Pancreatic neuroendocrine tumor: A rare case report

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Abstract
Pancreatic neuroendocrine tumors (NETs) are a heterogeneous group of tumors that arise in the endocrine cells of the pancreas. Despite being relatively rare, representing just 1–2% of all pancreatic neoplasms, the incidence of pancreatic NET has increased over the past two decades.We report a case of 44-year-old female patient presenting with history of long standing pain radiating to back, weight loss, decrease in appetite, nausea and vomiting along with jaundice. CECT Upper Abdomen showed soft tissue density mass at the lower end of Common Bile Duct with infiltration of 2nd part of duodenum causing biliary obstruction.The diagnosis is distal CBD cholangiocarcinoma. MRCP gave impression of periampullary soft tissue mass obstructing the terminal CBDwith associated up stream dilatation of biliary tree with cholelithiasis.Patient underwent Whipple's procedure (Pancreaticoduodenumectomy) on exploratory laprotomy. Grossly a growth measuring 3.5x2 cm seen in pancreas abutting CBD was seen. Onmicroscopic examination, diagnosis of Pancreatic neuroendocrine tumor was made which wasinvolving the duodenal wall and CBD.

Keywords: Neuroendocrine tumor, Pancreatic tumors, Pancreatoduodenectomy, Common Bile Duct.

Introduction
Pancreatic Neuroendocrine tumors (NETs) are a heterogeneous group of tumors that arise in the endocrine cells of the pancreas having two probable origins of pancreatic NET: mature endocrine cells in the pancreas (e.g., a-, b-, d- and c-cells) and multi-potent stem cells that are differentiated into endocrine and exocrine cells in the pancreas.[1]Although being relatively rare, representing just 1–2% of all pancreatic neoplasms,[2] the incidence of pancreatic NET has increased over the past two decades. Individuals ranging anywhere from 50 to 70 years of age are found more commonly associated with them.[2]

Neuroendocrine cells can develop into tumors, many of which grow slowly and others that can be very aggressive and spread to other parts of the body.The neuroendocrine system is composed of cells that have characteristics comparable to nerve cells and hormone-producing endocrine cells.The clinical presentation of NETs primarily depends on whether they are functional or non-functional, and if they are functional, it depends on hormone.It can cause symptoms either due to mass effects and/or through the secretion of bioactive substances leading to discrete clinical syndromes (functioning tumors).[3,4]

Case History
A 44-year-old female patient presented with history of long standing pain radiating to back, weight loss, decrease in appetite, nausea and vomiting along with jaundice.All routine laboratory investigations along with Liver and Kidney function test were done.The investigations were in normal limits.CECTUpper Abdomen showed soft tissue density mass at the lower end of Common Bile Duct (CBD) with infiltration of 2nd part of duodenum causing biliary obstruction. A provisional diagnosis of Cholangiocarcinoma of the distal CBD was offered based on CT findings.MRCPgave an impression of periampullary soft tissue mass obstructing the terminal CBD with associated up stream dilatation of biliary tree with cholelithiasis.

After adequate preparation, an exploratory laprotomy was performed and the patient underwent Whipple's procedure (pancreaticoduodenectomy).On gross examination ofreceived pancreaticoduodenectomy specimen along with gallbladder, a growth measuring 3.5x2 cm was seen in pancreas abutting CBD. (Fig. 1).

Fig 1: Gross Specimen showing a grey-white tumor in the pancreas abutting common bile duct and extending up to the wall of the duodenum

Resected tumour margins were free from tumour.Duodenal area showed ulceration.Microscopic examination ofsections from the tumor showed ill defined nests of small uniform cells having central

nuclei and eosinophilic granular cytoplasm.(Fig. 2A,2B).

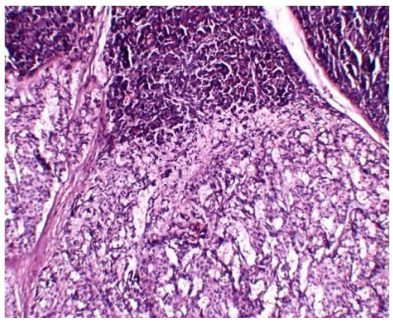

Fig. 2A: H&E(10X): Microscopic examination showing ill defined nests of small uniform cells

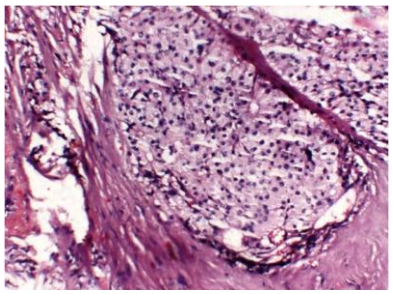

Fig. 2B: H&E (20X): Microscopic Examination shows nests of small uniform cells with central nuclei and eosinophilic granular cytoplasm

These nests were separated by vascularized stroma. Areas of necrosis and focal calcification were also seen. Mitotic figures were infrequent. Tumor was extending into the duodenal wall with focal ulceration of lining mucosa (Fig2C).

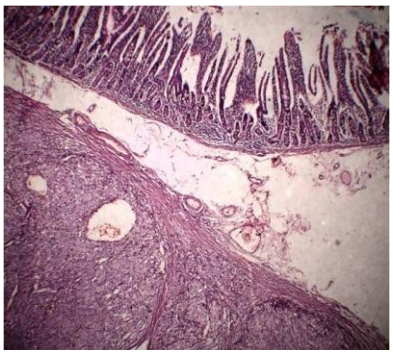

Fig 2C: H&E(10X):Tumor extending into the duodenal wall

Tumor was involving CBD. Diagnosis ofPancreatic neuroendocrine tumour was made which was involving the duodenal wall and CBD.

Discussion

Neuroendocrine tumors are rare, but their reported incidence has increased over the last decades, which is attributed to improved diagnostic modalities and surveillance. PNETs are a group of pancreatic neoplasms with high heterogeneity and a better prognosis than exocrine pancreatic cancer.[4-6]

PNETs are classified as two general categories, functional or non-functional, basedon the characteristic symptoms caused by the hypersecreted hormones. Functional PNETs are classified into insulinoma, glucagonoma, somatosatinoma, gastrinoma, VIPoma, Serotonin producingtumor, ACTH producing tumor. Insulinoma is the most common type of functional PNETs followed in decreasing order by gastrinoma, glucagonoma, VIPoma, somatosatinoma.[4]

Several studies havebeen performed on the pathogenesis of sporadic PNETs,which comprise 90% of all PNETs. In recent research it has been revealed that loss of chromosome1, 3p, 6q, 11q, 17p, or 22q and gains of chromosome 4or 9q have been somehow related toPNE

Ts. It is also reported that the loss of a tumor suppressor gene or the gain of an oncogene is the mechanism by whichchromosomal alterations cause PNETs, besides this stochasticchromosomal number changes are also possible. A fewgenes that regulate cell proliferation have also beenstudied. Inhibitors of cell proliferation, including the tumorsuppressor genesand, and the cyclindependent kinase inhibitor (CKI) p16 INK4a are usuallyintact in welldifferentiated PNETs, but p53 abnormalitiesare common in poorly differentiated PNETs. Theoncogene(cyclin D1) is often upregulated inPNETs, but the ras family oncogenes are not usuallydetected. Recently, an exome study of apparentlysporadic PNETs from 68 patients demonstrated that 44%of those tumors harbored mutations in thegene(the same gene, if inactivated, causes MEN1), 43%harbored mutations in two subunits of a transcription/chromatin remodeling complex [death domainassociatedprotein (DAXX) and thalassemia/mental retardationsyndrome Xlinked (ATRX)], and 14% harboredmutations in the mammalian target of rapamycin(mTOR) pathway.[3]

PNETs are classified as functioning or non-functioning depending on whether they cause hormonalhypersecretion syndrome . Functioning PNETs result inhormonal hypersecretion syndromes. Nonfunctioning PNETs cause nonspecific symptoms, such as vague abdominal pain, andcan be an incidental finding.For the nonfunctional pNETs, the clinical presentations are more likely to be associated with the symptoms of local compression and metastatic lesions, such as obstructive jaundice, pain and liver metastasis. They can also be broken down into well-differentiated and poorly differentiated PNETs taking into account the measurement of mitotic count and the expression ofnuclear antigen Ki-67.[4]

The role of serum tumor markers in diagnosing pancreatic NET is limited. CgA is a member of the chromogranin family and is often elevated in serum of patients with pancreatic NET. If hormonalhypersecretion syndrome is suspected,

appropriatebiochemical testing is performed to determine hormonalhypersecretion and followed by imaging, endoscopy, andbiopsy. Surgical resection is the only curative strategy for pancreatic NET. Cytoreductive surgery can control the secretion of activated hormones and improve the survival for patients with advanced pancreatic NET.[7]

Conclusion

With the occurrence of 1 every 100000 people, PNETs are a rare tumors; however, with the improved technology, they are being diagnosed more frequently every day. Due to this increase, the spectrum of treatment options has significantly grown.

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