Pathology

Diseases of the pancreas

Complication of acute pancreatitis (80% mild and self-limiting, 20% severe disease):

1. Shock
2. Peritonitis
3. Infection of pancreatic necrotic debris
4. Pseudocyst formation
5. Acute respiratory distress syndrome and acute renal failure

Pancreatic pseudocysts

- Localized areas of **necrotic** pancreatic tissue **rich** in pancreatic enzymes, surrounded by inflammatory and fibrous tissue forming cystic spaces **lacking** an epithelial lining
- Common sequel of acute pancreatitis
- 75% of all pancreatic cysts

2. Chronic pancreatitis: Is long standing inflammation with irreversible destruction of the **exocrine** pancreas, fibrosis and, in its late stages, loss of the **endocrine** parenchyma**.**

- ✓ Irreversible impairment in pancreatic function
- ✓ Most common cause → **long-term alcohol abuse**

Less common causes of chronic pancreatitis e.g. ***1.long-standing** pancreatic duct obstruction, ***2.hereditary pancreatitis** (due to mutations in the pancreatic trypsinogen gene, or the gene encoding a trypsin inhibitor), ***3.cystic fibrosis** or ***4.autoimmune** pancreatitis. {**40% no** recognizable predisposing factor}

Pathogenesis of chronic pancreatitis

Not well understood , however several theories have been postulated:

- Ductal obstruction by concretions: e.g. alcohol, may increase protein concentration of pancreatic secretions leading to ductal plugs
- Toxic- metabolic effects: Toxins (e.g. alcohol and its metabolites) have direct toxic effect on acinar cells
- Oxidative stress: alcohol can for e.g. generate free radicals
- Inappropriate activation of pancreatic enzymes due to mutations

.....The end result is deposition of collagen and fibrosis

Morphology of chronic pancreatitis

-Gross: Hard pancreas, with dilated ducts and calcified concretions

-Microscopical features: Parenchymal fibrosis, variable dilation of the pancreatic ducts, **acinar** loss and chronic inflammatory infiltrate. Islets of Langerhans at first are preserved but will eventually disappear.

Complications of chronic pancreatitis

- Severe pancreatic exocrine insufficiency and chronic malabsorption
- Diabetes mellitus
- Severe chronic pain
- Pancreatic pseudocysts (10%)
- Hereditary pancreatitis due to mutations in trypsinogen gene have 40% of developing pancreatic cancer

Pancreatic neoplasms

Classification of pancreatic tumors

***Benign epithelial tumors and precursors** e.g. Serous cystadenoma and mucinous cystic neoplasms
***Malignant epithelial tumors** e.g. Ductal adenocarcinoma and acinar cell carcinoma
***Pancreatic neuroendocrine neoplasms**
-Other pancreatic tumors e.g. mesenchymal tumors (e.g. lipoma) and lymphomas

-In addition, secondary tumors can occur in the pancreas

Serous cystadenomas

- About 25% of all pancreatic cystic neoplasms
- Female predominance
- Almost always benign
- Gross: Solitary mass, on cross-section: most cases show microcystic lesions (composed of numerous small cysts) containing **clear straw-colored fluid** (Sponge-like or honeycomb appearance)
- Histopathology : Small cysts lined by glycogen-rich uniform cuboidal epithelial cells

Mucinous cystic neoplasms

- ☒ 95% in women
- ☒ Usually arise in the body or tail of the pancreas
- ☒ They are precursors to invasive carcinomas
- ☒ Gross : Cyst filled with thick mucin
- ☒ Histopathology : Cyst lined by columnar mucin-producing epithelium with densely cellular stroma (like ovarian stroma)

Intraductal papillary mucinous neoplasms (IPMNs)

- Mucin-producing intraductal neoplasms
- More in males
- Frequently involve the head of the pancreas
- Lack the dense (ovarian like stroma)
- Arise in the main pancreatic duct or one of its major branch ducts
- Can progress to an invasive cancer

Ductal adenocarcinoma of the pancreas

- Is an invasive pancreatic epithelial neoplasm with glandular (ductal) differentiation
- Represents about 90% of pancreatic malignant tumors
- Has a high mortality rate (one of the top of the list of killers from malignancies)
- Elderly: peak age 60-80 years

Pathogenesis and etiology of pancreatic carcinoma

***1. Genetic factors:** It arises as a consequence of inherited and acquired mutations in cancer-associated genes

***Hereditary pancreatitis** has 40% lifetime risk for pancreatic cancer

***BRCA2** gene mutations are the most common known cause of familial pancreatic cancer

***2. Precursor lesions:**

- The **most common** precursor lesions of pancreatic cancer arise in small ducts and ductules, and are called **pancreatic intraepithelial neoplasias** (PanINs)
- Mucinous cystic neoplasms
- Intraductal papillary mucinous neoplasms

***3. Environmental factors** (smoking (doubles the risk, is the strongest factor), chronic pancreatitis, diabetes mellitus, obesity)

Morphology of pancreatic ductal adenocarcinoma

Location : head 60%, body 15%, tail 5% and 20% diffusely involve the pancreas

Gross : Hard poorly defined mass

Histopathology : Most are ductal adenocarcinomas

Note: Most carcinomas of the head of the pancreas obstruct the distal common bile duct. In contrast, carcinomas of the pancreatic body and tail do not impinge on the biliary tract and may be large and widely disseminated at diagnosis.

Thank you