Mucin-Producing Cystic Neoplasms of the Liver: Current Update on Nomenclature, Pathogenesis & Cross-Sectional Imaging Features

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No Financial Disclosures
Aims / Objectives

Review the updated nomenclature of the mucin-producing cystic neoplasms of the liver

Discuss the pathogenesis & pathological features with special emphasis on evolving tumor entity – ‘intraductal papillary neoplasms of the bile duct’

Describe CT and MR imaging findings of these tumors & how to differentiate them from non-neoplastic cystic lesions & cystic metastases
Introduction

• Biliary cystadenoma and cystadenocarcinoma are the blanket words that have been used to describe mucin-producing cystic neoplasms of the liver
• Recent advances in pathology have led to their updated classification into two different groups that differ in clinical, histological, radiological features & prognosis: Hepatic mucinous cystic neoplasms (MCN) & Intraductal papillary neoplasms of bile duct (IPNB)

• Preoperative differentiation between MCN and IPNB is important; in addition, they should be differentiated from non-neoplastic cystic lesions & cystic metastases
• Imaging plays a pivotal role in diagnosis, surgical planning & follow-up.
Classification

- Hepatic Mucinous cystic Neoplasms (MCN)
  - Unilocular & Multilocular
- Intraductal papillary neoplasms of bile duct (IPNB)
  - Duct-ectatic Mass-forming Cystic type
- Cystic Metastases
  - Ovarian & colorectal cancer
- Non-neoplastic cysts
  - Solitary Bile duct Cyst & Complex hepatic cyst

Zen et al. Modern pathology 2011
Cyst forming
Mass forming
Duct ectatic

Mucin producing cystic neoplasms of liver

Sub epithelial ovarian stroma

Intraductal papillary neoplasm of bile duct (IPNB)

Mucinous Cystic Neoplasm (MCN)

Hepatic MCN vs. IPNB: How Do They Differ?

• Subepithelial Ovarian-Like Stroma – Hepatic MCN
• Bile duct Communication – IPNB

Zen et al. Histopathology 2014
Hepatic MCN

- Cyst forming epithelial neoplasm composed of mucin producing epithelium & associated with **ovarian-type subepithelial stroma**.
- About 5% of hepatic cystic lesions; mostly in females, 90% are histologically benign; central liver location is more common
- Previously classified as cystadenoma & cystadenocarcinoma; now the synonymous terms used are noninvasive and invasive MCN respectively

Pathogenesis

- Develops from endodermal immature stroma or primary yolk sac cells implanted during embryogenesis. The prevalence of hepatic mucinous cystic neoplasm in segment IV may support an **implant origin** as hamartomatous lesions commonly develop in segment IV
- Expression of estrogen & progesterone receptors in ovarian-like subepithelial stroma also supports a **putative role for female hormones** in the tumorigenesis.

Zen et al. Modern pathology 2011
Hepatic MCN: Pathology

- Multilocular cystic mass, lined by columnar epithelium & contain ovarian-like stroma
- Can have elevated serum Ca 19-9.
- CK7 positivity, occasionally positive MUC5AC & MUC2
Hepatic MCN: Imaging Findings

- Multiloculated cystic mass with enhancing septations & rare solid components
- Upstream biliary dilatation is uncommon
- No bile ductal communication or intraductal filling defects
- No downstream ductal dilatation
Hepatic MCN: Imaging Findings

Despite of large size, no significant biliary dilatation & no bile duct communication

Characteristic MRI findings of hepatic MCN in two different patients
Intraductal Papillary Neoplasm of the Bile ducts (IPNB)

- Biliary papilloma & papillomatosis
- Intraductal type of cholangio carcinoma
- Papillary type of bile duct carcinoma
- Mucin-producing bile duct tumor

Macroscopically identifiable papillary tumor within the bile ducts
May or may not have mucin production

Intraductal Papillary Neoplasms of the bile duct
- Polypoidal (Classic type)
  - No mucin production
- Cystic type
  - Abundant mucin production

Most commonly seen in 50-70 years age group without gender predilection
- Intermittent abdominal pain, jaundice and cholangitis are the most common clinical manifestations
- Intrahepatic bile duct is the most common site of origin for IPNB (69%) followed by extrahepatic bile duct (22%) & hilar location (9%)
- Hepatolithiasis increases the risk of IPNB, which explains its relative increased incidence in Asian countries with higher incidence of hepatolithiasis and Clonorchiasis
IPNB: Pathogenesis

Develop from stem cells in bile ductules, bile duct epithelium or peribiliary glands

- Mucin-forming
- Duct-ectasia without identifiable mass
- Cystic type

Interplay of two factors: Epithelial proliferation & mucin secretion decides the formation of mass forming, predominant duct ectatic & cystic types of IPNB

- Dilated ducts with papillary mass
- Mass formation
- Predominant epithelial proliferation
- Predominant mucus secretion
- Superficial spread along biliary epithelium
- Dilated ducts filled with mucin without mass

Lim et al. AJR 2011
Cystic IPNB: Pathogenesis

IPNB arising from biliary ductal epithelium → Intraductal papillary mass → Mucin overproduction with increased intraductal pressure → Cystic or aneurysmal biliary ductal dilatation

Cystic variant of IPNB

IPNB arising from peribiliary glands → Blockage of conduit between the gland and bile duct → Progressive dilatation of gland with mucin → Cystic or diverticulum like dilatation

Lim et al. AJR 2011
IPNB: Pathology

- Intraductal papillary proliferation with fibro vascular cores, dilated ducts with or without mucin hypersecretion
- Multiple visible masses
- Can change into invasive carcinomas (tubular adenocarcinoma or mucinous type) & express CK20
• Intraductal filling defect with papillary mass
• **Ductal dilatation**— downstream as well as upstream ductal dilatation, can be segmental, lobar and diffuse depending on the location
• Crowded bile ducts with hepatic parenchymal atrophy
• Multilocular cystic mass with ‘bunch of grapes’ appearance; enhancing mural nodule
• Ductal communication
IPNB: Imaging Classification

- Predominant segmental or lobar ductal dilatation
- No visible mass
- Hepatic segmental or lobar atrophy

Mass forming IPNB

- Intraductal papillary mass
- Biliary ductal dilatation

Duct-ectatic IPNB

- Cyst with papillary excrescences arising from the wall
- Biliary ductal dilatation

Cystic IPNB

Yoon HJ et al. Abdominal Radiology 2013

Lim et al. AJR 2008 & AJR 2011
Mass-Forming IPNB

Bile ductal dilation with enhancing intraductal masses
Duct-ectatic IPNB

Diffusely dilated bile ducts without any identifiable intraductal mass

Abundant mucus in the bile ducts
Cystic IPNB

Eovist MRI clearly shows intrabiliary extension of tumor

Cystic lesions with bile ductal communication & biliary dilatation
MCN vs. IPNB: How Do They Differ on Imaging?

MCN

- Multiple intracystic septations
- Minimal mural nodularity; rare solid components
- No bile duct dilatation / communication

Cystic IPNB

- Multilocular cystic lesion.
- Enhancing mural nodule.
- Presence of bile duct dilatation & communication
Solitary Bile Duct Cyst

- Most common non-neoplastic cystic lesions of liver present, seen in 2.5% of population
- About 10% of MCNs manifest as unilocular cystic lesions, which are difficult to differentiate from solitary simple cysts

Complex Hepatic Cyst

- Simple cyst with multiple episodes of infection and/or hemorrhagic resulting in minimally thickened septations & echogenic debris
- Mimic hepatic MCN
MCN / IPNB vs. Simple/Complex Hepatic Cyst

**Imaging features that favor Neoplasms:**
- Multiloculated or multicystic mass.
- Internal septations: Central > peripheral.
- Upstream biliary dilatation.
- Downstream biliary dilatation
- Enhancing mural nodules
- More common in left > right hepatic lobe.
- Perilesional transient hepatic attenuation difference
- Coexistence of fewer than 3 cysts
Mucin-Producing Cystic Metastases

Metastases from adenocarcinomas of the ovary and colon/rectum

Abundant production of mucin by acinar tissues & glandular structures in mucinous adenocarcinomas

Cystic Metastases mimic MCN/IPNBs

Mucin-Producing Cystic Metastases from Colon Cancer
Mucin-Producing Cystic Metastases from Colon Cancer

- Multifocal/diffuse distribution
- Multilocular appearance
- Enhancing internal septae & Mural nodules
- Post-treatment calcifications
Management

MCN
• **Enucleation or segmental liver resection**
• Noninvasive MCN has a propensity for recurrence & malignant transformation
• Treatment should therefore be complete surgical resection

IPNB
• **Segmental liver resection** due to propensity for superficial spread along the bile duct & recurrence after aspiration or enucleation

Watchful waiting may be one of the treatments options for MCN, unlike in IPNB where surgery is the only treatment option owing to the high probability of malignancy.

Solitary bile duct cysts / complex hepatic cysts are managed conservatively or by aspiration followed by sclerotherapy or fenestration, and therefore misdiagnosis of MCN/IPNB as SBC / complex cyst may lead to inappropriate management & recurrence.
MCN / IPNB: Complications & Prognosis

- Obstructive jaundice & cholangitis
- Intraperitoneal rupture, hemorrhage within cyst or compression of portal vein.
- **Malignant transformation:** Risk is as high as 15% in MCN & 40-80% IPNB; Always treat IPNB as malignant lesion.
- Recurrence: Fenestration, aspiration, sclerosis, internal drainage, marsupialization, or partial resection with or without cavity ablation can result in recurrence rate as high as 80% to 90% in both tumors
- 5 year survival rate of 80% after complete resection of tumor with negative margins in IPNB.

Cholangiocarcinoma developing in mass forming IPNB

Cholangiocarcinoma developing in cystic IPNB
Mucinous adenocarcinoma developing in IPNB

High-grade dysplasia in IPNB
Mucinous cystic neoplasms of liver are divided into MCN & IPNB on the basis of sub-epithelial ovarian stroma (MCN) and bile ductal communication (IPNB).

In every case of cystic hepatic lesion, look for biliary dilatation and ductal communication, otherwise diagnosis of IPNB can be missed!!

Radiologists should be aware of differentiating imaging features between MCN and IPNB, as there are significant differences in surgical management, follow-up and prognosis.

Mucinous cystic neoplasms of liver should also be differentiated from non-neoplastic cystic lesions and complex hepatic cysts.

Cross sectional imaging modalities like CT, MRI & MRCP play an important role in preoperative diagnosis & differentiation between these entities.
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