Pancreas I.-Acute and chronic pancreatitis

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Development

- Anatomical malformations
  - ectopic pancreas
    - Ectopic islands of pancreatic tissue may occur almost anywhere in the gastointestinal tract
    - Present in approximately 2% of autopsy specimens
    - Rarely symptomatic
    - Most commonly located in gastric antrum, with central dimple representing rudimentary duct
    - Rarely give rise to neoplasm or focal pancreatitis
  - pancreas annulare
  - pancreas divisum
  - junctional disorders of the common bile- and pancreatic duct
THERAPY OF ANOMALOUS PANCREATOBILIARY JUNCTION

Sphincterotomy or sphincteroplasty is recommended for such patients with pancreatitis.

Surgical resection is generally recommended for extrahepatic choledochal cysts because they have a frequency for cholangiocarcinoma of approximately 10%.
CONGENITAL PANCREATIC CYSTS

True single congenital cysts are extremely rare.

Female predominance

- asymptomatic palpable mass
- Epigastric pain, jaundice, and vomiting related to compression of surrounding visceral structures

Most commonly located in the tail and body of the pancreas and are typically unilocular cysts with

Size is from microscopic up to 5 cm in diameter

Ductal communication is rare.
Pancreatic trauma: mechanism of injury:

Blunt abdominal trauma
- traffic accident
- children bicycle accident
- frequently combined with multiorgan injury
- penetrating wounds

Mechanism of trauma
- Contusion
- Transsection or rupture

Treatment:
- Drainage in contusion
- Resection in rupture
- Distal resection in case of transsection of body and tail
- Pancreatic head resection in head injury
Basic considerations of acute pancreatitis

• The acute pancreatitis is not a surgical disease

• Considering the course and severity, various clinical forms are exist

• Tools for the early and reliable prognosis are not in hand

• The treatment strategy is frequently uncertain, though Evidence Based guidelines, and recommendations are available.
Definition of acute pancreatitis

Acute pancreatitis comprises different entities with regard to pathomorphology, clinical course, severity, and risks of disease:

- interstitial-edematous pancreatitis,
- necrotizing pancreatitis withinfected or sterile necrosis, with or without intrapancreatic andextrapancreatic fatty tissue necrosis, pancreatic abscess, and pseudocystic lesion after pancreatitis.

Acute pancreatitis is generally defined as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ systems.
Definition of acute pancreatitis

Acute pancreatitis displays inflammation of pancreatic tissue secondary to acinar cell necroses. Apoptosis prevails in mild acute pancreatitis, necrosis in severe acute pancreatitis. In mild acute pancreatitis, the morphologic changes range from interstitial edema to minimal fat and exocrine tissue necrosis. In severe acute pancreatitis, large confluent areas of pancreatic tissue necroses, frequently accompanied by hemorrhage into the tissue, are found.
POTENTIAL FACTORS CONTRIBUTING TO THE SYSTEMIC MANIFESTATIONS OF ACUTE PANCREATITIS

- Oxigen-derived free radicals
- Bradykinin
- Pro-inflammatory cytokines (IL-1, IL-6, IL-8, tumor necrosis factor-A, platelet activating factor)
- Complement
- Antioxidants (gluthione and other compounds containing sulthydryl groups)
- Anti-inflammatory cytokines (eg:IL-2, IL-10, IL-1, receptor antagonist)
- Others?
Etiology

- Alcohol-induced acute pancreatitis
- Biliary acute pancreatitis
- Congenital anomalies related acute pancreatitis
- Metabolic, infectious, drug related AP

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Mortality

- All 7.8 %,
  - mild 1.0 %,
  - severe 16.1 %
Alcohol-induced acute pancreatitis

- Alcoholic acute pancreatitis is generally milder than pancreatitis of other etiology
- More frequent in young males
- First and consecutive attacks of pancreatitis
- There is no difference in survival compared to biliary pancreatitis
- First alcoholic attack is even worse
- Pseudocysts and fluid collections are more frequent
- Alcohol withdrawal syndrome develops in about 25%
- The outcome of acute alcoholic pancreatitis is mainly defined by the recurrence of attacks of pancreatitis and the development of chronic pancreatitis.
**Biliary acut pancreatitis**

- Gallstone-associated pancreatitis results from the passage of stones through the sphincter of Oddi
- **Common channel hypothesis**
  - Bile reflux is the trigger for pancreatitis
  - The pressure in the pancreatic duct is in fact two to three times higher than that in the bile duct
- **Duodenal reflux hypothesis**
- **Ductal hypertension hypothesis**
  - Strictures/Tumor
  - ERCP
  - Helminth
- **Two-phase hypothesis**
  - Edema of the head of the pancreas or ampulla after passage of a gallstone
  - Repeated transient obstruction due to passage of multiples small stones
  - Large stone impacted in the distal main bile duct causing compression of the main pancreatic duct which lies alongside
  - Impaction of a larger stone at the ampulla of Vater itself
ACUTE PANCREATITIS ASSOCIATED WITH CONGENITAL ANOMALIES

• Pancreas divisum
  – Even though pancreas divisum is a congenital malformation, initial presentation with pancreatitis in the third and fourth decades is most common.
  – Complete / incomplete dorsal and ventral duct alteration / relative obstruction

• Treatment: relief of obstruction
  – Sphinteroplasty
  – Pancreatojejunostomy
  – Duodenum preserving head resection

• Anomalous pancreaticobiliary ductal union (APBDU)
  – common channel is greater than 15 mm in length
  – BP – bile duct to pancreatic duct
  – PB – pancreatic duct to bile duct

• APBDU has been considered a factor:
  – pancreatitis, choledochal cyst,
  – gallbladder cancer and adenomyomatosis,
  – common bile duct cancer, choledolithiasis,
  – pancreatic carcinoma
ACUTE PANCREATITIS ASSOCIATED WITH CONGENITAL ANOMALIES

• Annular pancreas
  – Annular pancreas is identified with obstruction or pancreatic inflammation in adults, usually in the third decade or later
  – Additionally, annular pancreas is associated with a high rate of associated congenital anomalies
  – Surgical correction of annular pancreas:
    • Diamond duodenoduodenostomy
    • Duodenojejunostomy
    • Gastrojejunostomy should be avoided
ACUTE PANCREATITIS:
METABOLIC, INFECTIOUS, AND DRUG-RELATED DISEASES

- Primary (hereditary, familial) hypertriglyceridemia
- Hereditary lipoprotein lipase deficiency
- Apolipoprotein C-II deficiency
- Familial hypertriglyceridemia and chylomicronemia
- Secondary hypertriglyceridemia
  - Alcohol
  - Diabetes
  - Pregnancy
- Drugs
  - Thiazide, diuretics, tamoxifen, retinoids, beta-blockers
- Mumps, Coxsackievirus type B, Varicella-zoster virus, HIV, Cytomegalovirus, Hepatitis
ACUTE PANCREATITIS

Diagnosis

• Contrast-enhanced CT is the single most efficacious imaging modality for the initial evaluation of patients with acute pancreatitis.
• It should be performed first in patients with clinically known or suspected acute pancreatitis.
• Other modalities, such as US, MRI, angiography, and barium studies are reserved for more specific evaluation of complications initially detected with CT.

Treatment

– Pain treatment
– Fluid resuscitation
– Nasogastric suction
– Nutrition
– Adequate therapy of organ failures
– Prevention of infected pancreatic necrosis
– Selective gut decontamination
– Endoscopic sphincterotomy
– Timing of cholecystectomy

• Treatment of pancreatic necrosis
PROGNOSIS in AP

1. Scoring systems:  
   Ranson, Balthasar, Glasgow, APACHE II

2. Tests that relate to the degree of SIRS:  
   granulocyte elastase, TNF-α, IL-6, IL-8, CRP

3. Tests that relate to the activation of pancreatic proenzymes:  
   trypsinogen, trypsinogen activation peptide (TAP), trypsin-alpha1-protease inhibitor, carboxypeptidase B activation peptide (CAPAP)

4. Tests that measure leakage of enzymes
Treatment

- Pseudocysts
- Pancreatic fistula
  - External
  - External pancreatic fistulas are common sequelae of infected necrosis and of interventions designed to manage infected severe necrotizing pancreatitis.
  - The majority of fistulas are low output and close spontaneously.
  - Endoscopic or surgical intervention should be considered if the fistula persists beyond 12 weeks, is difficult to drain because of high output or skin irritation, or if local complications develop.
- Pancreatic fistula
  - Internal
  - In the case of the rarely diagnosed internal pancreatic fistula, surgical treatment is indicated in most cases.
  - The surgical approach to internal fistulas is focused on the treatment of the underlying disease, mainly infected pancreatic necrosis. Once infected necrosis is treated adequately, internal fistulas will generally close rapidly.
  - Gastrointestinal fistulas most frequently develop after surgical necrosectomy and can be managed conservatively in most cases.
Definition of chronic pancreatitis

Chronic pancreatitis is a clinical syndrome defined by groups of signs and symptoms characteristic of longstanding inflammation of the pancreas.
**Etiologic classification of chronic pancreatitis and pancreatic fibrosis**

**Chronic pancreatitis**
- Alcoholic
  - manifestation
  - alcoholic CP around the age of 40
  - gender distribution: male 80%
  - alcohol intake (> 80 g/die = 1 ltr. wine, 2.5 ltrs. beer)
  - different additional factors are needed, but are unknown

- Hereditary
- Autoimmune
- Metabolic (hypercalcemia, hyperlipidemia)
- Tropical
- Idiopathic
- Chronic pancreatitis associated with anatomic abnormalities*

**Pancreatic fibrosis not associated with symptoms of chronic pancreatitis**
- Pancreatic fibrosis in the elderly
- Cystic fibrosis†
- Pancreatic fibrosis in long-term insulin-dependent diabetes mellitus
- Hemochromatosis
Chronic pancreatitis
Pathogenesis of pain

- local complications
- alterations of blood flow
- intraductal - intraparenchymal hypertension
- inflammatory neural involvement
- neuro-immuno pathway
Exocrine Insufficiency

- normal pancreatic secretion: 2 ltrs/day
- amount of secreted enzymes: 10 times more than needed to ensure normal digestion
- fat digestion failure occurs earlier in the course of exocrine insufficiency than impairment of other food contents
- Steatorrhea
- weight loss
- bacterial overgrowth
- deficiency of fat soluble vitamins
- (A, D, E, K)
Diagnosis of Chronic Pancreatitis

= based on morphological findings

Function tests play a minor and only complementary role in the diagnosis of CP.

Morphological diagnosis of CP by imaging procedures

– easy in advanced stages of the disease
– difficult in early stages of CP
Imaging procedures

• Computed tomography
  • Sensitivity  56 - 95 %
  • Specificity  85 - 100 %
  • most sensitive method for detection of pancreatic calcifications

• Endoscopic Ultrasound

• Endoscopic retrograde Cholangiopancreaticography

• Magnetresonance Tomography / Magnetresonance cholangiopancreaticography

• Transcutaneous Ultrasound
EUS changes as predictors for CP

Parenchymal features
- focal areas of reduced echogenicity [p 0.009]
- hyperechogenic foci (> 3 mm) [p 0.05]
- gland size, cysts, accentuation of lobular pattern

Ductular features
- irregular caliber of MPD [p 0.03]
- dilatation of MPD [p 0.04]
- dilatation of side branches [p 0.05]
- narrowing, duct wall echogenicity, calculi
Treatment options – Pain

• medical treatment options
  – dietary (stop alcohol intake)
  – drug therapy (antiinflammatory, analgetic)
    • NSAIDʻs (and PPI)
    • Opioids
      – inhibition/suppression of secretion
• invasive treatment
  – endoscopic stenting, stone removal
  – ESWL
Treatment options – Pain

Inflammation
„Immunopathogenesis“
- antiinflammatory substances (NSAID)
- analgesics (e.g. Tilidin)
- enzymes

Obstruction
ductal / parenchymal hypertension
- octreotide
- therapeutic endoscopy

Complications
- compression of adjacent organs

therapeutic endoscopy (e.g. cyst drainage), surgery
Why do we Operate in Chronic Pancreatitis?

- **PAIN** -> 80-90%
- **Complications** -> 60-70%
  - Compression syndrome
  - Pseudocyst
  - Septic complications
  - Fistula
  - Ascites
  - Pleural effusion
  - Malabsorption
Factors Determining the Choice of Procedure

- Operative Morbidity and Mortality
- Early and Late Results
- Subsequent Operations
- Exocrine and Endocrine Function
- Survival and Quality of Life
- Morphology of the Pancreatic Lesion
- Dilation of Duct ( > 6-8mm)
- Site of Focal Lesion
  - head, body, tail
- Relation to Surrounding Structures
- Multiple Lesions
- Etiology
  - obstructive, diffuse
  - calcification
Types of operations in chronic pancreatitis

• Decompressions
  – transduodenal „double plasty”
  – distal decompressions
    • DuVal, Puestow- Gillesby, Partington-Rochelle
• Cyst drainage
  – external
  – internal
  – excision, resection
It is of basic importance in clinical practice; the differential diagnosis of the lesions

Main questions of differentiation:

• Inflammation and tumor
• Cystic lesions
• Complications of pancreatitis vs. Other GI diseases
• Inflammation and tumor
  • Factors of uncertainty:
    • Clinical symptoms are overlapping
    • Tumor markers, genmutations expressions difficult
    • Effectivity of imaging procedures’ – subjective factors
    • Mostly the analysis of the removed specimen is the most effective method

• Histology vs. Cytology
  • The wedge biopsy is uncertain: superficial
  • Frozen sections are difficult to evaluate
  • Cytology: High reliability but BUT ONLY IN THE HANDS OF EXPERIENCED CYTO-PATHOLOGISTS
Cystic lesions

- True cysts 2%
  - Congenital cyst - solitaire, multiple
  - Cystic fibrosis
- Parasitic origin 1%
- Retention cyst 5%
- Inflammatory pseudocyst 75-80%
- Neoplastic origine 8-15%
Recognition of complications of chronic pancreatitis

• Pseudocyst, abscess
  – Dangers of conservative or endoscopic treatment!

• Fistula
  – pancreatogenic ascites, exsudative pleuritis

• GI bleeding - Wirsungorrhagia
  – pseudoaneurism

• Compression syndrom
Changing Trends in the Surgical Management of Chronic Pancreatitis

- Organ preservation in resection
  - Total pancreatectomy avoidable
  - Whipple replaced by Pylorus Preservation
  - Duodenum preservation
    - Beger: subtot. head resection and double jejunal anastomosis
    - Flautner & Tihanyi: subtot. head resection and pancreatogastrostomy
    - Tihanyi: total head resection and pancreatogastrostomy
    - Limitation of ductal drainage to ducts >6-8mm. Alternative is the “V” excision
    - Combination of drainage with head resection (FREY)
    - Application of combined drainage procedures
KEY POINTS

Chronic alcoholism is responsible for up to 80% of cases of chronic pancreatitis.

The type of alcohol and the manner of consumption do not correlate with disease severity, but the severity of chronic pancreatitis does appear to increase with the amount and duration of alcohol consumption.

It takes almost a 90% loss of functional pancreas for symptoms of malabsorption (diarrhea, steatorrhea) to develop.

Although imaging studies such as transabdominal ultrasound and CT may be used to diagnose chronic pancreatitis, ERCP is the gold standard for diagnosis.

Patients with chronic pancreatitis have an increased risk of pancreatic cancer.
KEY POINTS

Analgesics and oral pancreatic enzymes are the first-line treatment for chronic pancreatitis.

In the presence of a dilated pancreatic duct (7 mm), longitudinal pancreaticojejunostomy (Puestow procedure) can provide pain relief in more than 80% of patients.

Resection therapy is indicated for chronic pancreatitis in the absence of a dilated pancreatic duct.

Pancreaticoduodenectomy has a success rate of between 60% and 80% in patients with disease confirmed predominately to the head of the pancreas.

Patients with chronic pancreatitis have a decreased life expectancy in comparison to the general population.
Conclusion

- pain is the most frequent symptom in patients with chronic pancreatitis

- several non-operative treatment options should be integrated in the treatment concept

- in case of pancreatic exocrine insufficiency - pancreatic enzyme replacement therapy