Hereditary Pancreatitis

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Honey V. Reddi, PhD
Prevention Genetics, Marshfield, WI

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AACC
Pancreatic Function

**HORMONES**
- Insulin
- Glucagon

**DIGESTIVE ENZYMES**
- Proteases (Trypsin, Chymotrypsin)
- Lipase
- Amylase

http://pathology.jhu.edu/pc/BasicOverview3.php
(Reproduced with permission)
Types of Pancreatitis

➢ Acute

- An inflammatory response to pancreatic injury
- Is usually non-progressive and mostly painful
- Serum amylase and lipase concentrations are elevated
- Involves a large portion of the pancreas and a predominantly neutrophilic inflammatory response
Types of Pancreatitis

➢ Chronic
  ▪ Progressive inflammatory and fibrotic changes in the pancreas resulting in permanent structural damage
  ▪ Leads to impairment of exocrine and endocrine function
  ▪ May be asymptomatic over long periods of time, present with a fibrotic mass, or have pancreatic insufficiency without pain
Chronic Pancreatitis - Demographics

- Incidence
  - Because of its varied presentation and clinical similarity to acute pancreatitis, the true global prevalence is unknown
  - In Europe (EUROPAC Study) the prevalence has been evaluated to be 1 in 300-800,000
  - Estimated 12 cases per 100,000 women and 45 cases per 100,000 men
  - The average age at diagnosis is 35 to 55 years
Chronic Pancreatitis - Demographics

➢ Etiology

- Chronic alcohol use accounts for 70%
- Idiopathic factors – 20%
- Genetic Factors – 1-2%
- Autoimmune pancreatitis – 5-6%
- The TIGAR-O (Toxic-metabolic, Idiopathic, Genetic, Autoimmune, Recurrent and severe acute pancreatitis, Obstructive) classification system is based on risk factors for chronic pancreatitis
TIGAR-O Classification

**Obstructive**: Pancreatic divisum, duct obstruction, post traumatic pancreatic duct scars

**Toxic-Metabolic**: Early or late onset, tropical calcific pancreatitis

**Idiopathic**: Alcohol, tobacco, medications, toxins, hypercalcemia, hyperparathyroidism

**Genetic**: Mutations in PRSS1, SPINK1, CFTR

**Recurrence**: Post necrotic, recurrent acute pancreatitis, vascular disease

**Auto-Immune**: Isolated or syndromic autoimmune pancreatitis

**IBS or Primary Biliary Cirrhosis-Associated Pancreatitis**
Hereditary Chronic Pancreatitis

- HP or HCP [OMIM #167800]
  - Autosomal dominant or recessive pattern of inheritance
  - High penetrance
  - Causes chronic pancreatitis in both children and adults
  - Patients with HCP are at a higher risk for pancreatic cancer
  - Great example of locus heterogeneity
HP – Clinical Considerations

➢ Primary manifestations are:
  ▪ abdominal pain
  ▪ maldigestion due to pancreatic exocrine dysfunction, and
  ▪ diabetes mellitus due to islet cell damage

➢ Median ages of first symptoms and diagnosis is about 10yrs and 19yrs, respectively

➢ HP is associated with a markedly increased risk for pancreatic cancer
Genes involved in HP

- Mutations in 4 genes are known to be involved
  - Cationic trypsinogen gene (*PRSS1*)
    - Located on 7q34, accounts for 52-81% of cases
  - Serine protease inhibitor Kazal type 1/Pancreatic secretory trypsin inhibitor (*SPINK1/PSTI*)
    - Located on 5q32, accounts for 50% of cases
  - Cystic fibrosis transmembrane conductance regulator (*CFTR*)
    - Located on 7q31; accounts for 20-55% of cases
  - Chymotrypsin C (*CTRC*)
    - Located on 1p36; acts as a modifier gene
Model of Inherited Pancreatitis

Testing for HP

- Indications for testing for PRSS1 or SPINK1 mutations in asymptomatic patients should be one of the following:
  - Recurrent unexplained attacks of acute pancreatitis and a positive family history
  - Unexplained chronic pancreatitis and a positive family history
  - Unexplained chronic pancreatitis without a positive family history
  - Unexplained pancreatitis episode in children
Differential diagnosis for HP

- **CYSTIC FIBROSIS**
  - ~70-80% of CF patients have pancreatic insufficiency

- **ANATOMIC ANOMALIES**, metabolic disorders, trauma and inflammatory bowel disease (IBS)

- Other rare differential diagnoses include:
  - hyperlipidaemia type I
  - familiar (hypocalciuric) hypercalcaemia (FBH)
  - hereditary hyperparathyroidism
  - autoimmune pancreatitis (adult-hood)
Treatment and Management of HP

➢ Primarily management of symptoms
  ▪ Pain control (analgesics)
  ▪ Pancreatic enzyme supplement to suppress pancreatic exocrine secretion.
  ▪ Cessation of alcohol intake and smoking.
  ▪ Eat small meals that are low in fat.
  ▪ Surgery may be indicated for patients who fail first line of therapy (as mentioned above) or if there is a suspicion of pancreatic cancer.
References

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