Vasoactive Intestinal Peptide-Secreting Tumor (VIPoma)

Forest Washington, MD
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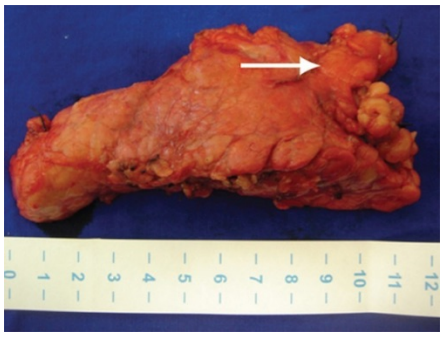
Pathophysiology

Also Known as "VIP-Producing Neuroendocrine Tumor", "Vasoactive Intestinal Peptide-Secreting Neoplasm", or "VIP-Secreting Tumor of the Pancreas"

Definition [1]

- Vasoactive Intestinal Peptide (VIP) Secreting Neuroendocrine Tumor
- Most Commonly Arise from Islet Cells of the Pancreas (75-90%) [2]
- *See Pancreatic Neuroendocrine Tumor (PNET)
- Other Potential Sites: [2-5]
    - Lung
    - Colon
    - Liver
    - Adrenal Gland or Sympathetic Ganglion – More Common in Infants and Pediatric Patients
        - Neuroblastoma
        - Ganglioneuroma
        - Pheochromocytoma
        - Paraganglioma



Distal Pancreatectomy Specimen with a Peripancreatic VIPoma (Arrow) [15]

Distribution and Size

- Most Common in Body or Tail of the Pancreas (70-75%) [6-8]
- Usually Solitary with Rare Multicentric Masses (5%) [9,10]
- Most are Large (> 3 cm) [6,11]

Malignancy

- Most are Malignant and Have Metastasized at the Time of Diagnosis (60-80%) [9]
- 5% Have Multiple Endocrine Neoplasia Type 1 (MEN-1) [12]

Epidemiology

- Median Age: 40-50 Years [2,13,14]
    - Between Ages 2-4 Years in Children [4]
- More Common in Females (65%) [14]

Presentation

VIPoma Syndrome

- Also Known As:
    - Watery Diarrhea, Hypokalemia, and Achlorhydria (WDHA) Syndrome
    - Verner-Morrison Syndrome
    - Pancreatic Cholera
- Classic Triad: [2,4]
    - Watery Diarrhea
        - Profuse and Persists with Fasting (> 700 mL/Day but Can Be Over 6 L)
        - Tea-Colored Odorless Stools
        - Profound Diarrhea Can Lead to Electrolyte Imbalances and Non-Anion Gap Metabolic Acidosis
    - Hypokalemia
        - Due to Diarrhea, Aldosterone Synthesis, and Direct Excretion by Enterocytes
    - Achlorhydria (HCl)
        - Due to the Inhibition of HCl Secretion by Gastric Parietal Cells

Additional Symptoms [2,4,16-18]

- Flushing (15-30%)
- Hyperglycemia (20-50%)
- Hypercalcemia (25-50%)
- Nausea and Vomiting
- Lethargy
- Weakness
- Muscle Cramps
- Weight Loss

Diagnosis

Diagnosis

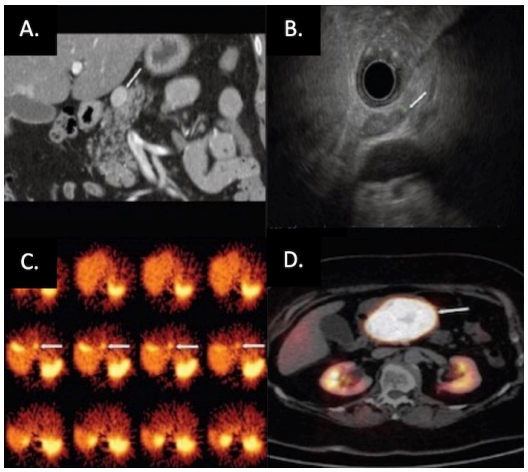
- Primary Diagnosis Made by Demonstrating High Serum VIP Levels (> 200 pg/mL) [19,20]
- Biopsy Not Required but Can Be Used for Grading [21]

TNM Staging

- Same System Used for all Pancreatic Neuroendocrine Tumors [22]
- *See Pancreatic Neuroendocrine Tumor (PNET)

Localization

- Initial Imaging: Noninvasive (CT or MRI) [23,24]
- Somatostatin Receptor Imaging [23,24]
    - Consider if Initial Imaging Fails to Localize
    - Options:
        - *Somatostatin (Octreotide) Receptor Scintigraphy (SRS)* – Classic Test Used
        - *Functional PET Scan (Ga-68 DOTATATE)* – Becoming More Prevalent with Higher Sensitivity
- If Noninvasive Imaging Fails: Invasive Imaging
    - *Endoscopic Ultrasound (EUS)* – Generally Preferred Next Step [25]
    - *Selective Visceral Angiography*



PNET on Imaging: (A) CT, (B) EUS, (C) SRS, (D) Functional PET [26]

Treatment

Initial Medical Therapy [27-29]

- Aggressive Fluid Resuscitation
- Electrolyte Replacement
- Somatostatin Analogs (Octreotide/Lanreotide) May Be Needed to Control Diarrhea
- Additional Agents for Refractory Diarrhea:
    - Glucocorticoids
    - Clonidine
    - Loperamide

Surgical Resection (Treatment of Choice) [2,30,31]

- Definitive Treatment: **Surgical Resection**
  - Head/Neck: Pancreaticoduodenectomy
  - Body/Tail: Distal Pancreatectomy (Concurrent Splenectomy if Malignancy is Suspected)
  - Entire Pancreas: Total Pancreatectomy
- May Consider Enucleation for Small Tumors (< 2-3 cm) – Controversial Due to High Malignancy Rates
  - Additional Requirements: Single Lesion, ≥ 2-3 mm From the Main Pancreatic Duct, Well-Encapsulated, and No Local Invasion
- Due to High Rates of Metastases, Surgical Resection is Often Not Feasible [9]

Liver-Directed Therapy

- Resection of Metastases if Able
- Radiofrequency Ablation (RFA) or Cryoablation [32]
- Hepatic Artery Embolization [33,34]

Additional Options in Surgically Unresectable Disease

- Somatostatin Analogs (Octreotide/Lanreotide) to Decrease Hormonal Secretion and Control Symptoms [28,29]
- Other Molecular-Targeted Agents:
  - Everolimus [35]
  - Sunitinib [36]
- Peptide Receptor Radionuclide Therapy (PRRT) [37,38]
- Chemotherapy [39,40]
- Radiation Therapy [41,42]
  - Pancreatic Neuroendocrine Carcinomas Were Previously Considered to be Resistant to Radiation

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