WELL DIFFERENTIATED NEUROENDOCRINE CARCINOMA OF PANCREAS- A CASE REPORT

MARTINA
Department of Pathology, THANJAVUR MEDICAL COLLEGE

Abstract : Pancreatic Endocrine tumors (PET) are uncommon neoplasms that generally present with symptoms of hormone overproduction (syndromic). Non functional tumors (non syndromic) show an endocrine differentiation but lack the clinical syndrome of hormone over production. This is a case report of a 60 years old male with a non functioning pancreatic endocrine tumor. Immunohistochemical study was carried out to confirm the diagnosis. This case is reported for its rare incidence.

Keyword : Neuroendocrine, pancreas, non-functional

INTRODUCTION:
Pancreatic Neuroendocrine tumors are rare neoplasms of the pancreas accounting for less than 2% of all pancreatic primary malignancies. Functional neoplasms of the pancreas are gastrinomas, insulinomas, glucagonomas and somatostatinomas. Approximately half of the pancreatic neuroendocrine tumors are non-functional and have an indolent behaviour. Due to lack of specific symptoms they present with locally advanced or metastatic disease. Most of the pancreatic neuroendocrine tumors are associated with MEN-1 syndrome that includes tumors in pituitary and parathyroid along with pancreatic tumors.

CASE HISTORY : A 60 years old man presented with the complaints of upper abdominal pain and a feeling of fullness in the upper abdomen. On examination there was a palpable mass in the epigastric region for one week duration. He did not have any symptoms related to any excess hormone secretion. He was evaluated with ultrasonogram of abdomen and was found to have a hypoechoic lesion in the left upper quadrant probably arising from the head of pancreas. CT scan revealed a sharply delineated solid mass measuring about 12 x 10 x 8 cms located in the head of pancreas. Intraoperatively a well circumscribed and encapsulated tumor was seen in the pancreatic head and no evidence of local infiltration or adhesion was noted. The tumor was enucleated from the head of pancreas and was sent for histopathological examination.

GROSS EXAMINATION :
figure1 - circumscribed mass showing grey white areas with necrosis and haemorrhage

The tumor was a well encapsulated globular soft tissue mass measuring 10 x 10 x 8 cms with areas of focal congestion over the surface. A small nodule measuring about 0.5 cm diameter was found adherent to the surface. Cut surface showed predominantly grey brown and grey tan areas with a central foci of necrosis (figure-1). Multiple sections from several areas were sampled.

MICROSCOPY:
figure -2- low power view showing nests of uniform cells

Sections from the mass showed histopathological features of a pancreatic neuroendocrine tumor composed of nests of uniform cells with moderate amount of cytoplasm and a round nucleus with ’salt and pepper’ like chromatin distribution. The nests were separated by delicate fibrous septa. Mitotic count was more than 2 per 10 HPF. No obvious angioinvasion or perineural invasion was observed. A foci of normal pancreatic tissue was seen adherent to the tumor. The nodule over the tumor showed a lymph node with metastatic deposit from the same tumor (figure -4). As the patient was asymptomatic no further hormone analysis was done except for blood sugar which was normal.
An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
University Journal of Pre and Para Clinical Sciences

IMMUNOHISTOCHEMISTRY:
IHC was performed with Chromogranin A on the tumor proper and in the lymph node metastatic deposit which showed diffuse cytoplasmic positivity thus confirming the neuroendocrine origin of the tumor (figure-5,7). Ki 67 labelling index was also done and showed >2% positivity (figure -6).

DISCUSSION:
Pancreatic endocrine tumors arises from the multipotent epithelial cells within the pancreatic ductules. Peak incidence is during the sixth decade with equal distribution among the sexes though according to the SEER( Surveillance Epidemiology and End Results) there is a slight male preponderance. These tumors may be functionally active or inactive depending upon the hormonal secretion. It has been found that due to lack of symptoms most patients present with locally advanced or metastatic disease. Patients may present with abdominal pain(35-78%), anorexia and vomiting (20-35%), intra-abdominal hemorrhage, jaundice or a palpable mass. They occur commonly in the head of pancreas though the occurrence in the body and tail has also been reported. Our case also presented as a mass in the head of pancreas. The pancreatic neuroendocrine tumors are well circumscribed, soft, homogeneous and yellow to tan coloured tumors. Cystic spaces may be seen. Histopathology is the gold standard in establishing a preoperative and definitive diagnosis. The cells are arranged in a nested, trabecular, gyriform, acinar, rosette like or solid patterns with rich vasculature. The tumor cells are uniformly round with salt and pepper chromatin and moderate amount of cytoplasm. Neuroendocrine cells are characterised by expression of marker molecules like synaptophysin, Chromogranin-A and Neuron specific enolase. Non functioning tumors may well show immunohistochemical positivity for hormones, neuropeptides or neurotransmitters. The WHO classifies the pancreatic neuroendocrine neoplasm into (1)well differentiated neuroendocrine tumor with benign or uncertain behaviour ; (2)well differentiated neuroendocrine carcinoma with low grade malignant behaviour and(3) poorly differentiated neuroendocrine carcinoma with high grade malignant behavior based on the tumor size mitotic count per 10 HPF, ki 67 labelling index, vascular invasion, extrapancreatic invasion and metastasis to lymph nodes and liver. Most approximately 60-100% are classified as well differentiated endocrine carcinomas. Our tumor was 10 cms and the mitotic count was less than 2 per 10 HPF and a single regional lymph node also showed metastatic deposit and so was classified as well differentiated neuroendocrine carcinoma with low grade malignant behaviour. Diagnostic imaging techniques include Somatostatin-Receptor Scintigraphy(SRS), ultrasonography, computed tomography and MRI. Laboratory assessment of chromogranin A (CgA) is a general tumor marker for neuroendocrine tumors. Aggressive surgery for locally advanced non-functioning pancreatic NETs may prolong survival is the treatment of choice. Other treatment available are Radiofrequency ablation, biotherapy with somatostatin analogues(SSA) or interferon.  

PROGNOSIS:
Overall 5-year survival is 30-63%, with a median survival of 72 months. Aggressive surgery may increase survival to 63- 82%.
The tumor has a good prognosis where the long term survival can be expected even in the presence of metastasis\cite{8}.

**CONCLUSION:**
Pancreatic neuroendocrine tumor accounts for < 2 % of all neoplasms of the pancreas and their clinical behaviour is much more indolent than that of adenocarcinoma of the pancreas. They occur at an elderly age group. Histopathology remains the gold standard for preoperative diagnosis. The tumor has a very good prognosis inspite of metastasis.

**REFERENCES:**