Clinical Chemistry Trainee Council
Pearls of Laboratory Medicine
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TITLE: Hereditary Pancreatitis

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Slide 1:
Hello, my name is Honey Reddi. I am a Clinical Molecular Geneticist at Prevention Genetics in Marshfield, Wisconsin. Welcome to this Pearl of Laboratory Medicine on "Hereditary Pancreatitis."

Slide 2:
The Endocrine function of the Pancreas includes the secretion of hormones such as Insulin and Glucagon, while the exocrine portion of the pancreas is responsible for the secretion of digestive enzymes such as trypsin, chymotrypsin, lipase, and amylase.

Slide 3:
There are two main types of Pancreatitis: Acute and Chronic.
Acute pancreatitis is an inflammatory response to pancreatic injury, is usually extremely painful, and non-progressive, with elevated serum amylase and lipase concentrations.

Slide 4:
Chronic pancreatitis, on the other hand, is a progressive inflammatory change resulting in permanent structural damage, leading to impairment of both endocrine and exocrine functions of the pancreas. Chronic pancreatitis may be asymptomatic over long periods of time, present with a fibrotic mass, or have pancreatic insufficiency without pain.

Slide 5:
Due to a similar clinical presentation as acute pancreatitis, though the true prevalence of chronic pancreatitis is unknown, a European study did estimate a prevalence of 1 in 300-800,000 individuals. Within genders, estimated numbers are about 12 cases for women and 45 cases for men per 100,000 individuals, indicating a predilection for males with an average age of diagnosis between 35-55 yrs.

Slide 6:
Etiology for chronic pancreatitis primarily includes alcohol abuse accounting for over 70% of cases. Idiopathic factors account for about 20% of cases, with genetic causes being responsible for 1-2% of cases. The TIGAR-O classification system for chronic pancreatitis is, therefore, based on the risk factors associated with this disease.

Slide 7:
TIGAR-O stands for Toxic-metabolic, Idiopathic, Genetic, Autoimmune, Recurrent and severe acute pancreatitis, and Obstructive with the individual components listed in the slide. For the rest of the presentation, my focus will be on Hereditary Pancreatitis, which occurs due to causes mentioned under the tab "GENETIC" and is the topic of this presentation.

Slide 8:
Hereditary Pancreatitis, or HP/HCP as it is called, is inherited in an autosomal dominant fashion and causes disease in both adults and children. Individuals with HP are demonstrated to be at a higher risk for pancreatic cancer. HP is a great example for locus heterogeneity since it does involve multiple genes.

Slide 9:
Primary manifestations for HP mimic acute pancreatitis and include abdominal pain and maldigestion. Onset of diabetes mellitus is also observed due to islet cell damage.

Slide 10:
The genetics of HP is a bit complex. There are multiple genes involved, including the Cationic trypsinogen gene (*PRSS1*); the Serine protease inhibitor Kazal type 1/Pancreatic secretory trypsin inhibitor (*SPINK1/PSTI*); and the Cystic fibrosis transmembrane conductance regulator (*CFTR*). Involvement of each of the genes accounts for about 50% of cases for an overall etiology ranging from 20-80%. Chymotrypsin C (*CTRC*) is believed to function as a modifier for HP.

Slide 11:
In the normal pancreas (left), trypsin that is prematurely activated within the pancreas is inhibited by *SPINK1* followed by trypsin and mesotrypsin, preventing autodigestion. In inherited pancreatitis (right), mutations in *PRSS1* or *SPINK1* lead to an imbalance of proteases and their inhibitors, leading to autodigestion, resulting in pancreatitis. The role of *CFTR* is yet to be clearly understood, while *CTRC* is thought to function as a modifier. AP= activation peptide.

Slide 12:
Genetic testing for HP requires the presence of at least one of the following indications:

- Recurrent unexplained attacks of acute pancreatitis + a positive family history
- Unexplained chronic pancreatitis + a positive family history
- Unexplained chronic pancreatitis without a positive family history
- Unexplained pancreatitis episodes in children

Slide 13:
When doing differential diagnosis for HP, one should keep in mind that about 70-80% of CF patients have pancreatic insufficiencies that can manifest as chronic pancreatitis. Other anatomic anomalies such as trauma or irritable bowel syndrome (IBS) also need to be considered. Rarer diseases such as hyperlipidaemia type I, familial (hypocalciuric) hypercalcaemia (FBH), hereditary hyperparathyroidism, and autoimmune pancreatitis in the case of adults should also be considered.

Slide 14:
Treatment of HP primarily involves the management of symptoms, particularly pain, which is an integral component of treatment. Pancreatic enzyme replacement is also a first line of therapy. Surgery is an option that may be considered depending on the extent of damage; however, it needs to be kept in mind that a complete pancreactectomy results in permanent insulin-dependent diabetes.

Slide 15: References

Slide 16: Disclosures

Slide 17: Thank You from www.TraineeCouncil.org
Thank you for joining me on this Pearl of Laboratory Medicine on “Hereditary Pancreatitis.” I am Honey Reddi.