

Nonfunctional Pancreatic Neuroendocrine Tumors: A Retrospective Review and Early Detection facilitated by EUS and Novel CORE biopsy techniques

Neil R Sharma^{1,2,3} M.D., Alexander Perelman⁴ D.O., MS, Akshay Sharma^{5,6} M.D., Christina Zelt⁷ RN, MSN, Colin S Linke^{8,9} D.O., Kevin Lowe^{1,2} M.D., PhD., Saurabh Gupta^{1,2} M.D.
¹Parkview Health, ²Parkview Physicians Group, ³Indiana University School of Medicine, ⁴University of Connecticut Health Center, Farmington, CT
⁵Detroit Medical Center, ⁶Wayne State University School of Medicine, ⁷Parkview Research Center, ⁸Loyola University Medical Center, ⁹Lincoln Memorial University-DeBusk College of Osteopathic Medicine

Background

- An estimated 48,960 people were diagnosed with pancreatic cancer in 2015.
- Pancreatic neuroendocrine tumors (PNET) account for approximately 3% of all pancreatic cancers. The more common, "non-functioning neuroendocrine tumors" (NF-PNET) produce vague symptoms with delayed diagnosis and thus a poor prognosis.
- Symptoms indicative of NF-PNETs are usually caused by the growth and spread of the tumor and can include: feeling a mass in the abdomen, weight loss, abdominal and back pain, jaundice, diarrhea, and indigestion.^{1,2}

Objective

- To analyze diagnosis, treatment and outcome data of patients diagnosed with NF-PNET at a large tertiary community referral hospital and evaluate Changes in diagnosis and outcomes that may be effected by implementing high quality EUS and novel needle biopsy.

Methods

- A retrospective chart analysis was conducted on patients diagnosed with NF-PNETs at a large tertiary community hospital from 2013 to 2016.
- All patients were seen through the Advanced Interventional Endoscopy & GI Oncology Program and underwent multi-disciplinary review of diagnosis, staging, and treatment planning.
- Charts were audited for: patient demographics, symptoms, tumor characteristics, whether patients underwent EUS guided needle biopsy (EUS-FNB), any test results for certain biomarkers, treatments, and survival post- diagnosis.

Results

- The cohort consisted of 13 patients with a total of 14 NF-PNETs, with sizes ranging from 1.01cm to 9cm, 61.5 % of which were less than or equal to 2cm.
- Initially high resolution CT was utilized in patient evaluation, but had difficulty identifying tumors under 4cm in 15% of patients.
- All lesions found on EUS were confirmed with novel EUS guided CORE biopsy rather than Fine Needle Aspiration (FNA).
- All samples were stained for biomarkers to confirm diagnosis; 100% tested positive for chromogranin and synaptophysin.
- Eight of 13 patients (61.5%) underwent surgical resection; seven of whom are currently living.
- Three patients were treated with chemotherapy alone, with only a single survivor at 21 months.
- Two patients declined surgery or medical intervention and remain under close surveillance 8 and 27 months from initial diagnosis.

Imaging And Tables

#	Age at Dx	CT+	Stage	Size (CM)	Location	Biomarkers (+)	Treatment	Survival (months)
1	43	CT+	T1N0M0	1.2, 1.6	Head and Tail	C+ S+ K+	Surgery	Alive (18)
2	47	CT-	T1N0M0	1.01	Body	C+ S+	Surveillance	Alive (27)
3	41	CT+	T1N0M0	1.14	Head	S+ C+	Surgery	Alive (35)
4	35	CT+	T1N0M0	1.4	Body	C+, S+	Surgery	Alive (24)
5	73	CT-	T2N0M0	2	Body	C+, S+, K+	Surgery	Alive (22)
6	51	CT+	T3N0M0	3.5	Head	S+	Surgery	Alive (41)
7	76	CT+	T3N0M0	2.7	Head	C+, S+	Surgery	Deceased (1)
8	47	CT+	T3N0M1	9	Tail	C+, S+	Surgery	Alive (8)
9	60	CT+	T3N1M1	3.7	Head	S+	Chemo	Deceased (7)
10	64	CT+	T3N1M1	17	Head	K+ S+ C+	Chemo	Deceased (4)
11	46	CT+	T4N1M1	8	Head	C+	Y90, Chemo	Alive (21)
12	72	CT+	T1N0M0	1.3	Tail	C+S+	Surveillance	Alive (8)
13	34	CT+	T2N0M0	6.5	Tail	C+S+	Surgery	Alive (38)

C- chromogranin; S- synaptophysin; K- Ki67

Table 1: Patient characteristics including initial imaging findings, TNM stage, location and size of tumor. Also, demonstrating management approach and survival at time of study.

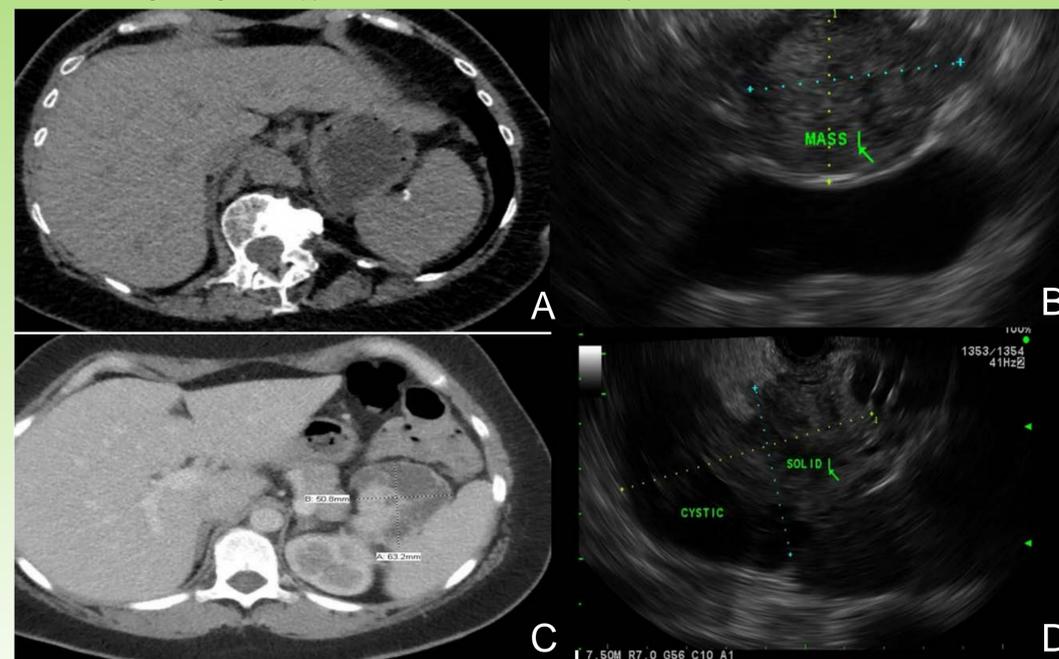


Figure 1: Comparing patient five's CT without evidence of PNET (A) with EUS for the same patient demonstrating a 2 cm mass in the body of the pancreas (B). We also demonstrate a large 6.5 cm PNET on CT (C) and EUS (D) for patient thirteen.

Pathology

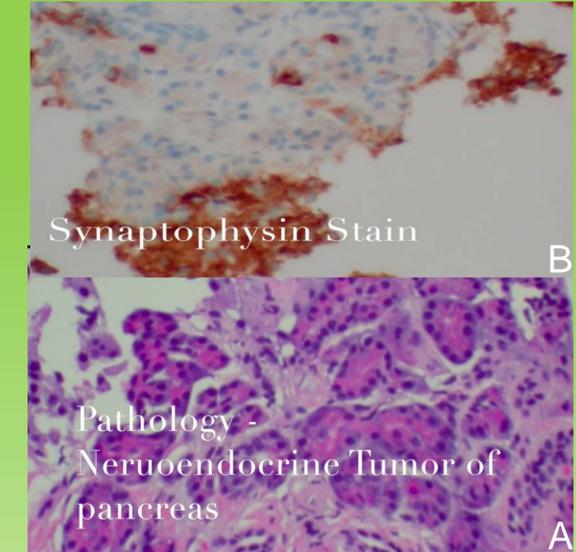


Figure 2: Histologic example with immunohistochemistry of PNET with H&E (A) and Synaptophysin (B).

Conclusion

- The use of EUS for imaging and confirmation with CORE biopsy may account for the smaller size of lesions detected in this study and earlier detection may improve long term survival.
- While radiological modalities, including CT, MRI, PET may detect an abnormal mass, EUS can inspect the pancreas with greater detail and enable earlier detection of lesions.
- EUS guided CORE biopsies – with the use of novel tissue acquisition needles - can obtain large histologic samples to be stained for biomarkers, including chromogranin, synaptophysin, and Ki67.
- Early detection can improve survival rates which depend on various factors including tumor characteristics and resectability. Increased sensitivity of EUS in the hands of a dedicated interventional endoscopist with advanced training and multidisciplinary review may improve detection, planning and treatment of PNETs.

Citations

- American Society of Clinical Oncology (ASCO). (2015). Types of cancer. Cancer.Net. <http://www.cancer.net/cancer-types>
- National Institutes of Health (NIH). (March 2015). Pancreatic Neuroendocrine Tumors (Islet Cell Tumors) Treatment (PDQ®). http://www.cancer.gov/types/pancreatic/patient/pnet-treatment-pdq#section/_11.