Case Report

Primary pancreatic lymphoma in a human immunodeficiency virus-positive patient

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ABSTRACT

Primary pancreatic lymphoma (PPL) is a rare occurrence. Lymphoma involving the pancreas may be seen more often. The incidence of non-Hodgkin's lymphoma (NHL) is expected to increase in patients suffering from acquired immune deficiency syndrome (AIDS) and also as age increases that is beyond sixth decade. NHL involving the pancreas is often seen in AIDS patients; however, PPL in a human immunodeficiency virus patient is uncommon and consists of a handful of case reports. Obstructive jaundice as a presentation is unusual. Histological diagnosis is often required to differentiate it from pancreatic adenocarcinoma, though there are certain features on computerized tomography and magnetic resonance imaging that favor lymphoma. We here describe a case of PPL in a young patient of AIDS who presented with obstructive jaundice and a palpable lump. Radiological features suggested it to be an adenocarcinoma. However, biopsy and immunohistochemistry helped to get the final diagnosis.

Key words: Acquired immune deficiency syndrome, pancreas, primary pancreatic lymphoma

INTRODUCTION

Gastrointestinal tract is the second most common site of non-Hodgkin's lymphomas (NHLs) after nodal lymphoma, accounting for 15-20% of all NHL cases.[1] Stomach is the most common site of extranodal gastrointestinal lymphoma. Although secondary involvement of the pancreas is seen often in cases of gastrointestinal lymphoma, primary pancreatic lymphoma (PPL) is an extremely rare disease that can mimic pancreatic carcinoma.[2] Fewer than 2% of extra-nodal malignant lymphomas and 0.5% of all pancreatic masses constitute PPL.[3,4] The incidence is expected to be higher in patients of human immunodeficiency virus (HIV) but occurrence of PPL in acquired immune deficiency syndrome (AIDS) is limited to case reports. Significant, however, is the fact that PPLs are potentially treatable. Until date, more than 150 cases of PPL have been reported in the English-language medical literature, but only two case reports of HIV and PPL.[5] There have been case reports of PPL from India, but HIV and PPL together is not yet reported from the subcontinent.[5]

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CASE REPORT

The 35-year-old male, painter, resident of Govandi coming from lower socioeconomic class had presented to us with anorexia (progressive, hardly able to take 1 chapatti/meal but no fear of eating) and fatigability for 6 months. Besides, he had weight loss of 15 kg generalized pruritus and yellow discoloration for 25 days. He also complained of right hypochondriac dull aching abdominal pain for 15 days before admission and development of loose, watery, nonbloody motions, 6-8 times/day, without urgency, tenesmus or incontinence for 7 days. There was no history of fever, night sweats, cough, nausea, vomiting, hematemesis, chronic drug intake, worms in stool, chronic or recurrent diarrhea, abdominal distention, altered sensorium, night blindness, tingling, numbness, bleeding from any site, bone pain, rash or joint pain. He had a history of tuberculous effusion, 5 years back for which he had taken anti tuberculous treatment for 6 months. He was a chronic tobacco addict and an alcoholic for 19 years. He gave a history of repeated unsafe sexual exposure. On examination, his weight was 37 kg with a body mass index of 16.01 kg/m^2. He was hemodyanamically stable

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with presence of pallor, icterus, cachexia, pellagrous skin changes and generalized scratch marks. There were no stigmata of chronic liver disease. On abdominal examination there was upper abdominal fullness with a swelling, approximately 4 cm × 2 cm, epigastric, soft, nonfluctuant, noncompressible, subcutaneous which freely moved over underlying structures [Figure 1a and b]. There was the hepatomegaly of 10-12 cm, firm, smooth, rounded edge and nontender. Palpable spleen of 2 cm was there with a large globular palpable gall bladder (GB). Other system examination was normal. Complete blood count showed anemia, microcytic, hypochromic type. Serum bilirubin was 16.2 mg/dl with 70% direct fraction. Alkaline phosphatase was 4102 IU/ml with alanine transaminase and aspartate transaminase being 98 and 154 IU/ml respectively. Serum lactate dehydrogenase and cholesterol was elevated. Stool and urine were normal. Enzyme linked immunosorbent assay for HIV turned out positive with a CD4 count of 76. Hepatitis B surface antigen and anti-HCV were negative. Ultrasound showed liver enlarged with normal echogenicity, spleen 12.1 cm, GB over distended 12 cm and normal portal vein. A 7.5 cm × 7 cm × 5.7 cm sized nearly well-defined heterogenously hypoechoic lesion in close proximity to inferior vena cava (IVC), in the region of head, neck and uncinate process of pancreas engulfing the terminal portion of pancreatic duct (PD) and common bile duct (CBD) with dilated PD (5.5 mm), CBD (3 cm), right hepatic duct, left hepatic duct and intra hepatic biliary radicals (IHBR) was seen. A 1.1 cm × 1.5 cm sized cystic lesion with 3 mm sized hypoechoic specks noted within the rectus muscle plane in the right upper part of the epigastric region was seen suggestive of cysticercosis. On computerized tomography (CT) abdomen bulky head and uncinate process of the pancreas seen with 6 cm × 6 cm × 5.7 cm sized mildly enhancing hypodense lesion, dilated CBD (2.9 cm), PD (7 mm) and IHBR, grossly distended GB, loss of fat planes with IVC and few discrete peri pancreatic lymph nodes. Lymph nodes away from peri pancreatic region were not enlarged. Spleen was mildly enlarged. No free fluid was detected. All these features were suggestive of pancreatic adenocarcinoma. Magnetic resonance cholangio pancreaticography also corroborated with the same findings [Figure 2a-c]. Serum carcino embryo antigen was 0.72 (n < 3.0), while serum CA 19 9 was 566.8 (n < 37). A CT guided biopsy was taken which was suggestive of undifferentiated lymphoma cells, high-grade lymphoma cells [Figure 3a-b]. Cells were positive for CD20 (B cell marker) and CD45 (leukocyte common antigen), but negative for CD3 (T cell marker) and CD138 (plasma cell marker). High resolution CT Thorax was normal except few fibrous strands in right upper lobe. Hence, the diagnosis was changed from pancreatic adenocarcinoma to AIDS (CD4-76) with PPL (Ann Arbor IIE) with obstructive jaundice and rectus muscle cysticercosis. diarrhea of the patient responded to antibiotics but the patient was deemed unfit for chemotherapy and endoscopic retrograde cholangio pancreaticography and expired.

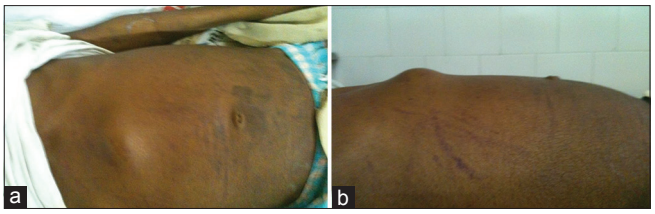

Figure 1: (a and b) Abdominal lump in the patient

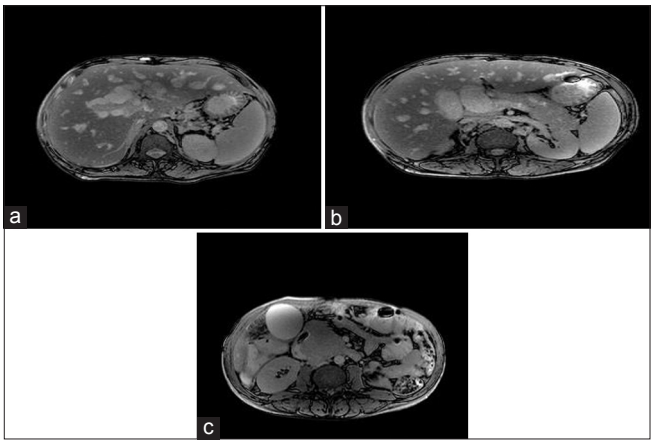

Figure 2: Magnetic resonance cholangio pancreaticography changes seen in the patient. (a) Dilated intra hepatic biliary radicles. (b) Grossly dilated common bile duct. (c) Grossly dilated gallbladder and homogenous lump arising from pancreas

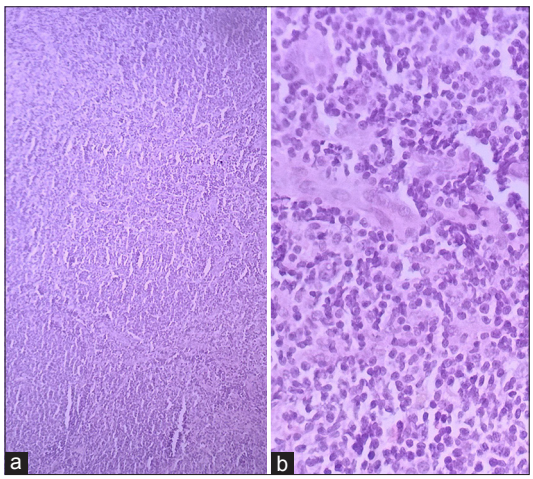

Figure 3: Histopathology from ultrasonography guided biopsy-H and E staining at low power (×10) (a), in high power (×40) (b), CD20 staining

DISCUSSION

Lymphomas are classified as Hodgkin's and non-Hodgkin's types. NHLs often involve extra-lymphatic organs, but Hodgkin's lymphomas rarely do so. NHLs may originate from extra-lymphatic organs, and pancreas may be involved about 30% times. Isolated PPL is very rare, and most of them are NHLs.[6] B cell type is most common and less commonly

T cell type is seen, though a recent case report of natural killer cell type has been published.[7]

PPL most commonly presents in fifth to sixth decade, though some studies show a decade or two earlier.[8] PPL has various clinical manifestations. Abdominal pain (83%) and abdominal mass (58%) are the two main presenting symptoms.[9] Weight loss, nausea and vomiting are other symptoms.[10] Diarrhea, pancreatitis, gastric outlet obstruction, obstructive jaundice may also be present but rare. Although head is the most common site obstructive jaundice is not common. Size of lymphoma masses are generally >6 cm and often reaching 10 cm. The constitutional symptoms of lymphoma are less common in PPL. Gastrointestinal bleeding and ascites may be presenting features.[8]

Computerized tomography appearance may help to differentiate PPL from pancreatic adenocarcinoma but is not definitive. CT is by far the most common imaging technique used to diagnose and characterize PPL. Two different morphologic patterns can be seen on a CT scan of PPL: A localized, well-circumscribed tumoral form and a diffuse enlargement with infiltration or replacement of the majority of the pancreas.[11] The diffuse infiltrating type of PPL can appear similar to acute pancreatitis. The well-circumscribed tumoral form of PPL can often appear similar to pancreatic adenocarcinoma.[11] Magnetic resonance imaging (MRI) is an excellent modality for detecting and diagnosing pancreatic lesions as well as assessing the extent of involvement since the tissue contrast is far superior compared with CT. In general, pancreatic lymphomas appear as homogeneous, low-signal-intensity, focal nodular areas on T1-weighted image, with variable, low or high signal intensity on T2-weighted image, and a generally circumscribed, less-enhanced area relative to surrounding parenchyma on DCE-MRI.[12] Tumor marker Ca19-9 may also be elevated in malignancies, of the upper gastrointestinal tract, including PPL.[11] Radiological guided percutaneous fine-needle aspiration of the pancreas is very useful in experienced hands as small amount of tissue is available. Endoscopic ultrasound has greatly improved the accuracy of diagnosis and obtaining diagnostic tissue, and a large number of reports of its success in diagnosis have been recently published.[13] Immuno-histochemical stains and flow cytometry are essential for diagnosis of PPL as it is extremely difficult to diagnose on hematoxylin-eosin stains alone. Tissue biopsy may have to be considered as cytological diagnosis may not be adequate for diagnosis.[13,14] Wallace *et al*. has described diagnostic criteria for PPL: (1) Absence of superficial or mediastinal lymphadenopathy on chest CT. (2) Normal leukocute count. (3) Mass in the pancreatic region with lymph nodes limited to pancreatic region only. (4) No hepatic or splenic involvement.[11]

The presence of PPL in a patient with HIV/AIDS has been described only twice in the literature.[15,16] In a report by Jones *et al*.,[15] PPL was diagnosed on the basis of percutaneous biopsy as was our patient. In another case report by Loots *et al*.[16] the diagnosis was made only after pancreatico duodenectomy for suspected pancreatic adenocarcinoma. Both the cases were treated with cyclophosphamide, anthraquinone, vincristine, prednisolone (CHOP) therapy and had responded to treatment like a patient without HIV.

The role of surgery and radiotherapy in the treatment of PPL is controversial. Surgery would not be recommended unless nonsurgical diagnosis is unsuccessful, the most common of surgery being a lack of preoperative diagnosis. Battula *et al*.[17] proposes surgery as a treatment in view of high recurrence on chemotherapy. As PPL tumors are large surgery is difficult and complications more. Risk of postoperative pancreatic fistula is also high.[18] In localised intermediate and high-grade NHL, chemotherapy using the CHOP regimen plus adjuvant radiotherapy is superior to chemotherapy alone. Intensive chemotherapy regimens without radiotherapy have been shown to be superior to CHOP plus involved field radiotherapy.[19] Laparoscopic modality of surgery has been described recently.[20] Whether there is a benefit of adjuvant radiotherapy to more intensive chemotherapy regimens is not known. Multimodality therapy in PPL may lead to complications like biliary sepsis, due to the frequent presence of biliary stents, and risk of neutropenia. There was no uncontrolled stent-related mortality or biliary sepsis in one study and chemotherapy did not have increased biliary complications.[21] Metal stents are better than plastic stents for long-term patency.

CONCLUSION

Primary pancreatic lymphoma is a rare but potentially curable pancreatic tumor and mandates pathological diagnosis of all pancreatic masses, as its treatment and prognosis differ from adenocarcinoma. AIDS and PPL is a rare occurrence, and a percutaneous biopsy is warranted in such patients before embarking upon surgery. Nonoperative diagnosis may avoid the need for surgery, as outcomes with chemotherapy and radiotherapy without surgical resection compare favorably to surgical series.

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