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Isolated non-Hodgkin’s lymphoma of the pancreas: Case report and review of literature

ABSTRACT
Background: Isolated primary pancreatic lymphoma (PPL) is a rare extra-lymphatic non-Hodgkin’s lymphoma comprising less than 1% of all extra-lymphatic lymphomas. It is seen in people of advanced age and there is a slight male preponderance. It is difficult to diagnose; the vague presenting symptoms and nonspecific laboratory/radiological findings make it difficult to differentiate the condition from pancreatic adenocarcinoma. Histopathological examination is of paramount importance to conclusively establish the diagnosis since the treatment involves lymphoma protocols, and prognosis and survival in PPL are considerably superior to that in adenocarcinoma pancreas.

Case Report: We report a case of isolated PPL diagnosed after Tru-Cut biopsy and immunohistochemistry after a thorough staging workup.

Result: The patient was treated with multi-agent combination chemotherapy followed by radiotherapy.

Discussion: A review of literature was done using a Medline search to determine the incidence and prevalence of isolated PPL and to note the diagnosis and management of previously reported cases.

Conclusion: An exceedingly rare entity, isolated PPLs need to be differentiated from pancreatic adenocarcinomas by histopathological evaluation since management is on the lines of other extralymphatic lymphomas and prognosis is significantly better.

KEY WORDS: Case report, histopathology, isolated primary pancreatic lymphoma, literature review, radiology, treatment

Primary pancreatic lymphoma (PPL) is a rare variety of extra-lymphatic non-Hodgkin’s lymphoma with a slight male preponderance; it presents with vague abdominal symptoms and an epigastric mass. More than 25% of non-Hodgkin’s lymphomas originate from extra-lymphatic organs; some involve the pancreas. However, isolated PPL is extremely rare, with less than 1% incidence. In a review of 207 cases of malignant pancreatic tumors, there were only three cases (1.5%) of pancreatic lymphoma.

Laboratory investigations and radiological studies cannot definitively differentiate this entity from pancreatic adenocarcinoma. Histopathological examination is essential to conclusively establish the diagnosis for these tumors. Treatment involves chemotherapy and radiation therapy using lymphoma protocols, and the prognosis and survival rates are significantly better than that of pancreatic adenocarcinoma. We report a case of isolated PPL diagnosed and treated at our institute and present a review of current literature on PPL.

CASE REPORT

A 42-year-old male farmer presented to our institute with 5 months’ history of obstructive jaundice, abdominal discomfort/distention, and yellowish discoloration of the eyes. At presentation his general condition was good; he had mild icterus and a Karnofsky performance score (KPS) of 80. Physical examination revealed non-tender hepatomegaly (5 cm below the right costal margin), without any other organomegaly or peripheral lymphadenopathy. Other systemic examination was unremarkable.

The hematological profile revealed increased total bilirubin (11.09 mg%) and direct bilirubin (8.79 mg%). Liver enzymes were raised, with serum alkaline phosphatase: 527 U/l, SGOT: 115 U/l, and SGPT: 82 U/l. Serum viral markers, including HIV, HBsAg, and HCV were nonreactive. Tumor markers included CA 19.9: 1130.57 U/ml, AFP: 1.06 ng/ml, and CEA: 1.7 ng/ml. A contrast-enhanced computed tomography (CECT) of the abdomen and pelvis showed a 8.93 × 6.47 × 9.91 cm large, lobulated, heterogeneously enhancing, soft tissue mass in the preaortic region, encasing the celiac and superior mesenteric arteries and the left renal vein, with compression of the inferior vena cava. The mass also extended into the hepatoduodenal ligament, obstructing the common bile duct and causing...
associated dilatation of the intrahepatic biliary radicals. The lesion was found to be arising from the body of the pancreas. The spleen and liver were normal. Pelvic examination did not reveal any abnormality [Figure 1]. A True-Cut biopsy from the abdominal mass was performed. The histopathological evaluation revealed round or ellipsoid lymphoma cells arranged diffusely, with scanty cytoplasm, thick chromatin, and clear nuclei suggestive of non-Hodgkin’s lymphoma - diffuse large B-cell type. Immunohistochemical staining revealed tumor cells positive for CD20 and BCL2 and negative for CD3, CD5, CD10, CK, EMA, synaptophysin, chromogranin, and neuron-specific enolase [Figure 2]. Bone marrow was uninvolved.

The final diagnosis was primary non-Hodgkin’s lymphoma of the pancreas: stage-IaEX. The treatment comprised of a combination of multiagent chemotherapy (R-CHOP) for six cycles, with 50% dose reduction in the first cycle in view of the deranged liver function and full doses in subsequent cycles, followed by involved-field radiotherapy. Blood investigations done after 6 courses of chemotherapy revealed total bilirubin: 0.89 mg%, serum alkaline phosphatase: 179 U/l, SGOT: 44 U/l, and SGPT: 41.0 U/l. Chest radiograph was within normal limits. CT scan done after completion of chemotherapy revealed significant regression of the primary pancreatic mass and the abdominal mass, with a few residual enlarged lymph nodes surrounding the celiac and superior mesenteric artery. The common bile duct compression was also relieved. The patient further received adjuvant involved-field radiation therapy to the pancreas and regional nodes, using the 3-D conformal technique and delivering a dose of 45 Gy in
25 fractions @ 1.8 Gy per fraction over 5 weeks. The patient completed the planned treatment without any interruptions or major complications. A follow-up CT scan of the abdomen and pelvis revealed complete regression of the disease.

### REVIEW OF LITERATURE

PPL is an extremely rare condition comprising only 0.2–4.9% of all pancreatic malignancies and less than 1% of cases of non-Hodgkin’s lymphoma.\(^1\) This tumor demonstrates a strong male preponderance (male to female ratio of 13:3) and affects relatively older patients (median age of 57.5 years).\(^2\)

It is diagnosed more commonly in immunosuppressed individuals, such as transplant recipients or HIV affected people. A possible causative link may be Epstein Barr virus infection.\(^3\) There have been reports of PPL diagnosed after radical resection. Percutaneous fine-needle aspiration cytology obtained under radiological guidance requires expert interpretation and is handicapped by the difficulty in performing immunohistochemistry on such limited material. Histopathological examination is usually mandatory to obtain a definitive diagnosis since symptoms and radiological features are quite similar to those of other pancreatic masses. The majority of the patients present with vague abdominal complaints such as dyspepsia, nausea, flatulence, abdominal cramps, jaundice, reflux, weight loss, bowel obstruction, palpable abdominal mass, and even diarrhea. Sometimes the clinical presentation mimics acute pancreatitis. Obstructive jaundice is less common than in pancreatic cancer. B-symptoms are uncommon at presentation.\(^4\) Ultrasound examination of the abdomen reveals the cause of the above symptoms in the form of a hyperechogenic mass located commonly in the pancreatic head, although tumors of the body and tail are also reported. Computed tomogram shows the characteristic diffuse enlargement of the head and body of the pancreas, with associated peripancreatic, periportal, and paraaortic lymphadenopathy.\(^5,6\) Merkle et al. reported that the presence of a bulky localized tumor in the pancreas, without significant dilation of the main pancreatic duct, supports a diagnosis of pancreatic lymphoma over adenocarcinoma.\(^7\) Enlarged lymph nodes below the renal vein also rules out pancreatic cancer and favors a diagnosis of pancreatic lymphoma. With current MRI techniques, evaluation of the origin and macroscopic infiltration of regional structures is possible due to the high intrinsic soft tissue content resolution. This facilitates good localization of masses in the region of the head of the pancreas.\(^8\)

Histopathologically, two different morphologic patterns of pancreatic involvement are seen in patients with PPL - a localized, well-circumscribed tumoral form and a diffusely enlarged infiltrating form replacing most of the pancreatic gland.\(^9\) Diagnostic criteria for PPL, as defined by Dawson et al., include: 1) neither superficial lymphadenopathy nor enlargement of mediastinal lymph nodes on chest radiography; 2) a normal leukocyte count in peripheral blood; 3) main mass in the pancreas with lymphnodal involvement confined to the peripancreatic region; and 4) no hepatic or splenic involvement.\(^10\) Diagnostic laparoscopy and directed biopsy from the head of pancreas lesion will reveal the nature of the lesion in most cases.\(^11\) CA 19.9 levels are normal or slightly elevated, allowing differentiation from pancreatic cancer.\(^12\) Most cases are primary low-grade non-Hodgkin’s lymphoma of the B-cell type. Many patients present after primary surgical excision or partial pancreatectomy or even Whipple’s procedure performed on exploratory laparotomy. However, if diagnosed preoperatively, the treatment strategy involves chemotherapy and radiotherapy on the lines of non-Hodgkin’s lymphoma, with surgical intervention being reserved for those cases requiring biliary or gastric bypass to relieve the symptoms.\(^13\) The most common regimens include CVP, CHOP, and MACOP-B. The addition of Rituximab to the CHOP regimen increases the complete response rate and prolongs event-free and overall survival in patients with diffuse large-B-cell lymphoma, without a clinically significant increase in toxicity.\(^14,17\) The role of radiation therapy in the management of PPL is not well defined. Local radiotherapy up to a total of 40 Gy has been used as consolidation after chemotherapy.\(^15\) Cure rates of up to 30% are reported for patients with PPL, which is much better than the dismal 5% 5-year survival rate in patients with pancreatic adenocarcinoma.\(^13,17\) To summarize, PPL is a rare variety of extranodal lymphoma presenting with nonspecific symptoms and yielding nonpathognomonic findings on laboratory and radiological investigation; the diagnosis can be confirmed on histopathological examination. Treatment results are significantly better than that for pancreatic adenocarcinomas and every effort should be made, therefore, to have an accurate pretreatment diagnosis and staging and to treat such patients with a combination of multiagent chemotherapy and adjuvant radiation therapy.

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