Comparison of Clinicopathologic Factors in 122 Patients with Resected Pancreatic and Ileal Neuroendocrine Tumors from a Single Institution

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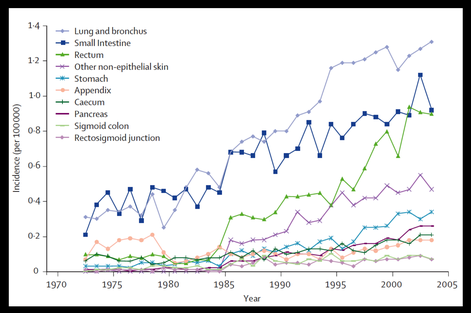
Introduction

- Gastroenteropancreatic Neuroendocrine Tumors (GEP NETs)
- NETs are rare tumors
  - Annual Incidence: 2.5-5 cases per 100,000
  - SEER: five-fold increase in incidence over past 30 years
- Ileal NETs (INETs) and pancreatic NETs (PNETs): two important subtypes
  - Share common clinical and pathologic features
  - Can differ in outcome and behavior



Increased incidence of carcinoid tumors, US population 1973-2005. Data from SEER database, US National Cancer Institute (Adapted from Modlin et al. Lancet; Jan 2008.

Aims

1. Compare clinicopathologic factors between patients with resected INETs and PNETs
2. Determine the incidence of preoperative elevation of biochemical markers
3. Examine survival in INETs and PNETs

Methods

- Retrospective chart review
  - Demographics and clinical symptoms
  - Preoperative imaging and biomarker levels
  - Pathology
  - Octreotide therapy
- Statistics
  - Student's t-test, ANOVA
  - Kaplan-Meier method for survival

Results

- Between 1998-2010, 141 patients underwent resection of GEP NETs
  - 52 with INETs, 70 with PNETs
  - 19 other (duodenal, rectal, gastric, colonic, appendicial, and liver)
  - 53% males
  - Mean age (years): 56.3 ± 13.7
- Median follow-up: 30 months (range 1 - 156)

Clinicopathologic and treatment related variables

Variable	INETs (%)	PNETs (%)	P
Age (years ± SD)	58.4±12.1	54.7±14.6	0.061
Gender (males/total)	32/52 (61.5)	33/70 (47.1)	0.115
Symptoms			
Abdominal Pain	18/52 (34.6)	33/70 (47.1)	0.165
Flushing	23/52 (44.2)	10/70 (14.3)	<0.001
Diarrhea	33/52 (63.4)	11/70 (15.7)	<0.001
Pathology and treatment			
Size on Pathology (cm)	2.0±0.9	4.2±2.4	<0.001
Vascular Invasion	42/44 (95.5)	41/68 (60.3)	<0.001
Nodal status			<0.001
N0	7 (14.9)	25 (49.1)	
N1	40 (85.1)	26 (50.9)	
Differentiation/Grade			0.484
Well/Low	40 (76.9)	45 (68.2)	
Mod/Intermediate	10 (19.2)	15 (22.7)	
Poor/High	2 (3.8)	6 (9.1)	
M1 disease	40/52 (76.9)	26/70 (37.1)	<0.001
Multiple Primaries	13/52 (25.0)	6/70 (8.6)	0.05
Octreotide Rx	46/51 (90.2)	30/70 (42.8)	<0.001
Imaging and biomarkers			
Radiologic Image Size (cm)	2.0±2.6	3.4±2.2	<0.001
Chromogranin A*	25/32 (78.1)	19/35 (54.3)	0.036
Pancreastatin*	35/40 (87.5)	16/38 (42.1)	<0.001
Serotonin*	36/40 (90.0)	17/40 (42.5)	<0.001
Glucagon*	3/30 (10.0)	6/31 (19.4)	0.253
VIP*	0/26 (0.0)	2/27 (7.4)	0.255
Gastrin*	2/27 (7.4)	5/36 (13.9)	0.349
Pancreatic Polypeptide*	4/11 (36.4)	5/24 (20.8)	0.283

*Values refer to the number of patients with levels above the upper normal limit

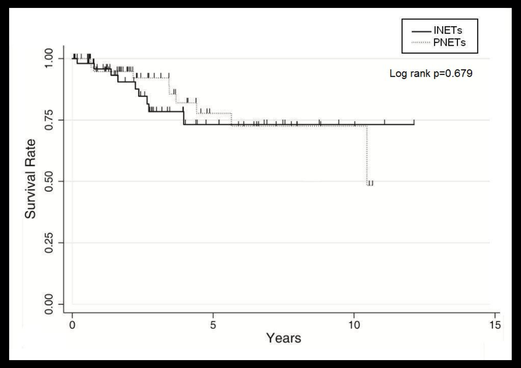
Results of Octreoscans and CT scans

	INETs n (%)	PNETs n (%)
Octreoscan		
Negative Scan	4 (8.3)	3 (6.6)
Primary Tumor* Only	13 (27.1)	25 (55.6)
Metastasis Only	15 (31.2)	6 (13.3)
Primary Tumor* and Metastasis	16 (33.3)	11 (24.4)
Total	48	45
CT		
Negative Scan	4 (7.8)	2 (2.9)
Primary Tumor Only†*	5 (9.8)	42 (60)
Nodal Involvement Only	5 (9.8)	-
Nodes and Mets	4 (7.8)	-
Metastasis Only	20 (39.2)	1(1.4)
Primary Tumor, Nodes, and Metastasis	13 (25.5)	25(35.7)
Total	51	70

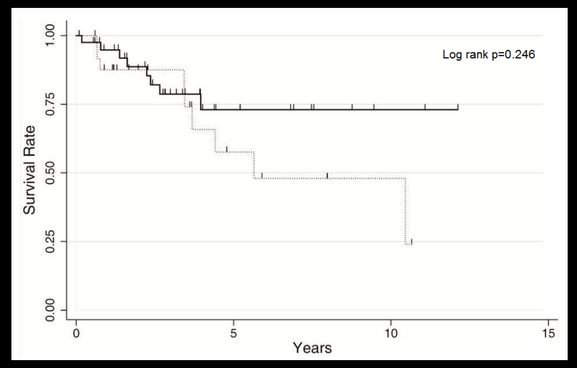
* For INETs, primary tumors were often indistinguishable from adjacent nodes and are combined in this table

† Thickening of the ileum/small bowel is considered evidence of a primary lesion.

Overall Survival



Survival: M1



Discussion

- Patients with INETs presented more often with nodal and distant metastasis, had a higher incidence of elevated biomarker levels, and more frequent symptoms as compared to those with PNETs. While these findings imply a more aggressive behavior exhibited by INETs, we found no difference in survival between these two groups. Therefore, the contrary argument, that INETs actually have a more indolent tumor biology, should be entertained.
- We also found that currently available biomarkers are not selective enough to differentiate INETs from PNETs, and that both octreoscans and CT scans were more useful in identifying primary tumors in patients with PNETs versus INETs (or their adjacent nodes).
- Finally, the strategy of surgical resection of the primary with hepatic debulking (where feasible) led to favorable survival in our patients. Unfortunately, proof that this approach results in improved survival is unlikely to ever be supported by randomized clinical trials, because these tumors are rare, present heterogeneously, and patients may not accept being assigned to the control group. Therefore, clinicians who take care of these challenging patients will continue to have to make decisions based upon the best retrospective data available.