

Vesalius SCALpel™ : Carcinoid and Endocrine Pancreas

Carcinoid

most common GI neuroendocrine tumor

age 2nd to 9th decade

55% GI origin, 30% bronchial, 1.5% of GI neoplasms

enterochromaffin cells crypts of Lieberkuhn

from diffuse population of neuroendocrine cells

stimulate intense desmoplastic reaction

symptoms: diarrhea, flushing, bronchospasm

octreotide (somatostatin analog) suppresses release of serotonin from metastatic tumors

controls diarrhea

no effect on valvular R heart disease

poor response to chemotherapy

foregut: bronchial, gastroduodenal

lung: some ability to detoxify vasoactive peptides (serotonin, substance P)

associated with valvular fibrosis R heart

no decarboxylating enzyme, normal 5HIAA

gastroduodenal 7% of carcinoids, most benign

increasing identification on EGD

small local resection/subtotal gastrectomy

associated with atrophic gastritis, H2 blockers, hi gastrin

less likely to be malignant

large: total gastrectomy or Whipple

pancreas very rare, may present with syndrome, may need Whipple

GI distribution: 45% small intestine (ileum), 20% rectum, 16% appendix, 11% colon, 7% stomach

midgut: ileum, appendix (to mid-colon), capable of producing syndrome

appendix:

most common appendiceal tumor

if < 2cm and base not involved appendectomy alone

> 2cm R hemicolectomy, 98% 5y survival/good prognosis

goblet cell carcinoid/adenocarcinoid intermediate malignant potential

R hemicolectomy may be safest option

small intestine

2nd most common, most ileum 28%

desmoplastic reaction in adjacent mesentery predisposes to presentation as small

bowel obstruction, most common presentation

high incidence of lymph node metastasis

aggressive resection including hepatic mets for syndrome

54% 5y, 21% if metastatic

hindgut: colorectal rarely symptomatic

colon: 11%, mimic adenocarcinoma, 4-5cm

60% mets (site with greatest chance of metastasis)

rectum: 2nd most common 20%

syndrome rare, better prognosis
85% solitary, < 2cm 4% metastatic, > 2cm 80% metastatic
75% 5y survival
remove endoscopically at 4-13cm

syndrome

5hydroxytryptophan decarboxylated (by those carcinoids with enzyme) to serotonin which is metabolized to 5 HIAA in liver
liver mets allows serotonin (also histamine, kallekrein, catechols, prostaglandin, substance P) to directly enter systemic circulation where they cause symptoms
flushing (head and trunk), diaphoresis, nausea/vomiting, bronchospasm, lacrymation
right heart valvular disease
pellagra-like skin condition
ovaries: venous drainage bypasses liver

liver mets

slow growing, hepatic resection to debulk beneficial
recurrence amenable to radiofrequency ablation (RFA), embolization

Endocrine pancreas

hormone secreting cells

alpha: glucagon
beta: insulin
delta: somatostatin, gastrin
D2 cells: vasoactive intestinal peptide (VIP)
F cells: pancreatic peptide

beta cells in center of islets surrounded by others

originate from common endodermal stem cells (not neural crest/APUD as previously thought)

hypervascular pancreatic lesions almost always neuroendocrine

needle Bx not effective for Dx, only 20% of neuroendocrine cells stain with IHC

neuroendocrine tumors radioresistant

adenomas produce one or more peptides including: ACTH (2%), parathormone, calcitonin, growth hormone, CCK, catechols

85% functional, 15% non-functional

hormone producing islet cell tumors
60% insulin, 20% gastrin, 5% VIP
25% association with MEN1

insulinoma (beta)

Whipple's triad: symptomatic hypoglycemia, documented low glucose, resolution with IV glucose
glucose/insulin ratio < 1 often (40%)

bizarre mentation sometimes mistaken for mental illness (neuroglycopenic symptoms)

fasting hypoglycemia, elevated insulin, elevated C-peptide (portion broken off to activate insulin) or pro-insulin

small (<1.5cm), 85% solitary, red-brown, 90% benign, 10% malignant

CT/MRI (10-60% Dx), arteriogram (30-90% Dx), pre-op US (20-65%; handicapped by colon gas), nuclear scan, venous sampling (25-85%), intraop US most effective

2/3 diagnosed pre-op

enucleate, excise, debulk larger, resect palpable nodes

MEN1: 5-10% of MEN1 patients have insulinoma

2nd most common functioning pancreatic neuroendocrine tumor in MEN1

often multicentric, may need subtotal pancreatectomy

suppress residual tissue with somatostatin lifelong

30-80% of MEN1 pts have pancreatic/duodenal neuroendocrine tumors

gastrinoma (D, delta cells)

concentrated duodenum (70%) and head of pancreas (25%)(gastrinoma triangle)

multicentric v insulinoma

duodenal more multicentric, less malignant potential than solitary sporadic

pancreatic gastrinoma

sporadic 60% malignant

(ZE described '55, prior Rx total gastrectomy before somatostatin)

gastrin > 1000 diagnostic

degree of elevation proportional to tumor burden

chromogranin A not diagnostic but increased in most ZE

30% of gastrinoma patients have MEN1 (higher than insulinoma)

MEN1 associated ZE not aggressive, hard to cure, radical resection v treat gastrin

70% benign, most survive extended period

most common functioning pancreatic neuroendocrine tumor in MEN1

jejunal ulceration rare

exclude other causes of elevated gastrin: chronic renal failure, short bowel, antral G-cell

hyperplasia (rare), truncal vagotomy, gastric outlet obstruction (decompress stomach

before measure gastrin)

secretin inhibits normal cells, but powerful secretagogue for gastrinoma gastrin

Dx: somatostatin (octreotide = somatostatin analog) receptor scan most sensitive > CT,

MRI, US, selective angio

CT or MRI stage multicentric or malignant

submucosal duodenal tumors hard to find, intraop endoscopy with transillumination helps

glucagonoma (alpha cells)(1st case '74)

M=F in most recent series, rarely associated with MEN1

chromogranin A marker

larger 3-5cm, 80% malignant, 50% metastatic @ Dx

always in pancreas, 90% body and tail (alpha cell distribution)

glucose intolerance, increased glucagon level, diabetes, wt. loss, neuropsychiatric

(4Ds: diabetes, dermatitis, DVT, depression)

necrolytic migratory erythema 70% by time of Dx, skin rash, cellulites, (decrease amino

acids, catabolic effect of glucagon?)

face, perineum, extremities

papules/plaque enlarge, coalesce to 14d, then central clearing

glucagons > 500pg/ml, > 1000 diagnostic

86% localization by CT

paradoxical increase glucagon with secretin challenge

good chance localization CT/MRI (larger lesions)

Rx: pancreatic resection, debulking mets especially for symptomatic; hepatic a.
embolization, radiofrequency ablation
suppress w octreotide

VIPoma (Vermer-Morrison/WDHHA, '58)(delta2 cells)

rare, small

binds to receptors on intestinal epithelial cells, activate cell adenylate cyclase & cyclic AMP
production causing water and electrolyte secretion into lumen

secretory watery diarrhea, hypokalemia, hypochloremia, alkalosis

symptomatic VIPomas are usually solitary, > 3cm

age 30-50, 85% pancreas, 15% association with ganglioneuroma (90% benign)

75% body and tail: increased VIP with profuse diarrhea

50% malignant, 60-80% metastatic at time of Dx

5% association with MEN1

enucleate or pancreatectomy

debulking helps symptoms

streptozotocin chemo, suppress with somatostatin

somatostatinoma (delta cell)(described '77)

rare, < 20 cases reported

50% pancreatic, 2/3 head

most malignant, metastatic @ Dx

when in duodenum usually symptomatic mass v other neuroendocrine duodenal tumors

only 10% experience syndrome

mild diabetes: strong suppression of insulin & other glucagon

cholelithiasis: suppression of biliary secretion, lytes and water, increase lipid in bile,
inhibit CCK

diarrhea +/- steatorrhea (inhibits pancreatic enzyme and bicarbonate secretion, impairs
intestinal absorption of lipids)

excise

non-functioning islet cell tumors (50%)

small percent of pancreatic masses but better chance of resection than exocrine pancreatic
cancer

90% of non-functioning islet cells tumors malignant

usually head, yellowish

resect for palliation pain bleeding, good results, long term survival

future direction: somatostatin-linked targeted chemotherapy

octreotide

somatostatin analog

somatostatin produced by hypothalamus

switches off pituitary growth hormones, decreases splanchnic blood flow,
inhibits gastrin, VIP, secretin, motilin, pancreatic polypeptide
very short acting (minutes)

octreotide

more stable, long acting

counters effects of flushing and diarrhea from carcinoid and VIP secreting adenomas

decreases splanchnic blood return to liver in portal hypertension/variceal bleed

References:

Pasieka J. What's new in general surgery: endocrine surgery. JACS 199(3), Sept. '04: 437-445.