Non-neoplastic disease of the pancreas

- No indication for surgical resection of non-neoplastic disease (except end-stage chronic pancreatitis)
- Unexpected benign disease in 5-13% of pancreatic resections

Consensus

When to perform a pancreaticoduodenectomy in the absence of positive findings?

A consensus statement by the International Study Group of Pancreatic Surgery

Consensus statements

- In the presence of a solid mass in the head of the pancreas that is suspicious for malignancy, biopsy proof is not required before proceeding with PD when AIP is not suspected (strong recommendation).
- Vast majority of lesions are neoplastic/malignant
- Obtaining a positive biopsy can be difficult and time-consuming
- (Ill-founded) issues over needle track seeding

Suspicion of malignancy

- Mass
- Jaundice
- Dilatation of the bile duct or pancreatic duct
- Double duct sign
Suspicion of malignancy

- mass
- jaundice
- bile duct or pancreatic duct dilatation
- double duct sign

<table>
<thead>
<tr>
<th>Mass</th>
<th>PD and/or CBD dilatation</th>
<th>PA confirmed diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>Malignant</td>
<td>Total</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>10 (68%)</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>10 (89%)</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>27 (61%)</td>
</tr>
</tbody>
</table>


Non-neoplastic disease of the pancreas

- Mass
  - Solid
  - Cystic

- Double/single duct dilatation

- Pancreatitis
  - Autoimmune
  - Acute inflammatory
  - Tumour
  - Infectious
- Ectopic
- Retention cyst
- Pseudocyst
- Enterog. duplication cyst
- Periampullary lesions
  - Ectopia
  - Ectopic pancreas
- Ectopic glandular tissue
  - Adenomyomatous hyperplasia of the ampulla
  - Diverticulum
  - Pancreas annulare
- Cholangitis/cholelithiasis

Groove pancreatitis

Syn. paraduodenal pancreatitis, cystic dystrophy of the duodenum

Pancreas annulare
Non-neoplastic disease of the pancreas

- Mass
- Solid
  - Pancreatitis
  - NOS
  - Autoimmune
  - Follicular
  - Groove
  - Vasculitis
  - Infectious
- Cystic
  - Retention cyst
  - Pseudocyst
  - Enterog. duplication cyst

- Double/single duct dilatation
  - Periampullary lesions
  - Ectopia
  - Groove pancreatitis
  - Adenomyomatous hyperplasia ampulla
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Retention cysts

Pseudocysts
Duplication cyst
Non-neoplastic disease of the pancreas

Autoimmune pancreatitis: mimicry of PDAC

- Inhomogeneous signal; tumour mass
- Stricture of pancreatic duct
- Type 1:
  - Pancreatic infiltration
  - Bile duct stricture
  - Enlarged lymph nodes
  - Enlarged ampulla of Vater
  - Involvement of SMV
  - Para-aortic extension
Focal AIP

AIP

Portal vein

Infectious pancreatitis

Â tuberculosiscs
Infectious pancreatitis
- tuberculosis
- actinomycetes
Male, 52 yr
Chronic pancreatitis diagnosed 8 years ago
In recent months: gradual deterioration, weight loss, abdominal pain
CT:
- Suspicion of ill-defined mass in head of pancreas
- Extension into duodenum
- Enlarged peripancreatic lymph nodes
- Whipple’s resection

Pancreatic tuberculosis and actinomycosis
- Seldom
- Can occur in isolation
- Can mimic pancreatic cancer:
  - Pancreatic mass
  - Infiltration of surrounding tissues, incl. SMV
  - Lymphadenopathy
  - Liver lesions
- Occasional low fever, night sweats
- Actinomyces: in patients with chronic pancreatitis and pancreatic/bile duct stent
Endocrine cell hyperplasia

Insulin (brown) & glucagon (red)

Secondary (reactive) endocrine cell hyperplasia

- Often in association with pancreatic atrophy
- Focal or diffuse
- Islets: increased in number and size
- Multihormonal expression preserved, but usually with a relative increase of glucagon-producing cells
- Cave: perineural growth

Somatostatin

Reactive endocrine cell hyperplasia
Endocrine cell hyperplasia (primary)

- Diffuse and specific increase in the number of one particular endocrine cell type (e.g., α-cells)
- Can affect α-, β-, and PP-cells
- Histological diagnosis
- Clinically heterogeneous

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Pt age</th>
<th>Clinical picture</th>
<th>Hormone serum level</th>
<th>Histology</th>
<th>Mutation</th>
<th>Risk for NET</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Newborn</td>
<td>Hyperinsulinaemic hypoglycaemia</td>
<td>Increased</td>
<td>Focal/Diffuse: Enlarged islet, All cell types represented</td>
<td>ATP-sensitive K⁺ channel</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Adult</td>
<td></td>
<td>More and larger islets, increased number of cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Adult</td>
<td>Glucagonoma syndrome</td>
<td>Increased</td>
<td>More and larger islets, increased number of α-cells</td>
<td>Glucagon receptor inactivation</td>
<td>Yes (glucagonoma &amp; other)</td>
</tr>
<tr>
<td></td>
<td>No syndrome</td>
<td>Normal / increased</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>Adult</td>
<td>No syndrome</td>
<td>Increased</td>
<td>More and larger islets, increased number of PP-cells</td>
<td></td>
<td>No</td>
</tr>
</tbody>
</table>

Reactive endocrine cell hyperplasia

Insulin (brown) & glucagon (red)

Yu Run - J Clin Endocrinol Metab 2014;99:748
Glucagon cell hyperplasia

- Islets > 250 μm
- Increased number of islets
- Overwhelming increase in the number of α-cells
- Reversal of β/α-cell ratio in all the pancreatic sections examined
- No MEN1 or von Hippel-Lindau disease

<table>
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<tr>
<th>o-cell hyperplasia</th>
<th>Reactive (Mahvash disease)</th>
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<tr>
<td>GCGR (Glucagon receptor)</td>
<td>Mutated</td>
</tr>
<tr>
<td>Serum glucagon</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Presenting symptoms</td>
<td>Nonspecific</td>
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Liver —— Glucose output —— Glucagon —— o-cells
α-cells are intrinsically normal, but as a consequence of hormonally driven α-cell neogenesis (not increased proliferation), the α-cell population becomes hyperplastic.

In animal models, the disease is reversible upon restitution of GCGR expression.

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<tr>
<td>Endocrine microadenoma / PET</td>
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Glucagon-cell hyperplasia (primary)

- Overwhelming increase in the \( \alpha \)-cell number
- Reversal of \( \beta/\alpha \)-cell ratio in all the pancreatic sections examined
- No MEN1 or von Hippel-Lindau disease
- Age: 25–74 yr
- Diffusely enlarged pancreas; diffuse labelling on Octreotide scan

Octreotide scan: increased tracer activity in pancreatic remnant

Glucagon-cell hyperplasia (primary)

- Overwhelming increase in the \( \alpha \)-cell number
- Reversal of \( \beta/\alpha \)-cell ratio in all the pancreatic sections examined
- No MEN1 or von Hippel-Lindau disease
- Age: 25–74 yr
- Diffusely enlarged pancreas; diffuse labelling on Octreotide scan
- Require continuous surveillance
- Pharmacologically induced?

\( \rightarrow \) Incretins: glucagon-like peptide 1 (GLP-1) analogs inhibit glucagon release from \( \alpha \)-cells and induce \( \alpha \)-cell hyperplasia

Glucagon-cell hyperplasia

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<tr>
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<td>Wild type</td>
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<td>PET</td>
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Glucagon-cell hyperplasia

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Pancreatic polypeptide (PP-) cell hyperplasia
- Rare: 8 cases published
- Enlarged islets, ragged PP cell clusters, DICs
- Disruption of spatial & quantitative relation between 4 islet cell types
- DD: PP cell-rich islets in posterior part of pancreatic head

Pancreatic polypeptide (PP-) cell hyperplasia
- Rare: 8 cases published
- Enlarged islets, ragged PP cell clusters, DICs
- Disruption of spatial & quantitative relation between 4 islet cell types

Octreotide scan: diffuse labeling of entire pancreas
No clear-cut clinical syndrome; some in association with gastrinoma / hypergastrinaemia
Underlying aetiology unclear
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