Case Report

A Case Report of Duodenal Psammomatous Somatostatinoma

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Abstract

Somatostatinoma is a neuroendocrine tumor; its incidence in the duodenum around the ampulla of Vater is rare, and it is often not associated with secretory manifestation. The authors report a case of a female with an ampullary (Vater) tumor displaying neuroendocrine nuclear features, psammoma bodies, and the positivity for immunohistochemical panel of neuroendocrine tumors. The patient was presented with some features compatible with somatostatin secretion-associated syndrome; albeit with normal serum levels of the hormone. Initial attempt of complete resection failed, and the involved margins were revised with a subsequent surgery, and the patient showed an uneventful course on follow-up for two years.

1. Introduction

Neuroendocrine tumors are a group of tumors with a variable malignant potential. In the Gastrointestinal tract, they are classified topographically into fore, mid and hindgut tumors. Most of the tumors arise in the mid-gut, distally more than proximally [1].

Only 2% of neuroendocrine tumors occur in the duodenum. Five types have been recognized in the duodenum and the upper jejunum: G-cell tumor (gastrinoma), D-cell tumor (somatostatinoma), well-differentiated tumors, poorly differentiated tumors/small cell carcinoma, and gangliocytic paraganglioma [1–3].

According to the IARC-WHO Blue Book, neuroendocrine tumors span a spectrum from well to poorly differentiated tumors. Mitosis and tumor necrosis dictate the classification [1].

The somatostatinoma syndrome is defined by a pentad of clinical features; diarrhea, cholelithiasis, diabetes mellitus, weight loss and hypochlorhydria.

Somatostatinoma syndrome is often associated with pancreatic neuroendocrine tumors; duodenal tumors are mostly asymptomatic, and only a small fraction of cases (10%) is symptomatic [3].
Duodenal somatostatinoma arises exclusively in or in the vicinity of the ampulla of Vater. These tumors are solitary in 90% of cases, while familial tumors and syndrome-associated tumors might be multiple [2].

2. Case Report

2.1. History and examination

A 39-year-old female from West Kordofan State/Sudan presented in July 2012 to a private clinic run by a general physician in Alnohod city complained of vague abdominal pain and indigestion for two-month duration. She has been diagnosed with irritable bowel syndrome (IBS) and received antispasmodic medications since. She has no diarrhea or steatorrhea.

On examination, she was found as obese with BMI (31), not pale jaundiced or cyanosed. Her abdomen was soft and pendulous. The liver and the spleen were not palpable. Other clinical examinations were unremarkable.

Blood chemistry revealed adverse lipid profile with high cholesterol = 260mg/dl, LDL cholesterol = 150mg/dl, HDL cholesterol = 42mg/dl, normal bilirubin, alkaline phosphatase X3 upper normal level (done one week postoperatively), Post Prandial Glucose = 14 mmol/L, normal bicarbonate and electrolytes levels. The fasting serum somatostatin level = 7.9pmol/L, which falls within the normal reference range for adults (10–22 pg/mL) [4] (in two different occasions in two different labs two-weeks apart).

Abdominal ultrasonography revealed two small echogenic gallstones with a thin-wall gall bladder. No features consistent with cholecystitis were seen. The liver showed no echogenic masses.

With the persistent of her symptoms, the patient was referred to Khartoum Teaching Hospital (a reference Hospital in Sudan) in August 2012. The attending gastroenterologist planned for upper GIT endoscopy. The procedure showed a 2.7 cm polypoid mass with a smooth glistening surface at the level of the 2nd duodenal segment protruding from the ampulla of Vater, and the surrounding duodenal mucosa was unremarkable.

An incisional biopsy was obtained and sent to the authors’ lab (Central Laboratory Administration, Histopathology-lab). The received specimen was tiny, fragmented and poorly preserved with crush artifacts and was not optimal for a proper histopathological interpretation, nevertheless the ghosted outlines of the nested growth gave the impression of a neuroendocrine tumor.
A definitive surgery was planned after four-weeks interval (October 2012) for the attempt of complete surgical resection. The tumor was approached through laparotomy, excisional attempt succeeded via Ampullectomy (including the polypoid tumor) with electrocautery dissector, intraoperative examination of the duodenum revealed increased thickness overlying the affected area.

2.2. Gross description

The specimen received were fixed in formalin; the external surface was grayish white in color with small punctate hemorrhage on its surface. The mass measured 2.7 cm and consisted of a polyp with a small segment of its base, with three accompanying lymph nodes, sized 1x, 6x, and 7x each.

Serial longitudinal sections were done to reveal relation with the deep surgical margin.

The cut sections showed a yellowish white surface with a slight gritty sensation upon trimming. No cystic degeneration, necrotic or hemorrhagic central foci noted. The tumor specimen were all processed for microscopic examination.

The third subsequent margin revision biopsy was composed of a pancreatico-gastro-duodenectomy resection specimen.

2.3. Microscopic description

Microscopic examination of the polypoid mass revealed a circumscribed mass composed of glandular structures and packets of cells surrounded by abundant, delicate vasculature. Glandular lumen showed psammomatous bodies about 25–60 um in diameter. Periodic Acid Schiff luminal secretions were detected focally.

The constituent tumor cells are columnar, with basally oriented nuclei. The cytoplasm ranges from eosinophilic to clear. The nuclei showed monotony; some are vesicular with prominent nucleoli. No mitotic activity or necrotic foci were appreciated in the adequate biopsy submitted (Figure 1).

Immunohistochemical studies were positive for synaptophysin, CD56, chromogranin, CK and weakly for CDX-2; a collective of a neuroendocrine differentiation markers.

The deep surgical margin was involved, the base of the polypoid mass showed infiltrating glands traversing and dissecting through pancreatic acini (Figure 2).
Figure 1: The upper microscopic slide (H&E) shows nests, trabeculae, and ribbons of columnar cells with clear to eosinophilic cytoplasm surrounded by a rich vascular network. The lower shows psammoma body in the center of the field.

The tumor is well-differentiated, Grade 1 – according to the WHO criteria (< 2 mitoses/10 HPF (50 fields were counted using X40), and no necrosis).

The World Health Organization Criteria for diagnosing malignancy are a size > 2 cm, increased mitosis, and the presence of tumor necrosis [3].

The pTNM (Pathological Tumor, Node, Metastasis staging system) staging according to the AJCC manual [5] is T3 (tumor invades the pancreas), No (no regional lymph node
Figure 2: The upper histopathological slide shows the invasive front of the tumor traversing and dissecting through pancreatic acini. The lower slide shows the tall columnar clear tumor cells forming trabecula and nests with small punctate classifications.

metastasis, three were obtained), Mo (no distant metastasis), and R1 (surgical margin is grossly negative, microscopically positive).

Surgical revision for the deep margin was advised, and a second pancreatoco-gastro-duodenectomy procedure performed two month later, and all the surgical margins and accompanying lymph nodes (= 6 nodes) were negative of tumor deposits.
3. Discussion

The first case of duodenal somatostatinoma was reported in 1979. Duodenal somatostatin-producing endocrine tumors, which belong to the group of gastrointestinal, endocrine tumors, are rare neoplasms that have a prevalence of 1 in 40 million [6, 7].

Due to the relatively large number of D cells, 40% of the reported somatostatinoma originated from the upper intestinal tract (50% in the duodenum and 50% in the ampulla with only one case reported in the jejunum) [6].

The Peri-ampullary of Vater region is a specialized anatomical structure in the 2nd part of the duodenum composed of both ampulla and papilla. The ampulla constitutes common bile duct and pancreatic duct with variable anatomical combination patterns. The papilla is observed as a mucosal protrusion into the duodenal lumen. The area showed multiple intersections of different types of mucosa (small intestine, pancreatic duct, and biliary duct epithelia) and associated underlying supporting tissue [8].

About 105 case reports hits in PubMed (accessed December 7, 2016), about 93% are sporadic and 7% familial. Familial cases are usually associated with Neurofibromatosis-1, Multiple Endocrine Neoplasia-1, Tuberous sclerosis or Vhon Hippel Lindau syndromes [9–13], all of which were excluded in the patient.

Duodenal tumors tend to be smaller averaging between 13 and 75 mm and 18 mm as a medium size, compared to pancreatic tumors with a median size of 42.5 mm. In this case, the tumor size was 2.7 cm. There is a strong correlation between the size of the tumor and its behavior; larger tumors tend to have lymph node and liver metastasis that were not observed in this case supporting the previous findings [14]. In the current case, some features of somatostatinoma syndrome were evident (diabetes mellitus and gallstones), but not yet fulfilling the criteria for the diagnosis.

Somatostatin is an inhibitory hormone to various endocrine and exocrine hormones but due to the binding proteins in the plasma that rapidly inactivate the hormone it mainly acts in paracrine fashion [15]. Accordingly, the somatostatinoma syndrome is rare in duodenal somatostatinomas.

The diabetic range plasma glucose observed in this case could be explained by the inferential inhibition of somatostatin on insulin and diabetogenic hormones leading to a mild degree of diabetes and less ketoacidosis that could be observed in patients with somatostatinoma. Another plausible explanation is the coincidental DM in the patient, reflecting the high prevalence of diabetes mellitus in Sudan [16]. In this case,
the fasting somatostatin level was within normal reference range. And the postprandial plasma glucose was diagnostic for diabetes.

The patient had many features of the metabolic syndrome, consolidated by a high postprandial glucose, adverse lipid profile, and BMI.

In the literature most of the duodenal somatostatinoma are non-secretory [1]. Episodic secretion of the somatostatin hormone or decline in the secretory function of the tumor with the tumor advancement is a likely remote possibility.

Gallstones are observed in 27% of duodenal somatostatinoma together with a massively dilated gallbladder [15]. Although gallstones were detected in our patient, the gallbladder was not dilated and showed normal wall thickness.

In a subset of cases, metastatic disease is evident at diagnosis mainly in the liver (10%) and lymph nodes (35%). This might be related to the late presentation at the diagnosis due to non-secretory attribute of the tumor [17].

Liver and lymph nodes metastasis in the present case were excluded by Clinical, CT-Abdomen, ultrasonic and surgical exploration; however, Endoscopic ultrasononography was not done due to limited accessibility of this important diagnostic imaging in the authors’ country. The long follow-up disease free survival supports the absence of metastasis and lymph node involvement notion.

The deep surgical margin was involved, and review of the surgical margin was advised. Subsequent radical surgery was done through Whipple pancreatico-gastro-duodenectomy after two months’ interval. The revised surgical margin was free. The patient showed no features of recurrence at six, twelve months and two years’ follow-up visits (last visit in May 2014).

Forty percent of patients with somatostatinomas died at intervals ranging from 1 week to 14 months after diagnosis, whereas 60% of patients were alive from 6 months to 5 years after diagnosis. Thus, the syndrome is associated with a high malignant potential, and it is important to be approached aggressively in management and to attempt to remove all tumor tissue with a clear surgical margin. Surgical extirpation of the tumor provides the only chance of cure [18].

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Author Contributions

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References


