



A Case of a Large Non-Functional Pancreatic Neuroendocrine Tumor: A Case Report and a Review of the Literature

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Abstract

In patients with non-functioning pancreatic neuroendocrine tumors, surgical resection is a viable option for many. Although rare, the general surgeon should be familiar with the workup, evaluation and treatment of these tumors. PNETs account for 1% of all pancreatic tumors, the majority of which are non-functional. The location variation of these can be significant making surgical planning challenging. Although PNETs can occur sporadically, they have been found to be associated with MEN-1, Von Hippel-Lindau, and neurofibromatosis type 1. PNETs, also called Islet cell tumors, are pancreatic neoplasms that are derived from islet cells within the pancreas. Non-functioning PNETs are typically found incidentally on imaging. However, patients with larger PNETs may present with abdominal pain, mass effect, obstructive symptoms, or metastatic disease. Surgical resection in these patients can be curative or palliative.

Introduction

JL is a 59 year-old female with a past medical history of morbid obesity with lap band that presented to her family medicine clinic on May 6th, 2019 complaining of fatigue for several months. She reported a lack of appetite, 20 pound unintentional weight loss and malaise. She had been worked up previously for hypothyroidism and was started on levothyroxine with minimal relief of symptoms. However, after starting on levothyroxine, she reported continued lethargy and fatigue. At this initial visit to her primary care provider, she was noted to have abdominal fullness measuring approximately 10 cm in diameter. Due to the fullness in the abdomen, the primary care provider ordered a CT scan of the abdomen and pelvis with IV contrast and basic lab work. She was also scheduled to see her bariatric surgeon for removal of Lap band.

Case Presentation

Imaging

CT abdomen pelvis findings: There is a large solid vascular heterogeneous mass involving most of the body and tail of the pancreas. This measures approximately 12 cm × 12 cm × 11 cm. The mass pushes the stomach anteriorly and stomach laterally. Etiology of mass is uncertain based on imaging. Could represent pseudopapillary tumor or neuroendocrine tumor but is non-specific (Figures 1-3).

The patient then presented to the bariatric/general surgery office after referral from primary care for concerns of pancreatic mass. The patient has noted early satiety over the past several months as well as weight loss and fatigue. The abdominal exam revealed a large, central abdominal mass. CT report and images were reviewed. CT pancreas protocol was ordered at this time. The patient also underwent MRI abdomen with and without contrast. This revealed a large mass centered in the tail region of the pancreas with a couple arterially enhancing liver lesions concerning for metastases. Large hemangioma also noted in the left hepatic lobe. CT angiography of the abdomen and pelvis revealed the hepatic lesions were consistent with hemangioma. CA-19-9 was within normal range. No other significant laboratory findings at that time. Oncology was consulted and the patient was scheduled for distal pancreatectomy with splenectomy.

Operative report: July 26th, 2019

Patient taken for distal pancreatectomy, partial gastrectomy with Roux-en-Y gastrojejunostomy, splenectomy, gastric band and port removal.

In the preoperative area informed consent was obtained and all questions were answered. She

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Figure 1: CT abdomen pelvis findings.

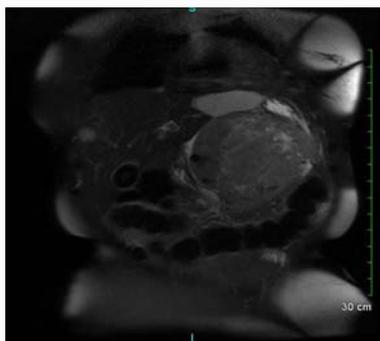


Figure 2: MRI abdomen w/w/o contrast (T1).

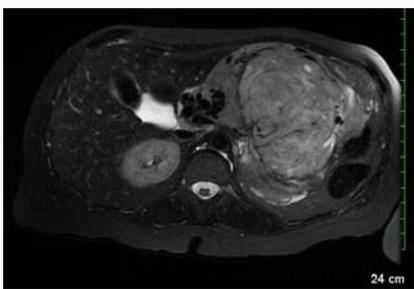
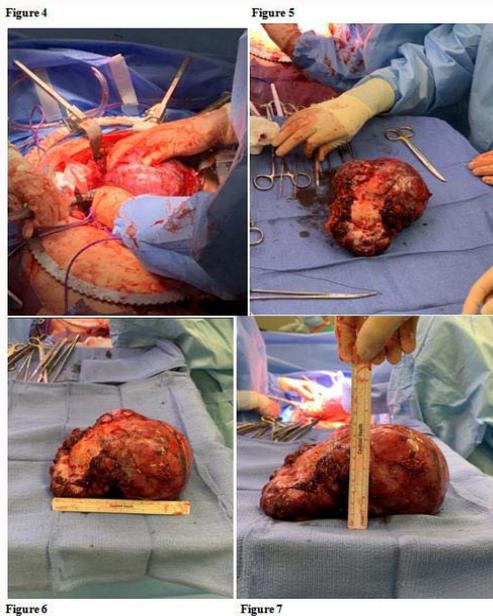


Figure 3: MRI abdomen w/w/o contrast (T2).

was wheeled back to the operating room and placed supine on the operating table. She was placed under excellent general endotracheal anesthesia and a left arterial line and right internal jugular central venous catheter was inserted. A Foley catheter was placed to monitor resuscitation. The patient was prepped and draped in the usual sterile fashion using Chloraprep and a surgical time out was performed.

A midline laparotomy incision was made with a ten blade from xiphoid to suprapubic. It was taken down using Bovie electrocautery until we entered the peritoneum. When we had good visualization of our abdomen, we used LigaSure to take down any adhesions for better visualization. We immediately noticed, on inspection, a hemangioma on the liver and a large 15 cm mass displacing the stomach downward. We inspected and palpated the rest of the abdomen and checking small bowel, did not notice any other masses or abnormalities. We entered the lesser sac through the gastrocolic ligament and took the ligament laterally and medially to make room, we took down the short gastrics with good hemostasis. The mass was adherent to the antrum of the stomach. We used LigaSure to dissect it free from the superior stomach, however, we noticed it would not free from the distal stomach/antrum. We came across the stomach with an echelon stapler, utilizing a green load proximal to the antrum.



Figures 4-7: Operative images.

We then, using combination of LigaSure and stick ties (3-0 vicryl) were able to obtain hemostasis as we went. Despite this, the tumor was bleeding profusely. As we were dissecting lateral to the tumor the LigaSure came across the splenic hilar vessels. We then took the spleen with two echelon white loads. Hemostasis was achieved. We were able to bluntly dissect with our fingers behind the neck of the pancreas and came across it with an echelon white load. With one whiter load we were able to free the mass from the peritoneal attachments and adhesions to nearby structures and deliver it. It was at least 15 cm in diameter and close to 5 lbs. We then transected the duodenum distal to the antrum using Echelon blue load and removed the antrum. We turned our attention to the gastric band and freed it from the capsule using Bovie electrocautery and then removed it from the stomach and abdomen. Next starting at ligament of Treitz we traveled down 50 cm and transected it with 2 white loads. We then measured out 80 cm of jejunum distally for the alimentary limb. We secured the jejunojejunostomy with a running 3-0 vicryl suture and created two enterotomies. We used the echelon to staple our jejunojejunostomy and closed the remaining enterotomy with running 3-0 Vicryl. We then took the proximal end of the alimentary limb and secured it to the distal stomach remnant. We created two enterotomies with the Bovie and stapled with the echelon to create our gastrojejunostomy. We then closed our remaining enterotomy with the running vicryl suture. We were satisfied with our repair. We took one more look in the abdomen and ensured hemostasis with Surgiflo and 3-0 Vicryl stick ties in our dissection bed, where small unnamed vessels were bleeding. We were happy with our hemostasis and closed our mesenteric defects with Ethibond running suture, tacking the jejunum to the mesentery after we closed the majority of the defect to ensure that it would not slide though superiorly. We then removed the port from inside of the abdominal wall and closed the fascial defect with a figure of 8, 0-vicryl suture. Finally, we closed the abdomen with 0 PDS in running fashion. The skin was closed with staples and dressed with abdominal pads and tape. All counts were correct (Figures 4-7).

Estimated blood loss intraoperatively: 2L

Table 1: WHO 2010 Grading system based on mitotic count and Ki-67 indices (ENETS).

Grade	Differentiation	Ki-67 index %	Mitotic Count/10 HPF
G1(low)	Well	<= 2	<2
G2(intermediate)	Well	3-20	2-20
G3(high)	Poor	>20	>20

Table 2: Tumor staging.

Tumor staging	Description
TX	Cannot be assessed
T0	No evidence of tumor
T1	<2 cm, limited to pancreas
T2	2 cm to 4 cm, limited to pancreas
T3	>4 cm limited to pancreas
T4	Involving adjacent organs or blood vessels

Table 3: Nodal staging.

Nodal Staging	Description
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis present

Patient received 4 units of packed red blood cells, 4 units of fresh frozen plasma

Mass Measurements: 15 cm × 9 cm × 10 cm, 80oz

Post-operative report

The patient was transferred to the intensive care unit postoperatively. The patient was mobile the following day after surgery on July 27th, 2019, able to get up out of her bed and move to her chair. She remained NPO at this time as she had not yet had a bowel movement. The patient's postoperative blood loss anemia remained stable. On July 28th, 2019, Post-operative day #2, the patient remained mobile and was able to walk around the unit. She had still yet to pass a bowel movement. On July 30th, 2019, Post-operative day #3, the patient was noted to be hypoglycemic at 56. The patient was started on D5W at 75 mL/h and Accu-Cheks ordered every 4 h. The patient remained NPO as she had not yet passed a bowel movement. On July 31st, 2019, post-operative day #4, the patient's hypoglycemia had improved and she had been advanced to a full liquid diet as she began passing flatus. D5W was discontinued as were the Accu-Cheks. The patient maintained excellent pain control with her pain medication regimen. On August 1st, 2019, Post-operative day #5, the patient noted that she did have a bowel movement over the course the previous evening and continued passing flatus. She was advanced to a regular diet and was tolerating it well without nausea or vomiting. Her only complaint at that time was mild incisional pain. The patient was medically cleared for discharge with instructions to follow-up with the surgeon on August 9th and follow-up with her primary care physician and oncologist in 1 to 2 weeks.

Follow up with surgeon: August 9th, 2019

The patient reported mild reflux but otherwise doing well. She was tolerating a diet, her post-operative pain had resolved and she had no new complaints.

Oncology consultation

Patient had been following with Oncology who had determined the staging of pT3pN0Mx well differentiated neuroendocrine carcinoma (G2). She was scheduled for PET scan and further workup

Table 4: Metastases staging.

Metastases staging	Description
M0	No distant metastasis
M1	Distant metastasis present

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Table 5: Stage.

0	Description
I	T1, N0, M0
II A	T2, N0, M0
II B	T3, N0, M0
III A	T4, N0, M0
III B	Any T, N1, M0
IV	Any T, Any N, M1

to evaluate concerning lesions in the liver. Pathology revealed negative margins.

Repeat CT done on October 29th, 2019

Interval increase in size of indeterminate hypodense lesion in the left hepatic lobe measuring 1.5 cm. Suspicious for metastatic disease. There are two additional subcentimeter lesions with a similar appearance, also worrisome for metastases. Recommend further evaluation with PET/CT. Findings suspicious for metastatic peri-portal lymph node measuring 1.8 cm × 1.3 cm. Improved post-surgical inflammatory changes. Persistent free fluid in rectouterine cul-de-sac. The liver lesions were determined to be hemangiomas per triple phase CT.

PET done on December 27th, 2019

Revealed no lesions of concern for metastatic disease.

Discussion

Pancreatic Neuroendocrine Tumors can be divided into two main subtypes: Functional and non-functional depending on their ability to secrete biologically active hormones [1,2]. In this discussion we will focus on the non-functional subtype which was described in the case.

Neuroendocrine tumors remain a rare pathology for the general surgeon. However, of all neuroendocrine tumors, pancreatic neuroendocrine tumors are the most common, making up 7% of all NET's. The overall incidence of PNETs appears to increase with age, with the peak being 65 years of age. Of all PNETs, non-functioning PNETs comprise up to 90% and are often asymptomatic. These tumors commonly present as advanced disease when metastatic complications arise [2].

Staging and prognosis of PNETs have changed in recent years, focusing on the mitotic counts and Ki-67 indices. Well differentiated tumors are determined to be lower grade as poorly differentiated tumors are higher grade (Tables 1-5).

As mentioned before, non-functional PNETs are often asymptomatic until the disease process is more advanced. The lack of hormonal function of these tumors makes symptomatology lacking or non-specific. Commonly, the presenting symptoms are due to mass effect from a large, growing tumor. This was the case in our patient which initiated her workup. These tumors are often found in the pancreatic head resulting in obstructive symptoms, both duodenal and pancreatic and biliary. Common symptoms include weight loss,

jaundice, and abdominal pain. The most common area of metastasis is hepatic. Often bilobar and multifocal [2].

90% of NF-PNETs are sporadic with up to 10% being genetically associated. Up to 75% of patients with multiple endocrine neoplasm type 1 eventually develop PNETs, most commonly, NF-PNETs. Of note, patients with von-Hippel Lindau syndrome do have an increased incidence of PNETs, up to 20% [2].

Diagnosics

The imaging modality of choice remains Computed Tomography with IV contrast if high suspicion of PNETs. PNETs typically appear well circumscribed with enhancing features with contrast, specifically during the arterial phase of CT. Referring back to Figure 1 above; the mass appears well circumscribed with arterial enhancement.

Alternatively, MRI is another option for diagnosis and operative planning of suspected PNETs. PNETs display low signal intensity with T1 weighted and high intensity on T2 weighted images. Referring to Figures 2 and 3, the intensity difference can be observed [2].

Treatment

Surgical resection of symptomatic NF-PNETs remains the treatment of choice and is suggested in ENETS consensus Guidelines [3]. Surgical resection is often the only curative option for patient with pancreatic neoplasms. Patients with NF-PNETs may benefit from symptomatic relief as well as curative outcomes depending on pre-operative staging. Patients with obstructive symptoms will likely need operative intervention regardless of respectability for symptomatic relief. Per the ENETS guidelines, these patients may undergo tumor resection with hepatic metastasis resection concomitantly. However, if a pancreaticoduodenectomy is performed, large hepatic resection should be avoided.

In patients with <2 cm NF-PNETs, observation has been suggested, however, safe resection remains the recommendation as it may be curative. Larger lesions, however, are likely to require surgical resection [3].

NF-NETs remain to be primarily treated with surgical resection. According to a large retrospective study done by Hill et al. [4] patients with NF-NETs exhibited significant survival benefits in all stages of surgery. The results revealed that patients benefit from surgical resection in local, regional and metastatic disease. Overall, the median survival difference in patients undergoing surgical resection was 114 months vs. 35 months in patients not undergoing resection. It has been suggested that small <1 cm, low grade tumors may be surgically enucleated. However, with larger masses, more extensive operations may be required. Typically, PNETs located in the head of the pancreas should be considered for pancreaticoduodenectomy, whereas distal pancreatectomy should be the operation of choice for lesions located in the body and tail. Splenic preservation is typically an intra-operative decision and does not appear to affect overall outcomes. For smaller lesions requiring distal pancreatectomy, a minimally invasive approach may be feasible and has been shown to reduce morbidity; mortality, operative blood loss, and length of hospital stay [2].

Any lesion >2 cm or lesions with calcification are recommended to undergo simultaneous lymphadenectomy.

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