Cystic Tumors of the pancreas

Firas Obeidat

Introduction

- The diagnosis rate has increased to an estimated 2.6 cystic lesions per 100 indivisuals per year.

- **This increase is secondary to**:
  - Better quality of imaging modalities.
  - Lower threshold of doing CT scan for any abdominal pain.
  - Aging population.

Introduction

- Based on WHO classification, cystic lesions of the pancreas are categorized as:

Neoplastic:

- Intraductal papillary mucinous neoplasms (IPMNs).
- Mucinous cystic neoplasms (MCNs).
- Serous cystadenomas (SCAs).
- Solid pseudopapillary neoplasms (SPTs).

Nonneoplastic:

- Pseudocysts.

Introduction

- **<u>The neoplastic lesions are further categorized as</u>**:
  - Mucin-producing (IPMNs, MCNs).
  - Nonmucin-producing (SCAs, SPTs).

- The mucinous cysts are considered malignant precursor lesions and are covered with endoderm derived columnar epithelium.
- The nonmucinous cysts are lined by simple cuboidal epithelium.

Clinicopathologic Variables

- The majority of patients with pancreatic cysts will have nonneoplastic inflammatory pseudocysts secondary to pancreatitis.
- Pseudocyst is an localized pancreatic fluid collection surrounded by granulation tissue.
- It may develop in as many as 50% of patients who experience acute pancreatitis.
- 20% of unexplained pancreatitis occurs because of the presence of cystic neoplasms.

Diagnostic evaluation of Pancreatic cystic lesions

- CT scan.
- MRCP.
- EUS (mucinous versus nonmucinous).
- Fluid analysis, (CEA > 192 ng/mL is the best predictor for mucinous lesions).
- Low glucose level has same diagnostic accuracy like CEA.
- Amylase level (Low amylase can exclude pseudocyst, but high level is not helpful as it may be high in IPMN,SCA,MCN).

Serous Cystadenoma (SCAs)

- Around half of patients are found incidentally.
- **In symptomatic patients, the most common manifestations are**:
  - Abdominal pain.
  - Palpable mass.
  - Weight loss.
  - Jaundice (infrequent).

SCAs

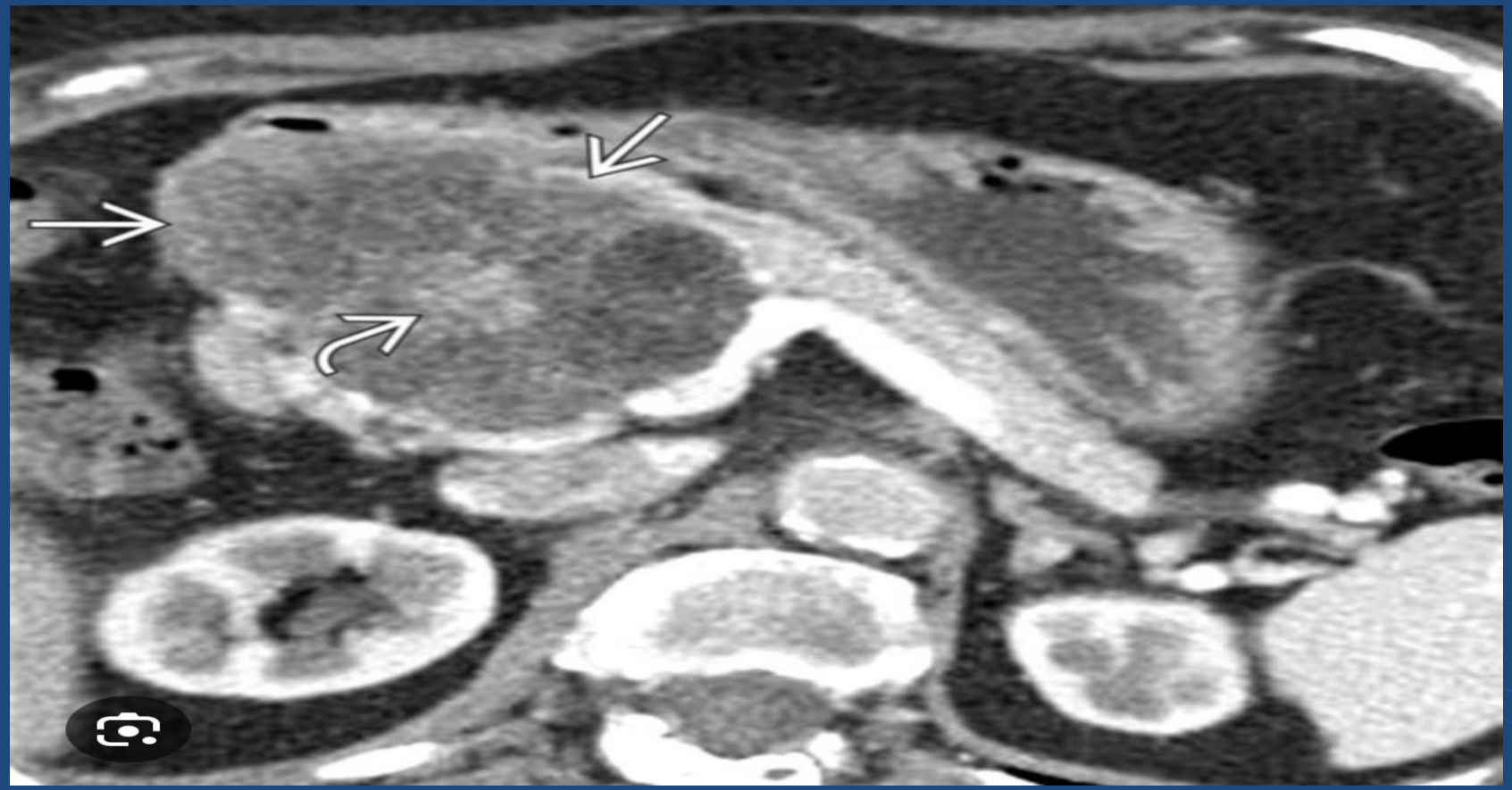
Characteristics:

- More in female, 60+ years.
- More in the head of the pancreas
- It is usually benign, serous cystadenocarcinoma is extremely uncommon and usually reported as case reports.
- Not more than 30 cases of serous cystadenocarcinoma have been reported in the literature.
- risk of malignancy is not more than 1% (female, old age, large cyst > 10 cm).
- Even with metastasis , long term prognosis was excellent.

SCAs

- Fluid analysis: serous, low CEA.
- Morphologic varieties (macrocystic, microcystic, mixed, and solid SCAs).
- Numeral number of small cysts (1-20 mm) Honeycomb appearance with calcified central scar.
- When it is in form of single large cyst (oligocystic), it is difficult to distinguish from MCNs.

SCA



Treatment

SCAs:

- The risk of cancer in asymptomatic lesions is less than 1%, while the risk of pancreatectomy is much greater.

Resection is indicated in the following conditions:

- Significant growth (some reports, large cysts >4 cm grow faster than smaller cysts and they recommend resection for cysts larger than 4 cm).
- Symptomatic.
- Technically feasible with good operative risk.
- Unclear diagnosis.
- When concern with invasive carcinoma excist.

MCNs

- Mucin producing cystic lesions.
- Many MCNs are discovered incidentally, when some may present with abdominal pain, vomiting, pancreatitis, back pain and rarely jaundice.
- Any macrocystic lesion in the distal pancreas in a female patient should be considered highly suspicious of MCN.
- In contrast to SCAs (microcystic) even if it is multilocular it is macrocystic.

MCNs

Characterestic:

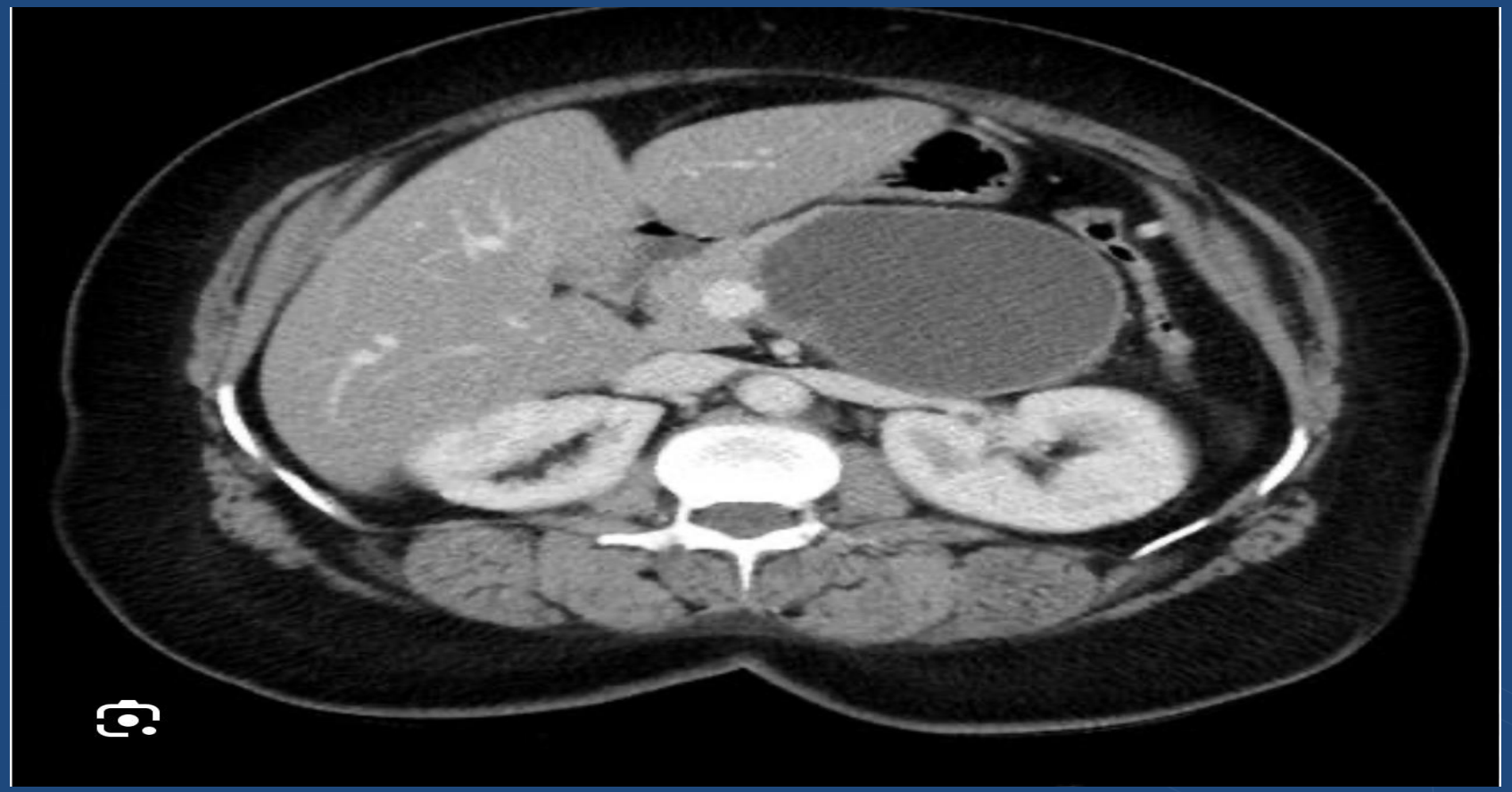
- Age of presentation 4th to 5th decade, almost exclusively in female. (9:1).
- Imaging characterestics: macrocystic, unilocular, more in the body and tail, peripheral “eggshell”cacification.
- Macroscopic features: tall columnar mucin producing epithelium ovarian type stroma.
- It has no connection with main pancreatic duct.
- Invasive or HGD potential 10-50%.
- Cyst fluid analysis: mucin, high in CEA.

MCNs

Factors associated with the risk of invasive carcinoma:

- Male gender.
- Pancreatic head and neck location.
- Larger MCN.
- Mural nodule.
- Duct dilation.

MCN



Treatment

MCNs

- 2012 international association of pancreatology (IAP) guidelines recommend resection for all MCNs regardless of size
- The european guidelines (2018) recommend resection in the following conditions:
  - Cyst > 4 cm.
  - Inhancing mural nodules.
  - Symptomatic cyst (jaundice, acute pancreatitis, new onset DM).
  - Asymptomatic patiens with syst < 4 cm can be safely followed every 6 months for one year then yearly.

Intraductal papillary mucinous neoplasms (IPMNs)

- IPMNs are epithelial tumors that arise from the main pancreatic duct or the branch ducts, causing ductal dilation from mucin production.
- Types: MD, BD, and mixed type.
- MD type high risk of malignancy, BD lesions often benign.
- Account for 15-30% of pancreatic cystic lesions.

Intraductal papillary mucinous neoplasms (IPMNs)

Characterestics:

- Occur equally in male and female, more in elderly (5^{th} to 7^{th} decade).
- MD type (segmental or diffuse dilation of MD> 5 mm) without other reasons for obstruction.
- BD type (grape like cystic lesions)
- Macroscopic features: mucin producing epithelium with papillae.
- Communicating with pancreatic duct.
- Risk of invasion or HGD : MD (36-100%) vs BD (12-30%).
- Cyst fluid analysis: mucin high CEA.

Intraductal papillary mucinous neoplasms (IPMNs)

Factors associated with the risk of invasive cancer:

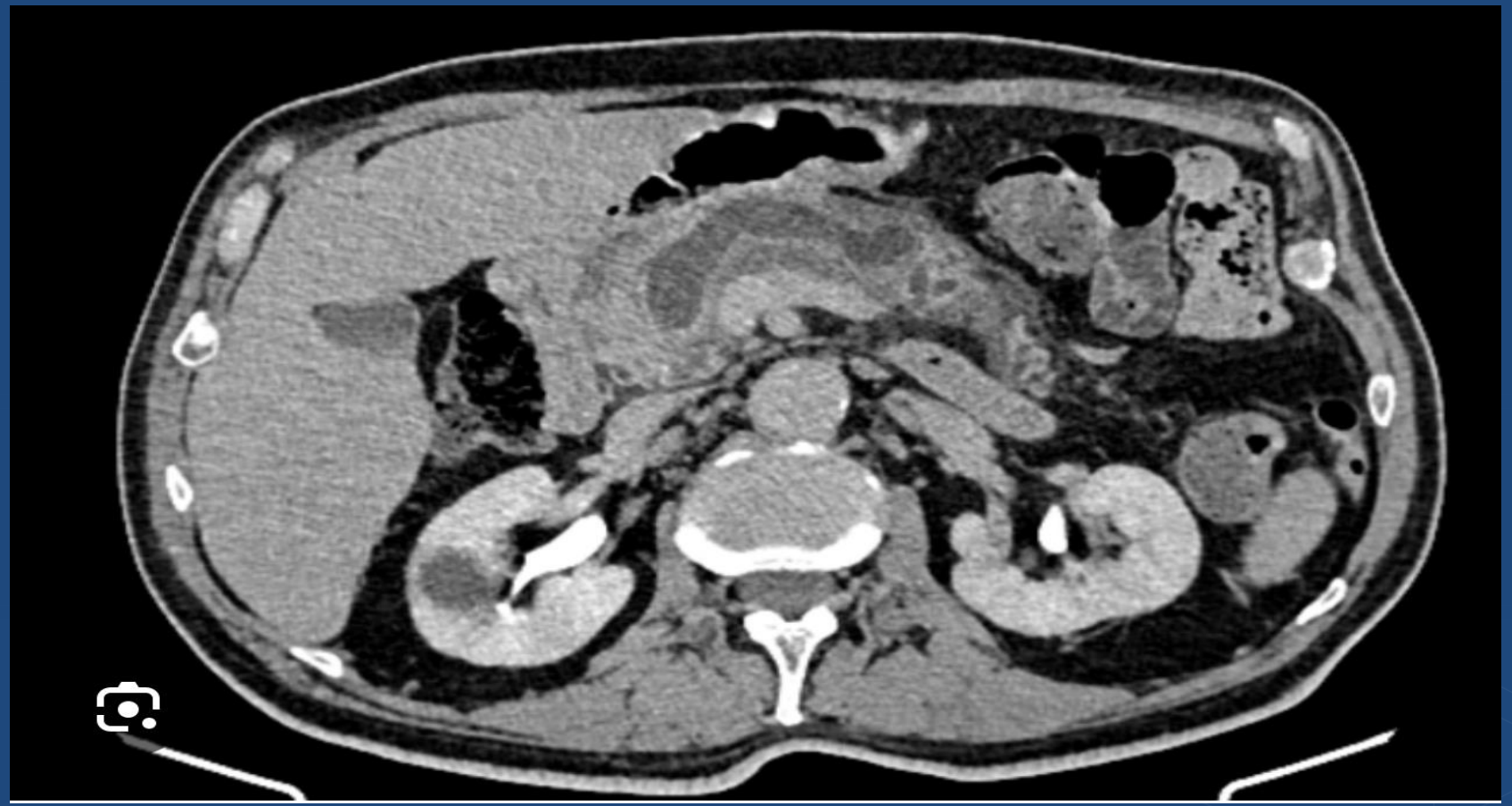
- Presence of symptoms like (jaundice, pancreatitis, new onset DM).
- Large cysts > 3 cm.
- Abrupt change in the calibre of pancreatic duct with pancreatic atrophy.
- Mural nodules.
- Main duct dilation.
- Cyst growth over time.
- Elevated CEA

Intraductal papillary mucinous neoplasms (IPMNs)

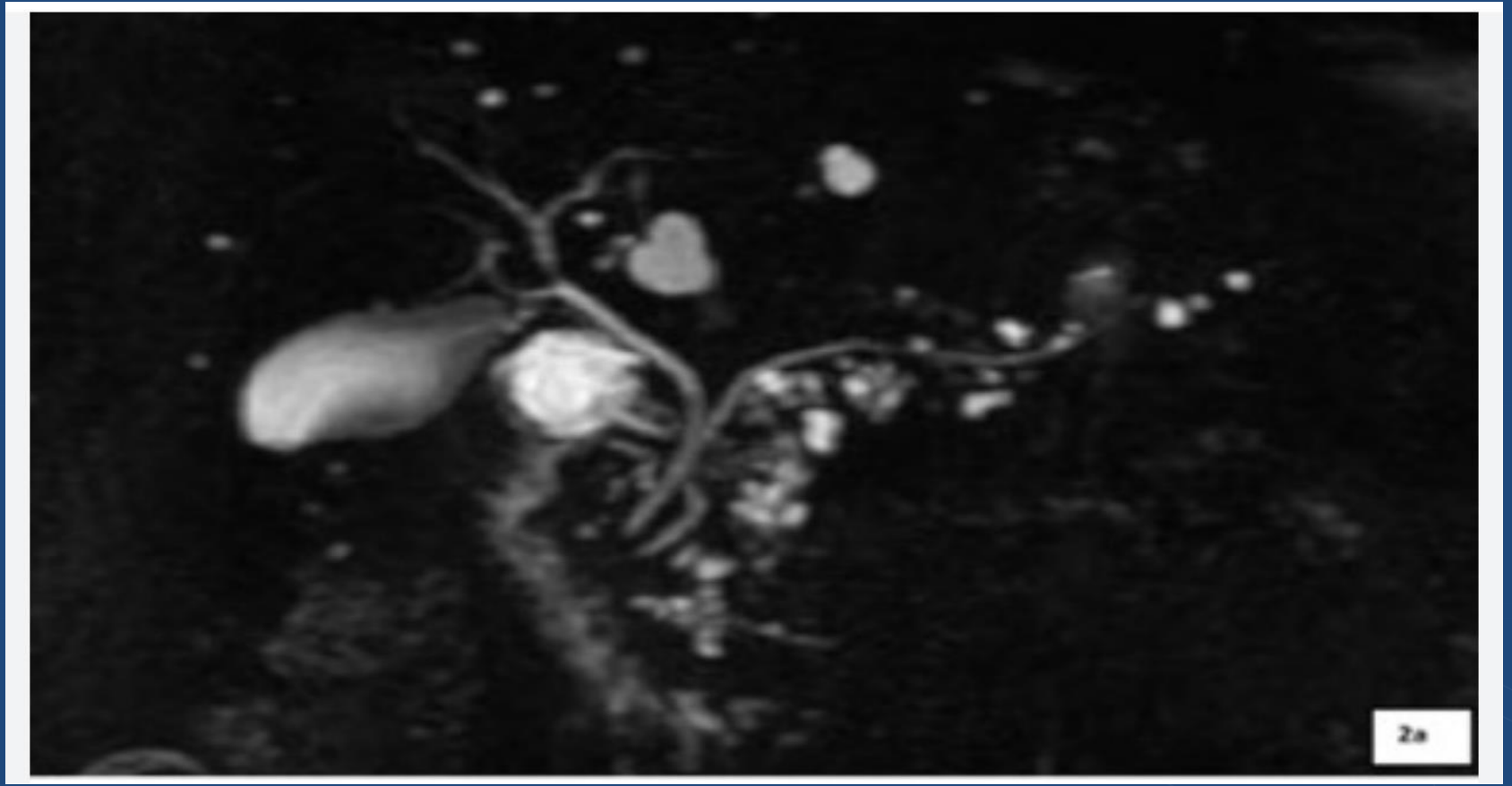
- Prognosis in IPMN adenocarcinoma is better than ductal adenocarcinoma (5 yr survival 43-60% vs 15%).

- Ductal adenocarcinoma is more associated with LN metastasis, advance T stage, perineural and vascular invasion.

IPMN-MD



IPMN-BD



Treatment

IPMN-MD:

- It is believed that most , if not all IPMN-MD will progress to invasive carcinoma.

- Operative resection is recommended because of high risk of HGD or invasive carcinoma.

Treatment

IPMN-MD:

- The European guidelines in 2018 defined main pancreatic duct dilation of 10 mm or greater is an absolute indication for surgical resection and 5-10 mm is a relative indication.

- IAP 2017 recommended surgical resection for all IPMN-MD with > 10 mm duct dilation and 5-10 mm is considered as “worrisome features” with no recommendation for immediate resection, but EUS evaluation is recommended.

Treatment

- The extent of surgical resection in IPMN-MD is controversial.
- The goal of surgery is to remove invasive carcinoma and HGD.
- Frozen section is mandatory to get free margin of resection.
- Positive margin for HGD suggest high risk for disease progression.
- LGD has low risk for disease recurrence.
- In some cases total pancreatectomy is indicated.

Treatment

IPMN-BD:

- 2017 IAP guidelines have classified the concerning radiographic features into:

"worrisome features" and "high-risk stigmata"

- Cysts with "high risk stigmata"should undergo resection without further testing:

- Obstructive jaundice (symptomatic).
- Enhancing mural nodule > 5mm.
- MD > 10 mm.

Treatment

- Cysts with “worrisome features”, should undergo further evaluation with EUS:
- Pancreatitis, Cysts > 3cm.
- Enhancing/thickened mural nodule < 5mm, MD 5-9 mm.
- Abrupt change in caliber of the PD with distal pancreatic atrophy.
- Lymphadenopathy, Increased serum level of CA19.9.
- Cyst growth rate > 5 mm/2yrs.

Treatment

- A multicentric study has analyzed the outcome and predectors of survival in nonoperative patients with presumed IPMNs:
- The authors found that patients with IPMN who had “worrrisome features”had a 5 year disease specific survival of 96% suggesting that conservative management is appropriate in these patients.
- On the other hand, the presence of of “high-risk stigmata” was associated with a 40% risk of IPMN-related death, indicating the policy of surgical resection in patients with “high risk stigmata”.

Treatment

- The 2018 European guidelines also have similar recommendations to the 2017 IAP for resection of IPMN-BD:
- **Absolute indication for surgery**:
  - Jaundice.
  - Cytology positive for high grade dysplasia or cancer.
  - Presence of contrast-enhancing mural nodule (>5 mm) or solid mass.

Treatment

- **<u>Relative indications for surgery</u>**:
- Growth rate > 5 mm /year.
- Increased serum CA19.9 level > 37 U/mL in the absence of jaundice.
- MD diameter 5-9.9 mm.
- Cyst size > 4 cm.
- New onset DM or acute pancreatitis.
- Contrast-enhancing mural nodules < 5 mm.

Solid pseudopapillary tumor (SPT)

Characterestics:

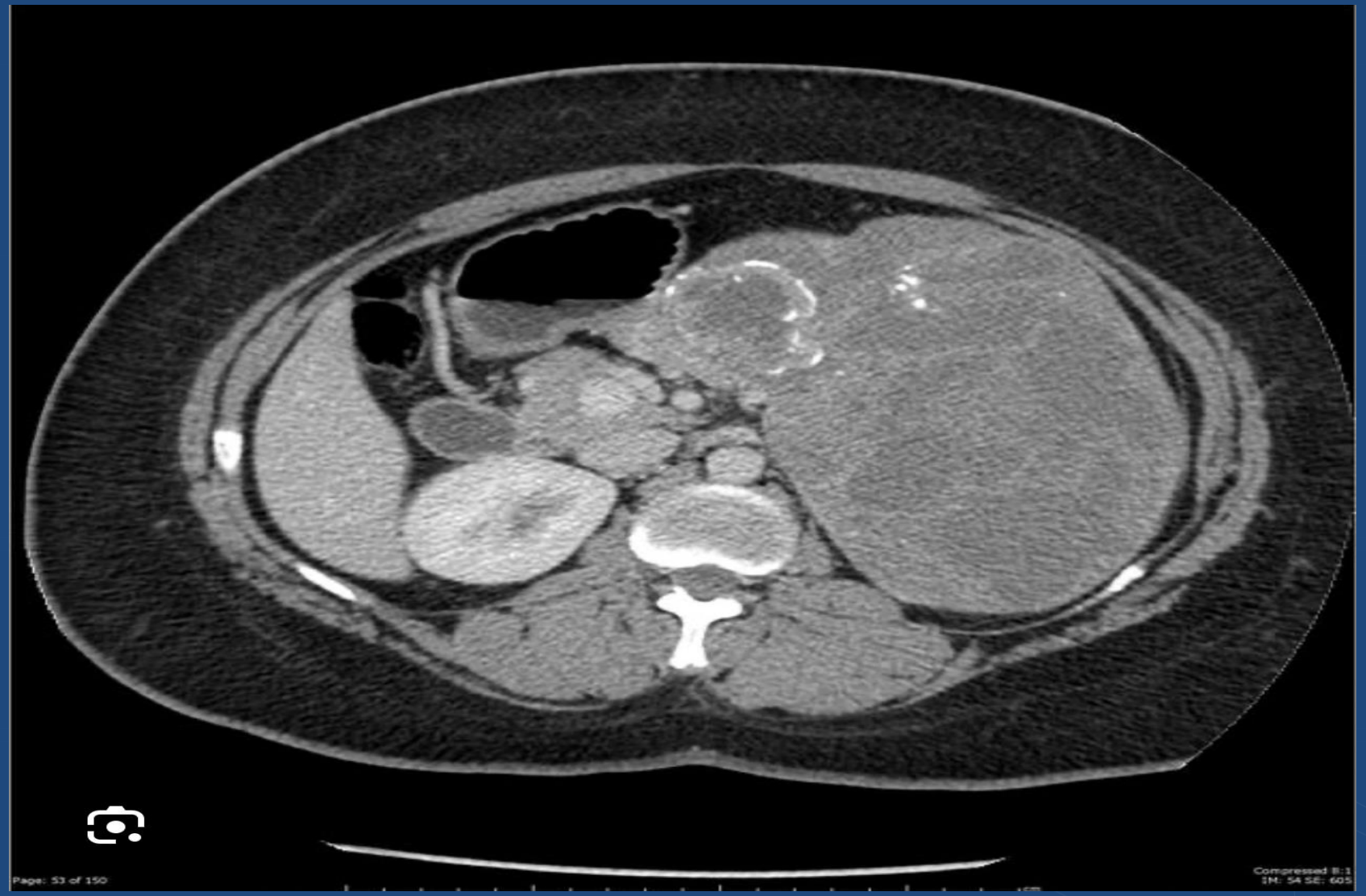
- Rarely cause ductal dilation because of the lack of invasion.
- No communication with the MD.
- 10-15% risk of invasion or HGD.
- Cyst fluid analysis: necrotic debris and blood.

Solid pseudopapillary tumor (SPT)

Characterestics:

- More in young female (2nd- 3rd decade).
- Imaging characterestics: macrocystic, encapsulating lesions with solid and cystic components, areas of hemorrhage and necrosis appearing as irrigular areas of hypodesities, sometimes calcfication.

- Difficult to differentiate from pseudocyst and other pancreatic cystic lesions. However, when a well-encapsulated pancreatic mass with cystic and solid components is encountered in a young female patient, SPTs should be at the top of the differential diagnosis.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Solid pseudopapillary tumor (SPTs)

- Also known as Frantz or Hamoudi tumors after the pathologists who first discribed this entity in 1950s.
- SPTs are rare tumors acoount for as many as 2.5% of resected pancreatic neoplasms
- Mean age 29 years, female to male ratio 9:1
- Most common presentation: abdominal pain and palpable mass,
- Some are asymptomatic around 30%.

Solid pseudopapillary tumor (SPTs)

- Acute rupture with hemoperitoneum is uncommon presentation.
- Typically cured with surgical resection.
- Vascular invasion is the most common cause of inability to resect these lesions.
- Metastatic disease present in 15% of patients.

Solid pseudopapillary tumor (SPTs)

Criteria for defining SPTs as malignant:

- Locally advanced disease with vascular invasion precluding resection.
- Lymph node or hepatic metastasis.
- Long-term survival is often possible despite the presence of metastasis and should not preclude resection in some cases.
- Male gender, positive margin, positive LN and presence of lymph vascular invasion were associated with a risk of of progression.