they concluded that two different morphologic patterns of pancreatic involvement are seen on CT: a localized, well-circumscribed tumoral form and a diffuse enlargement infiltrating or replacing most of the pancreatic gland.<sup>13</sup> CT imaging of our cases revealed a mass located at the head of pancreas.

In case PPL is included in the differential diagnosis, biopsy of the pancreatic mass may avoid surgical procedure.<sup>14</sup> FNAB of pancreatic masses is considered a safe, rapid, and easy procedure with high diagnostic accuracy. Fisher et al. reported their experience about endoscopic ultrasound-guided fine-needle aspiration biopsy regarding solid pancreatic lesions. They observed sensitivity, specificity, positive predictive value, negative predictive value, accuracy and false-negative rate of endoscopic ultrasound-guided fine-needle aspiration biopsy as 94.3%, 100%, 100%, 72.2%, 95% and 5%, respectively.<sup>15</sup> FNAB is valuable in the diagnosis of PPL. In most of the patients, the diagnosis can be established without surgery. Laparotomy may be required for definitive diagnosis in some cases.<sup>16</sup> The first case was diagnosed after major open surgery, however the second one was diagnosed by fine-needle aspiration biopsy accurately.

Treatments of PPL and other pancreatic malignancies are different. Periampullary tumors except PPL are treated by Whipple pancreaticoduodenectomy which carries high operative and postoperative morbidity and mortality.<sup>17,18</sup> In literature, it was cited that PPL patients treated with chemotherapy and/or radiotherapy – without resection did not have worse outcomes than operated patients.<sup>2,14</sup>

Chemotherapy is the treatment of choice for most patients with PPL. The most common chemotherapeutic regimen includes cyclophosphamide, doxorubicin, vincristine and prednisone. Complete remission can be expected with chemotherapy in 63% to 77% of patients with large B-cell lymphoma. Rituximab is a monoclonal antibody directed against the CD20 antigen. It has been combined with CHOP resulting in improved response rates up to 85%, and long-term survival in these patients.<sup>19</sup> Radiotherapy has only limited use in the treatment of PPL.<sup>14</sup> Potential concerns about the safety of radiotherapy in this region may be unnecessary, as toxicity has been substantially reduced

with three dimensional treatment planning and conformal delivery of radiotherapy.<sup>20</sup> After the chemotherapy, both of the patients had complete remission in follow-up period although the second patient has not undergone to tumor resection.

In conclusion, PPL should be considered in the differential diagnosis of pancreatic tumors because treatment and prognosis of PPL are utterly different. The diagnosis of PPL is based on histopathological examination. The simplest way for diagnosis is FNAB before surgery. FNAB should be planned in all patients with a suspected PPL in imaging studies.

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