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Intraductal Oncocytic Papillary Neoplasms

Clinical-Pathologic Characterization of 24 Cases,With An Emphasis on Associated Invasive Carcinomas

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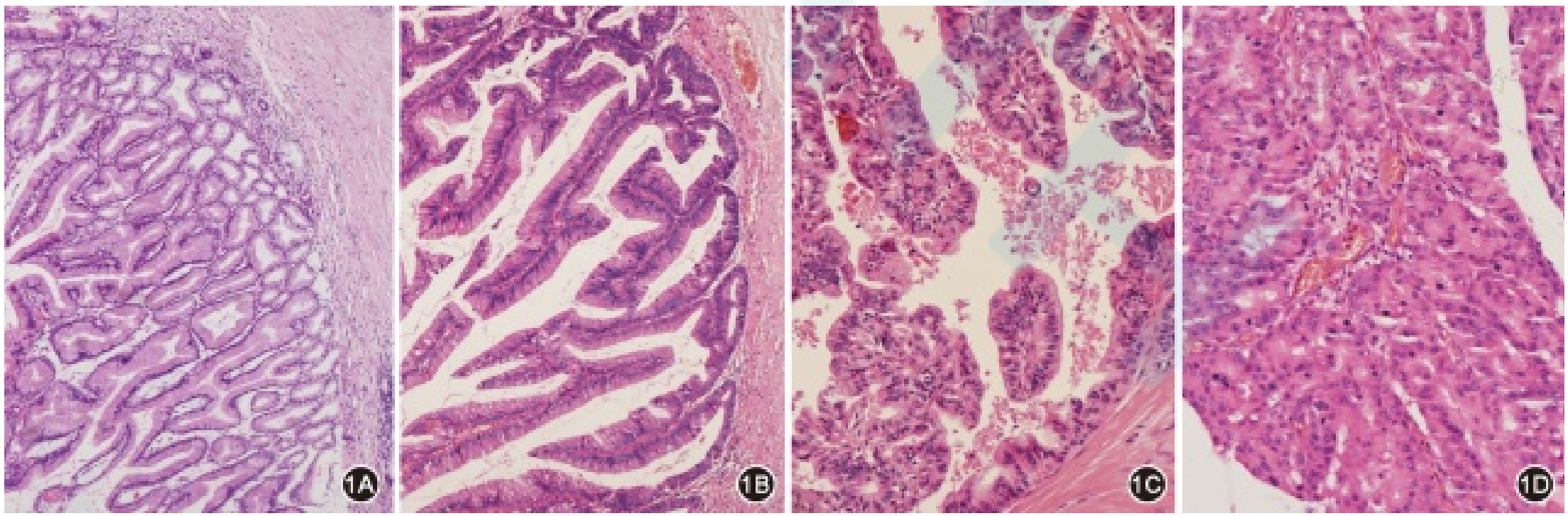
胰腺导管内乳头状黏液性肿瘤（intraductal papillary mucinous neoplasm，IPMN）

- 大体可见的导管内产生黏液上皮性肿瘤，主要发生在胰腺的主胰管及分支内。肿瘤上皮通常呈乳头状生长，黏液分泌及导管扩张程度不等，及不同程度的上皮异性增生。
- 根据细胞结构和主要分化方向，IPMN分为胃型、肠型、胰胆管型和嗜酸细胞型。



摘自中华病理杂志

胰腺导管内嗜酸性乳头状肿瘤（Intraductal oncocytic papillary neoplasm，IOPN）

- IOPN是IPMN的亚型。
- 大体形态一般都较大（5-6cm），灰褐色易碎结节，在大胰管内乳头状生长；
- IOPN通常为树枝状复杂增生的纤细乳头，乳头被覆2-5层立方状或柱状嗜酸性细胞，胞浆丰富、嗜酸，细胞核大而圆，形态均一，有单个偏位的核仁；
- 肿瘤细胞常见胞浆空泡，大小约为细胞的1/4，局部可形成筛状结构。相邻的乳头的上皮可发生融合，产生以小血管为中心的实性生长模式。

胰腺导管内嗜酸性乳头状肿瘤（Intraductal oncocytic papillary neoplasm，IOPN）

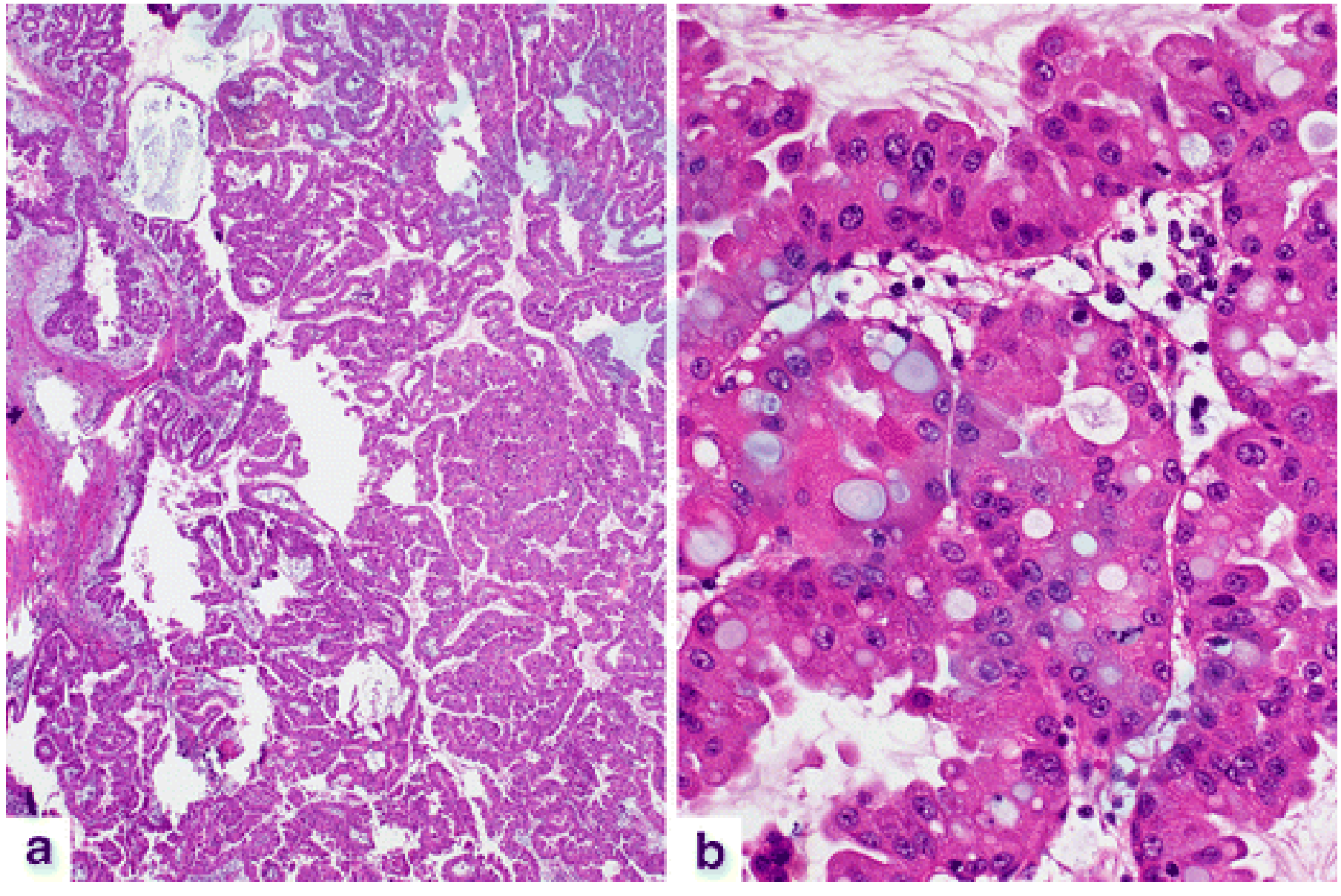


TABLE 1. Clinicopathologic Features of the Cases Analyzed

Features	N (%)
Mean age (range) (y)	59 (36-74)
Female/Male	15/9
Preoperative diagnosis	
Pancreatic ductal adenocarcinoma	5/12 (42)
Neuroendocrine tumor	1/12 (8)
Mucinous cystic neoplasm	3/12 (25)
Intraductal papillary mucinous neoplasm	3/12 (25)
Site	
Head	14/21 (67)*
Body/tail	6/21 (28)
Diffuse	1/21 (5)
Median tumor size (range)	4.5 (1-14)
Invasion	7/24 (29)
LVI	2/15 (13)
PNI	1/15 (7)
Lymph node metastasis	1/17 (6)
Positive margin	4/17 (24)
Follow-up	
Median follow-up (range) (y)	6.8 (0.1-18.5)
Died of postoperative complications or other causes	5/18 (28)
Died of disease	0/18 (0)
Alive with disease	0/18 (0)
No evidence of disease	13/18 (72)

*One of these IOPNs recurred in the tail and underwent completion pancreatectomy.

LVI indicates lymphovascular invasion; PNI, perineural invasion.

结果：IOPN大体形态

- 17例病例有详细的大体描述。
- 16/17例肿瘤呈单房或多房囊性。
- 其中8例内含乳头状突起或实行结节。
- 6例肿瘤囊肿中含有清亮黏稠液体。

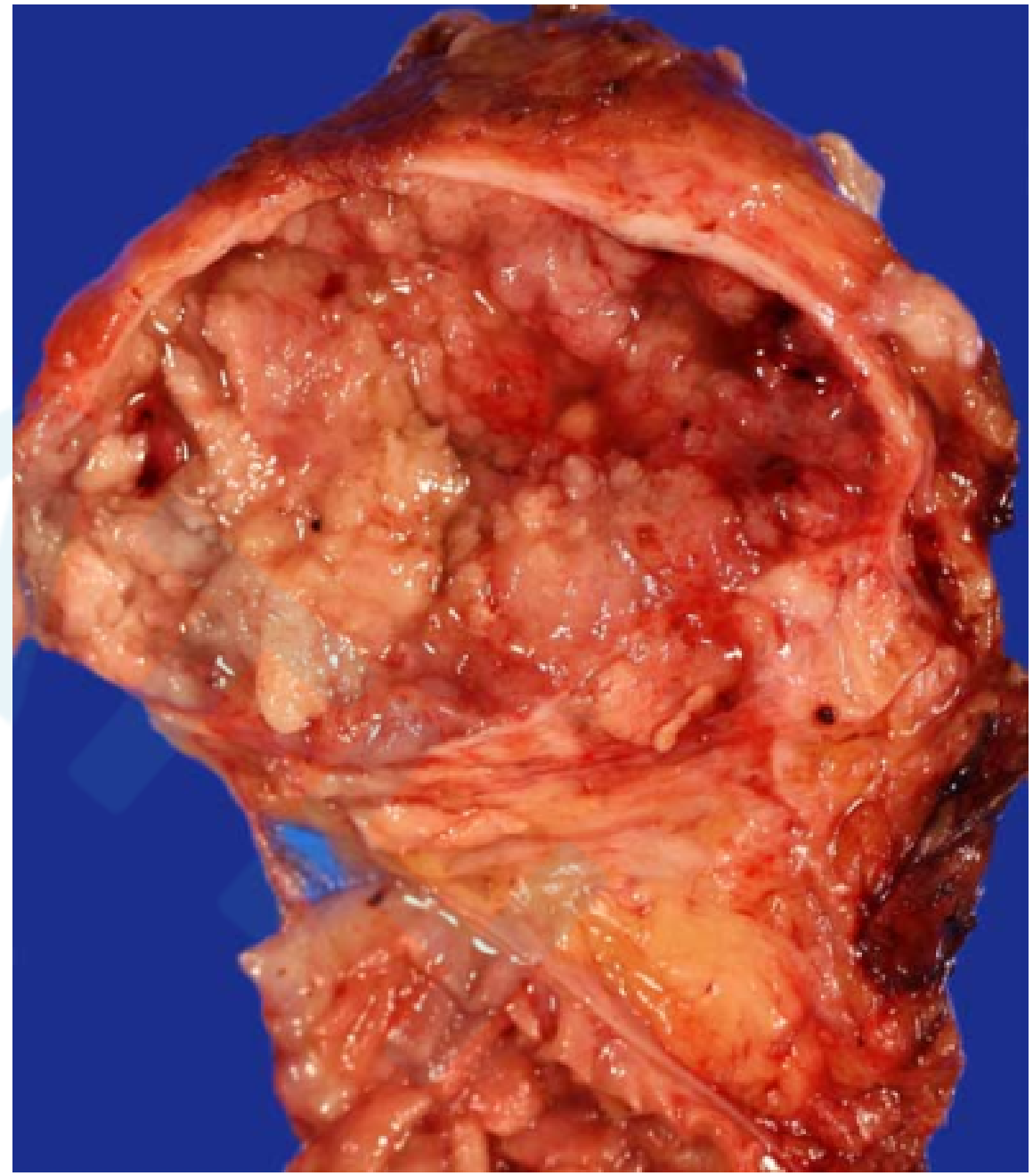
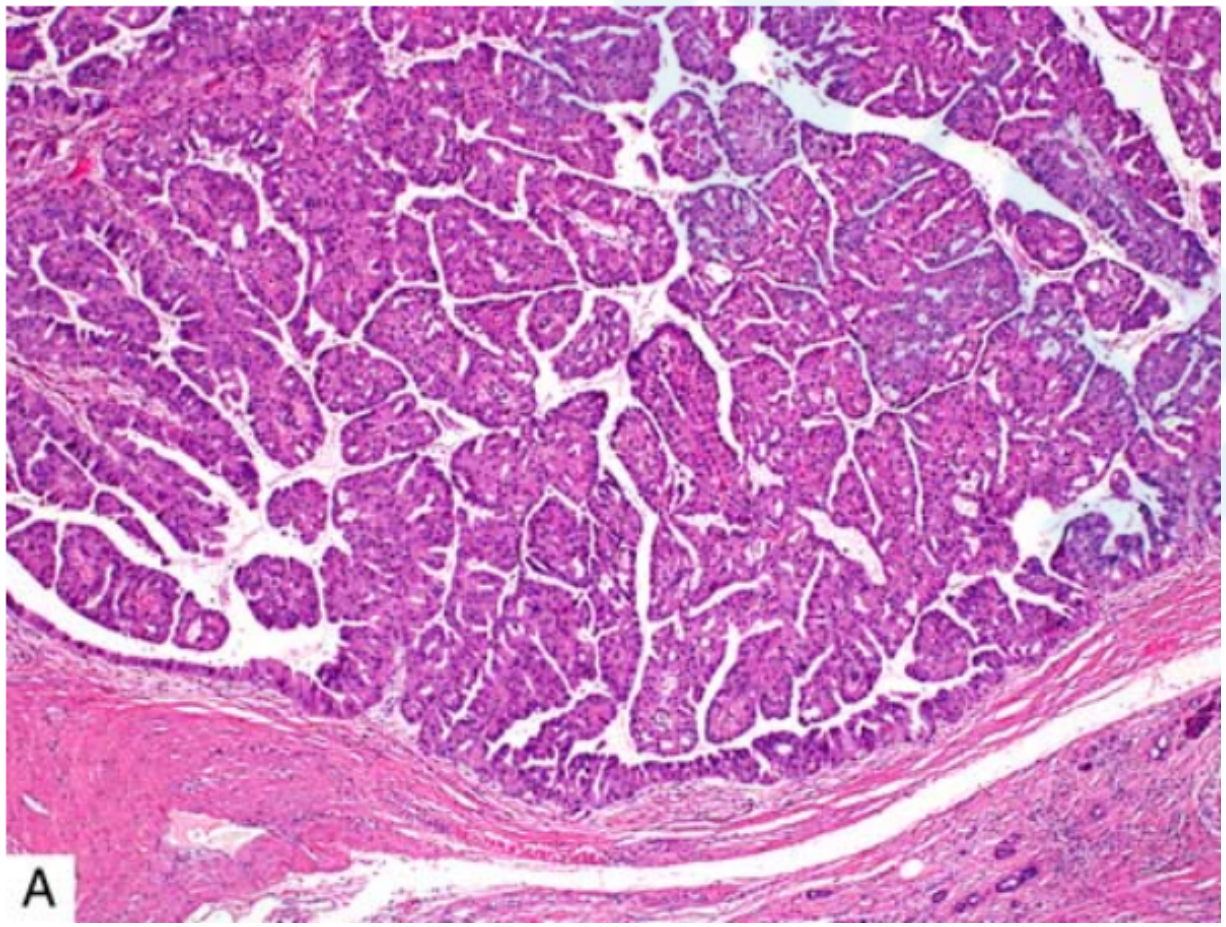


FIGURE 1. Macroscopic picture of IOPN with cyst lined by papillary excrescences.

结果：IOPN组织学形态



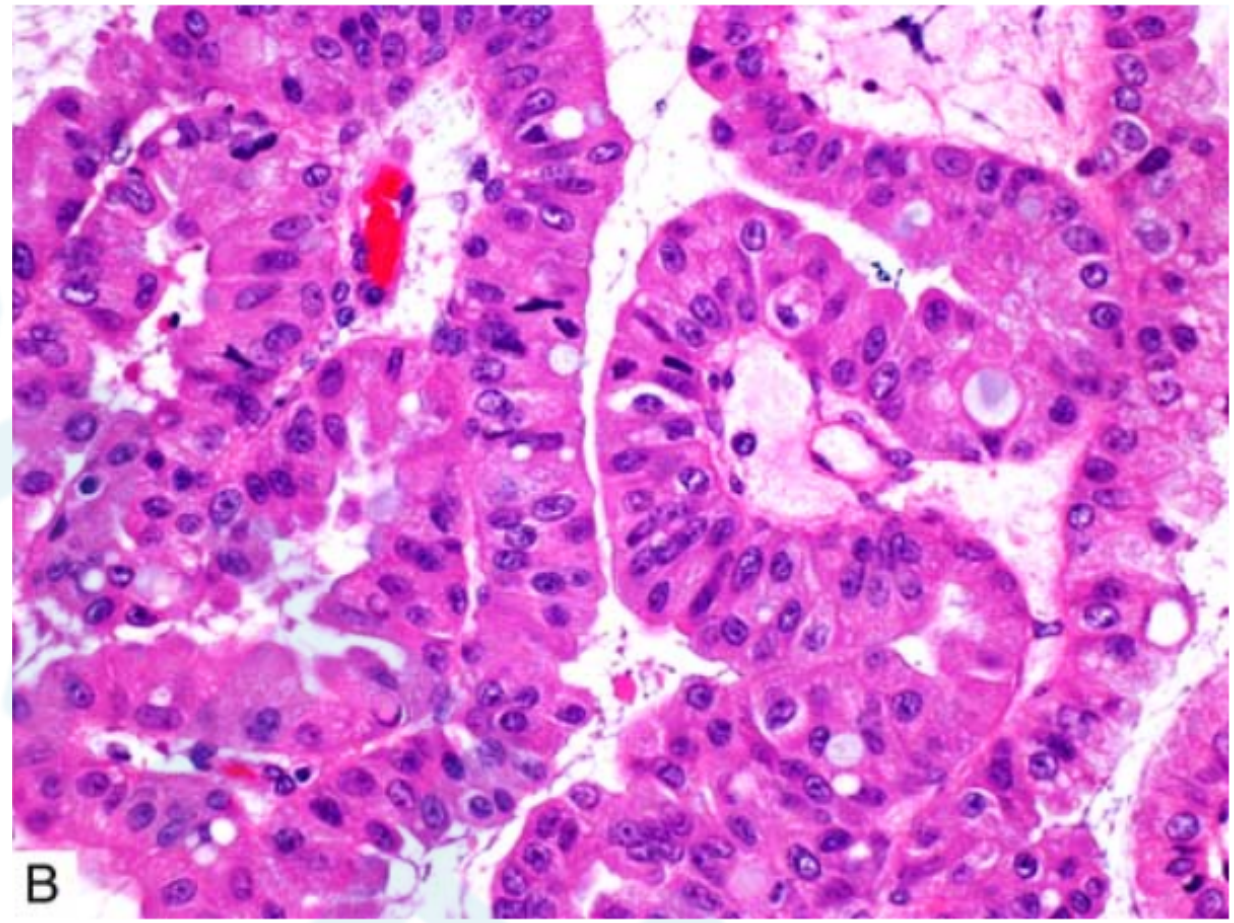


FIGURE 2. On microscopy, the lesion exhibits papillary architecture (A) with distinct oncocytic cytology and intracytoplasmic lumens (B).

IOPN伴浸润

- 7/24例IOPN含有浸润性成分。
- 其中5例，分期为pT1，浸润性成分通常仅限于导管周围或囊肿周围（即肿瘤细胞仅从导管边缘直接浸润到周围间质中）。
- 2例，分期为pT2，肿瘤组织侵及胰腺周围软组织或/和十二指肠壁。
- 7例病例中仅有一例具有淋巴结转移。

结果：IOPN伴浸润组织学形态

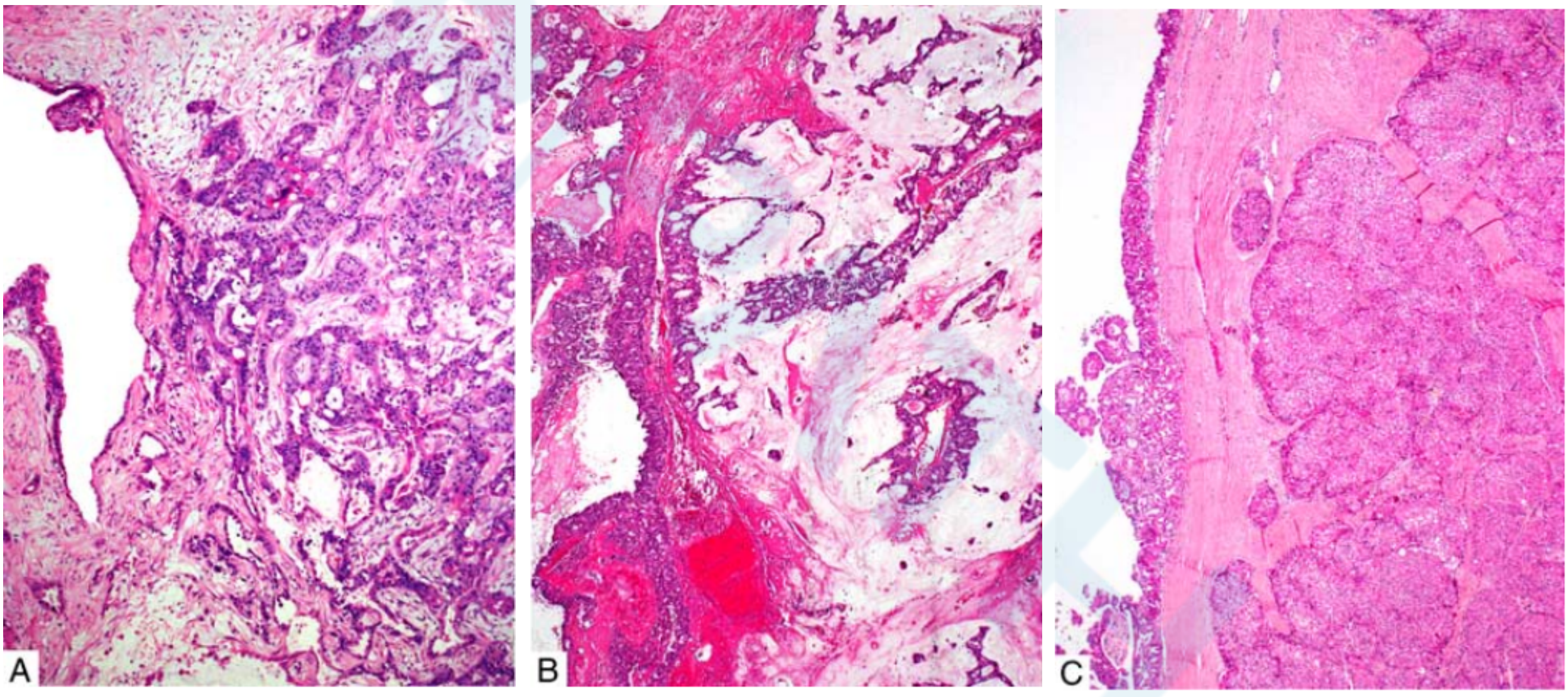
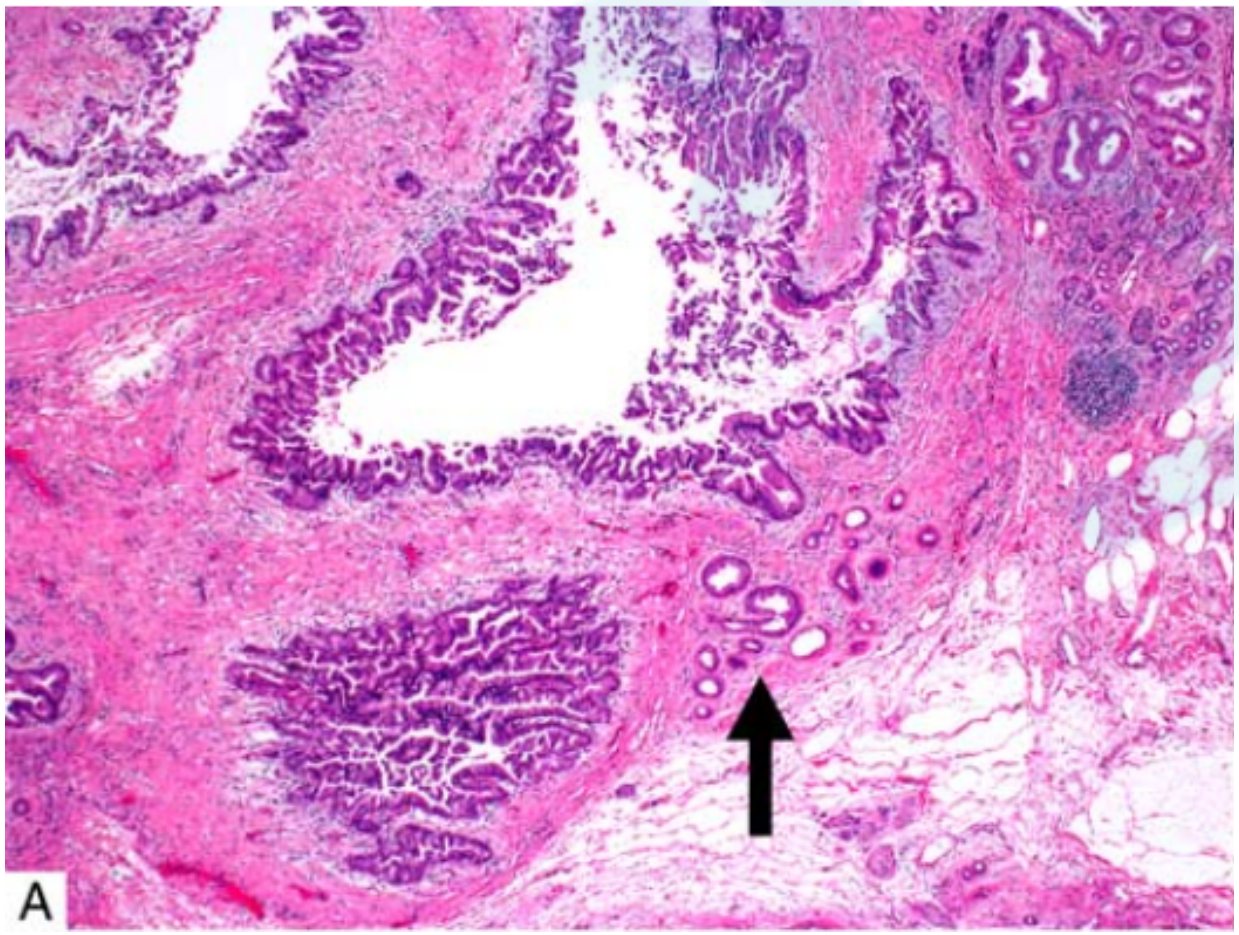


FIGURE 3. IOPNs can invade as small infiltrative tubules of oncocytic cells (A), as mucinous tumors with free-floating oncocytic cells (B), or as large nodules with pushing borders (C).

结果：IOPN假浸润



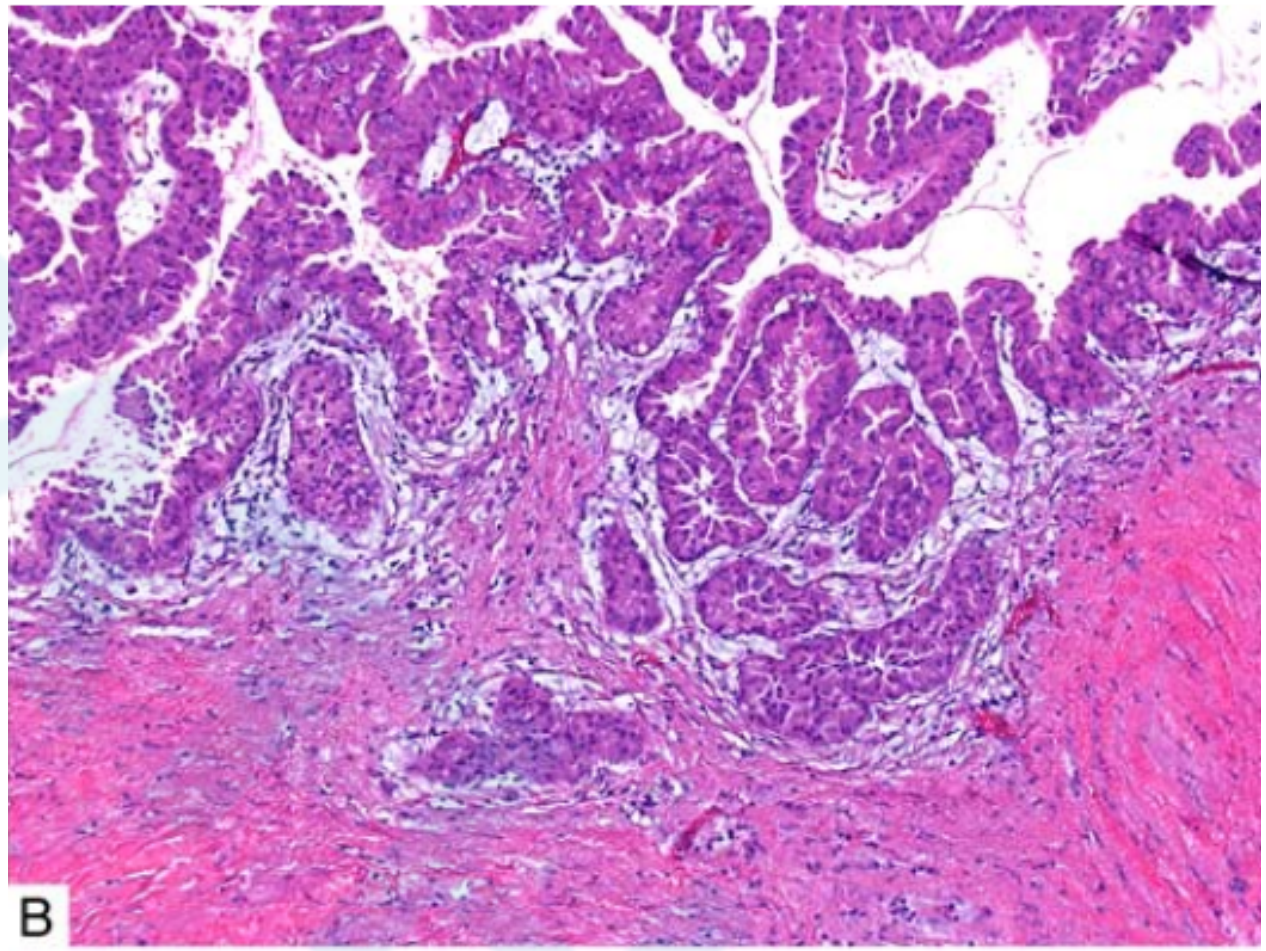
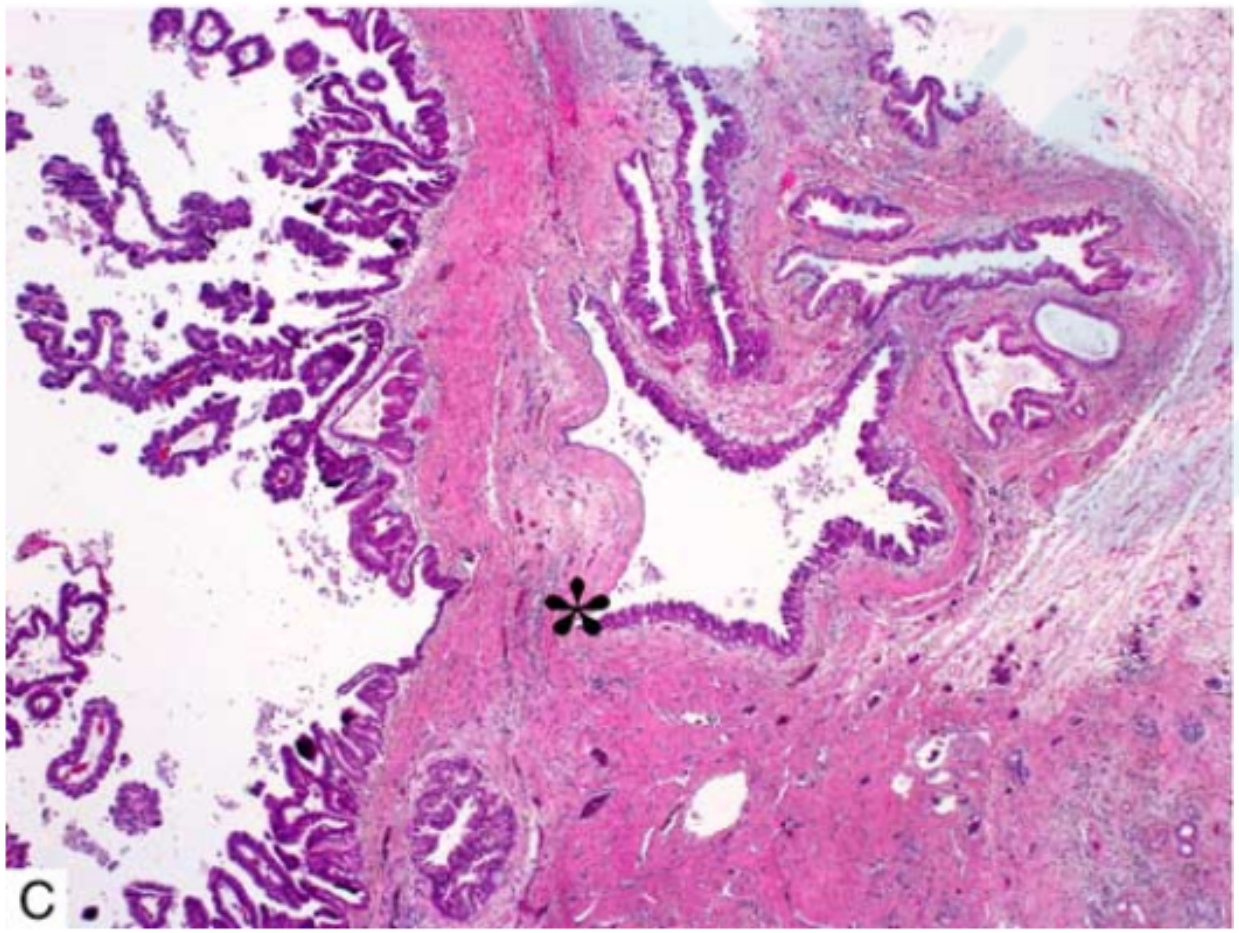
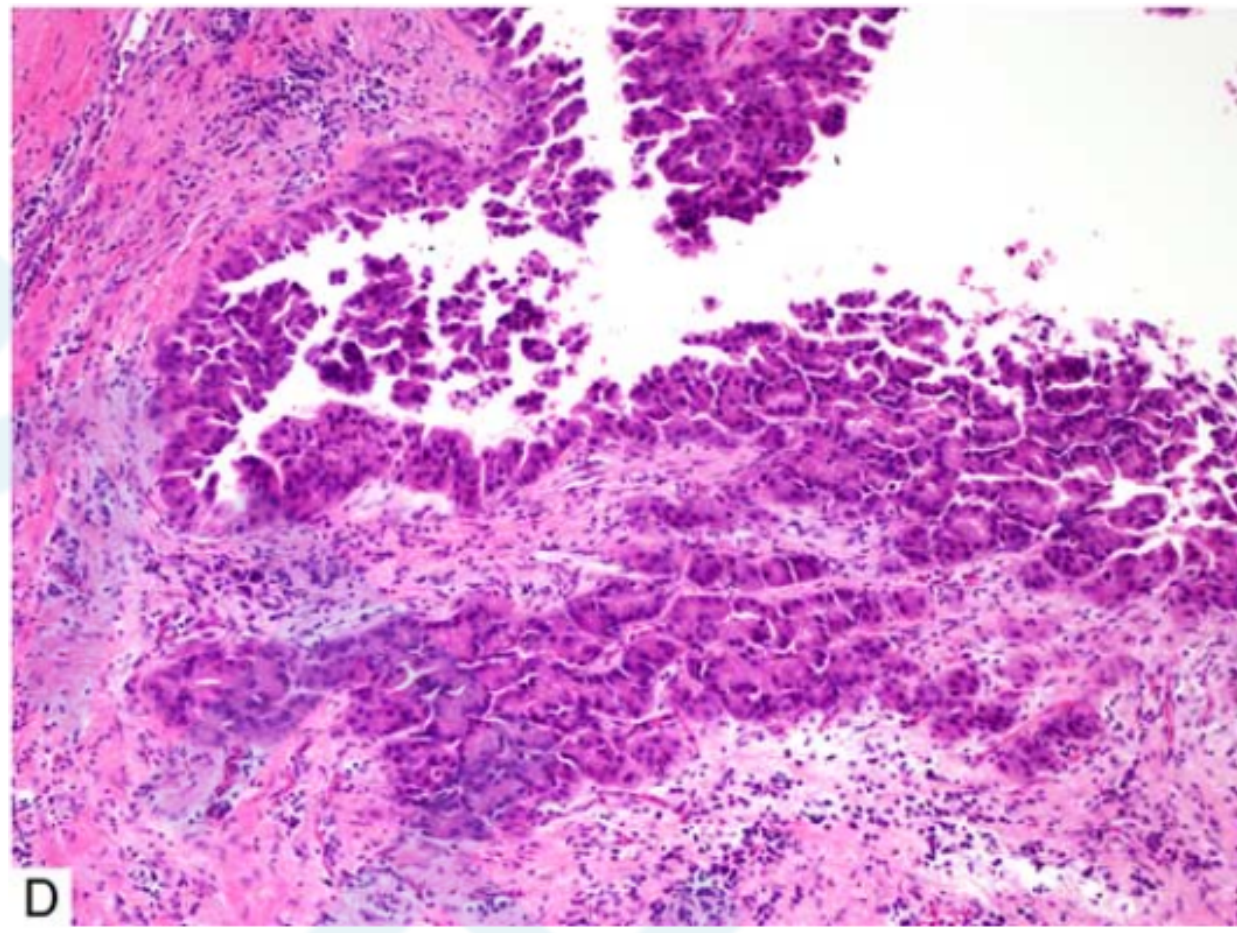


FIGURE 4. IOPNs may exhibit pseudoinvasive patterns including growing along adjacent benign ducts (arrow) (A), or myxoid stromal changes that simulate desmoplasia (B). If present, abrupt transition (star) from a morphologically normal epithelium to oncocytic epithelium within the same duct is helpful in recognizing pseudoinvasion (C). Tangential sectioning also mimics invasion by creating a complex appearance (D).

结果：IOPN组织学形态





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IPMN免疫组化

		MUC1	MUC2	MUC5AC	MUC6	CDX2
IPMN	intestinal	—	++	++	—	++
	pancreatobiliary	++	—	++	+	—
	gastric	—	—	++	—	—
	Oncocytic（IOPN）	+	—	+	++	—

+，可疑阳性；++阳性

——摘自消化系统WHO

结果：IOPN的IHC

TABLE 2. Immunoprofile of the IOPNs Analyzed

MUC1	50%
MUC2	29%*
MUC5AC	100%
MUC6	89%
CDX2	9%*
HepPar-1	61%

These results were previously published in part in Basturk et al.[6]
*MUC2 and CDX2 labeling was observed in goblet cells.

IOPN缺乏IPMN显著的肠分化，并且具有不同黏蛋白的表达模式。

肠型IPMN： CDX-2和MUC-2弥漫强阳性。

IOPN： MUC-6弥漫强阳性。

结果：IOPN的分子病理特征

- ✓ IOPN缺乏IPMN相关的或胰腺导管腺癌相关的基因突变。
- ✓ 在大多数胰腺导管肿瘤中普遍存在KRAS突变，但IOPN不存在。
- ✓ 最近的一项研究，对11例IOPN进行二代测序，发现IOPN在遗传学上的改变不同于胰腺其他类型的肿瘤。

结果： IOPN的预后

- 18例患者获得临床随访数据，随访时间为6-8年。
- 5/18例死于术后并发症或其他原因。
- 存活13/18例病例。
- 1名IOPN伴浸润成分的患者在手术后3-4年复发，并进行胰腺全切，预后良好。
- 浸润性的4例和非浸润性14例，10年总生存率没有差异，5年无复发生存率之间也没有差异。
- IPMN相关浸润性癌以导管腺癌为主，患者预后较差，手术后2年内病死率高。

总结

本文24例IOPN患者，大多数是女性，发生在胰头或钩突部，肿瘤大体呈单房/多房囊性，囊内充乳头状结节。

IOPN具有嗜酸性细胞的独特细胞学特征，嗜酸细胞具有单个大核仁；肿瘤细胞排列成树枝状、乳头状结构；胞浆内可见空泡，局部可融合成筛孔状结构。

与IPMN相比，IOPN的黏蛋白产生减少。

IOPN具有发展成浸润性癌的风险，但大多数是小面积浸润性癌，预后较好。

结论

IOPN具有独特的形态学、临床、分子和行为学特征，应将它归类为一种独特的肿瘤类型。

谢谢！