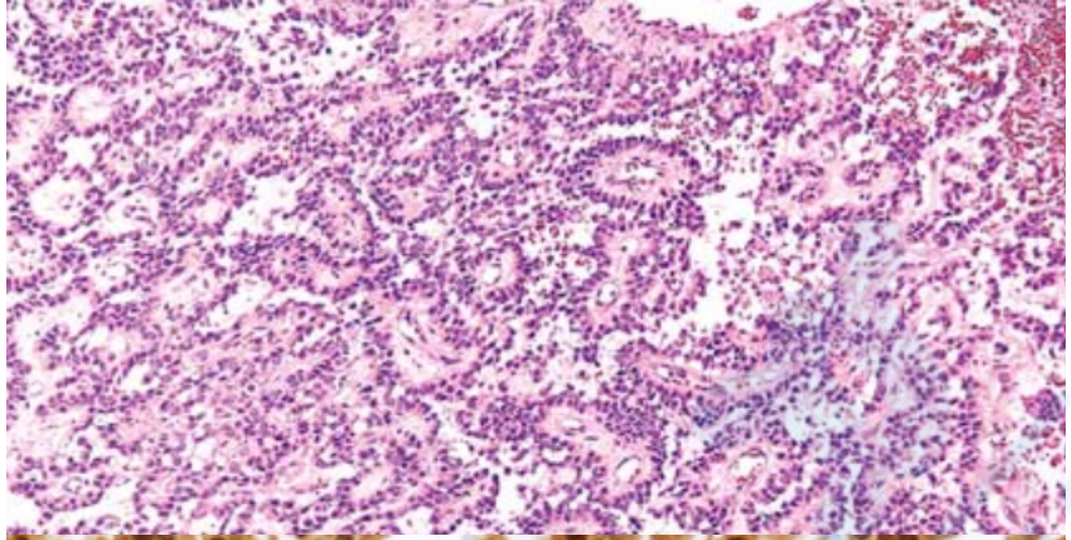
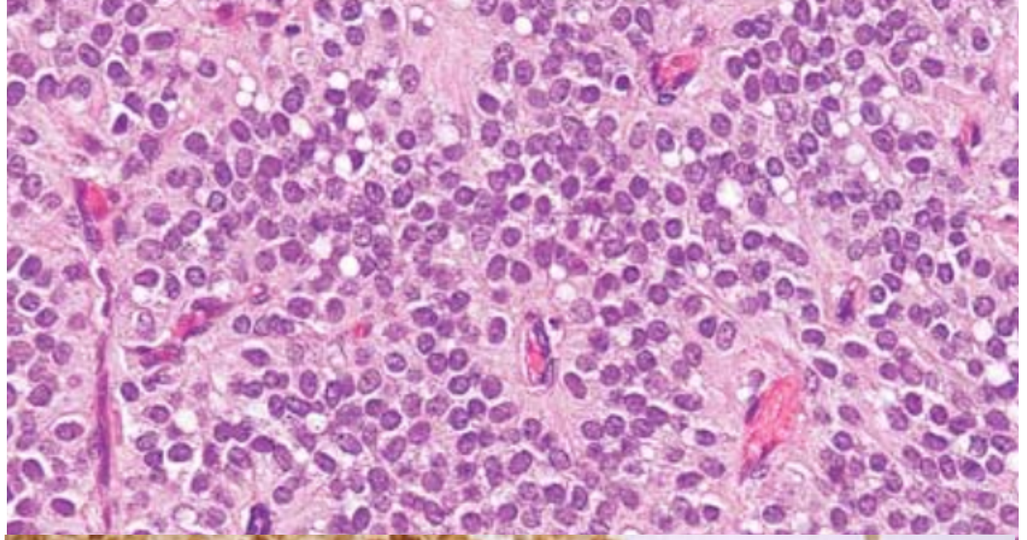
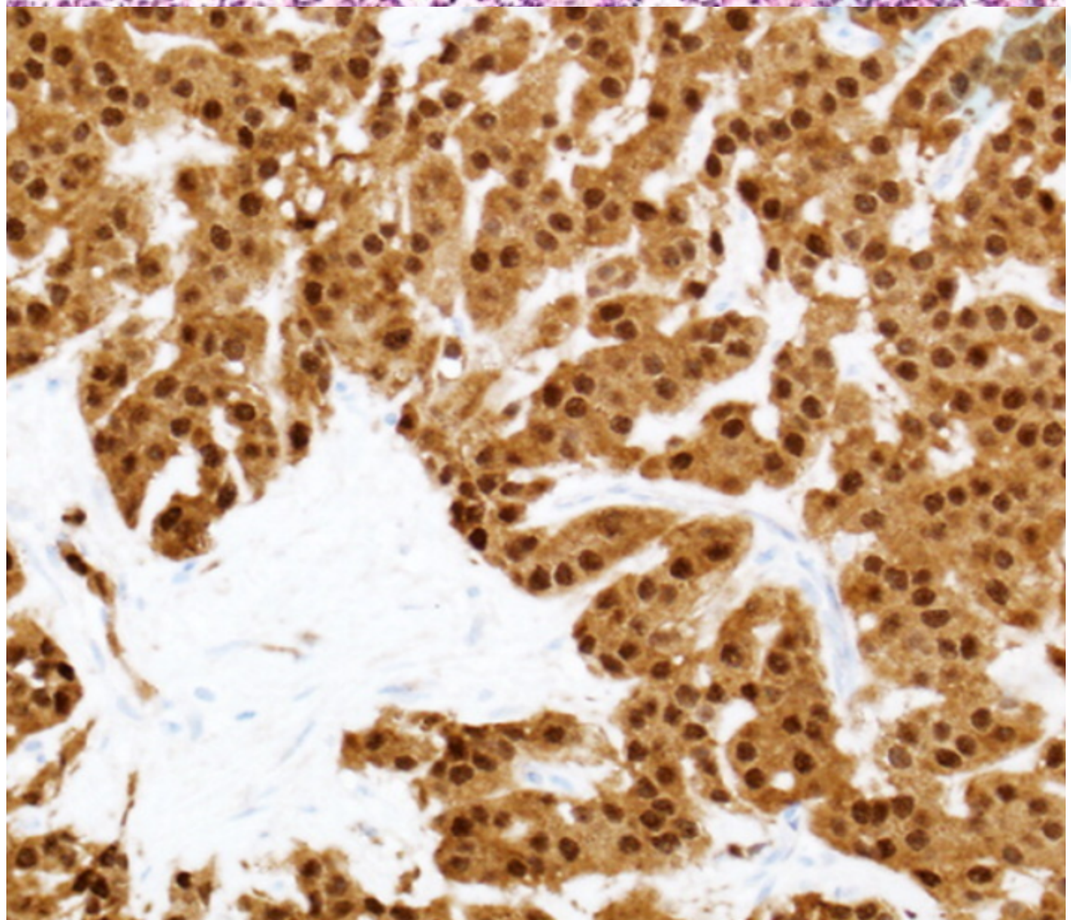
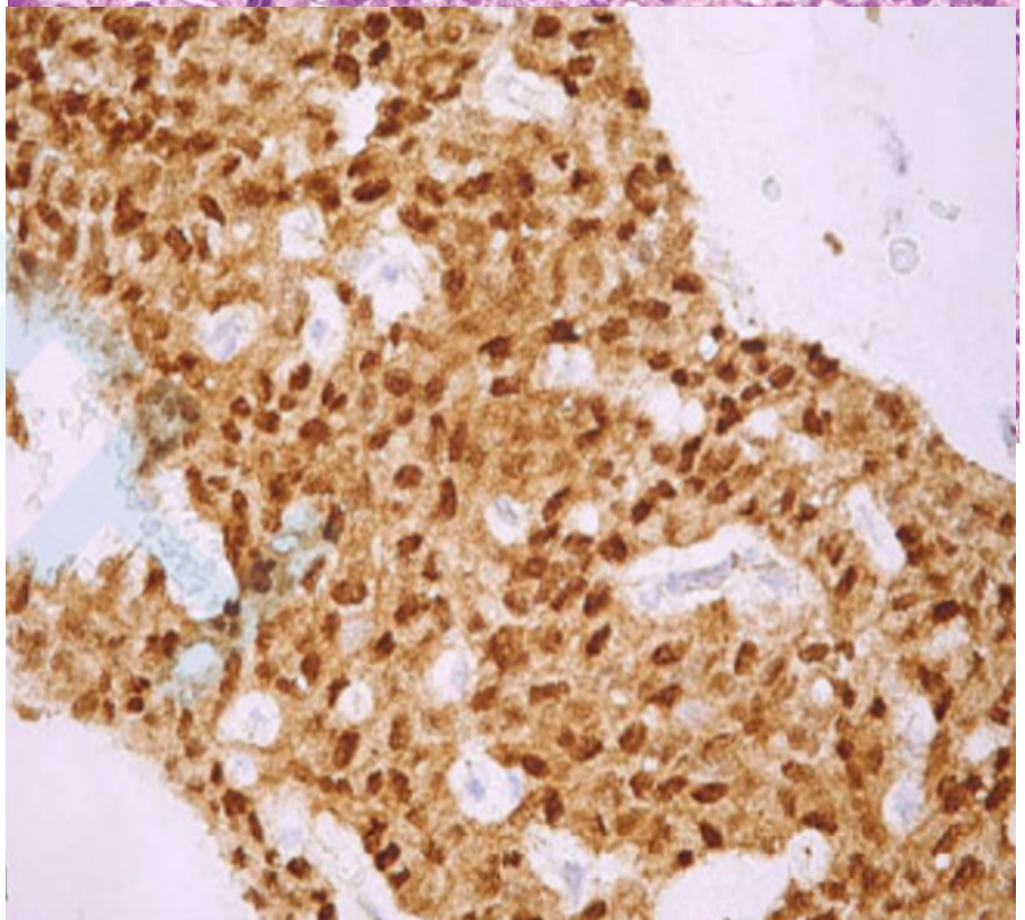








西京医院 XIJING HOSPITAL

PATH 西京病理

A Morphologic and Immunohistochemical Comparison of Nuclear β-Catenin Expressing Testicular Sertoli Cell Tumors and Pancreatic Solid Pseudopapillary Neoplasms Supporting Their Continued Separate Classification

Chia-Sui Kao, MD and Thomas M. Ulbright, MD†*

吴建锋

2020.09.07

Am J Surg Pathol 2020;44:1082–1091

BACKGROUND

BACKGROUND

实性假乳头状肿瘤Solid pseudopapillary neoplasm (SPN)

【定义】

由黏附性差的上皮细胞排列成实性、假乳头结构的胰腺恶性肿瘤

【ICD-O 】

8452/3

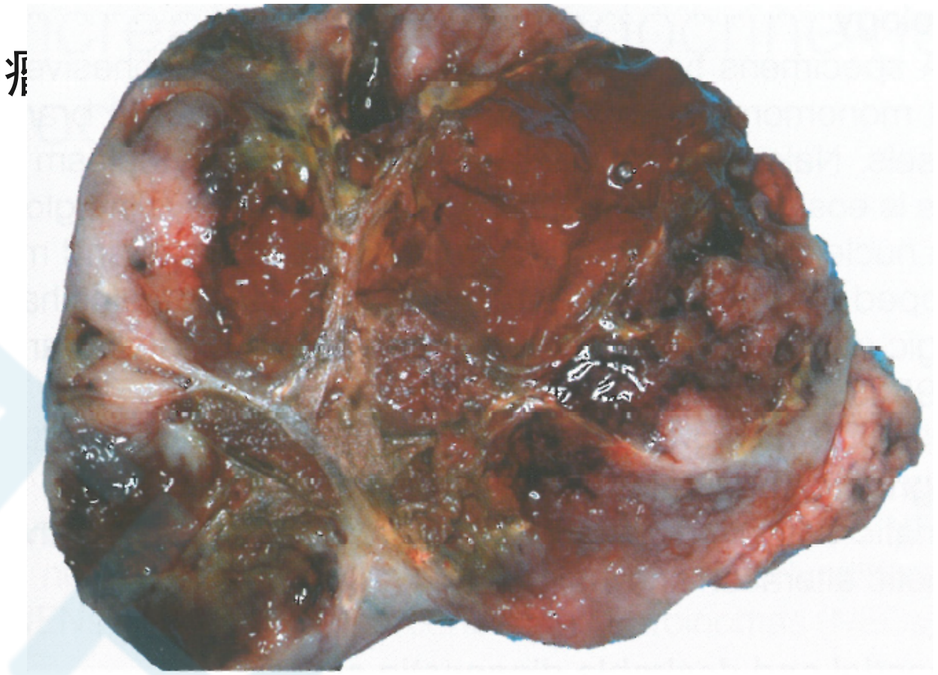
【流行病学】

绝大部分发生于年轻女性，占年轻人（<40岁）胰腺肿瘤40%

【大体特征】

巨大、圆形、实性肿物（平均8-10cm），

多有包膜，界限清楚，可见出血、坏死及充满坏死的囊性区



WHO Classification of Digestive System Tumours 5th Edition, 2019

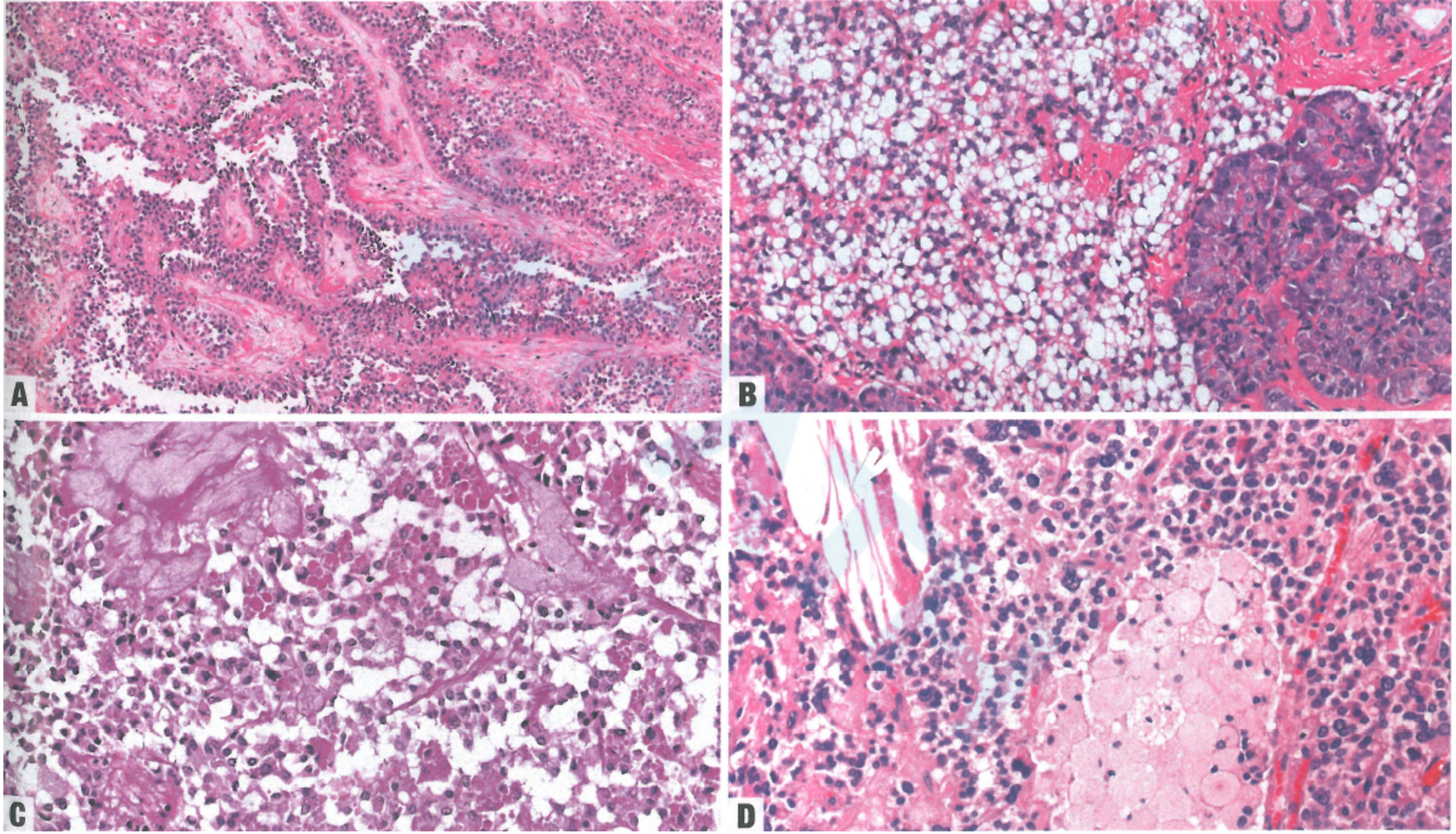
BACKGROUND

实性假乳头状肿瘤Solid pseudopapillary neoplasm (SPN)

组织学：

- 实性、假乳头样排列
- 肿瘤细胞一致，黏附性差，胞浆嗜酸或空泡状
- 间质玻璃样变性、黏液变性
- 纤维包膜多见
- 可见坏死、囊性变

WHO Classification of Digestive System Tumours 5th Edition, 2019



WHO Classification of Digestive System Tumours 5th Edition, 2019

BACKGROUND

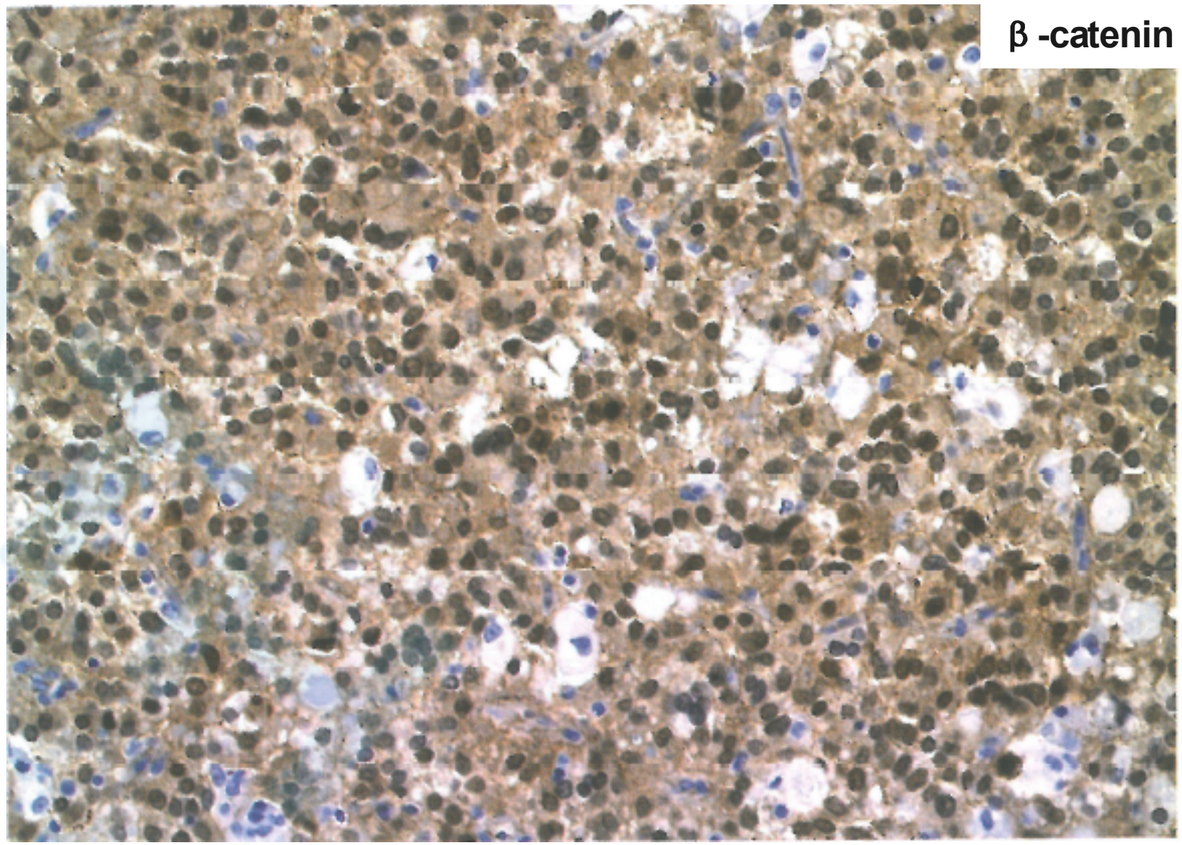
实性假乳头状肿瘤Solid pseudopapillary neoplasm (SPN)

免疫组化：

- β -catenin
- Cyclin D1，Vim，PR，CD10，CD56
- CK，CD117

基因改变：

CTNNB1 exon3突变



WHO Classification of Digestive System Tumours 5th Edition, 2019

BACKGROUND

Sertoli cell tumour, NOS (SCT)

【定义】

由性索细胞组成的肿瘤，常有局灶管状分化

【ICD-O 】

8640/1

【流行病学】

占睾丸肿瘤<1%，第二常见性索-间质肿瘤

【大体特征】

2-5cm，边界清楚，切面灰白色或黄色，实性、质软

少部分可见囊性区，出血、坏死罕见

WHO Classification of Tumours of the Urinary System and Male Genital Organs, 2016

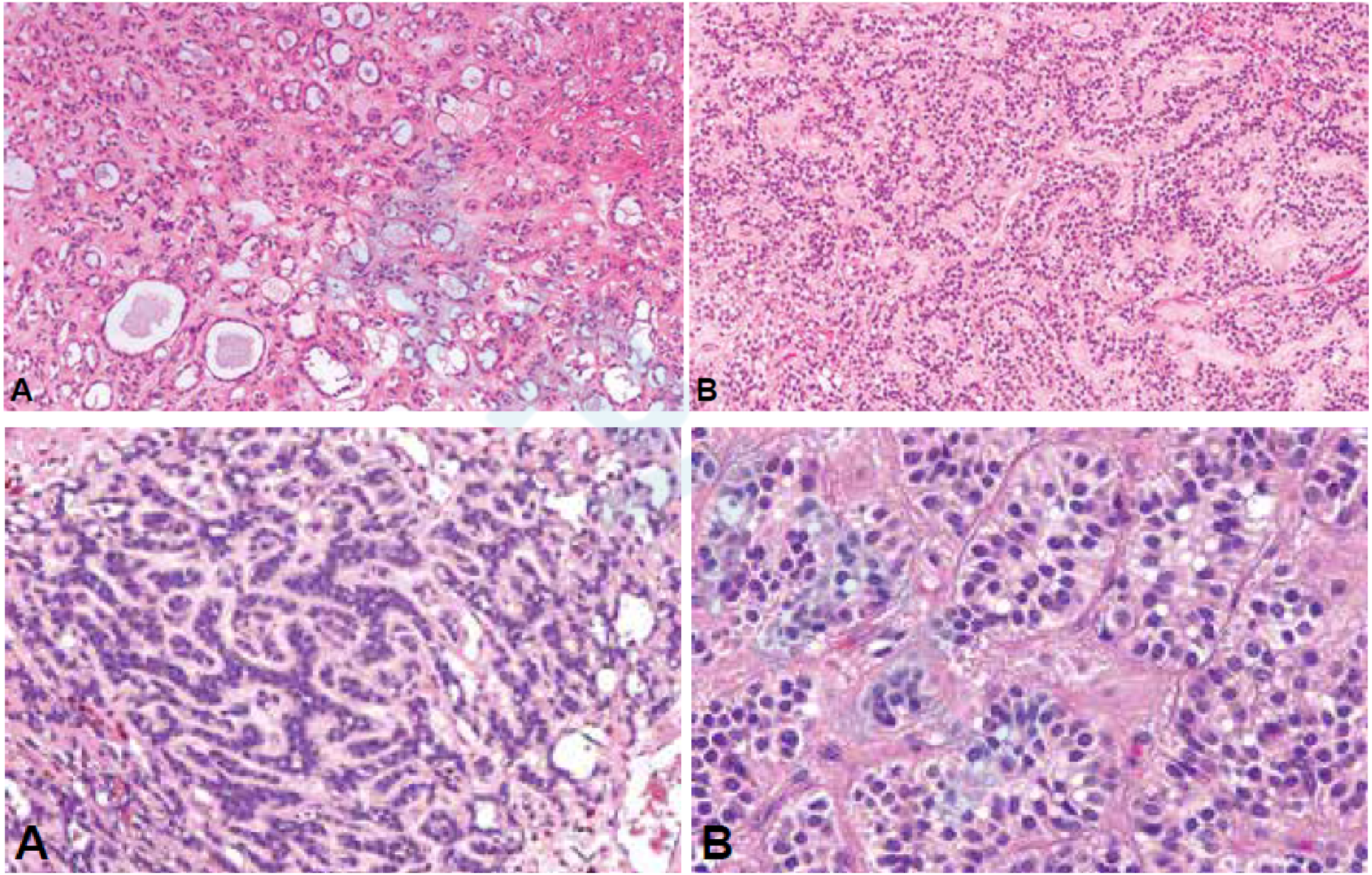
BACKGROUND

Sertoli cell tumour, NOS (SCT)

组织学：

- 结节状生长，细胞排列呈小管状，间质少
- 圆形或中空腺管状，实性或梁索状
- 局部区域可见囊腔形成
- 胞浆中等量，淡染至嗜酸性，胞浆内可见空泡
- 间质淋巴细胞浸润

WHO Classification of Tumours of the Urinary System and Male Genital Organs, 2016



WHO Classification of Tumours of the Urinary System and Male Genital Organs, 2016

BACKGROUND

Sertoli cell tumour, NOS (SCT)

免疫组化：

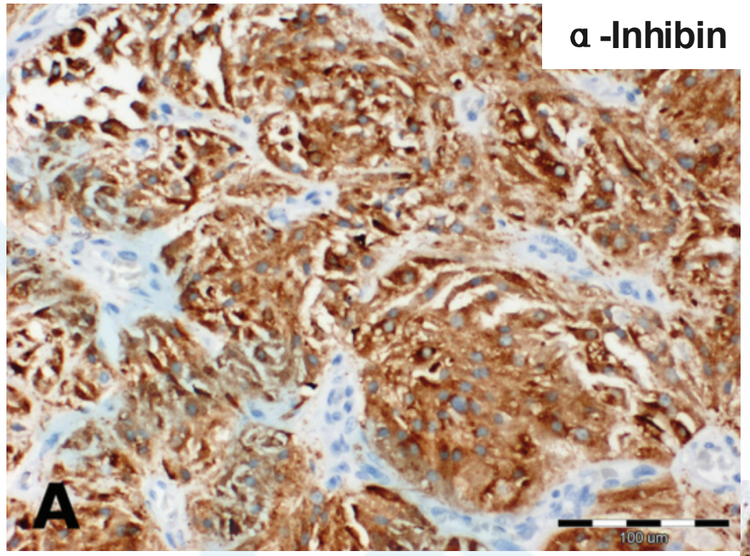
- β -catenin，α -Inhibin
- CR，SF-1，CD99，WT1，SOX9
- AE1/3，Cga，Syn

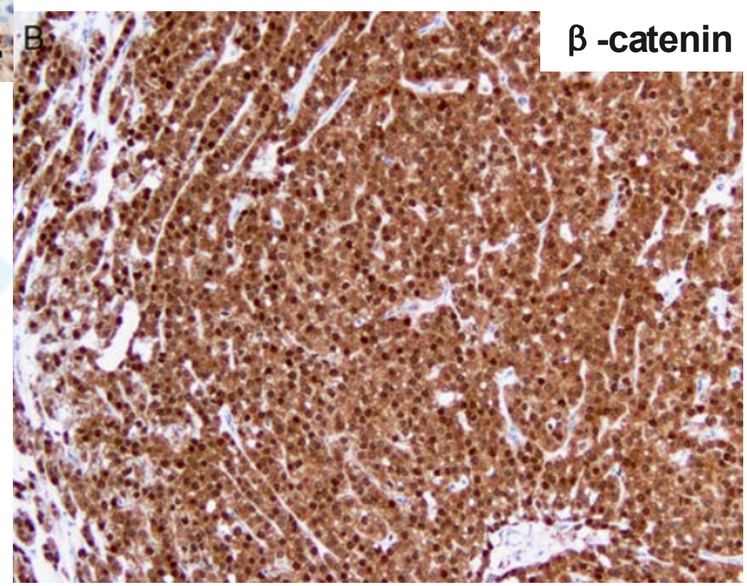
基因改变：

X染色体获得

2/19染色体部分或全部缺失

CTNNB1 exon3突变





WHO Classification of Tumours of the Urinary System and Male Genital Organs, 2016

BACKGROUND

Case study

Pancreatic analogue solid pseudopapillary neoplasm arising in the paratesticular location. The first case report☆,☆☆

Michal Michal MD[a], Stela Bulimbasic MD[b], Marijana Coric MD[b], Monika Sedivcova MSc[c], Dmitry V. Kazakov MD[d], Michael Michal MD[a,*], Ondrej Hes MD[d]

Human Pathology (2016) 56, 52–56

BACKGROUND

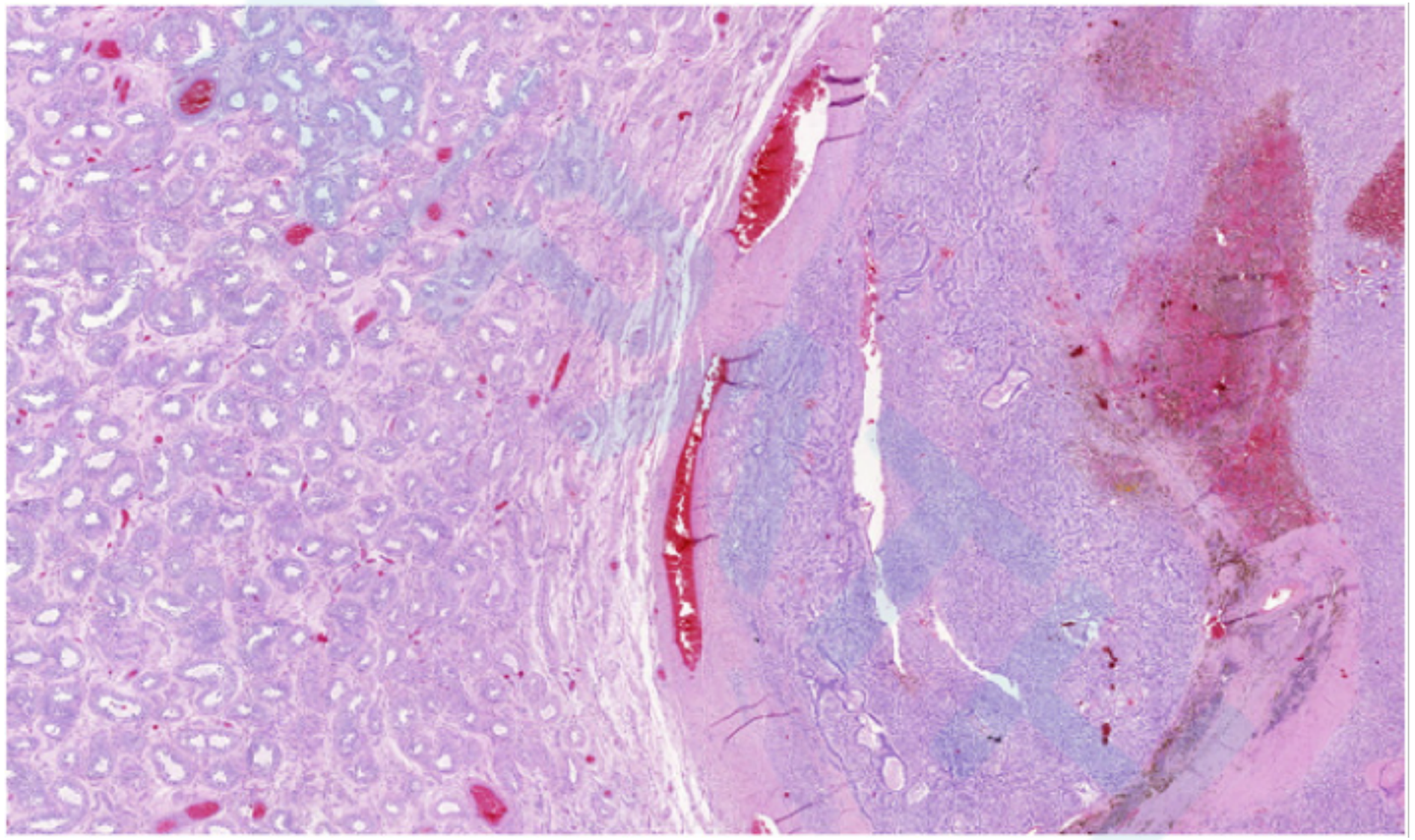


Fig. 1 The tumor was in the paratesticular position. In the septa of the neoplasm, there were deposits of hemosiderin, Gandy-Gamna bodies, and foamy macrophages as remnants of old hemorrhage.

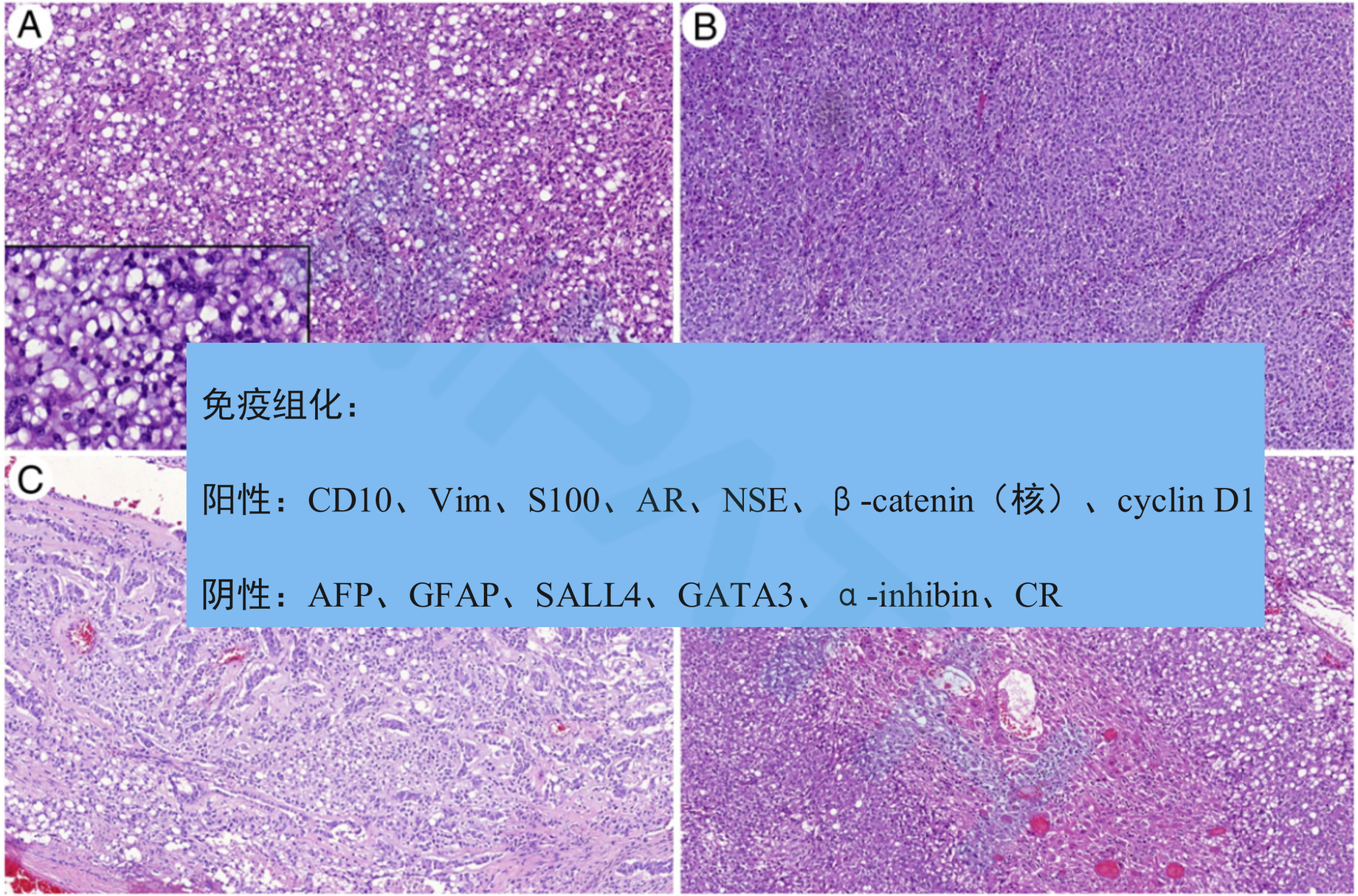


Fig. 2 A, The greatest part of the tumor represented signet ring cell component. This signet ring cell component gradually changed into the solid, non–signet ring cell areas (**B**), or these 2 components were intermixed (**C**). D, Small parts revealed oncocytic change, which was reminiscent of endometrial decidual change.

BACKGROUND

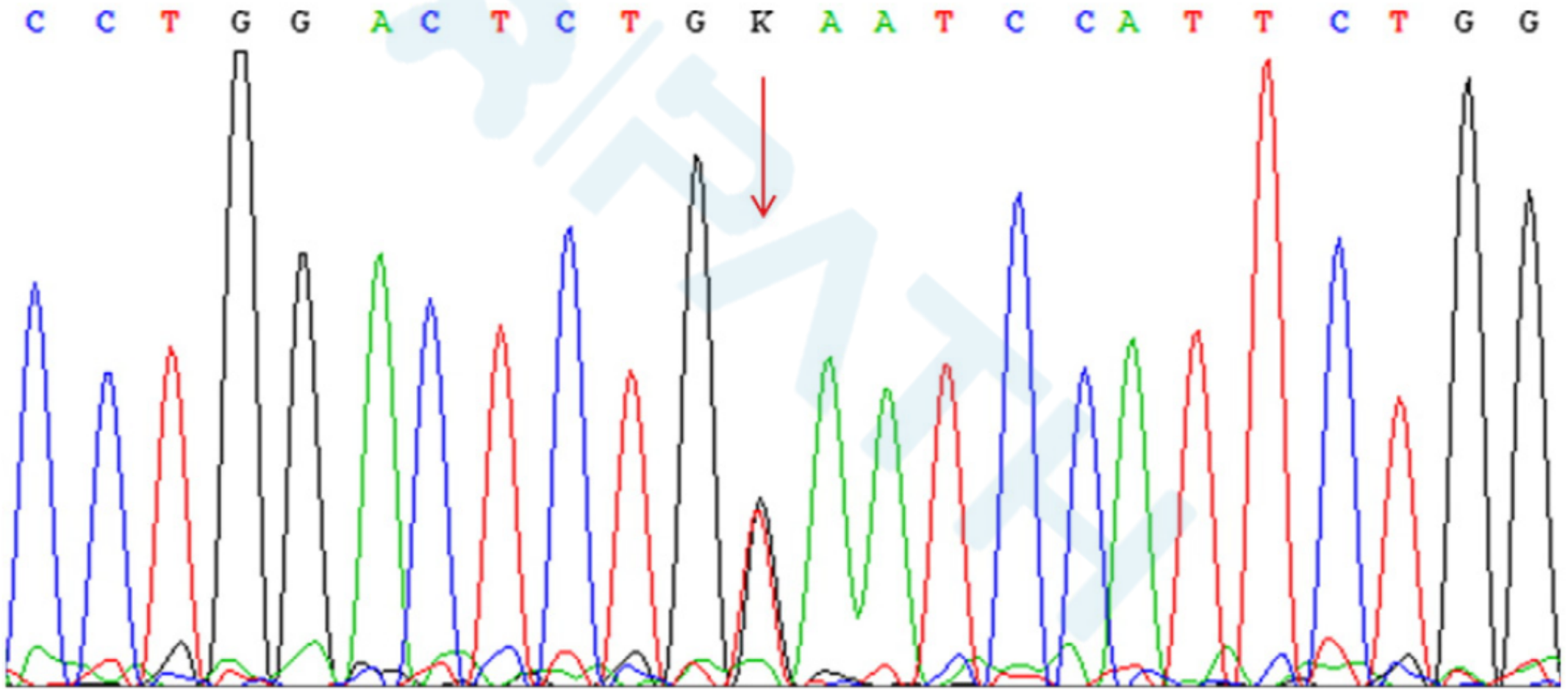


Fig. 4 The arrow shows the mutation c.101G>T/p. Gly34Val in exon 3 of the *CTNNB1* gene.

BACKGROUND

Primary signet ring stromal tumor of the testis: a study of 13 cases indicating their phenotypic and genotypic analogy to pancreatic solid pseudopapillary neoplasm☆,☆☆

Kvetoslava Michalova MD[a,*], Michael Michal Jr MD[a,b], Dmitry V. Kazakov MD[a], Monika Sedivcova MSc[c], Ondrej Hes MD[a], Ladislav Hadravsky MD[d], Abbas Agaimy MD[e], Maria Tretiakova MD[f], Carlos Bacchi MD[g], Arndt Hartmann MD[e], Naoto Kuroda MD[h], Stela Bulimbasic MD[i], Marijana Coric MD[i], Tatjana Antic MD[j], Michal Michal MD[a]

BACKGROUND

Solid pseudopapillary neoplasm (SPN) of the testis: Comprehensive mutational analysis of 6 testicular and 8 pancreatic SPNs

Kvetoslava Michalova[a,*], Michael Michal[a,b], Monika Sedivcova[c], Dmitry V. Kazakov[a], Carlos Bacchi[d], Tatjana Antic[e], Marketa Miesbauerova[a], Ondrej Hes[a], Michal Michal[a]

BACKGROUND

Because many SCTs-NOS share several of the morphologic and immunohistochemical features of pancreatic SPNs, as well as having exon 3 CTNNB1 mutations, the authors of these papers concluded that these 2 classes of neoplasm were the same.

BACKGROUND

研究目的

比较Sertoli细胞瘤（SCTs）与实性假乳头状肿瘤（SPNs）的组织学与免疫表型，进而评估两者是否为同一类肿瘤

MATERIALS AND METHODS

MATERIALS AND METHODS

Case and Slide Selection

A total of 18 cases of SCTs-NOS that showed strong and diffuse expression of nuclear β-catenin from 2002 to 2015 of Indiana University Health Partners were included in the study;

A total of 16 pancreatic SPNs from 2017 to 2019 were identified;

MATERIALS AND METHODS

Immunohistochemical

Nuclear reactivity: SF-1、FOXL2、SOX9、WT1

Cytoplasmic reactivity: α -inhibin

Both nuclear and cytoplasmic reactivity: Calretinin

Immunostains were scored for the extent (no staining =0; <10% =1; 10% to 50% =2; >50% = 3)

intensity of the staining (no staining =0; weak = 1; moderate=2; strong =3)

RESULTS

TABLE 1. Morphologic Features of Testicular SCTs-NOS and Pancreatic SPNs

Histologic Features	n/N (%) SCT-NOS*	SPN	*P* (Raw
Architecture			
Hollow tubules	9/17 (53)	0/16 (0)	**0.001**
Sheets/solid	7/16 (44)	15/16 (94)	0.005
Circumscribed/encapsulated	11/14 (79)	4/16 (25)	0.009
Cords/trabeculae	13/16 (81)	5/16 (31)	0.011
Papillae/pseudopapillae	4/17 (24)	11/16 (69)	0.015
Nests/clusters	15/16 (94)	8/16 (50)	0.016
Perivascular pseudorosettes	2/15 (13)	9/16 (56)	0.023
Cellular morphology			
Rhabdoid morphology	1/16 (6)	8/16 (50)	0.016
Signet-ring cells	7/16 (44)	11/16 (69)	0.285
Significant pleomorphism	1/17 (6)	2/16 (13)	0.601
Spindle cells	2/17 (12)	3/16 (19)	0.656
Pale cytoplasm	9/16 (56)	11/16 (69)	0.716
Foamy cytoplasm	5/16 (31)	5/16 (31)	1.000
Pale nuclei	5/16 (31)	5/16 (31)	1.000
Stromal characteristic			
Fibrosis	14/16 (88)	10/16 (63)	0.220
Perivascular edema/spaces	5/15 (33)	3/16 (19)	0.433
Hemorrhage	7/16 (44)	10/16 (63)	0.480
Myxoid/chondromyxoid stroma	5/16 (31)	5/16 (31)	1.000
Cysts	7/16 (44)	6/16 (38)	1.000
Other tumoral characteristics			
Psammoma bodies	0/17 (0)	3/16 (19)	0.102
Hyaline globules	1/16 (6)	5/16 (31)	0.172
Gamna-Gandy bodies	3/16 (19)	0/16 (0)	0.226
Cholesterol clefts	0/16 (0)	2/16 (13)	0.484
Lymphovascular invasion	1/17 (6)	0/16 (0)	1.000
Necrosis	3/17 (18)	3/16 (19)	1.000
Perivascular hyalinization	8/16 (50)	9/16 (56)	1.000
Globoid basement membrane material	4/16 (25)	4/16 (25)	1.000

	SCT-NOS	SPN
排列结构	✓ 边界清楚，包膜完整 ✓ 梁索状 ✓ 巢状、簇状 ✓ 小管状	✓ 实性、片状 ✓ 乳头/假乳头 ✓ 血管周假菊形团

	SCT-NOS	SPN
细胞形态	✓ 胞浆淡染、空泡状 ✓ 印戒样	✓ 横纹肌样形态 ✓ 胞浆淡染、空泡状 ✓ 印戒样

	SCT-NOS	SPN
间质特征	✓ 硬化，血管玻变 ✓ 出血、囊性变 ✓ 黏液样/软骨样间质	✓ 硬化，血管玻变 ✓ 出血、囊性变 ✓ 黏液样/软骨样间质

	SCT-NOS	SPN
其他特征	✓ Gamna-Gandy小体 ✓ 肿瘤坏死 ✓ 血管周水肿、基底膜样物质	✓ 玻璃样小球、砂粒体 ✓ 坏死、胆固醇裂隙 ✓ 基底膜样物质

RESULTS

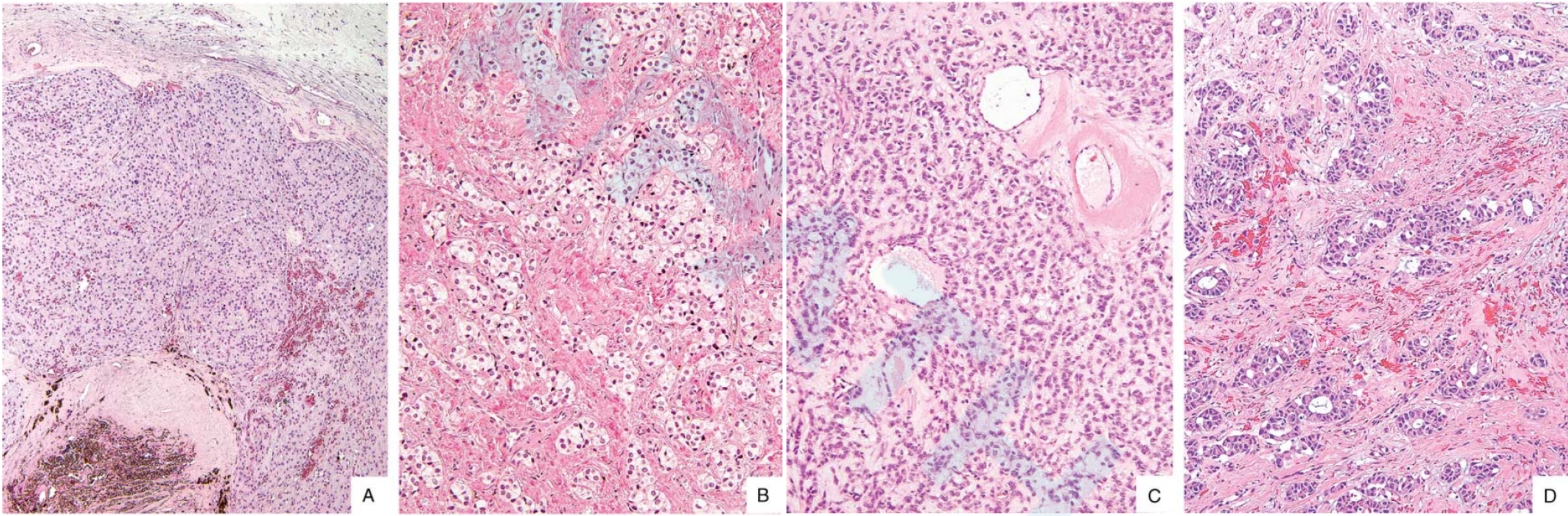


FIGURE 2. Features of SCT-NOS. A, A circumscribed and encapsulated tumor with sheets of cells with pale cytoplasm and a Gamna-Gandy body (bottom-left). B, Small nests and clusters of pale cells in a dense stroma. C, Cords of tumor cells in a myxoid stroma with perivascular hyaline change. D, Several hollow tubules and foci of fibrosis.

RESULTS

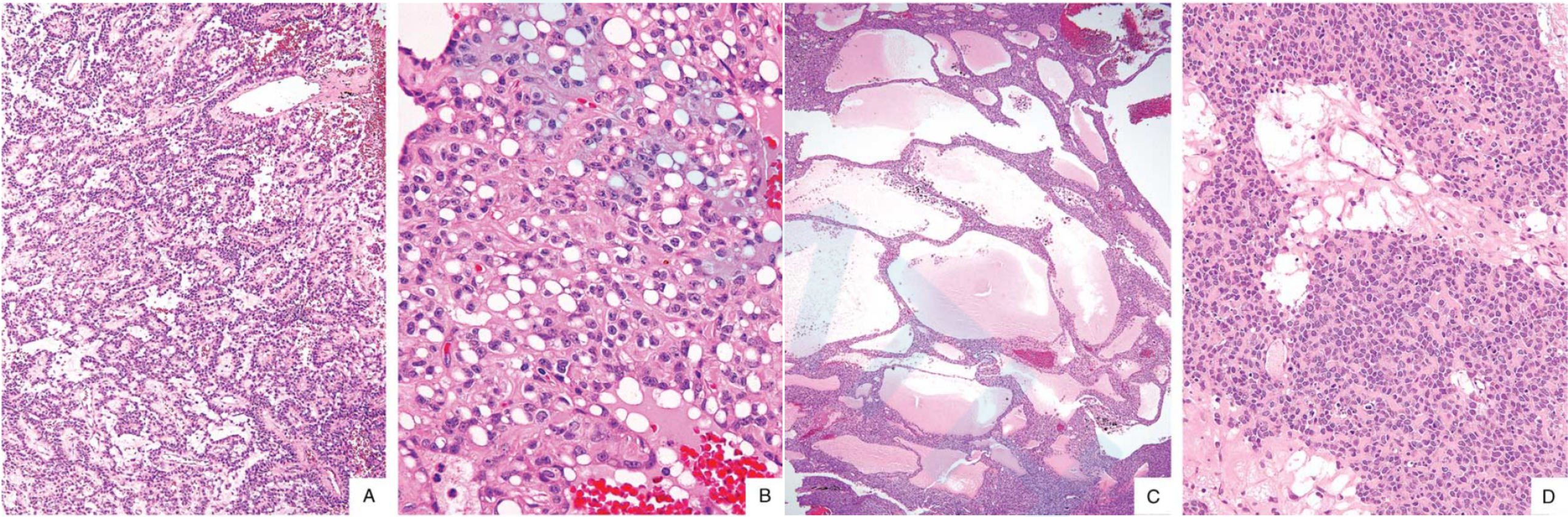


FIGURE 3. Features of SCT-NOS. A, Papillary growth results in structures resembling the Schiller-Duval bodies of yolk sac tumor. B, Large cytoplasmic vacuoles create a signet-ring appearance. C, Prominent cysts with edema fluid. D, Perivascular edema and bands of intercellular basement membrane-like material.

RESULTS

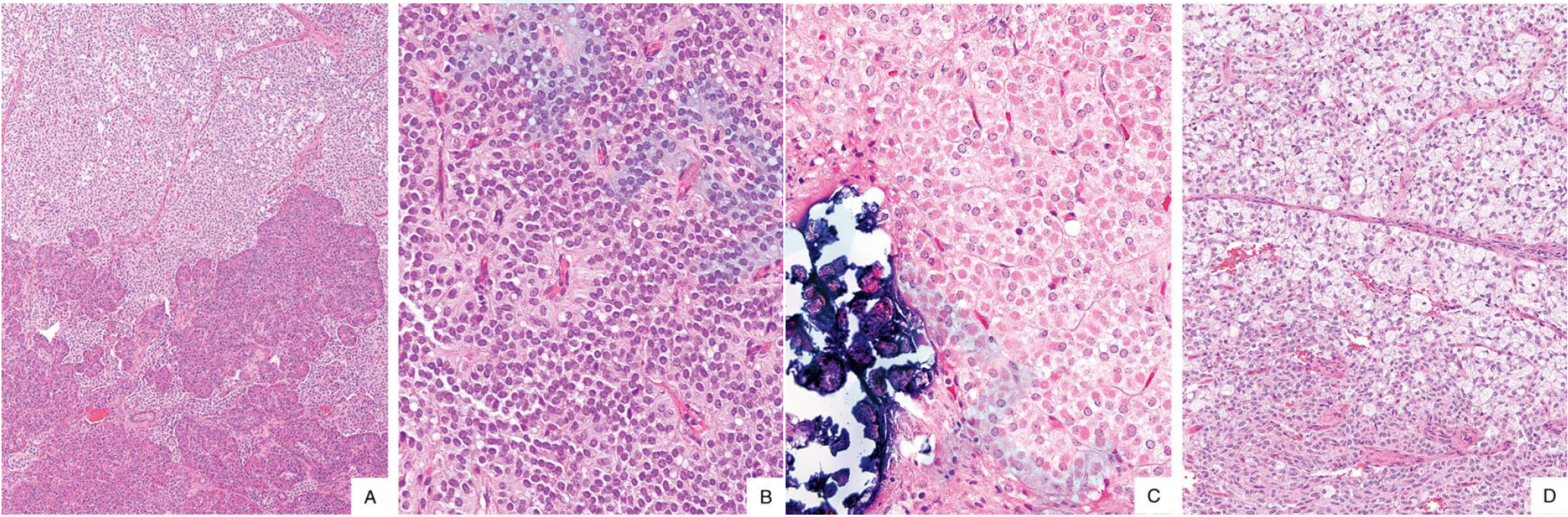


FIGURE 4. Features of SPN of the pancreas. A, Infiltrative growth of a solid pattern tumor into the pancreatic parenchyma (bottom). B, Perivascular pseudorosettes. C, Rhabdoid cytology and an aggregate of psammomatous calcifications. D, A large focus of foamy tumor cells.

RESULTS

TABLE 2. IHC Staining Results of SCTs-NOS and Pancreatic SPNs

Tumor Type	SF-1 (%; Mean IHC Score)	FOXL2 (%; Mean IHC Score)	SOX9 (%; Mean IHC Score)	Calretinin* (%; Mean IHC Score)	WT1* (%; Mean IHC Score)	Inhibin* (%; Mean IHC Score)
SCT-NOS	15/16 (94; 4.3)	13/15 (87; 3.9)	11/16 (69; 2.6)	9/15 (60; 1.3)	5/13 (38; 1.2)	5/17 (29; 1.0)
SPN	0/16 (0; 0)	0/16 (0; 0)	0/16 (0; 0)	0/16 (0; 0)	0/16 (0; 0)	0/16 (0; 0)
P (raw)	**5.6×10^{-8}**	**5.1×10^{-7}**	**6.7×10^{-5}**	**0.00025**	0.01084	0.0448

*Some cases that had positive results reported but no longer had immunostains available for review were included in the calculations of the percent of positive cases but were excluded from the determination of the IHC score.

Bolded *P*-values are statistically significant.

IHC indicates immunohistochemical.

RESULTS

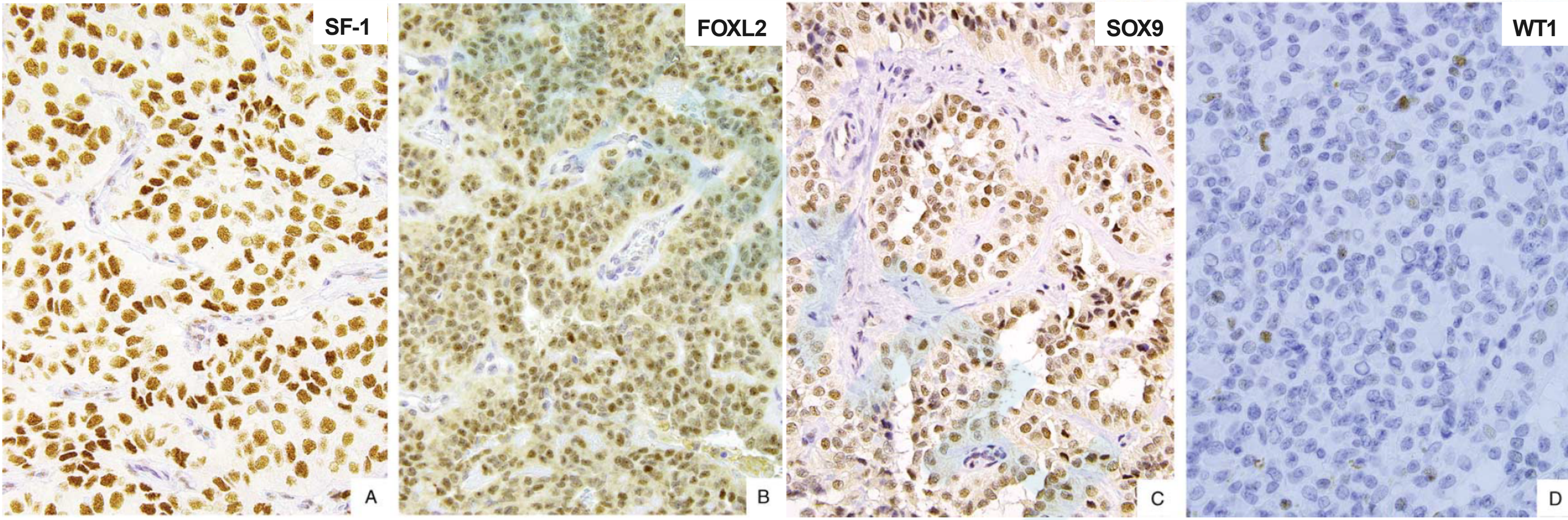


FIGURE 5. Immunohistochemical staining of SCT-NOS. A, Strong nuclear reactivity for SF-1. B, Nuclear and cytoplasmic reactivity for FOXL2. C, Nuclear reactivity for SOX9. D, Infrequent nuclear reactivity for WT1.

DISCUSSION

DISCUSSION

1) The recently reports of tumors in the male genital region with morphologic and genetic similarities to the SPNs concluded that these rare tumors are the testicular analog of pancreatic SPN rather than testicular SCT.

2) This study demonstrates that although testicular SCTs-NOS show morphologic overlap with pancreatic SPNs, their frequent tubular differentiation and immunoreactivity with different sex cord– stromal tumor markers are strikingly different from the findings in SPNs.

DISCUSSION

SF-1

1)The single most sensitive marker was SF-1, which showed nuclear reactivity in 15/16 SCTs-NOS (94%) and none of 16 SPNs.

2)In a comprehensive study of 219 adrenal neoplasms and non-neoplastic adrenal specimens, 98% were SF-1 positive and all 73 nonsteroidogenic neoplasms were negative.

3)Zhao et al found that all of 127 cases of ovarian sex cord–stromal tumor expressed SF-1.

4)The high frequency of SF-1 reactivity in our series thus provides very strong support for the sex cord differentiation of this neoplasm, and, conversely, the absence of SF-1 reactivity in the SPNs weighs heavily against its sex cord nature.

DISCUSSION

FOXL2

FOXL2 protein is the product of the *FOXL2* gene and is essential for normal ovarian development and the later differentiation of granulosa cells.

Its expression has been reported in 95/119 (80%) ovarian sex cord–stromal tumors, It is also expressed in the sex cord cells of gonadoblastomas, the lesional cells of juvenile granulosa cell tumor of the testis, a subset of pituitary adenomas, and in steroid cell tumors. No expression was found in a variety of 371 other ovarian neoplasms, including metastatic carcinomas.

The frequent FOXL2 expression in our cohort of SCTs-NOS of the testis strongly supports their sex cord–stromal nature.

DISCUSSION

SOX9

SOX9 expression by Sertoli cell precursors is an essential part of testicular development. Both immature and mature Sertoli cells show strong nuclear SOX9 expression. SOX9 nuclear expression was found in 6 of 11 juvenile granulosa cell tumors of the testis.

SOX9 expression may be seen in a variety of tumors, including chondrosarcoma, osteosarcoma, synovial sarcoma, Ewing sarcoma, gastric adenocarcinoma, pancreatic carcinoma, and colorectal adenocarcinoma.

Nonetheless, its restricted expression in our study to the SCTs-NOS and absence in the SPNs adds additional evidence to the dissimilarity of these 2 classes of neoplasm.

DISCUSSION

Calretinin and α-inhibin

We found the 2 traditional sex cord–stromal tumor markers, calretinin and inhibin, to be, in general, less sensitive for the recognition of SCTs-NOS than the others we studied.

Previously published series of SCTs found inhibin positivity that varied from 25% to 90%, while a recent study showed calretinin reactivity in 43%. Our study showed analogous results, with inhibin and calretinin reactivity in 29% and 60%, respectively.

Therefore, negative staining for either or both of these markers by no means excludes a diagnosis of SCT-NOS. In that circumstance, additional markers, preferably including SF-1 and β-catenin, should be used.

DISCUSSION

CTNNB1 (β -catenin)

This same mutation pattern, however, is found in a variety of diverse neoplasms, including desmoid-type fibromatosis, pilomatrixoma, basal cell adenoma of the salivary gland, hepatocellular adenoma, hepatocellular carcinoma, and hepatoblastoma, colorectal adenocarcinoma with high-frequency microsatellite instability, endometrioid adenocarcinoma, and others.

Therefore, the presence of *CTNNB1* exon 3 gene mutations are not specific and should not be considered a criterion for tumor classification without regard to morphologic and immunohistochemical features.

CONCLUSION

In summary, we have made an in-depth comparison of the morphologic and immunohistochemical features of nuclear β-catenin expressing testicular SCTs-NOS and pancreatic SPNs and found significant differences on both fronts. Our results make a strong argument for the continued separate classification of testicular SCTs-NOS, and we do not endorse the notion of a testicular analog of the pancreatic SPN at this time.

PATH

THANK YOU

感谢聆听