Diseases of exocrin pancreas. Maldigestion, malabsorption

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Anatomy

Anatomic specialties:

- Relation to biliary tract
- Retroperitoneal localisation
- Relation to surrounding organs
Anatomy

Heart
Spleen
Pancreas
Kidney
Diseases of exocrine pancreas

- Congenital anatomic anomalies
- Congenital metabolic disorders
- Acute pancreatitis
- Chronic pancreatitis
Anatomic anomalies

- **Pancreas divisum**
  - Most frequent, 3-6%
  - Fusion of the dorsal and ventral part is missing: additional papilla nearby the Vater’s papilla
  - Frequently no symptoms, but may cause acute recurrent or chronic obstructive pancreatitis
  - Conservative treatment, actually plastic surgery of the additional sphincter

- **Pancreas anulare**
  - Obstruction of duodenum
  - Symptoms of upper GI obstruction
  - surgery; retrocolic duodenojejunostomy
Congenital metabolic disorders

- Cystic fibrosis (CF)
- AR, 1/3000
- Mutation of CFTR (cystic fibrosis transmembrane regulator) protein, 7. chromosome, 1480 amino acids - polypeptide chain
- Chloride and other ion channels regulated by cAMP
- Influence on volume and ion-content of secrets
- Systemic disease! - airways, GI tract (meconium ileus, chronic pancreatitis, maldigestion, biliary cirrhosis), genital tract
Acute pancreatitis – pathogenesis

• 1-5/10 000/year, symptomfree (subclinical) cases!
• Early activation of proteolytic enzymes in zymogene granulums, retination instead of secretion, catepsin B → tripsinogene activation → other enzymes↑ → necrosis; protease inhibitors
• Proinflammatoric cytokines↑ → vasodilatation, permeability, oedema: **interstitial pancreatitis**
• Activated enzymes, leukocyte activation → necrosis of parenchyme and fatty tissue, ischaemia, bleeding, SIRS, multiorgan failure: **necrotising pancreatitis**
Acute pancreatitis – etiology

- Obstructive
  - Biliary (choledocholithiasis)
  - Pancreatic (p.divisum, PSC, eg.tu.)
  - Papillary (dysfunction of Oddi’s sphincter, tu., diverticulum, ascariasis)
- Toxic
  - **ALCOHOL**
  - Drugs (azathiprin, 6-mercaptopurin, L-aspariginase, sulfonamids, 5-ASA, FSD, thazids, ACEI, tetracyclin
- Infectious
  - Viral (mumps, hepatitis, Coxsackie, echo, CMV, HIV)
  - Bacterial toxins (Salmonella, Shigella, Camplyobacter, E.coli, Brucella, Legionella, Leptospira)
- Metabolic
  - Hypercalcaemia
  - Hypertrigliceridaemia
  - uraemia
- Autoimmune
- Ischaemic
- Genetic (inherited)
- Others
  - Iatrogenic (ERCP!)
  - Trauma
  - Penetrating duodenal peptic ulcer
- Idiopathic
Acute pancreatitis - symptoms

- Abdominal pain – belt shape, continuous, non-colic
- Nausea, vomiting
- Mild obstructive jaundice
- Fever
- Meteorism – paralytic ileus
- Muscular defense
- Tachycardy, hypotension
- Basal atelectasia, pleural effusion
Acute pancreatitis - symptoms

- Jaundice
- Periumbilical livid discoloration: Cullen’s sign
- Livid discoloration on the back: Turner’s sign
Acute pancreatitis – lab results

- Amylase, lipase
  - DiffDg: other causes of hyperamylasaemia
- CRP, leukocytosis, leukemoid reaction
- Signs of biliary obstruction (SeBi, SAP, GGT, SGOT, SGPT)
- Hyperglycaemia
- Hypertriglyceridaemia
- Hypocalcaemia, hypalbuminaemia, LDH,
- Hypoxia (ARDS), metabolic acidosis
Acute pancreatitis - imaging

- X-ray
- US
- CT (necrotising ~, complications)
- (MRI)
- MRCP (biliary ~)
- ERCP, EST, extraction of bile stones (biliary ~)
Acute pancreatitis - US
Acute pancreatitis - CT
Acute pancreatitis

- Ranson-Imrie prognostic criterias
- Simplified *Glasgow severity criterias* (within 48 hours everywhen)
  - Age >55 ys
  - WBC >15 000
  - LDH >600
  - Glu >11
  - Albumin <32
  - Ca <1.9
  - Arterial pO₂ <60 Hgmm
  - CN >7.5

*Severe pancreatitis: >3 criterias*
Acute pancreatitis - complications

• Local
  – Intra- és peripancreatic effusions, pseudoabscess (10-15%), abscess (3-4%)
  – Ascites (amilase and albumin high), fistula
  – Necrosis (5-10%), superinfected necrosis
  – Bleeding; thrombosis of splenic vein or sup.mesenteric vein; pseudoaneurysm; splenic rupture
  – Chronic pancreatitis

• Systemic (in 50% of necrotising ~)
  Activated proteolytic enzymes, systemic inflammatory response reaction, endotoxinaemia
  – ARDS, renal failure, sepsis, shock, coagulopathy, CNS symptoms, GI bleeding, disseminated necrosis of the fatty tissue
Acute pancreatitis - treatment

• Supportive care
  – NPO (nil per os) – carentia
  – Gastric drainage in case of vomiting, compression of duodenum
  – EN via nasojejunal probe (2. jejunal loop)
  – Iv. ion- and fluid restoration (no colloid due to ARDS)
  – Pain control (Dolargan)
  – Antibiotics (CP, imipenem, fluconazol)
  – ICU!!!

• Biliary intervention
• Surgery (necrosis, bleeding, pseudocyst)
• Plasma exchange (hyperTG)
Acute pancreatitis
Chronic pancreatitis

Morphology + function + patients’s complaints

- Irreversible, progressive destruction, inflammatory signs, fibrosis, lack of regeneration

- Pancreatic failure (both exocrin and endocrin), maldigestion – pancreatic cachexia

- Recurrent or continuous abdominal pain
Chronic pancreatitis

- Obstruction (protein plugs); Necrosis-fibrosis; Toxic/metabolic effect; indifficient detoxication (oxidative stress)
- **ALCOHOL** (70%)
- Non alcoholic (30%)
  - Inherited
  - Metabolic
  - Autoimmune
  - Tropic
  - Idiopathic
  - Obstruction of duct, stenosis (p.divisum, papillitis, duodenum diverticulum)
Chronic pancreatitis – symptoms

- Pain
- Steatorrhea
- Weight loss, cachexia
- Pancreatogenic diabetes mellitus (low insulin need)
Chronic pancreatitis - complications

- Pseudocysts (20%)
- Fistula (external/internal)
- Stenosis or thrombosis of splanchnic veins
- Duodenal peptic ulcer
- GI bleeding
- Subcutaneous fatty tissue necrosis on the legs
- Carcinoma (after 10 ys - 5%)
Chronic pancreatitis – diagnostics

• Imaging (US, CT, ERCP, MRI)
• Amilase, lipase
• Evaluation of exocrine functions
  – Functional tests (via probes or oral)
  – Indigestivity of stool, chimotripsin, elastase
• Evaluation of endocrine functions
  – Starving glucose
  – OGTT (glucose, insulin, C-peptid)
Chronic pancreatitis – CT
Chronic pancreatitis – ERCP
Chronic pancreatitis
Chronic pancreatitis – treatment

- Pain control: alcohol abstinency, NSAID, spasmylytics, anticholinergic drugs, H₂-blockers, PPI); epidural analgesia; surgery
- Management of exocrin failure: diet - 25% protein, 30% fat, 40% carbohydrates; pancreas enzyme extractions
- Management of endocrine failure: diet, OAD, insulin
- Treatment of complications

- Surgery: abolish outflow obstruction (duct plasty, stoma); partial/total removal of pancreas
- Endoscopic intervention: sphincter plasty, management/dilation of stenosis, biliary stenting
Chronic pancreatitis – surgery
Disorders of absorption

1. Altered digestion (luminal phase) – *maldigestion*
   - Stomach
     - More/less gastric juice
     - Previous surgery
       - Lack of acid/pepsin
       - Decreased movements
       - Fast transit
       - Lack of endogenic pancreas stimulation
   - Pancreas
     - CF
     - Chronic pancreatitis
   - Bile
     - Decreased synthesis – parenchymás hepatic disorder
     - Decreased outflow – cholestasis
     - Increased loss – diseases of terminal ileum
   - Others
     - Motility disturbance
     - Bacterial contamination
     - Drug affect
Disorders of absorption

2., Altered absorption (mucosal phase) – malabsorption

• Destroyed absorption
• Mucosal destruction
  – Primary diseases of small intestine
  – Secondary destruction of small intestine
• Decreased surface for absorption
  – Resection of small intestine
  – Diseases of small intestine
Disorders of absorption

3. Altered transport phase
   - Lymphatic disorders
     - Mesenterial lymphadenopathy
   - Vascular disorders
Diseases of small intestine

• Congenital
  – Lack of mucosalis disacharidases
  – Altered aminoacid transport
  – abetaliproteinaemia
• Infection
  – Viral, bacterial, parazitic, fungal, helmintic
• Bacterial overgrowth
• Coeliac disease
• Whipple-disease
• IBD/Crohn’ disease
• Tropical sprue
• Amyloidosis
• Sarcoidosis
• Tumors
Secondary destruction of small intestine

- Drugs
  - Laxatives
  - NSAIDs
  - Biguanids
  - Cytostatics
- Endocrin diseases
  - Hypo/hyperthyreosis
  - Hyperparathyreosis
- Cardiovascular (ischaemia)
- DM (autonom neuropathy)
- Neuroendocrin tu.
- AIDS
- PSS
Disorders of absorption – symptoms

- Weight loss (carbohydrates, protein, fat)
- Watery diarrhea (carbohydrates, bile acids/salts)
- Steatorrhea (fats)
- Weakness, fatigue (electrolytes (K, Ca, Mg, Fe), protein, folate, B₁₂)
- Anaemia (Fe, folate, B₁₂)
- Bone pain (Ca (osteomalacia), protein (osteoporosis), vitamin D (Ca-malabsorption))
- Paraesthesia, tetany (Ca, Mg)
- Neuropathy (B-vitamins)
- Oedema (protein)
- Amenorrhea (protein)
- Alopecia, fragile nails, hyperkeratosis (vitamin A)
- Nyctalopia, night blindness (vitamin A)
- Bleeding disorders (vitamin K)
- Glossitis, cheilosis (folate, nicotinic acid, B₁₂)
# Disorders of absorption – lab tests

<table>
<thead>
<tr>
<th></th>
<th>Malabsorption</th>
<th>Maldigestion</th>
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<tbody>
<tr>
<td>Serum</td>
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<tr>
<td>– Fe</td>
<td>↓</td>
<td>norm.</td>
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<tr>
<td>– Ca</td>
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<td>– Cholesterol</td>
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<tr>
<td>– Albumin</td>
<td>↓</td>
<td>sometime ↓</td>
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<tr>
<td>– Prothrombin</td>
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<td>sometime ↓</td>
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<tr>
<td>Stool</td>
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<tr>
<td>– Fat</td>
<td>&gt; 7g/24h</td>
<td>&gt; 7g/24h</td>
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<tr>
<td>• Neutral</td>
<td>norm.</td>
<td>↑↑</td>
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<tr>
<td>• Fatty acids</td>
<td>↑</td>
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Disorders of absorption – oral tests

- D-xilose
- OGTT
- Disacharid (lactose, sacharose) tests
- Iron tests
Disorders of absorption – functional tests

- $H_2$-expiation test
  - Lactose  lactose/intolerance
  - Laktulose  small intest. bacterial contam.
- $^{14}$C-triolein  fat
- Schilling-test  IF $\emptyset$, absorption of $B_{12}$
- SeHCAT-test  bilesalts
Coeliac diseases

• Glutensensitive enteropathy, non-tropical sprue
• Genetic predisposition, autoimmune enteropathy, villus atrophy, crypta hyperplasia, lymphocytic infiltration, complex malabsorption
• Not a childhood disease!
• Not rare!
• Even 20x difference between real prevalence and clinical presentation!
• Hungary 1:100
Coeliac disease

- Genetic predisposition DQA1*0501/DQB1*0201
- Glutene (α-gliadin, hordein, scalin)
- Autoantigenes (tissue transglutaminase, tTG)
- tTG is necessary for the activation of tissue transforming factor-β (TGF-β), essential for villus differentiation
- Clinical presentation depends on:
  - Altered immune response due to infection
  - First exposition to glutene
  - Glutene content of cereals
  - Duration of breastfeeding
  - First exposition to cow milk
Coeliac disease

• Classic form (in children, but even in adults, provoking event)
  NB!: Iron deficient anaemia, Ca deficient osteopenia, osteoporosis, diarrhea, habitual abortion, abdominal distension, steatosis hepatitis

• Asymptomatic

• Latent
Coeliakia – atypical symptoms, diseases

- Dermatitis herpetiformis Duhring
- Alopecia
- Stomatitis aphtosa
- Isolated elevation of transaminases
- PBC
- Epilepsia
- Polyneuropathiy
- MG
- DCM
- Hypo/hyperthyreosis
Coeliac – coincidence of other diseases

- Lymphoma of small intestine
- Other tumors of small intestine
- Autoimmune diseases
- DM1
- IgA-deficiency
- M.Sjögren
- Down sy., Turner sy.
- Addison-disease
Coeliac disease – diagnostics

- „Deep” small intestine biopsy – histology, Marsh classification Stage 0-4
- Serology (EMA, tTG spec. IgA 99%, IgG 98%; sens. IgA 93%, IgG 47%, bot both together 100%) – diagnosis, screening, follow-up
Coeliac disease
Coeliac disease
Coeliac disease – therapy

„DIET is the only cure we know”

• **Prohibited**
  - Wheat
  - Rye
  - Barley
  - Durum wheat
  - Malt
  - Beer
  - Prepared multiple content meals

• **Allowed**
  - Potato
  - Rice
  - Corn
  - Buckwheat
  - Sorghum
  - Millet
  - Bean
  - Pease
  - Soya
  - Fruits
  - Vegetables
  - Meat
  - Oat?