Rare case of primary duodenal somatostatinoma

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ABSTRACT

Neuroendocrine tumors develop from any part of the gastrointestinal tract. Duodenal neuroendocrine tumors constitute only 2.6% of all neuroendocrine tumors. Somatostatinomas are a type of neuroendocrine tumor. They are more common in the pancreas. We present a rare case of duodenal somatostatinoma. A 53-year-old male was presented with a complaint of upper abdominal pain. On evaluation, multi detector computed tomography showed heterogeneously enhancing hypodense mass in the medial wall of the second part of duodenum and head of pancreas measuring 3.1 × 2.8 cm. Whipples surgery was done and the microscopy showed neuroendocrine tumor with psammomatous calcification. On immunohistochemistry evaluation, the tumor cells were positive for Chromogranin, Synaptophysin, and Somatostatin. Hence, we reported this case as duodenal somatostatinoma.

Keywords: *Carcinoid tumor, Duodenal mass, Neuroendocrine tumor, Somatostatinoma, Whipples surgery.*

Neuroendocrine tumors are tumors derived from neuroendocrine cells that can develop from any part of the gastrointestinal tract. They can be broadly classified into functional and non- functional tumors based on their symptoms [1]. They can occur sporadically or as a result of hereditary predisposition syndromes such as multiple endocrine neoplasia type-1[MEN-1], Von-Hippel-Lindau's disease or neurofibromatosis type-1. Duodenal well-differentiated neuroendocrine tumors account for only 2.6% of all neuroendocrine tumors [2]. Somatostatin-producing neuroendocrine tumor of the duodenum constitute 18-21% of the neuroendocrine tumors [18].

Somatostatinomas are derived from somatostatin producing delta cells of the pancreas or from endocrine cells of digestive tract [3,4]. Pancreas is the most common site of somatostatinoma (68%), followed by the duodenum (19%), ampulla of vater (3%) and small intestine (3%) [5]. Somatostatinomas are malignant tumors that develop lymphnode or liver metastasis at the time of diagnosis [6]. Here, we present a case of duodenal somatostatinoma which was incidentally diagnosed in a patient who came for laparoscopic cholecystectomy.

CASE REPORT

A 53-year-old male was presented with complaints of upper abdominal pain for one month. On general examination, the patient was found to have gall bladder calculi. The patient was referred to our hospital for laparoscopic cholecystectomy. On examination, the patient was afebrile, with absensce of jaundice and anemia and had no generalized lymphadenopathy. His vitals were stable while the per abdomen was soft and non-tender.

On further evaluation, his ultrasound of the abdomen showed an irregular hypoechoic mass in the head of the pancreas measuring 3.7 × 2.8 cm with edematous duodenum. Also, there were few hyperechoic lesions in the liver and chronic cholecystitis. Multi detector computed tomography (MDCT) showed heterogeneously enhancing hypodense mass in the medial wall of the second part of duodenum and head of pancreas measuring 3.1 × 2.8 cm. Magnetic resonance imaging (MRI) showed duodenal wall thickening with infiltration of the head of the pancreas. Other lab investigations showed serum bilirubin 0.4mg/dl, Serum glutamic oxaloacetic transaminase (SGOT) -23U/L, Serum glutamic pyruvic transaminase

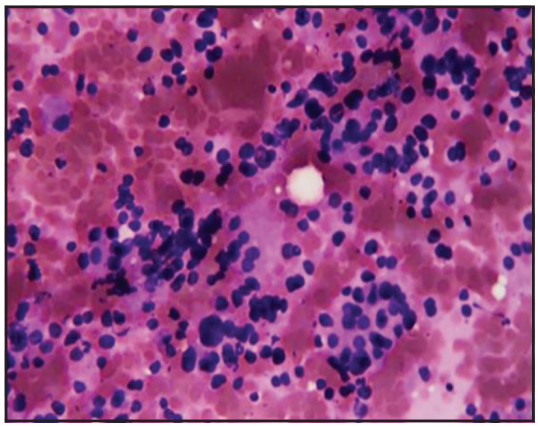

Figure 1: Endoscopic ultrasound guided FNAC from the lesion-acinar arrangement of neoplastic cells

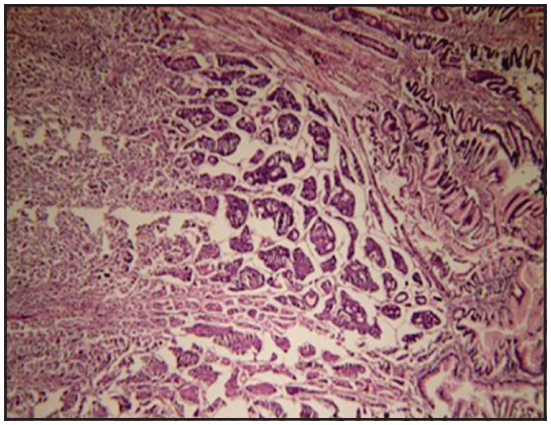

Figure 2: Low power view- H&E(Hematoxylin and Eosin) neoplastic cells arranged in nests

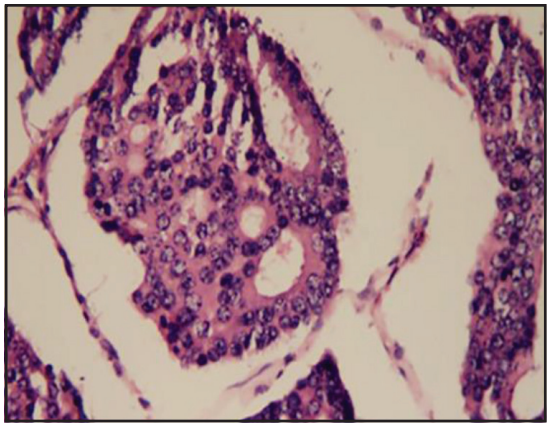

Figure 3: High power view- H&E stain shows psammomatous calcification

(SGPT) - 28U/L, cancer antigen (CA) 19.9-20.1U/ml, HbA1C-7.2%. Endoscopic ultrasound Fine needle aspiration cytology (EUS FNAC) was done from the mass which showed atypical cell clusters with focal acinar arrangement suggestive of malignancy (Fig. 1).

A provisional diagnosis of duodenal malignancy infiltrating the pancreas was made and surgery was the treatment of choice. The patient underwent Whipples surgery. Intraoperatively, there was a growth in D2 involving the head of the pancreas. Hepatoduodenal lymphnodes were enlarged. Uncinate process of the pancreas was adherent to the superior mesenteric artery. Cholelithiasis (multiple calculi) were found; one liver nodule measuring 3 cm was found. Frozen section biopsy was done which was negative for malignancy.

Gross examination of the specimen showed an ill defined mass measuring 4×3×2 cm in the second part of duodenum infiltrating the head of the pancreas. Mass was 0.5 cm proximal to the ampulla. All the resection margins, ampulla and bile duct were free of tumor infiltration. The microscopic examination showed that the tumor cells were arranged in nests and pseudo acinar pattern (Fig. 2). The cells were uniform with finely granular chromatin (Fig. 3). Psammoma bodies were found (Fig. 4).

On Immunohistochemistry evaluation, the neoplastic cells stained positive for chromogranin, synaptophysin and somatostatin (Fig. 5). Ki-67 labeling index was 7% hence we diagnosed it as Grade 2 well differentiated neuroendocrine tumor, primary duodenal somatostatinoma with infiltration into the pancreas and lymph node metastasis P (T3N1). At 6 month and one-year follow-up, abdominopelvic computed tomography showed no recurrent mass.

DISCUSSION

Somatostatinoma is a rare gastroenteropancreatic (GEP) endocrine tumor with an annual incidence of 1 in 4 million [7] and the median age is 54 years (range 24-84years) [8]. Somatostatin is a cyclic tetradecapeptide, widely distributed in normal human tissues and secreted by the hypothalamus, cerebrum, spinal cord, vagus nerve, delta cells in Langerhans islets of the pancreas, stomach, duodenum, and small intestine [9]. Somatostatin classified as the inhibitory hormone has an inhibitory effect on insulin, glucagon, gastrin, secretin, somatotrophin, thyrotropin, gastric inhibitory peptide, vasoactive intestinal peptide (VIP), growth hormone, thyroid stimulating hormone (TSH) and prolactin. This inhibitory effect of somatostatin leads to somatostatin syndrome also called as an inhibitory syndrome which consists of diabetes mellitus, diarrhea/steatorrhea, and cholelithiasis.

The somatostatin syndrome is more common in pancreatic somatostatinomas due to high levels of somatostatin secreted by these pancreatic tumors [10,11,12]. Our patient presented with diabetes mellitus and cholelithiasis which are the major manifestations of the inhibitory syndrome. Duodenal somatostatinomas are identified earlier than pancreatic counterparts because they are presented with abdominal pain, obstructive jaundice, cholelithiasis, vomiting, and abdominal bleeding [13].

Most somatostatinomas are incidentally diagnosed like in our case, where the patient had abdominal pain and while evaluating for cholelithiasis duodenal mass, infiltrating the pancreas was diagnosed. Computerized Tomography (CT), MRI, selective

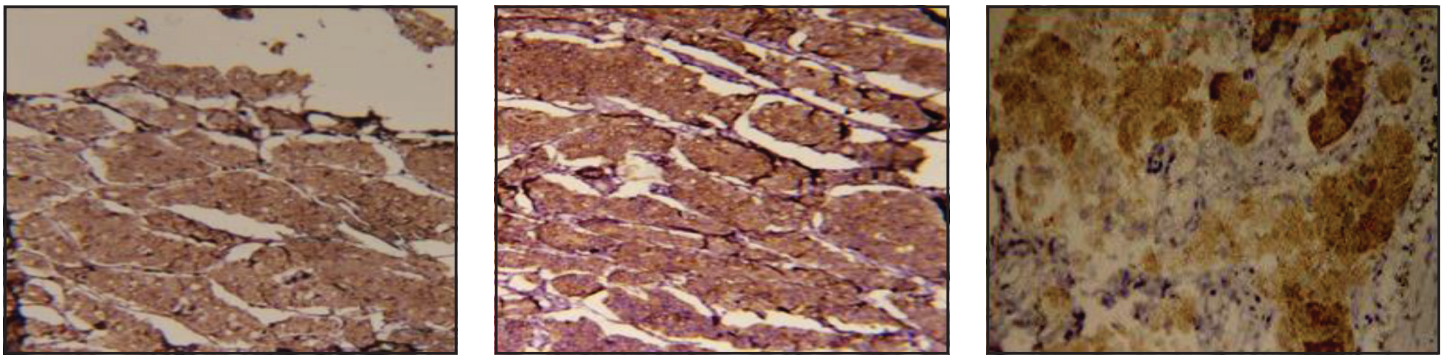

Figure 5: (a) IHC shows synaptophysin positivity. (b) IHC shows Chromogranin positivity. (c) IHC shows Somatostatin positivity.

Table 1 - Recommended grading system for well differentiated gastroenteropancreatic neuroendocrine tumors

Grade	Mitotic rate (per 2mm2)	Ki-67 index (%)
Well differentiated neuroendocrine tumor Grade1	<2	<3
Well differentiated neuroendocrine tumor Grade2	2-20	3-20
Well differentiated neuroendocrine tumor Grade3	>20	>20

arteriography of the celiac tripod and endoscopic retrograde cholangiopancreatography (ERCP) are useful diagnostic modalities for identifying the tumor [14].

On gross examination, somatostatinomas arising from the gastrointestinal tract are submucosal lesions with exophytic growth which can ulcerate or bleed. Pancreatic tumors are well circumscribed, grey-white to yellow tan nodule [15]. Duodenal somatostatinomas are smaller than pancreatic lesions. Histopathologic features of these tumors are similar to other neuroendocrine tumors. The neoplastic cells are arranged in nests, trebaculae or acinar pattern. Fewer mitotic figures are seen with little necrosis [16]. The most characteristic feature of somatostatinoma is the psammoma bodies [13].

Immunohistochemically, neuroendocrine tumors are positive for synaptophysin, chromogranin, and CD-56. Immunohistochemistry for somatostatin is positive in somatostatinomas [8]. Based on the mitotic rate or Ki-67 index neuroendocrine tumors are graded in WHO 2010 classification [18] (Table1). Adenocarcinoma is a close differential diagnosis for somatostatinoma. However, adenocarcinoma is negative for chromogranin, synaptophysin, and somatostatin. Kim JA et al reported a similar case of 58-year-old male with duodenal submucosal mass abutting the ampulla. Whipples surgery was done and on IHC evaluation the tumor cells stained for chromogranin, synaptophysin and somatostatin. After the 6 months follow up, the patient had no recurrent mass [21].

There is controversy regarding the role of surgery for duodenal NET between 10 and 20mm size. It is widely accepted that surgery is the treatment of choice for tumors >20mm in size [2]. Independent risk factors for primary tumor metastasis are invasion of muscularispropria, size >20mm and presence of mitotic figures [19]. Adjuvant chemotherapy for somatostatinomas is not recommended. In case of locally advanced disease or widespread metastasis tumordebulking, chemoembolization of the primary tumor and of hepatic metastasis, chemotherapy, somatostatin receptor (SSTR)- analogs (octreotide), and IFN-α can be used to control the clinical symptoms [20].

CONCLUSION

Good clinical evaluation and preoperative workup is the most important step in medical practice. A patient with abdominal pain and symptoms of cholelithiasis by proper evaluation found to have duodenal mass with pancreatic infiltration and ended up with Whipples operation. Hence the history which we elicit from the patient is just a tip of the iceberg. Only by thorough evaluation, we will be able to identify the rarest tumor which is hiding inside.

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