Hepatobiliary Mucinous Cystic Neoplasms With Ovarian Type Stroma (So-Called "Hepatobiliary Cystadenoma/Cystadenocarcinoma")

Clinicopathologic Analysis of 36 Cases Illustrates Rarity of Carcinomatous Change

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Background

- “ Hepatobiliary cystadenoma / cystadenocarcinoma” was interpreted to embrace essentially any epitheliallined cystic lesion occurring in the liver and biliary tract.

- cystic tumors in the pancreas : mucinous and serous

- ovarian type stroma(OS) → WHO Mucinous Cystic Neoplasms (MCN)

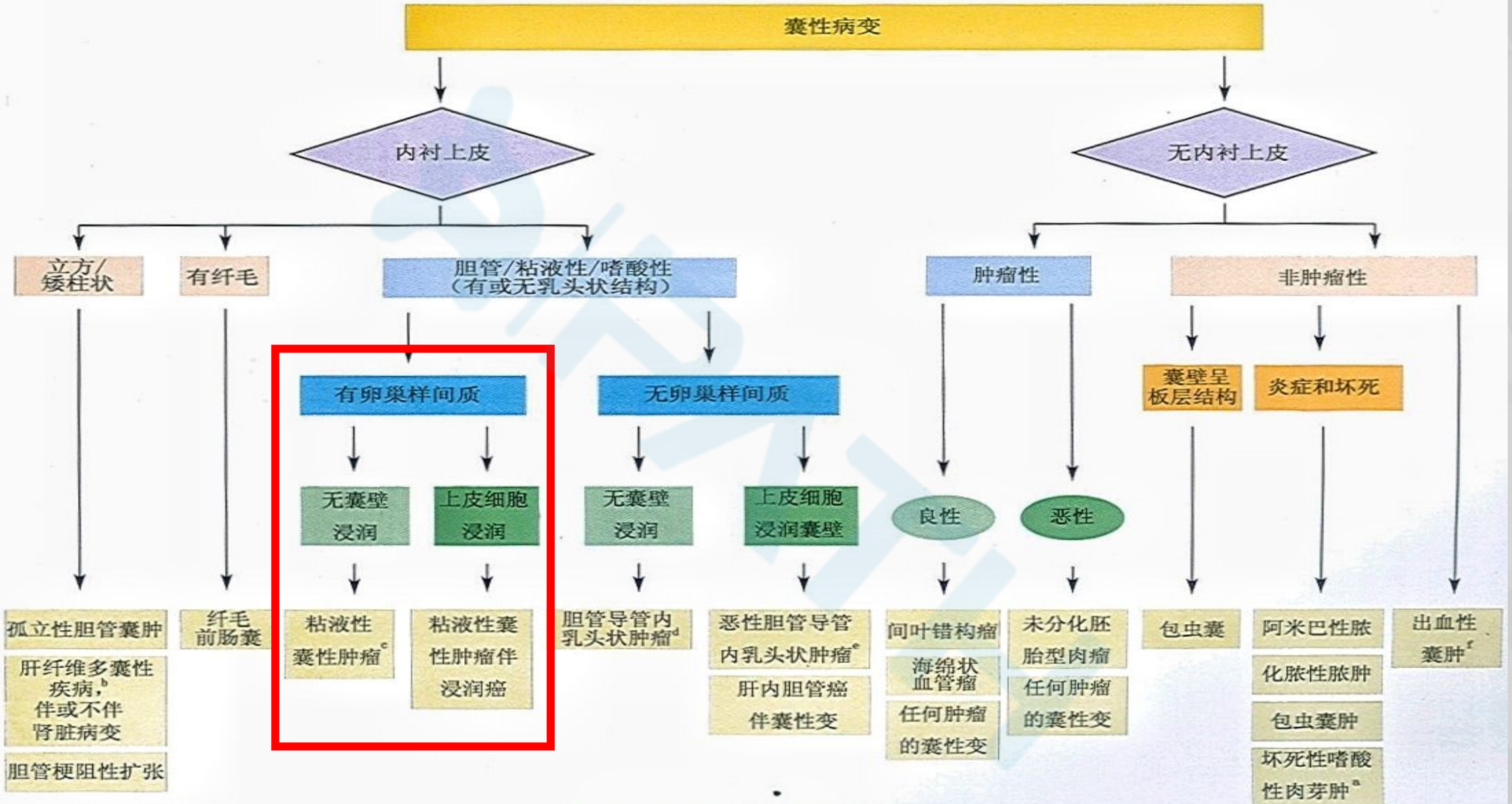


图10.105　肝脏束性病变的诊断规范

肝胆管粘液性囊性肿瘤（Hepatobiliary MCNs）

➢**WHO定义：**是一种囊性上皮性肿瘤，由立方或柱状粘液上皮及卵巢样上皮下间质构成，通常不与胆道相通。绝大多数患者为女性。

➢**卵巢样间质**（Ovarian Type Stroma，OS）：具有卵巢皮质基质的所有组织学和免疫表型特征，包括可能出现黄素化。

➢**ICD-O编码：**

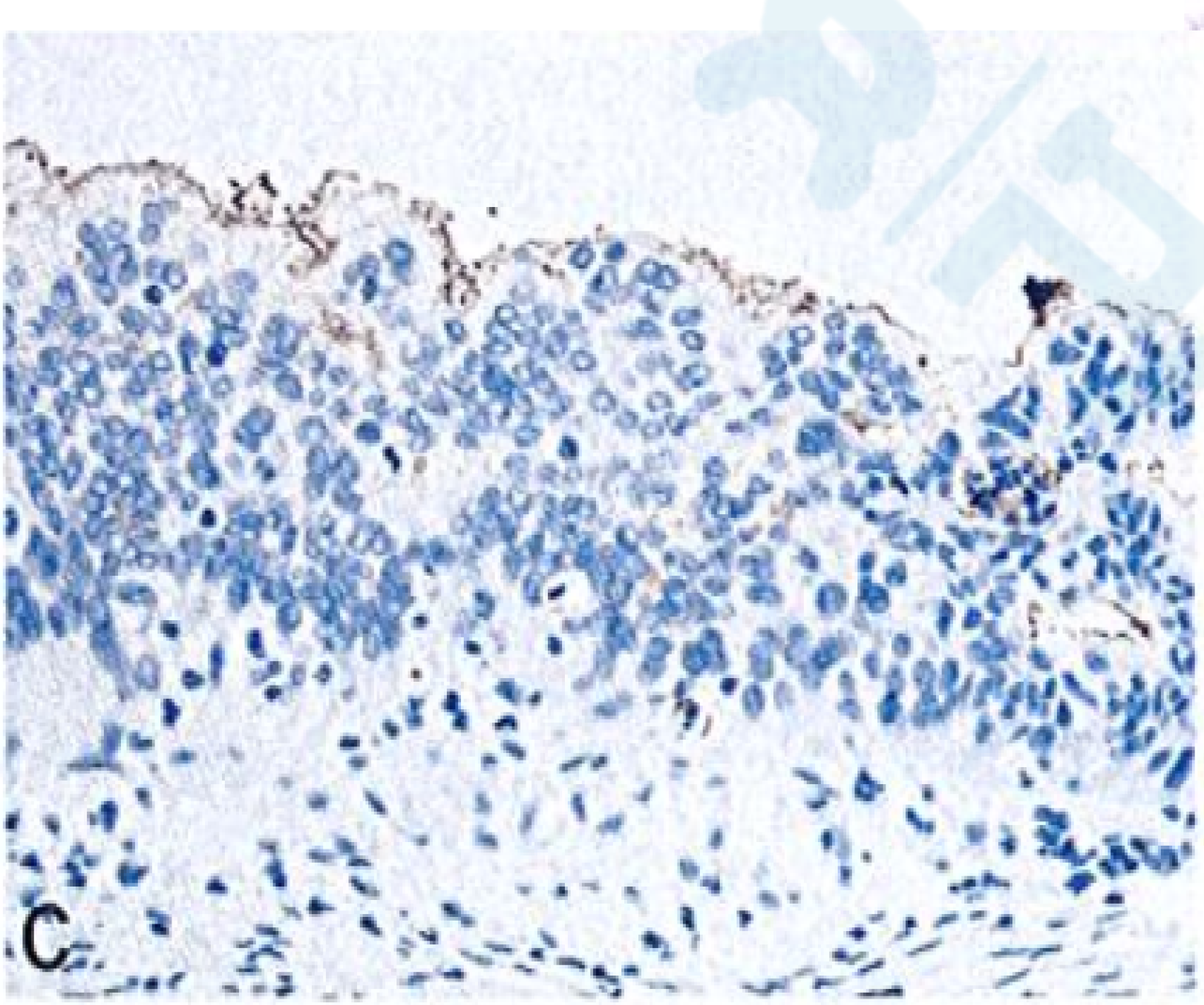
低级别或中级别上皮内粘液性囊性肿瘤	8470/0
高级别上皮内粘液性囊性肿瘤	8470/2
浸润型粘液性囊性癌	8470/3

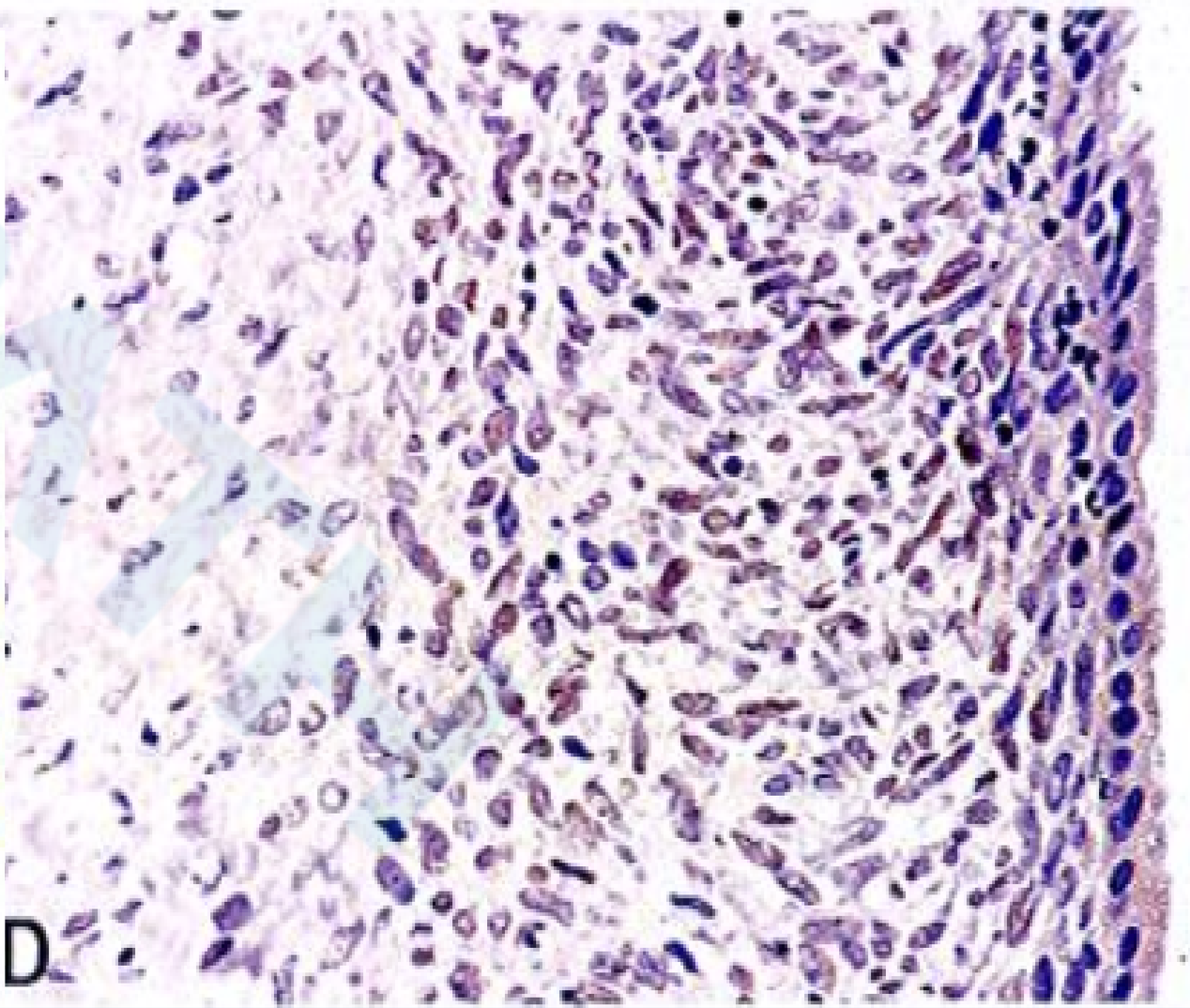
- **大体表现：**多为囊性肿物，直径2.5-28cm。囊内容物多为透明液体，有时可见出血和粘稠物，并不与较大胆管直接联通。浸润性癌时可见大的乳头状肿块或灰白色实性隆起区附在增厚的囊壁上。

- **免疫组化：**

  上皮细胞表达CK7、CK8、CK18、CK19、EMA、CEA

  间质表达vimentin、actin、desmin、ER、PR、α-inhibin 3





Purpose

- elucidate the relative frequency of hepatobiliary MCNs (as now defined by
the WHO by the presence of OS) among hepatic cysts

- determine its clinicopathologic characteristics

- establish the true frequency of carcinomatous changes in this tumor type

MATERIALS AND METHODS

229 cases (1994–2014) → 36cases

- 24 cases(hepatic or biliary cystadenoma / cystadenocarcinoma / mucinous cystic neoplasm)
- 12 cases(hepatobiliary cysts with ovarian-type stroma)

The amount of OS

- ➢Focal (< 25% of the cyst wall/lining sh
  OS presence)
- ➢ moderate (25% to 50%)
- ➢ substantial (> 50% to 75%)
- ➢diffuse (> 75%)

The lining epithelium was classified as either mucinous or biliary nonmucinous.

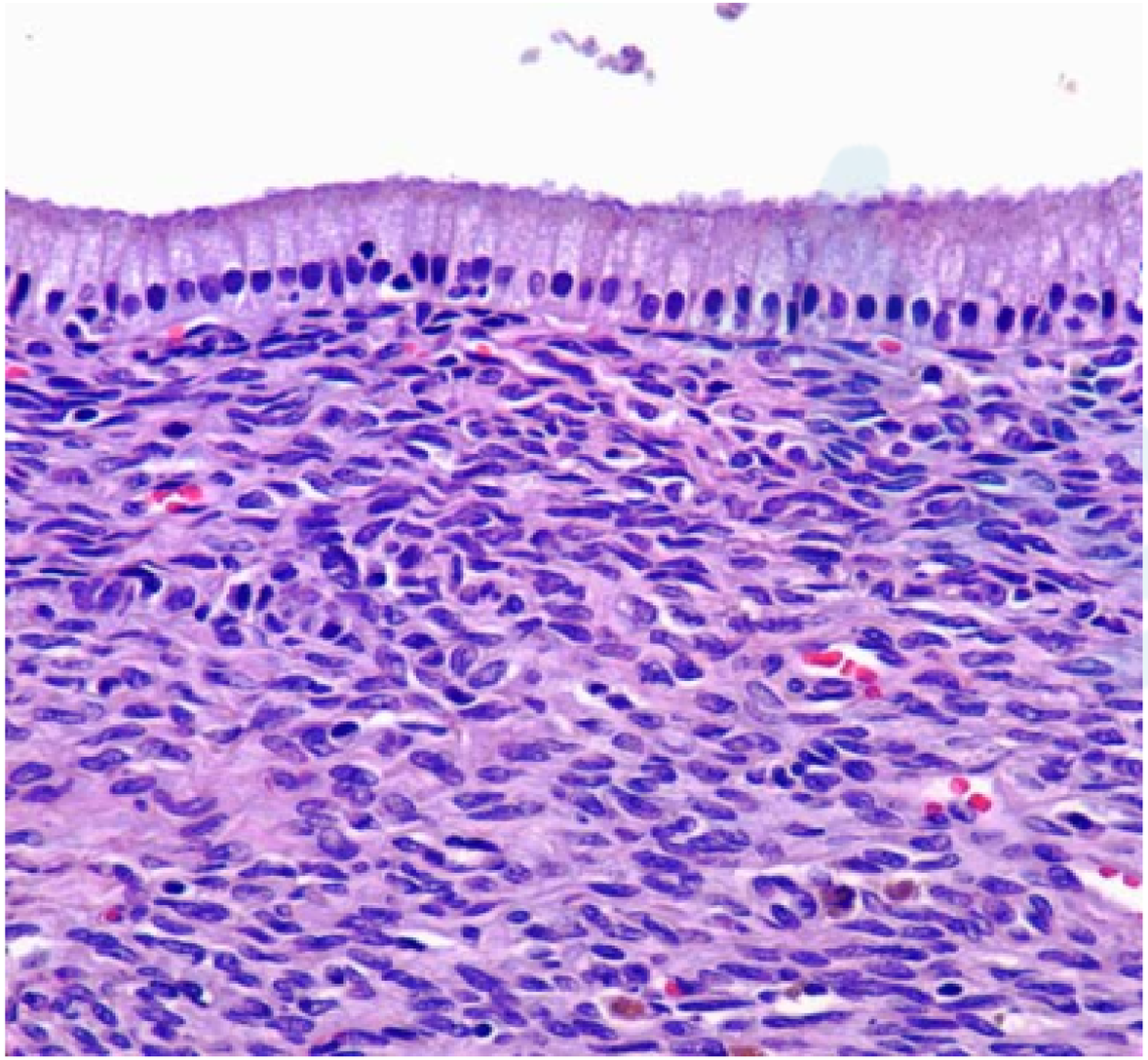


FIGURE 1. Tall columnar mucinous epithelium, as seen here, was seen at least focally in most of the cases. The ovarian stroma in this area is quite cellular (hematoxylin and eosin stain).

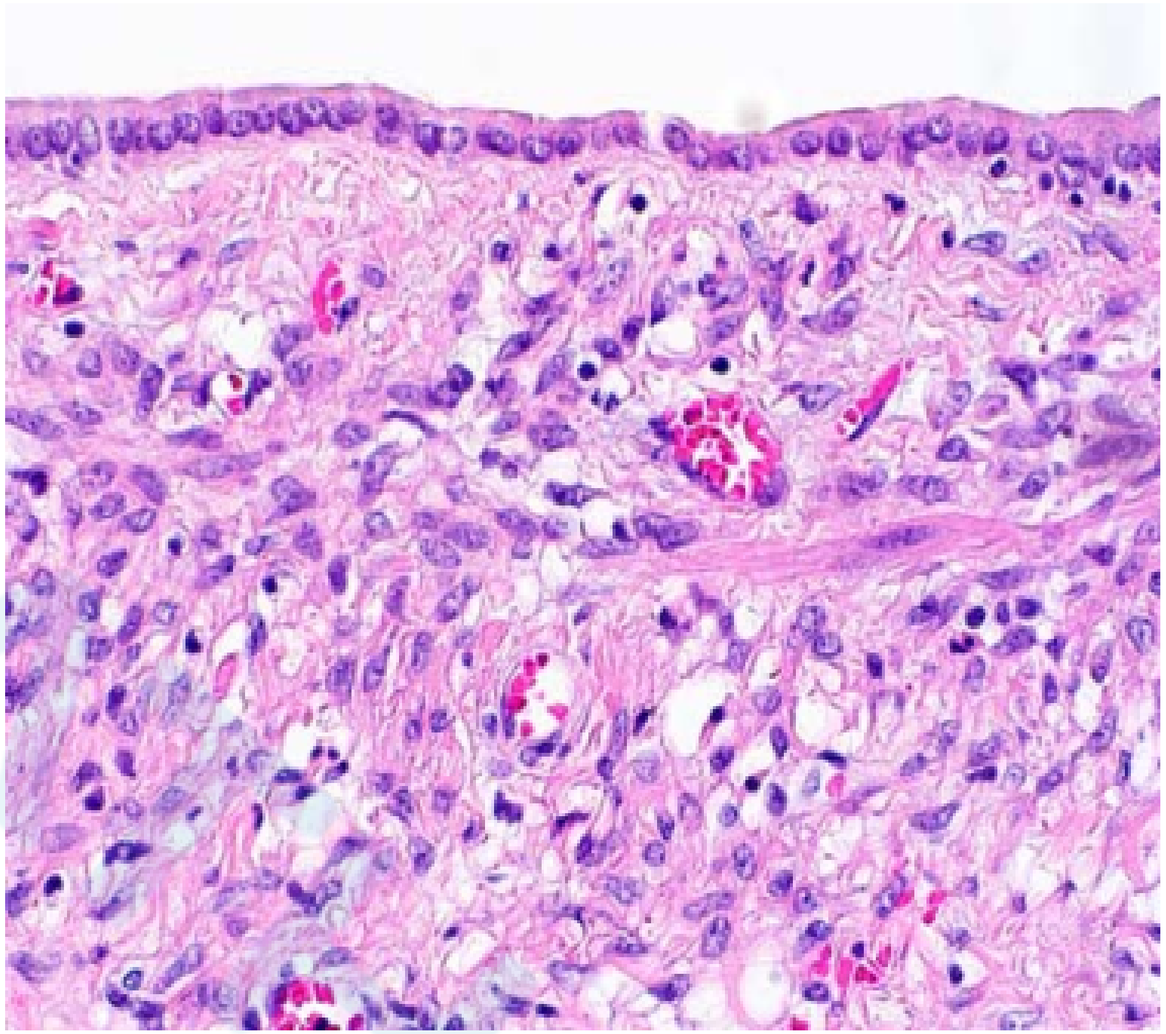
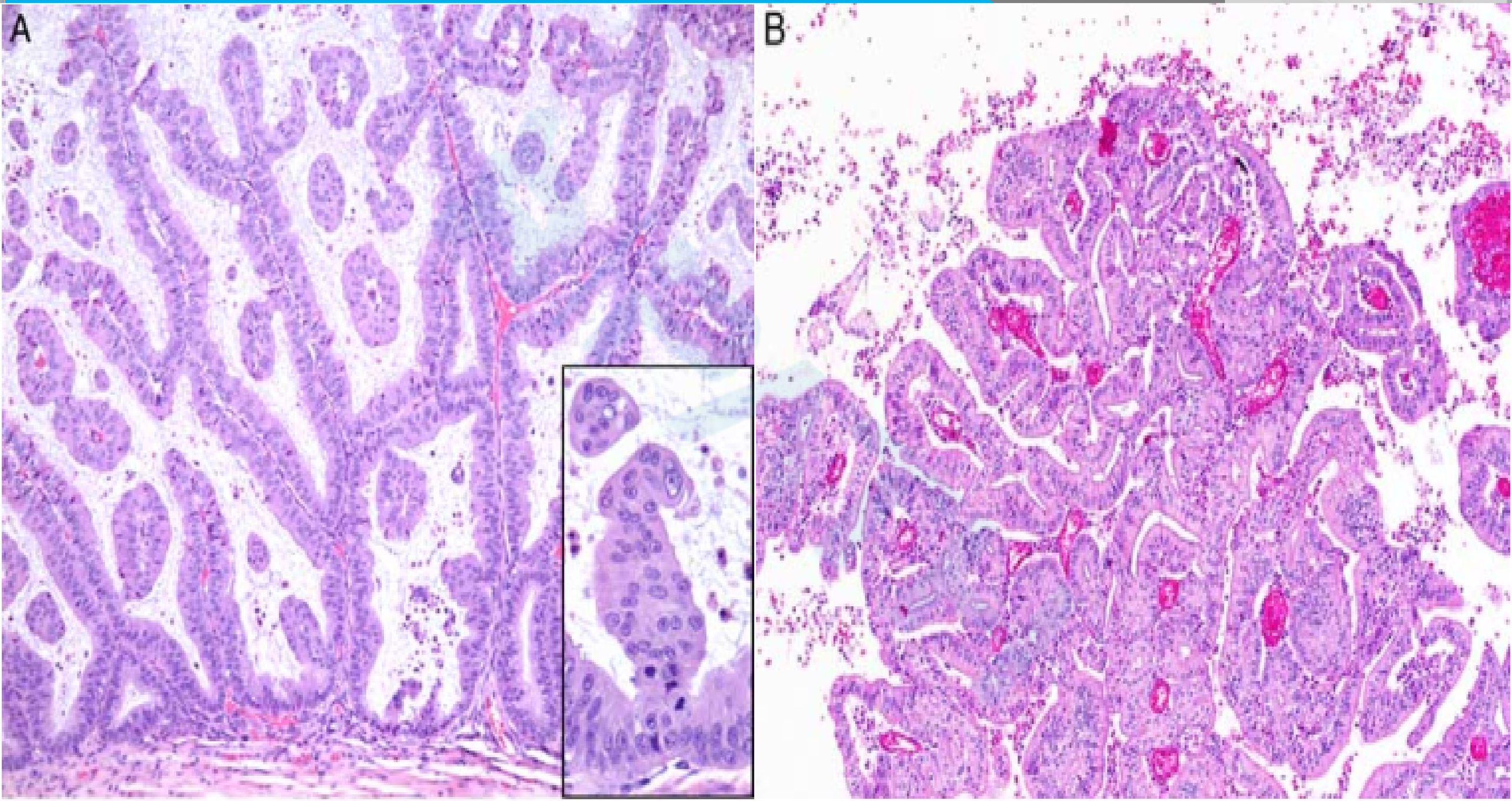


FIGURE 2. Nonmucinous cuboidal epithelium, as seen here, was seen at least focally in most cases and predominated in half. The ovarian stroma in this example is less cellular (hematoxylin and eosin stain).


A
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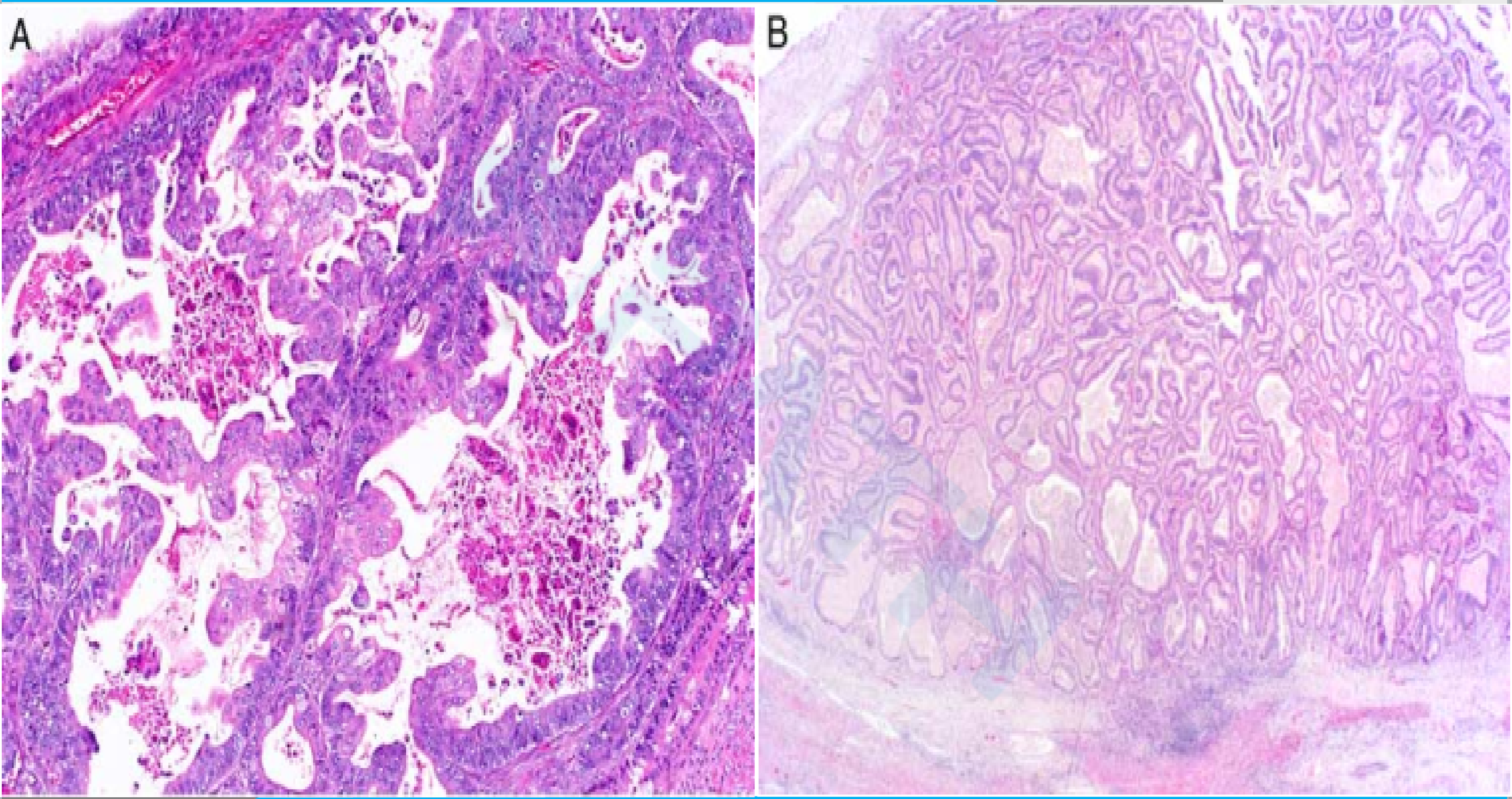
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TABLE 1. General Characteristics of 36 Hepatobiliary MCNs

Characteristic	n/N (%) Without Invasion	With Invasion
No. cases	34/36 (94.4)	2/36 (5.6)
Mean age (y)	50.4	61
Mean cyst (tumor) size (cm)	11.2	17.5
HGD/CIS	0	2/2 (100)
Mural nodule of any composition (≥1 cm)		
Prevalence	7/34 (20.6)	2/2 (100)
Mean size (cm)	1.5	2.2
Intracystic papillary epithelial nodule (≥1 cm)		
Prevalence	0	2/2 (100)
Mean size (cm)	NA	2.2
Left lobe	23/31 (74.2)	0
Central liver	1/31 (3.2)	0
Right lobe	4/31 (12.9)	1/1 (100)
Left lobe and extrahepatic bile duct	1/31 (3.2)	0
Extrahepatic bile duct exclusively	2/31 (6.5)	0
Diffuse OS prevalence	16/34 (47)	1/2 (50)
Focal OS prevalence	3/34 (8.8)	0
MCN in radiologic DDx	13/28 (46.4)	1/2 (50)
Malignancy in radiologic DDx	4/28 (14.3)	2/2 (100)

DDx indicates differential diagnosis; NA, not available.

1. all 36 cases (100%) occurred in women
2. predominantly in the left lobe of the liver (72%)
3. The mean tumor size was 11.6 cm (range, 5 to 23 cm)
4. The mean age was 51 years old (range, 28 to 76 y)
5. 29 cases (91%) were exclusively intrahepatic

Original Interpretation and Diagnoses

- 36 cases
  - 34 noninvasive MSN
    - 25 cases :hepatobiliary cystadenom mucinous cystadenoma,biliary cystadenoma
    - 9 cases mucinous cystic neoplasm
  - 2 cases with invasion
    - mucinous cystadenocarcinoma arising in cystadenoma
    - hepatobiliary cystadenocarcinoma with microscopic foci of invasion

Pathologic Findings

36 cases

- focal OS in 3(8%) (focal epithelioid cells with larger cytoplasm suggestive of luteinization in the OS)
- substantial OS in 16(45%)
- diffuse OS in 17(47%)

Frequency of Carcinoma

36 cases

- 34 noninvasive MSN
- 2 cases with invasion

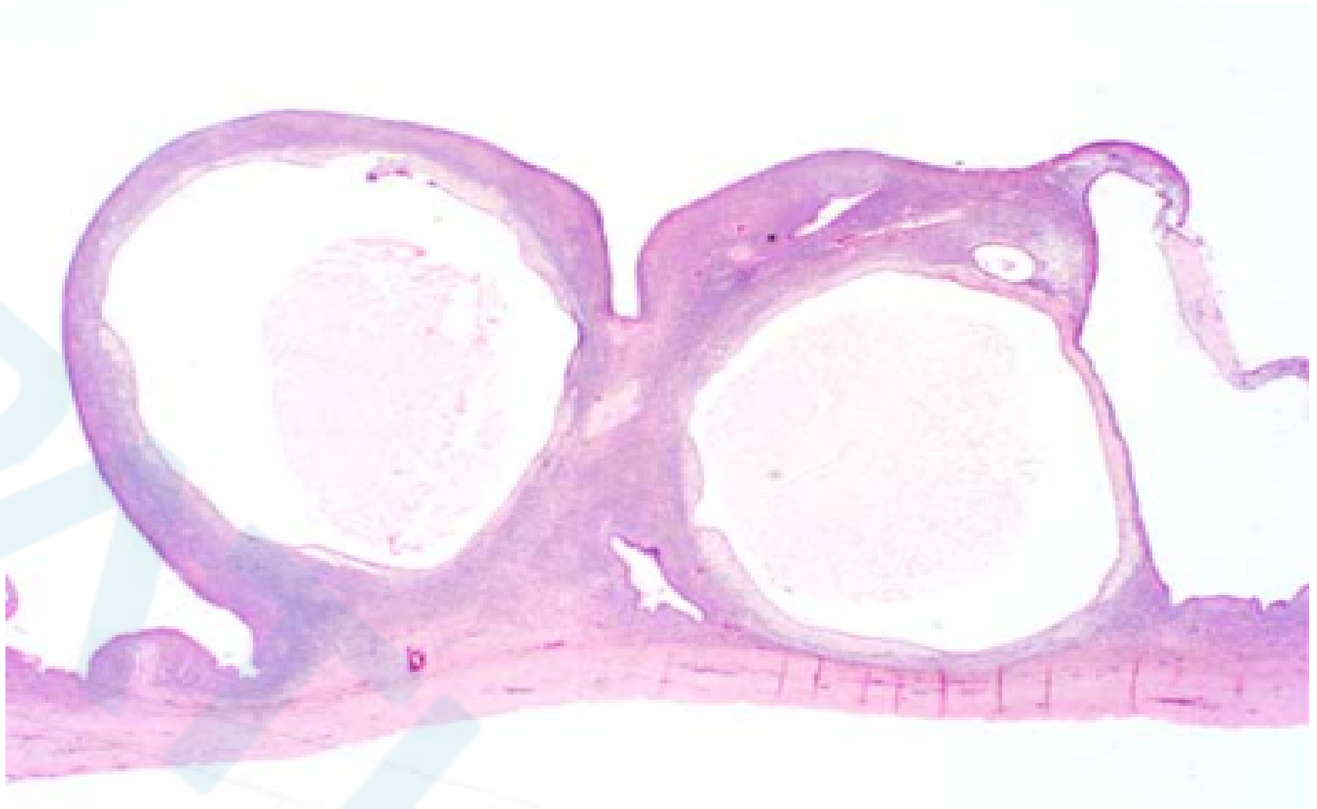

FIGURE 5. Many of the low-grade MCNs had grossly or microscopically detectable papillary/polypoid mural nodules. In this example, the nodule is created by protrusion of mural daughter cysts. This nodule measures 6 mm across and 3 mm tall. None of the low-grade MCNs had any polypoid/papillary nodules composed of complex epithelial proliferation (hematoxylin and eosin stain).

Follow-up

32 cases

- ➢29 were alive with no evidence of disease
- ➢ 2 patients had persistence/ recurrence of low-grade MCNs which were subsequently reresected (one after 7 mo and another after 15 y 11 mo)
- ➢1 patient was alive with reportedly “residual cysts” on MRI

2 invasive cases

- 1 had “residual cyst or hematoma” at 3.9 months
- 1 was without disease at 36.6 months

General Characteristics of 178 MCNs

	LGD	IGD	HGD/CIS	Invasive Carcinoma
No. of cases (%)	109 (61.2)	27 (15.2)	13 (7.3)	29 (16.3)
Mean # of blocks/cm of cyst (tumor)	3.6 (1–13)	3.8 (1.8–10)	4.5 (1.5–11.3)	3.4 (1.0–13.7)
Sex (M:F)	2:107	0:27	0:13	0:29
Location (head vs. body/tail)	2:107	0:27	1:12	0:29

F indicates female; M, male.

Clinicopathologic Findings	MCN With Invasive Carcinoma (n=29)	MCN Without Invasive Carcinoma (n=149)*	*P*
Mean age (range)	53 (23–81)	46 (29–80)	0.214
High CA19-9 (> 37U/L) (n [%])	7/11 (63.6)	10/43 (23.3)	0.011
High CEA (> 7ng/mL)	0/8	4/31 (12.9%)	0.284
Mean cyst (tumor) size (cm)	9.4	5.4	0.006
Intracystic papillary nodule (≥ 1 cm)			
Incidence (n [%])	23/29 (79.3)	13/149 (8.7)	0.000
Median size (cm)	2.3	1.6	0.05

*MCN with LGD, IGD, and HGD/CIS.

DISCUSSION

➢hepatobiliary cystadenoma /cystadenocarcinoma

Pathologic reexamination

25% of the cases have no OS

➢Close to 80% of the MCN/OS cases had not been classified as MCN in the original pathology diagnosis.

I. They occur (almost) exclusively in women.

II. They occur in perimenopausal women (mean age, 50 y).

III. They predominantly occur in the left lobe of the liver.

IV. in only half of the cases was OS diffuse and in the 2 cases with invasion the foci of malignancy were very focal

V. no mucinous epithelium was identified in 20% of the cases, and in close to half of the cases, nonmucinous epithelium was predominant.

VI. the relatively low frequency (6%) of carcinomatous changes in resected hepatobiliary MCN cases

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Original contribution

The expression of FOXL2 in pancreatic, hepatobiliary, and renal tumors with ovarian-type stroma☆,☆☆

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THANK YOU!