J Gastrointest Canc (2019) 50:324–327
DOI 10.1007/s12029-017-0010-2

CASE REPORT

Locally Recurrent Well-Differentiated Nonfunctioning Pancreatic Neuroendocrine Tumor Requiring Re-excision Including Portal Vein Resection

Rachel N. Saunders[1] · **Mathew Chung**[2]

Published online: 30 September 2017

Introduction

Pancreatic neuroendocrine tumors (PNETs) account for 1–2% of pancreatic neoplasms, and nonfunctional PNETs (NF-PNETs) are more common than functional. Well-differentiated tumors make up 90% of the PNETs [1–4]. Local recurrences rarely occur with few reported incidences in the literature [5, 6]. Treatment of local recurrences can be technically difficult. We report the first local recurrence requiring an aggressive surgical resection, which necessitated hepaticojejunostomy take down and resection of the portal vein and superior mesenteric vein with a reverse saphenous vein graft reconstruction.

Case Presentation

The patient is a 57-year-old female with a remote history of nonfunctioning pancreatic neuroendocrine tumor that measured 6.5 × 5 × 5 cm. She had presented with a non-tender abdominal mass without any other symptoms. She had no significant past medical history, and prior surgical history was only significant for a soft-tissue hemangioma removal from her back.

She underwent a pancreaticoduodenectomy, and she did well postoperatively. Pathology report demonstrated a low-grade neuroendocrine tumor with negative margins (mitoses and Ki-67 were not available). No lymph nodes were evaluated. She did not undergo adjuvant therapy. The patient underwent surveillance for 5 years with imaging and chromogranin A levels, none of which demonstrated evidence of recurrence. Her last chromogranin A level from 8 months prior to presentation was 53.

Later, she began experiencing symptoms of aortic insufficiency and was found to have an aneurysm of the aortic root. She underwent aortic root replacement. Surveillance imaging of her repair revealed an abnormality noted in the upper abdomen 11 years after her previous pancreaticoduodenectomy.

Dedicated computerized tomography (CT) scan of the abdomen and pelvis demonstrated a lobulated hypervascular mass that measured 3.5 cm in axial dimension and 7.5 cm in length in the right upper abdomen (Fig. 1). It extended from anterior to the inferior vena cava at L4 cephalad to the porta hepatis (Fig. 2). There was preservation of fat around the superior mesenteric artery, but the mass appeared to be intimately related to the portal vein either within it or in the wall of the vein. As a result, there were a large number of mesenteric venous varicosities in the left abdomen.

Octreotide scan revealed an oblong pancreatic head (remnant) mass with intense uptake of the radiotracer (Fig. 3), and no other focus of abnormal radiotracer uptake was seen in the abdomen or pelvis to suggest metastatic disease.

Ultrasound of the liver was performed to assess the hepatic vessels, which revealed normal spectral Doppler waveforms in patent hepatic and portal veins. There was no Doppler ultrasound evidence of portal venous hypertension, liver disease, or vein thrombosis.

Her chromogranin A level was 82. She denied any symptoms.

✉ Rachel N. Saunders
Rachel.saunders@spectrumhealth.org

[1] Spectrum Health/Michigan State University General Surgery Residency, 221 Michigan NE, Suite 402, Grand Rapids, MI 49503, USA

[2] Spectrum Health Hospital, Surgical Oncology, Michigan State University College of Human Medicine, 221 Michigan NE, Suite 402, Grand Rapids, MI 49503, USA

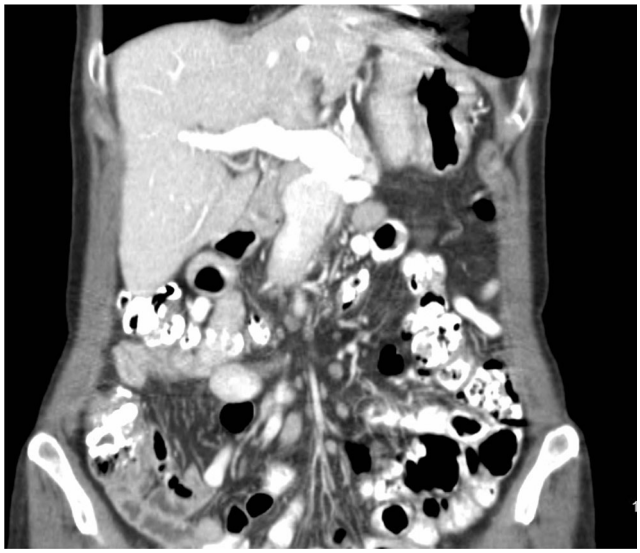

Fig. 1 CT of mass abutting portal vein

The patient was initially offered surgical resection, but she was hesitant and wanted to attempt other treatment options.

She received somatostatin analog injections. Repeat CT scan revealed the tumor had increased in size.

She then received 4000 cGy of radiation. Repeat imaging revealed that the mass had stabilized, but she became symptomatic. The patient elected to have the mass surgically removed.

A midline laparotomy was performed. In order to access the mass, the hepaticojejunostomy was taken down. The pancreaticojejunostomy was preserved. The mass was intimately associated with the inferior vena cava inferiorly, although a plane could be developed. Superiorly, the mass was intimately associated with the portal vein. No plane could be developed and an intraoperative ultrasound failed to reveal a plane. Part of the portal vein and superior mesenteric vein had to be resected en bloc. Reconstruction was then performed with a reverse saphenous vein graft.

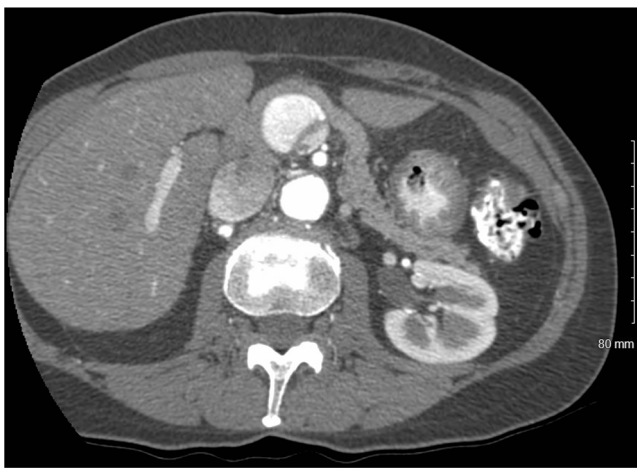

Fig. 2 CT of mass abutting the porta hepatis

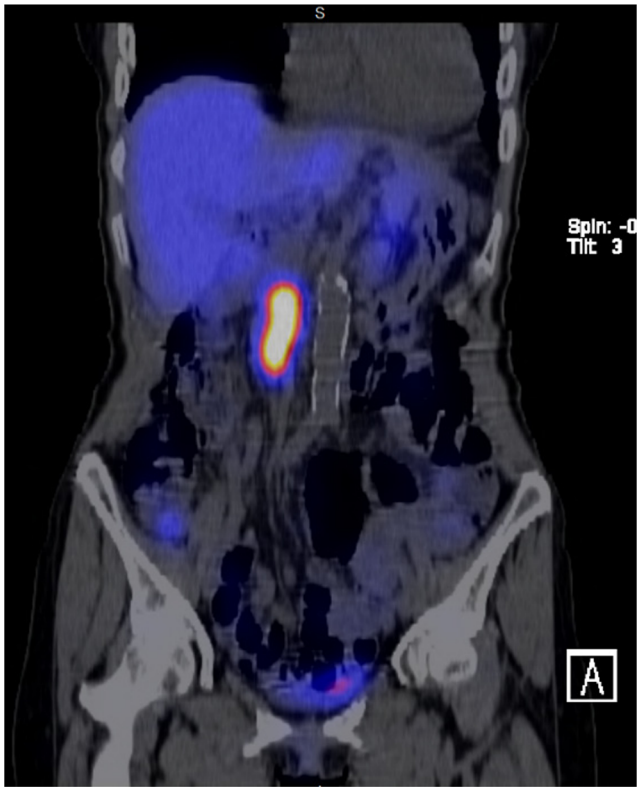

Fig. 3 Octreotide scan of mass and no evidence of metastatic disease

Pathology revealed a well-differentiated unifocal neuroendocrine tumor 6 cm in the greatest dimension (Fig. 4). The tumor invaded into the portal vein. It was well differentiated with < 2 mitoses/10 high-power fields (Fig. 5). Ki-67 was between 3 and 5% (Fig. 6).

The patient initially did well postoperatively. She had a hepaticojejunostomy leak, which was managed with a percutaneous transhepatic biliary (PTC) drain and the surgically placed Jackson-Pratt (JP) drains. The patient was discharged home postoperative day 17 tolerating a general diet and with

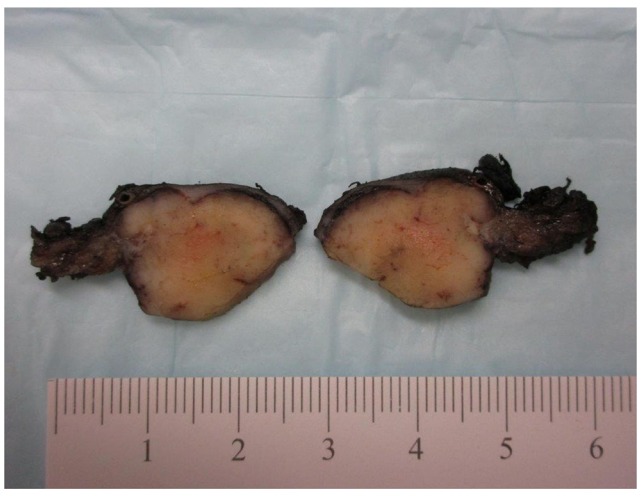

Fig. 4 The mass divided in the pathology department

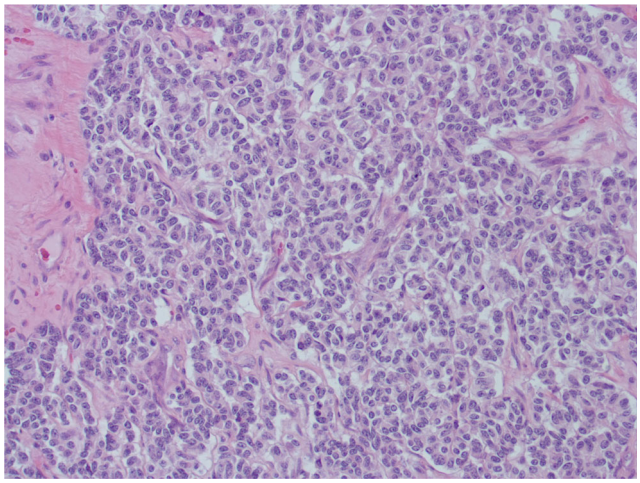

Fig. 5 H&E stain of mass ×200. This slide reveals the typical architecture and cytology of this tumor consisting of an overall nested pattern with thin fibrous septae, small blue round cells with a high nuclear to cytoplasm ratio, and round to oval nuclei with granular chromatin

the PTC drain clamped. Eventually, her PTC drain and JP drains were removed. In postoperative follow-up, she was doing well and did not have evidence of recurrence at one and a half years after surgery as evidenced by CT of the abdomen and pelvis with intravenous contrast.

Discussion

In this case, we presented a successful treatment of a locally recurrent PNET invading the portal vein after a pancreaticoduodenectomy with negative margins. There is limited data on locally recurrent well-differentiated PNET. Recurrences do occur, and it is important to understand who is at increased likelihood and what proper follow-up is.

When looking at recurrence, 6.7–11.4% of well-differentiated NF-PNETs recurred after resection [5, 6].

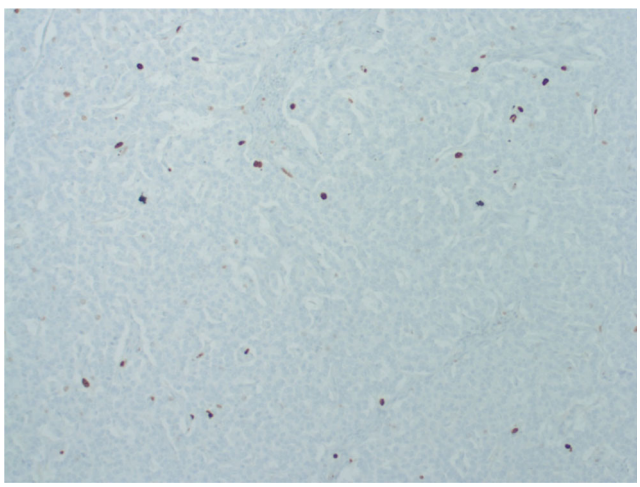

Fig. 6 Ki-67, a maker for cellular proliferation, stain of the mass

Recurrences ranged from 2.9–147 months with a median of 23 months after curative resection [5, 6]. Metastatic disease is more common than local recurrence [5, 6]. Primary lymphnodal PNETs have been described as well [7]. It is possible that this patient's mass arose from lymphnodal metastatic disease; although in this case, after discussing with our pathologists, it is not possible to know if that was the case.

Well-differentiated tumors make up the majority of the PNETs [8]. Altough generally associated with less aggressive tumors, the likelihood of well-differentiated PNETs recurrences is directly related to the Grade. The 2010 World Health Organization grading system is based off mitotic count and expression of nuclear antigen Ki-67, a cellular proliferation marker, and it divides well-differentiated tumors into two categories. Grade 1 (G1) is associated with a Ki-67 index < 3% and/or mitotic count < 2/10 HPF. Grade 2 (G2) is associated with a Ki-67 index 3–20% and/or mitotic count 2–20/10HPF. Recurrence rate has been shown to be increased with G2 disease, male gender, > 20 mm in tumor size, and the presence of lymph node metastasis, liver metastasis, lymphatic invasion, and neural invasion [6].

The original pathology report, which was performed before 2010, did not include the mitotic count or Ki-67 index. Based on the recurrent tumor's < 2 mitoses/10 high-power fields and Ki-67 was between 3 and 5%, the tumor would qualify as a G2.

The National Comprehensive Cancer Network (NCCN) currently recommends one post-resection CT or MRI 3–12 months after resection of well-differentiated PNETs. After 1 year, NCCN currently recommends an office visit and considering biochemical markers and CT or MRI every 6–12 months for up to 10 years. Follow-up is not different for G1 or G2 disease. The 2012 European Neuroendocrine Tumor's Society Consensus Guidelines recommend resected G2 disease follow-up every 6 months with imaging and chromogranin A levels [8]. For resected G1 disease, follow-up surveillance is not recommended. They do not recommend an end date to this follow-up, but no source is cited for this recommendation.

The only curative treatment for local disease is surgical resection, and it is the consensus treatment. Other potential options were pursued in this case secondary to a patient wanting to avoid another large surgery. Radiotherapy is not traditionally considered effective in neuroendocrine tumors. One study has evaluated radiotherapy as treatment for pancreatic neuroendocrine tumor [9]. In this study, 13% had a complete response, 26% had a partial response, 56% had stable disease, and 4% had progressive disease [9]. Our patient fell into the majority with stable disease.

The initial surgical resection of PNETs frequently requires en block resection of other organs. In one study, 21% of patients required portal vein resection [10]. Those patients requiring portal vein resection have been shown to increase mortality (11 vs. 3%) and morbidity (44 vs. 50%) [10].

Re-operation would logically increase the risk of mortality and morbidity and support the need for an experienced surgeon.

Due to the increased likelihood of recurrence with G2 disease and the difficulty with treating locally recurrent disease, longer surveillance should be considered in those patients. It would be logical to presume local recurrence primary treatment should be treated with surgical resection just as the primary tumor is. Due to the difficulty of operating in a re-operative field, locally recurrent disease should be surgical resected with an experienced surgeon.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

1. Yao JC, Eisner MP, Leary C, et al. Population-based study of islet cell carcinoma. Ann Surg Oncol. 2007;14:3492–500. https://doi.org/10.1245/s10434-007-9566-6.
2. Metz DC, Jensen RT. Gastrointestinal neuroendocrine tumors: pancreatic endocrine tumors. Gastroenterology. 2008;135:1469–92. https://doi.org/10.1053/j.gastro.2008.05.047.
3. Oberg K. Pancreatic endocrine tumors. Semin Oncol. 2010;37:594–618. https://doi.org/10.1053/j.seminoncol.2010.10.014.
4. Mckenna LR, Edil BH. Update on pancreatic neuroendocrine tumors. Gland Surg. 2014;3:258–75. https://doi.org/10.3978/j.issn.2227-684X.2014.06.03.
5. Schurr PG, Strate T, Rese K, et al. Aggressive surgery improves long-term survival in neuroendocrine pancreatic tumors: an institutional experience. Ann Surg. 2007;245:273–81. https://doi.org/10.1097/01.sla.0000232556.24258.68.
6. Tsutsumi K, Ohtsuka T, Fujino M, et al. Analysis of risk factors for recurrence after curative resection of well-differentiated pancreatic neuroendocrine tumors based on the new grading classification. J Hepatobiliary Pancreat Sci. 2014;21:418–25. https://doi.org/10.1002/jhbp.47.
7. Prithiviraj N, Godhi S, Saravanan MN, et al. Well differentiated lymphnodal neuroendocrine tumour: can they be primary? HPB. 2016;18:e455. https://doi.org/10.1016/j.hpb.2016.03.197.
8. Falconi M, Bartsch DK, Eriksson B, et al. ENETS consensus guidelines for the management of patients with digestive neuroendocrine neoplasms of the digestive system: well differentiated pancreatic non-functioning tumors. Neuroendocrinology. 2012;95:120–34. https://doi.org/10.1159/000335587.
9. Contessa JN, Griffith KA, Wolfe E, et al. Radiotherapy for pancreatic neuroendocrine tumors. Int J Radiat Oncol Biol Phys. 2009;75:1196–200. https://doi.org/10.1016/j.ijrobp.2008.12.044.
10. Birnbaum DJ, Turrini O, Vigano L, et al. Surgical management of advanced pancreatic neuroendocrine tumors: short-term and long-term results from an international multi-institutional study. Ann Surg Oncol. 2015;22:1000–7. https://doi.org/10.1245/s10434-014-4016-8.