ABSTRACT

Introduction

Somatostatinomas of the ampulla are rare neuroendocrine tumours with limited studies in the literature. These are often associated with familial genetic predisposition e.g. NF 1 and Von Hippel-Lindau Syndrome. Histology commonly shows classical features such as Psammoma bodies. The classical presentation with inhibitory syndrome is rare, but ampullary mass effects can cause an earlier presentation with potentially better outcomes with earlier intervention and treatment. Case series We report three cases of ampullary somatostatinomas: one sporadic and two familial, associated with neurofibromatosis type 1. The first patient presented with pruritus, the second with recurrent pancreatitis and the third, with elevated CA19-9 levels. Various preoperative localisation techniques were employed and one had an attempted endoscopic resection yielding involved margins. All patients underwent pancreaticoduodenectomy, of which one was laparoscopic assisted. The median size of the tumour was 10 mm and one patient had nodal involvement. All 3 patients have remained disease free at most recent follow up ranging from 1.5 to 11 years. Discussion Ampullary somatostatinomas can present early with mass related effects while inhibitory syndrome is rare. Early detection and intervention in ampullary somatostatinoma may contribute to better outcomes than pancreatic somatostatinomas. Long-term survival is achievable through pancreaticoduodenectomy for resectable ampullary somatostatinoma and laparoscopic approach is a feasible and viable option.

INTRODUCTION

Somatostatinoma is a rare neuroendocrine tumour (NET) with an annual incidence of 1 in 40 million [1]. 60% of somatostatinomas are pancreatic, with most others occurring in the duodenum or ampulla of Vater. Rarely, jejunal, bile duct and ovarian somatostatinoma as have been reported [2, 3, 4, 5, 6, 7, 8].

Somatostatinomas may be sporadic (93.1%) or familial (6.9%) and are associated with neurofibromatosis type 1 (NF1), Multiple Endocrine Neoplasia 1 (MEN1) and Von Hippel-Lindau syndrome. Sporadic and NF1-associated duodenal somatostatinomas show characteristic histological features of a pseudoglandular pattern and psammoma bodies, and these tumours are often localized to the ampulla of Vater. Only ten percent of somatostatinomas are functional tumours [9], and 60-70% of tumours are malignant. Nearly two thirds of patients with malignant somatostatinomas will present with metastatic disease. Duodenal and ampullary somatostatinomas are the least likely to metastasise, while those located in the pancreas or other sites have a higher tendency towards metastasis [9, 10, 11, 12]. We present a case series of 3 consecutive cases of ampullary somatostatinoma that were treated by pancreaticoduodenectomy (PD) with good outcomes.

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Keywords

Ampulla of Vater; Laparoscopy; Neuroendocrine Tumors; Pancreaticoduodenectomy; Somatostatinoma

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for chromogranin, synaptophysin and somatostatin, confirming the diagnosis of somatostatinoma. With no metastatic disease on imaging, the patient proceeded to open PD. Hospital stay was 7 days. Histopathology confirmed a 9×7 mm oval tumour at the ampulla of Vater, with immunoperoxidase staining positive for somatostatin (Figure 2). There was no nodal disease in 12 lymph nodes harvested. The patient was disease free at last follow up at 5 years.

Case #3

A Sixty-year-old lady with NF1 presented with an elevated CA19.9 at 250 (normal <37 Um/L), detected while being investigated for pelvic pain and postmenopausal bleeding. She was also noted to have an elevated bilirubin level of 61 mg/L. CT and MRI (Figure 3) of the abdomen demonstrated a small, enhancing lesion projecting into the duodenal lumen. Upper endoscopy demonstrated a 13 mm polyloid, submucosal ampullary mass in the duodenum with biopsy and immunohistochemistry suggestive of somatostatinoma. Staging positron emission tomography (PET) with gallium 68-labelled DOTA-octreotate (DOTATATE) scan failed to show uptake in the corresponding region. After discussion at a multidisciplinary team meeting, the patient underwent endoscopic mucosal resection of the ampullary tumour based on prior EUS findings that the lesion did not appear to invade the muscularis propria and submucosa. Histopathology showed a 15x12 mm somatostatinoma, with the deep margin involved.

The patient then proceeded to PD, which was initially attempted laparoscopically but converted to open due to dense adhesions from previous open cholecystectomy. She stayed for 10 days. The surgical specimen revealed no residual somatostatinoma, but noted a separate, benign 8 mm duodenal polyp, five duodenal gastrointestinal stromal tumours (GISTs) and a submucosal lipoma. Metastatic somatostatinoma was found in 2 of 11 lymph nodes. The patient was disease free when last reviewed 18 months postoperatively.

DISCUSSION

This paper presents 3 patients with ampullary somatostatinoma treated successfully with PD. Somatostatinomas are rare tumours that produce somatostatin, a cyclic peptide normally produced by the delta cells of the pancreas or endocrine cells of the digestive tract, along with the hypothalamus, cerebrum, spinal cord and vagus nerve. Somatostatin inhibits other gastrointestinal hormones including insulin, glucagon, cholecystokinin and gastrin. Excessive somatostatin levels can cause the classical inhibitory syndrome of diabetes mellitus, cholelithiasis, weight loss, diarrhoea and hypo/achlorhydria [13], however only 2.5% of patients with duodenal somatostatinoma experience the classical inhibitory syndrome [9].

Psammoma bodies (Figure 4) are the most distinctive features on histology, present in 49-68% of duodenal somatostatinomas [10, 12, 13, 14, 15]. Pancreatic somatostatinomas, however, have been noted not to consistently exhibit localisation, psammoma bodies or pseudoglandular pattern. Both pancreatic and duodenal somatostatinomas will often stain positive for synaptophysin and chromogranin A. Somatostatin may be the only hormone detected, however tumours cells may also stain positive for insulin, glucagon, pancreatic polypeptide (PP), and vasoactive intestinal peptide (VIP) [10].

Over half of somatostatinomas arise in pancreatic parenchyma. These tend to be larger and with higher risk of malignancy than duodenal tumours. By virtue of their anatomic position, ampullary tumours present earlier and are less likely to be malignant at presentation [16].

Somatostatinomas are the most common gastrointestinal neuroendocrine tumour seen in NF1 and are more likely to occur in the duodenum [11], in keeping
with our series. Of interest NF1 also increases the incidence of GISTs in up to 25% of patients with less than 5% being symptomatic [17]. Case #3 demonstrates this observation clearly.

Computed tomography or MRI scans are useful in evaluating these ampullary lesions, revealing size of the primary lesion, possible biliary dilatation from mass effect of the ampullary somatostatinoma, and at the same time identify any regional disease such as enlarged lymph nodes, or metastatic disease to the liver. DOTATATE PET is reported as superior to all other imaging modalities for localisation of small tumours and detection of distant liver, lymph node and bony metastases [19, 20], although this was negative for Case #3 where the primary lesion and the 2 nodes were negative on DOTATATE PET.

Endoscopy and endoscopic ultrasound (EUS) can be used to visualise and biopsy the ampullary lesion. EUS can assess for features of submucosal invasion, regional lymph node metastases and significant intraductal extension, which are all regarded as contraindications to endoscopic resection. Endoscopic ampullectomy has been reported as an effective treatment for small superficial lesions of the papilla [21], since ampullary somatostatinomas arise from crypt cells of duodenal mucosa. Despite adequate EUS assessment, there is still a 7% incomplete ampullectomy resection rate [22], as in our third case. Other reported complications include perforation (0-8%), bleeding (2-30%), acute pancreatitis (3-25%), cholangitis (0-5%) and papillary stenosis (0-8%) [12, 22]. Pancreatic duct stenting is recommended for reducing the incidence of postoperative pancreatitis [21].

Surgical resection is still the cornerstone for treatment of ampullary somatostatinoma, considering its malignant potential. While pancreatic somatostatinomas often present with metastasis, ampullary somatostatinomas present early with localised disease. Endoscopic ampullectomy has its role as mentioned, but disease invading beyond the submucosa or with nodal involvement, with no distant metastasis, can benefit from PD with clearance of loco-regional disease. Five-year overall survival after resection for localised somatostatinoma with no extranodal spread has been reported as 100%, and for patients with metastatic disease, 60% [9]. Unfavorable prognostic features for somatostatinomas include size >3 cm, poor cytological differentiation, regional/portal metastases and incomplete surgical resection [5]. As seen in our series, 2 patients had PD as the primary treatment and the third patient had PD after an endoscopic ampullectomy was attempted which showed positive margins. Even though in the third case there was no gross tumour left in the ampulla, there were 2 positive nodes which were removed with PD which were also not identified on preoperative imaging. While it is unknown if nodal clearance for somatostatinomas improve survival, empirically PD allows a more complete clearance of disease than ampullectomy alone. All three patients are still disease free at last follow up ranging from 18 months to 11 years.

One of the three cases in our series also had PD performed in laparoscopic-assisted fashion. Dissection was performed laparoscopically and anastomoses were performed with a mini-laparotomy. In our series, the operating time was longer laparoscopically but the patient recovered well and was discharged within a week from surgery. Histology also confirmed that the resection margins were adequate. This was also attempted for the third case but was converted to open after laparoscopy in view of dense adhesions from a previous open cholecystectomy. While laparoscopic PD is not the current gold standard approach worldwide, with appropriate case selection and expertise, we show that laparoscopic assisted PD can be safely done with good outcomes [22, 23, 24, 25].

Our case series highlights that ampullary somatostatinomas are rare, but should be a consideration in patients presenting with ampullary mass effects and a genetic
predisposition such as NF1. These 3 cases were managed over a period of almost 10 years, during which surgical, endoscopic and imaging techniques have evolved, accounting for some variations in approach. While selected small superficial lesions may potentially benefit from endoscopic ampullectomy, the risk of an involved margin or inadequate nodal clearance remains. PD remains the main treatment option with good long-term outcomes [26, 27, 28, 29, 30]. A laparoscopic approach to PD is a feasible option in selected cases of ampullary somatostatinoma with good outcomes.

Conflict of Interest

The authors declare no conflict of interest.

References