Primary pancreatic lymphoma camouflaged under the umbrella of spectrum of neuroendocrine tumors in somatostatin receptor imaging

ABSTRACT
Primary pancreatic lymphomas are very rare as compared to other pancreatic neoplasms. However, unlike carcinomas, pancreatic lymphoma is treatable with satisfactory cure rates. Somatostatin receptor (SSTR) positron emission tomography/computed tomography (PET/CT) with ⁶⁸Ga-DOTANOC is a well-established diagnostic modality in the management of neuroendocrine tumors (NETs). Over the years, it has been evident that any neoplasm with SSTR expression shows increased tracer uptake, lymphoma, being the most prominent one. Herein, we report a case of pancreatic mass, suggested as NET on fine-needle aspiration cytology referred to us for staging. Whole-body ⁶⁸Ga-DOTANOC PET/CT scan showed a large pancreatic mass with peripancreatic nodes, level I cervical nodes, cardiac, and left testicular masses which were initially thought to be possibly metastatic from pancreatic NET. However, immunohistochemistry (IHC) of the specimen was suggestive of B-cell Non-Hodgkin's Lymphoma. The present case emphasizes that pancreatic lymphoma is one of the potential differentials for pancreatic masses apart from NET on SSTR imaging. Noteworthy is the fact, that IHC plays a poignant role in the evaluation and is a mandatory tool for the management of tumors. Moreover, the whole imaging picture and clinical scenario ought to be given utmost importance for giving an affirmative diagnosis on imaging. SSTR expression in lymphomas may further obviate a remote fact that peptide receptor radionuclide therapy can be considered as an end of the line treatment for refractory lymphomas.

Keywords: Pancreatic neuroendocrine tumors, primary pancreatic lymphoma, somatostatin receptor expression in lymphoma, somatostatin receptor imaging

INTRODUCTION
Gastrointestinal lymphoma constitutes about 15%–20% of all extranodal non-Hodgkin's lymphoma (NHL). Primary pancreatic lymphoma (PPL) is a very rare tumor that may impersonate pancreatic carcinoma. Its incidence is <2% of all extranodal malignant lymphomas, and 0.5% of all pancreatic masses are PPLs.[1] Unlike adenocarcinoma, PPL is treatable with acceptable cure rates of 30%. The treatment consists of radiotherapy and chemotherapy with best results when both are given concurrently.[1]

Somatostatin receptor (SSTR) positron emission tomography/computed tomography (PET/CT) with ⁶⁸Ga-DOTANOC is a well-established diagnostic modality in the management of neuroendocrine tumors (NETs). Ga68-DOTANOC binds to SSTR subtypes 2, 3, and 5 with high affinity and is also known as a pansomatostatin receptor imaging agent. Over the years, it has been evident that any neoplasm with SSTR expression shows increased tracer uptake, lymphoma, being the most prominent one. Both low grade and malignant lymphomas with increased...
SSTR expression have been described, but at a much lower level compared to NETs.[2]

**CASE REPORT**

A 53-years-old male, suspected case of pancreatic NET, was referred to the Department of Nuclear Medicine and PET/CT for SSTR imaging. On review of history, he had presented with a progressively increasing epigastric pain associated with belching of 1-month duration. During clinical assessment at a local place, an epigastric mass was noted. Endoscopic ultrasound (EUS) elucidated a large mass arising from the body of pancreas. EUS-guided fine-needle aspiration cytology (FNAC) was done which showed clusters of cells in organoid pattern with stripped nuclear chromatin, suggestive of organoid neoplasm, possibly NET [Figure 1a and b]. 5 mCi of $^{68}$Ga-DOTANOC was injected intravenously and PET/CT imaging was performed 45 min later from the vertex of skull till mid-thigh.

Maximum intensity projection images [Figure 2] demonstrated SSTR overexpressing abnormal lesions in the neck, mediastinum, abdomen, and testes. A large mass arising from the body of pancreas with increased $^{68}$Ga-DOTANOC uptake was seen, measuring 10 cm × 14 cm × 14.6 cm in size, encasing and occluding the porto-mesenteric confluence and a standardized uptake value ($SUV_{max}$) of 16.8 [Figure 3].

$^{68}$Ga-DOTANOC avid left testicular mass measuring 11.7 cm × 8.1 cm × 11.0 cm with $SUV_{max}$ of 6.5 [Figure 4] and poorly enhancing lesion along the inferior wall of the right atrium with size of 4.3 cm × 2.5 cm and $SUV_{max}$ 5.8 [Figure 5a] were seen. Prominent peripancreatic nodes were seen which did not show any SSTR expression. However, enlarged level I cervical nodes were noted with increased $^{68}$Ga-DOTANOC uptake ($SUV_{max}$ 4.9) [Figure 5b]. No significant mediastinal lymph nodes were seen. Overall imaging features were suggestive of pancreatic NET with nodal metastases and possibly cardiac and testicular deposits.

However, immunohistochemistry (IHC) was suggestive of B-cell NHL. The cells stained positive for leukocyte common antigen, CD3 and CD20 positive and negative for chromogranin A and synaptophysin.

**DISCUSSION**

PPL are extremely rare tumors as compared to other pancreatic malignancies. They account for fewer than 2% of extranodal malignant lymphomas and 0.5% of all pancreatic masses.[1] It shows a male predominance (male-female ratio is 7:1).[3] Clinical spectrum includes abdominal pain (83%), abdominal mass (58%), weight loss (50%), jaundice (37%), acute pancreatitis (12%), small-bowel obstruction (12%), and diarrhea (12%).[1] Classic symptoms of NHL are present in <2% of patients.[3]

$^{68}$Ga-DOTA SSTR PET/CT has become the mainstay in the management of NETs over the years. However, with time, it became evident that false positives are common on SSTR imaging, such as tracer uptake in uncinate process of pancreas, inflammatory cells, meningioma, and other cancers such as renal cell carcinoma, primitive neuroectodermal tumor, and lymphoma.

Increased $^{68}$Ga-DOTANOC uptake is known to occur in all the malignant lymphomas, in particular, diffuse large B-cell and Hodgkin’s Lymphoma.[2] Even indolent lymphomas such as mucosa-associated lymphatic tissue (MALT) expressed SSTRs. Previously, SSTR imaging was considered an imaging modality to distinguish between gastric and extragastric MALT.[4]

The pancreatic mass in our case was suspicious for a NET based on FNAC, for which the $^{68}$Ga-DOTANOC PET/CT was performed.
PPL is a potential differential for pancreatic NET. Two morphologic patterns of PPL are noted,[5] well-circumscribed tumor predominantly in the head of pancreas or diffuse enlargement of the pancreas. Imperative findings to distinguish a PPL from other tumors would be a bulky, well-circumscribed mass, noninfiltrating, no duct dilatation, and no nodes below the level of renal veins.[5] On the other hand, NETs are usually small, well-circumscribed or large masses, hyperenhancing on arterial phase, located within the pancreas displacing surrounding structures with or without nodes. Frequently liver metastases are identified prior to the primary NET.[6]

Owing to the findings that lymphomas express SSTRs, there have been multiple studies evaluating SSTR imaging in diagnosis and therapy of lymphomas. It was noted that the density of SSTR expression in lymphomas was inferior to NETs and might not be sufficient for a therapeutic effect. However, lymphomas are radiosensitive tumors and SSTR expression established by an SSTR PET/CT widens horizons for peptide receptor radionuclide therapy (PRRT), which is well known for its palliative effect.[8] Hence, more prospective clinical trials have to be encouraged to assess the therapeutic effect of PRRT with Lu177-DOTATATE for refractory lymphomas.

**CONCLUSION**

PPL, though a rare entity, is a probable differential for suspected pancreatic NETs on SSTR imaging. Differentiating both the tumors is necessary as the management differs. $^{68}$Ga-DOTANOC SSTR PET/CT should be performed after a thorough confirmation with tissue biopsy and IHC. False positives are common in SSTR imaging and the total scan findings as a whole and clinical scenario should be kept in mind before arriving at a diagnosis.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients...
understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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