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Adenocarcinoma of the Rete Testis

Clinicopathologic and Immunohistochemical Characterization of 6 Cases and Review of the Literature

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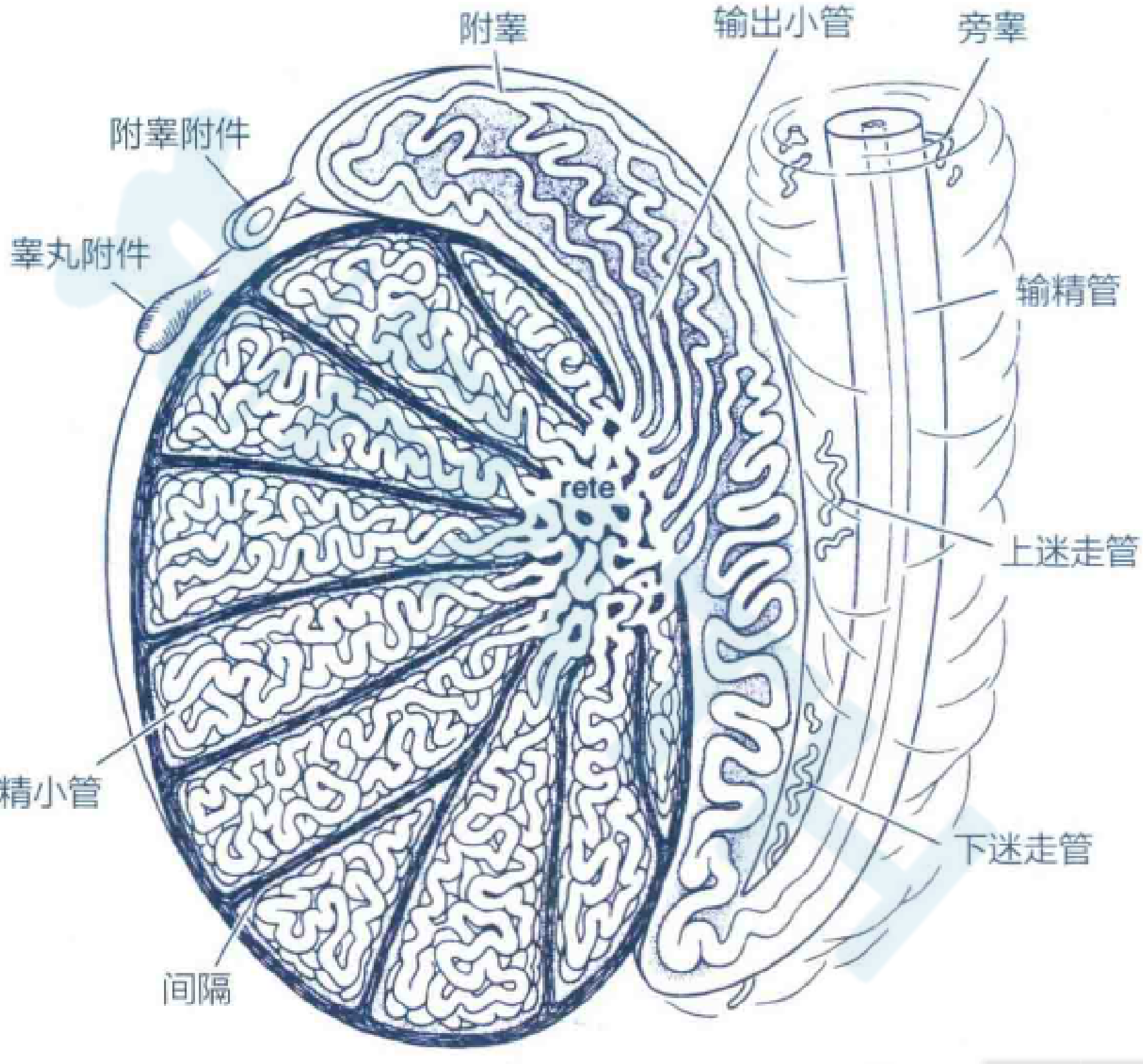
附睾
输出小管
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间隔

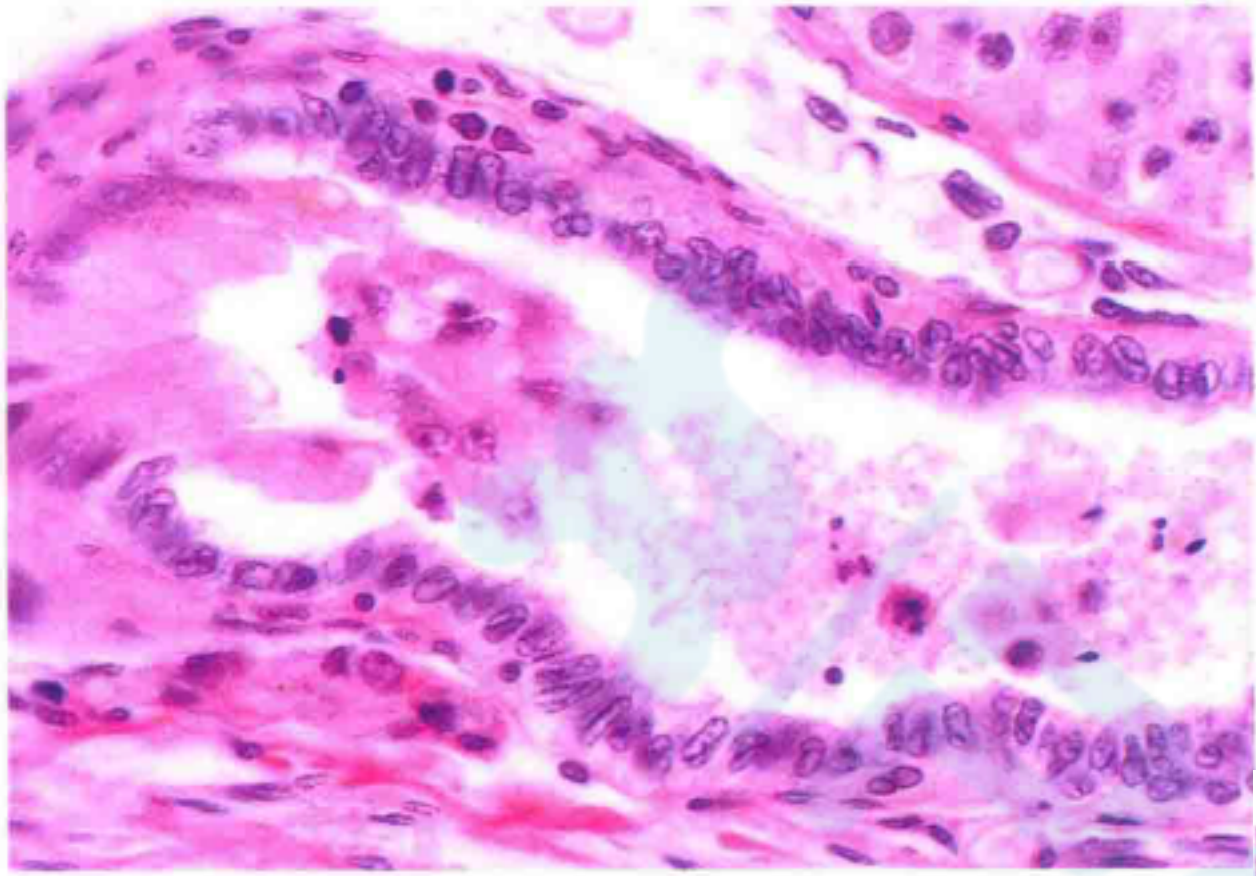


图 37.18　睾丸网间隔部与生精小管末端的连接处。注意 Sertoli 细胞“凸”进睾丸网的管腔。睾丸网上皮为矮柱状

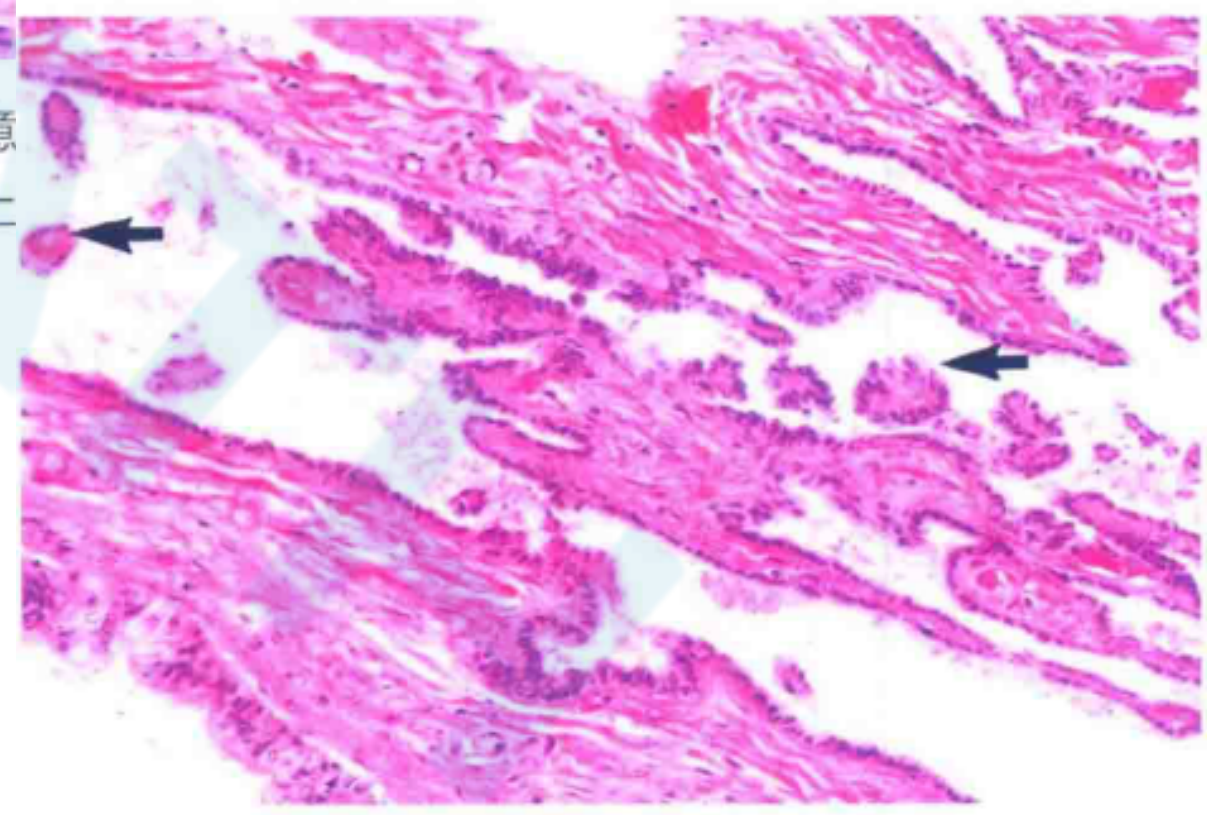


图 37.19　睾丸网，纵隔部分，可见不规则海绵样管道和管腔内网索（箭头）的横切面

MATERIALS AND METHODS

- **Six cases of adenocarcinoma of the rete testis.**
- **Immunohistochemical**

CK7、CK20、AE1/AE3、EMA、S100、calretinin、WT-1、CK5/6、MOC31、BerEP4、PAX8、OCT3/4、SALL4、CD30、NKX3.1、PSA

RESULTS

Clinical Features

TABLE 1. Clinicopathologic Characteristics of Rete Adenocarcinoma Cases

Case No.	Age (y)	Laterality	Race	Past History	Procedure	Tumor Size (cm)	RPLN Metastasis	Distant Metastasis	Time to Metastasis (months)	RPLND	Adjuvant Chemotherapy	Follow-up Period (m)	Outcome
1	74	Right	White	No significant history	Orchiectomy	—	No	Yes	At diagnosis	No	Yes	12	Died of disease
2	61	Right	White	No significant history	Orchiectomy	3.3	Yes	No	At diagnosis	Yes	Yes	8	Alive
3	55	Left	White	No significant history	Orchiectomy	2	Yes	No	At diagnosis	Yes	Unknown	3	Alive
4	56	Right	White	right hydrocelectomy	Orchiectomy	—	Yes	No	At diagnosis	Yes	No	3	Died of disease
5	63	Left	NA	No significant history	Orchiectomy	9	Yes	No	At diagnosis	NA	Yes	NA	NA
6	76	Right	White	Right hydrocelectomy	Orchiectomy	—	Yes	Yes	15	Yes	No	40	Died of disease

NA indicates not available.

- The mean age at diagnosis was **64 years** (range: 55 to 76 y);
- **4 patients** had retroperitoneal lymph node metastasis and 1 additional patient had both retroperitoneal lymph node and pulmonary metastases;
- **Three patients died** within 40months of diagnosis (range: 3 to 40 m）

Pathologic and Immunohistochemical Features

TABLE 2. Histomorphologic Characteristics of Rete Adenocarcinoma Cases

Case No.	Glandular	Papillary	Solid	Corded/ Trabecular	Glomeruloid	Nested	Micropapillary	Cribriform	Pale Eosinophilic Cytoplasm	Clear Cytoplasm	Geographic Necrosis
1	+	+++	+	−	−	−	−	−	++	+++	Focal
2	+++	+	+	−	+	−	−	+	+++	+	Extensive
3	+	+	+++	+	−	+	−	+	+++	++	Absent
4	+++	+	+	+	+	−	+	+	+++	+	Absent
5	+	+	+++	−	−	−	−	−	+++	+	Extensive
6	++	+	+++	+	+	+	+	−	++	+++	Absent

+ (< 25%), ++ (25% to 50%), +++ (> 50%).

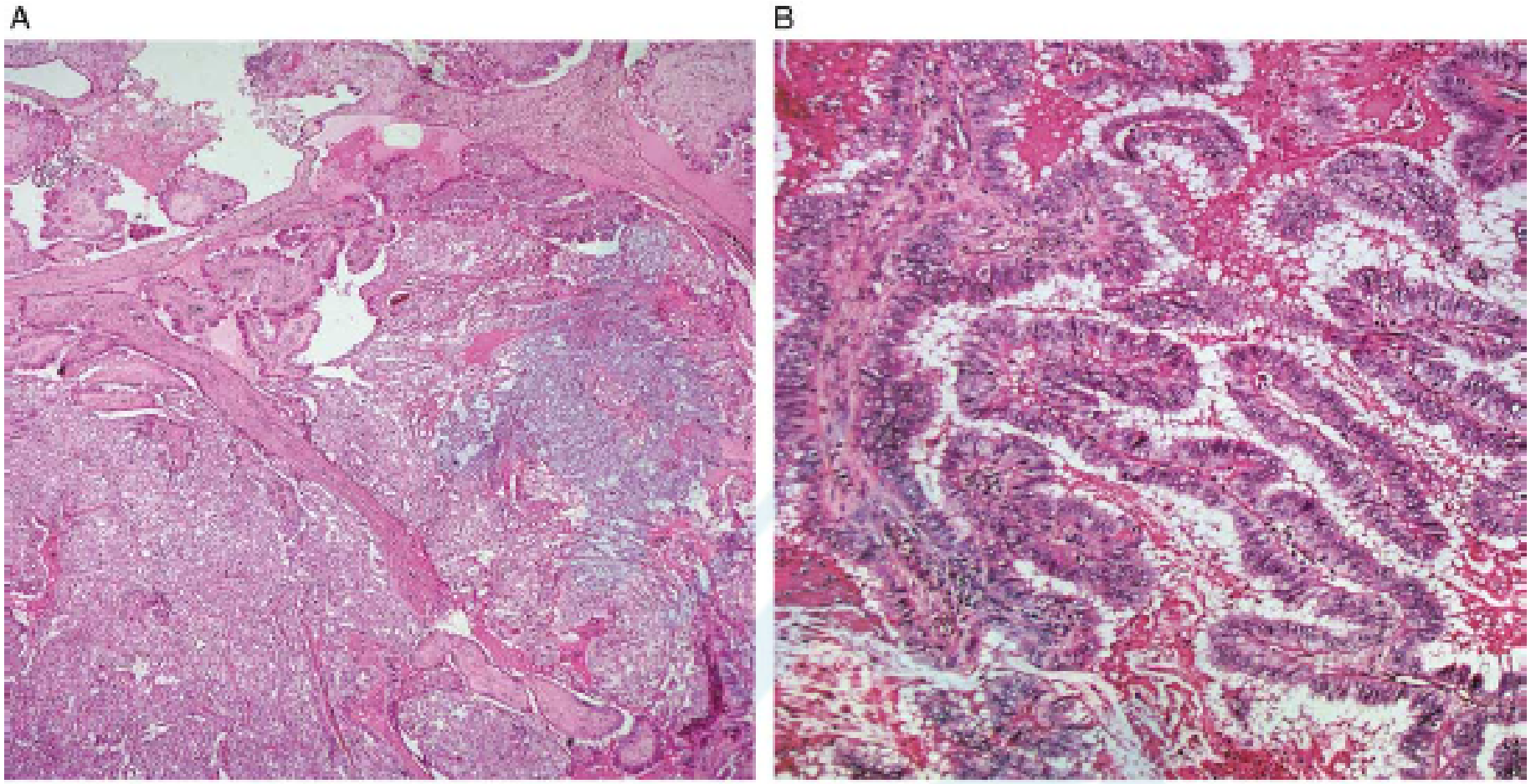


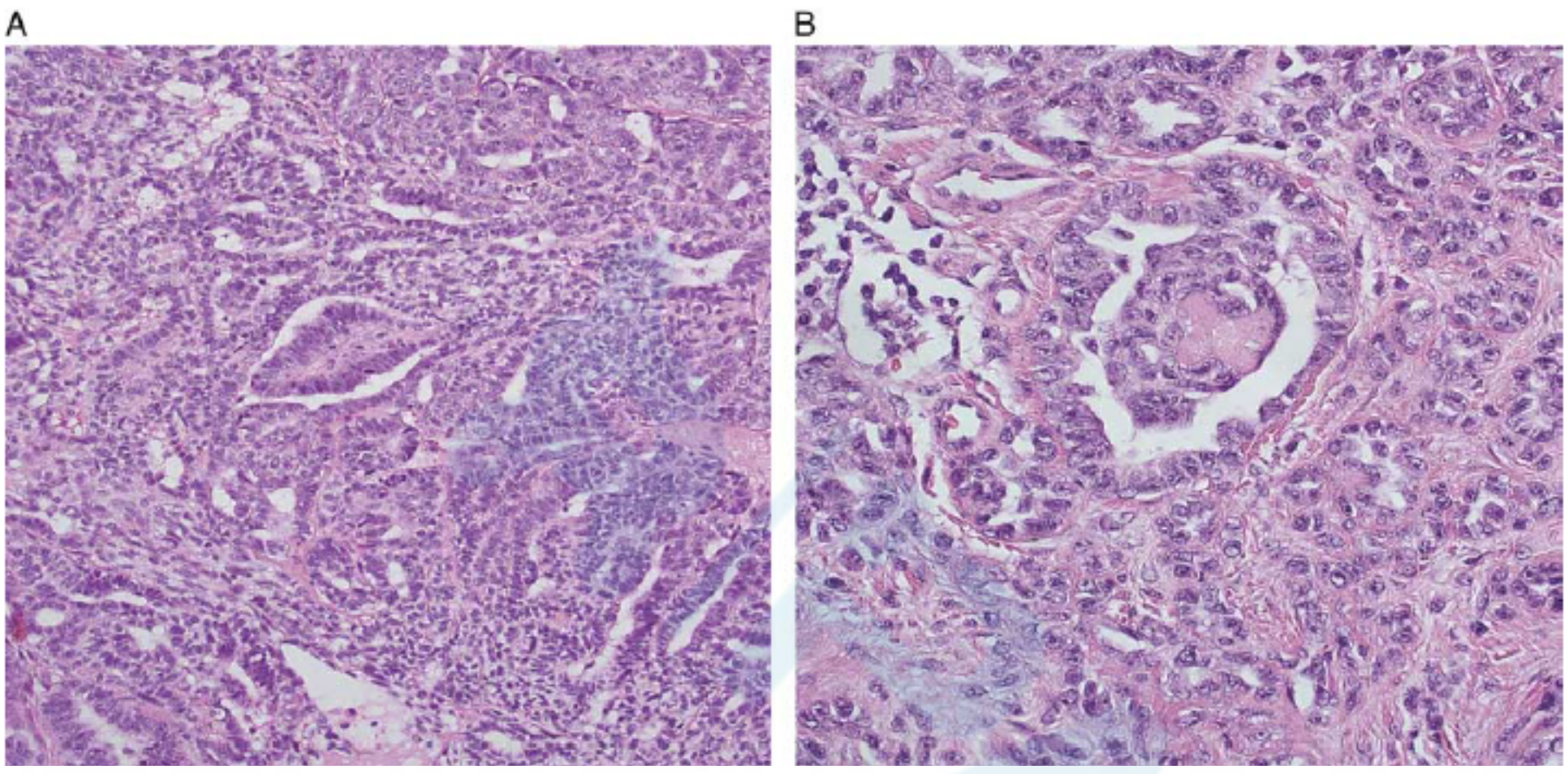
FIGURE 1.

A, **Papillary and solid pattern** in an adenocarcinoma of the rete testis with extensive intrarete growth.

B, High power showing columnar tumor cells on delicate fibrovascular cores.

C, **Nests of clear cells** are interspersed with branching, tubular glands.

D, **Transition** between eosinophilic and clear tumor cells. Some of the latter have spindled profiles.



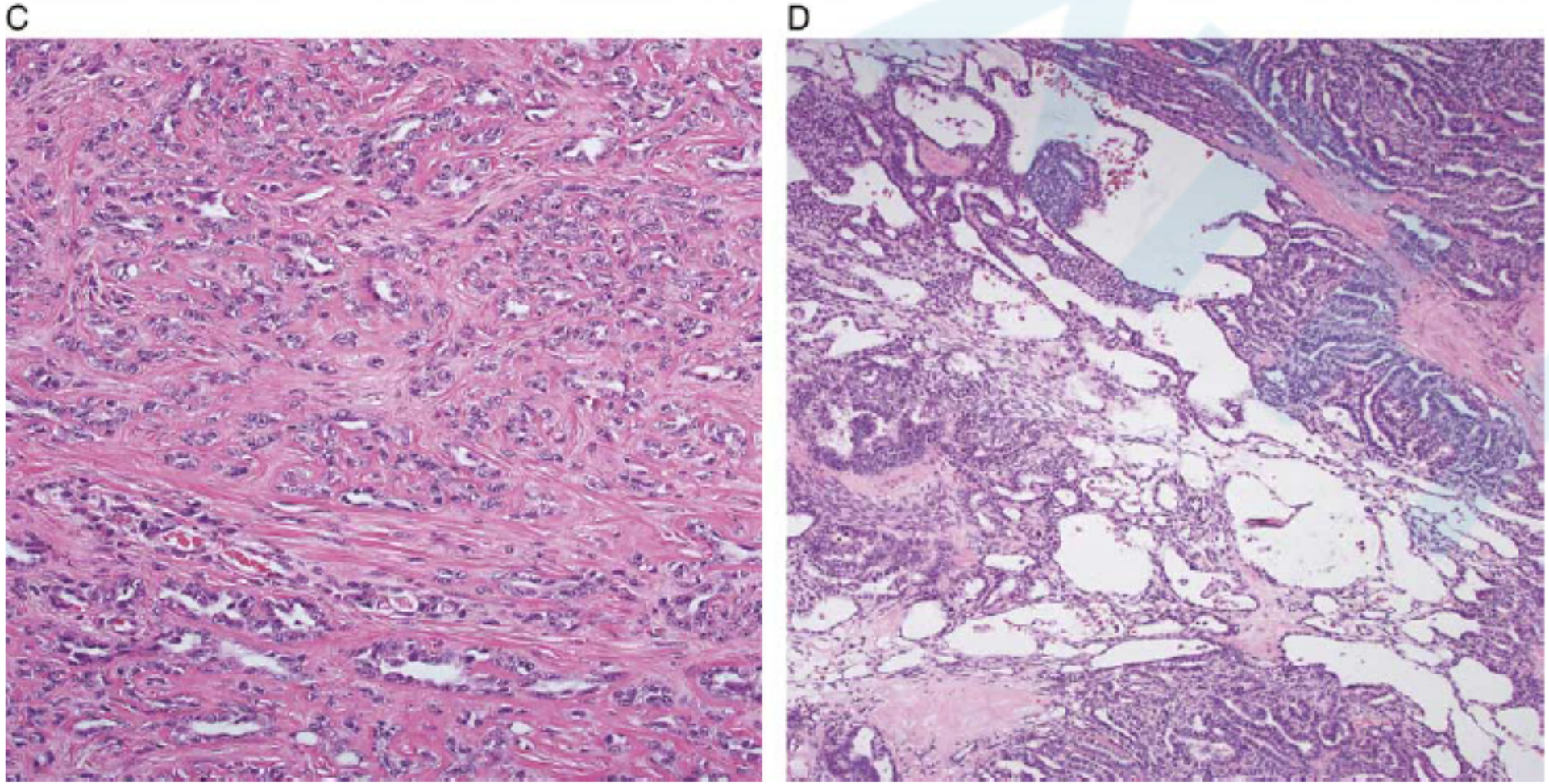


FIGURE 2.

A, A **papilla** projects into a small space with surrounding glands.

B, A **glomeruloid** appearance caused by an intraglandular papilla with globular hyalinized material.

C, **Cords and slit-like** glands in a dense, partially hyalinized stroma.

D, Rete adenocarcinoma with branching glands, occasional **papillae** and **microcystic and macrocystic** change.

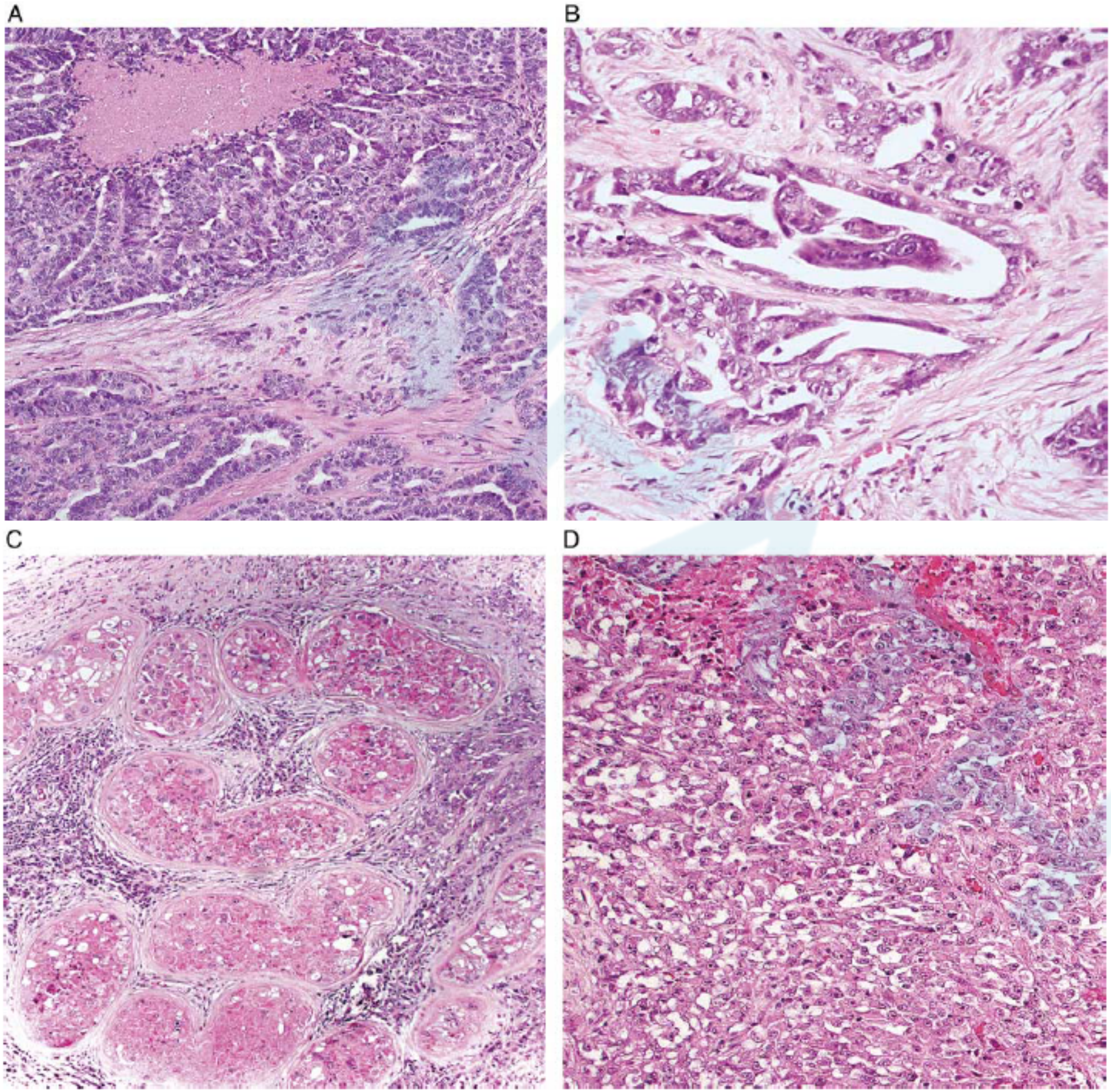


FIGURE 3.

A, A **cribriform** pattern with central necrosis.

B, **Micropapillary** pattern in a desmoplastic stroma.

C, Extension into and between the seminiferous tubules, with intratubular comdeo-type necrosis, **mimicking** a common appearance of embryonal carcinoma.

D, Sheets of highly pleomorphic cells with **necrosis** (top).

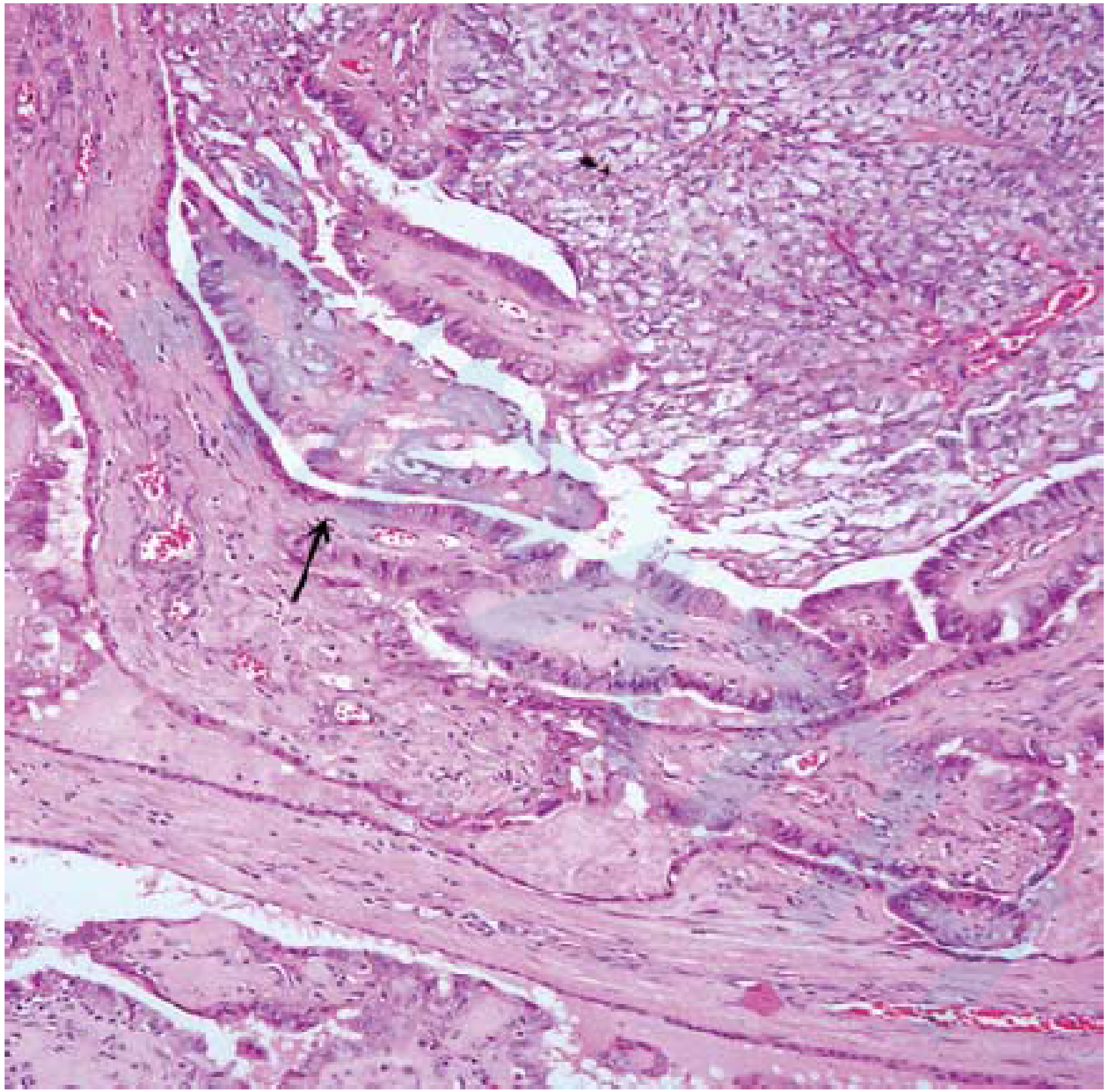


FIGURE 4. Transition (arrow) from benign rete testis epithelium to malignant epithelium within the rete tubules.

TABLE 3. Immunohistochemical Characteristics of Adenocarcinoma of the Rete Testis Cases (n = 5)

IHC Stains	Negative	Focal (5%-25%); Intensity	Intermediate (25%-75%); Intensity	Diffuse (>75%); Intensity	Percent of Positive Cases (%)
AE1/AE3 Ab	0	0	0	5; 3+	100
CK7	0	0	2; 3+	3; 3+	100
EMA	0	1; 3+	2; 3+	2; 3+	100
Vimentin	0	0	2; 3+	3; 3+	100
WT-1	0	1; 1+	0	3; 2+/3+	80
CK5/6	1	1; 3+	1; 3+	2; 3+	80
BerEP4 Ab	1	1; 2+	2; 3+	1; 3+	80
MOC-31 Ab (n = 4)	1	0	1; 3+	2; 3+	80
PAX8	0	0	2; 2+/3+	1; 2+	60
Calretinin	0	0	1; 3+	1; 3+	40
CK20	5	0	0	0	0
Inhibin	5	0	0	0	0
S100-P	5	0	0	0	0
OCT 3/4	5	0	0	0	0
SALL4 (n = 4)	4	0	0	0	0
CD30 (n = 4)	4	0	0	0	0
PSA (n = 4)	4	0	0	0	0
NKX3.1 (n = 4)*	4	0	0	0	0

*In one case, focal <5% staining was present, and therefore, considered negative.
1+ indicates weak; 2+, moderate; 3+, strong; Ab, antibody.

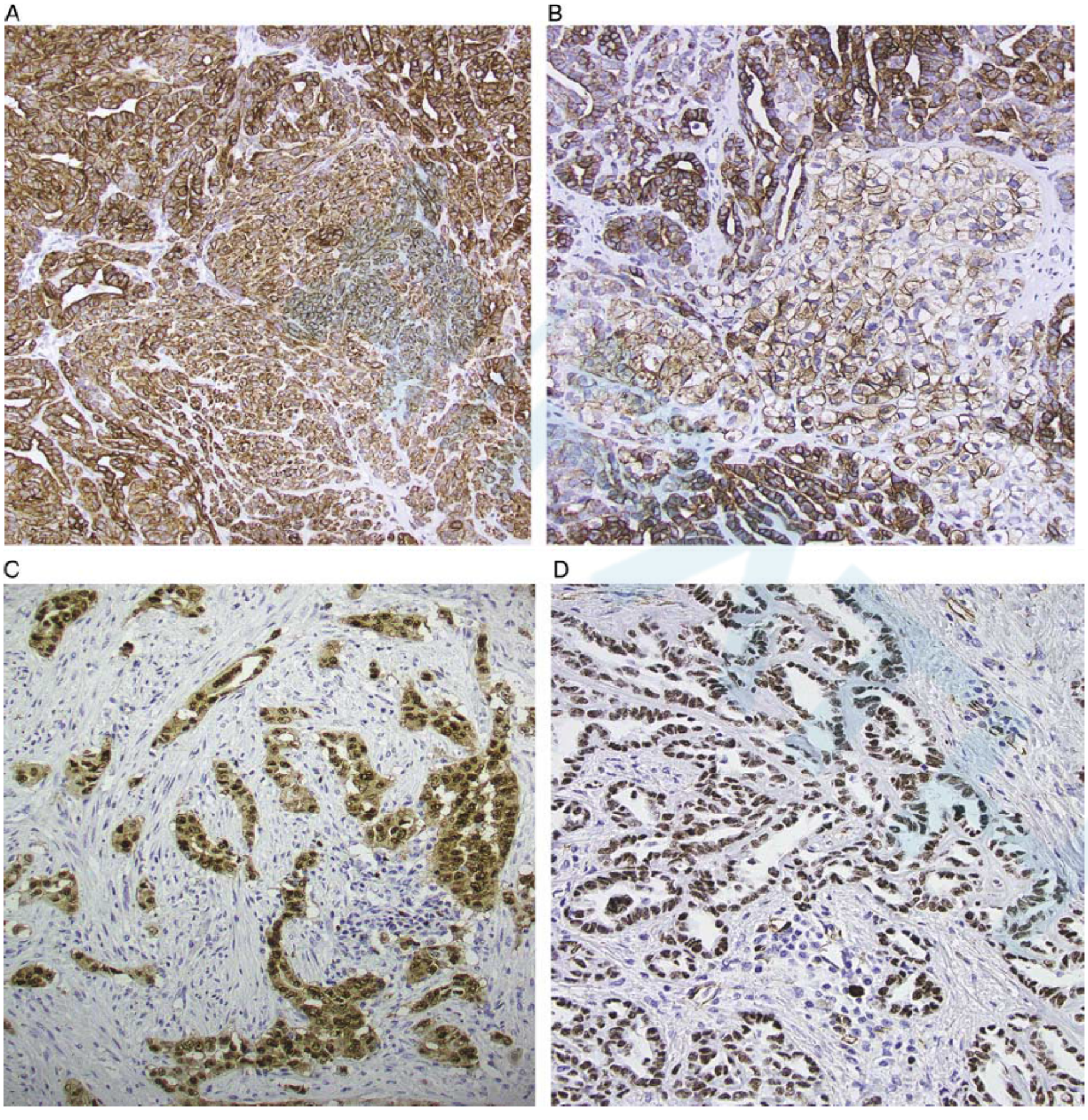


FIGURE 5.
A, Tumors are consistently positive for cytokeratin **AE1/AE3**.

B, Clear cell nests and solid areas stain less intensely than glandular areas for **CK7**.

There is nuclear staining for **PAX8** (C), and **WT-1** (D).

TABLE 4. A summary of the Clinicopathologic Parameters of the Reported Cases of Adenocarcinoma of the Rete Testis, Including this Series*

Age (y) (n = 78)	
Mean	54
Range	17-91
Laterality (N = 69) (n [%])	
Right	37 (53.6)
Left	31 (44.9)
Bilateral	1 (1.5)
Race (N = 29) (n [%])	
Caucasian/ white	25 (86)
Asian	2 (7)
Indian	1 (3.5)
Black	1 (3.5)
Relevant history (N = 70) (n [%])	
Mass/swelling	46 (66)
Hydrocele	25 (36)
Pain	16 (23)
Maldescended testis	6 (9)
Outcome	
Metastatic status (N = 69) (n [%])	
Metastasis	46 (67)
No metastasis	23 (33)
Survival status (N = 54) (n [%])	
Alive	26 (48)
DOD	25 (46)
DOC	3 (6)

*See Supplementary Table (Supplemental Digital Content 1, http://links.lww.com/PAS/A722) for individual case details and references.

- It mostly occurs in middle-aged to older patients at a mean age of 54 years;
- The great majority (86%) of reported cases occurred in white patients;

TABLE 5. A Summary of the Pathologic Features of Rete Adenocarcinoma Cases Reported in Literature, Including this Series*

Parameter	No. Cases
Mean size (cm)	3.8 (range, 0.2-10.2)
Transition from normal to neoplastic epithelium (n = 39)	23
Invasion into testicular parenchyma only	8
Invasion into testicular parenchyma and/or adjacent structures	7
Histology	
Architecture (n = 45)	
Papillary/tubulo-papillary	40
Glandular	23
Solid	20
Slit-like	8
Glomeruloid	6
Nested	5
Cribriform	5
Micropapillary	3
Biphasic (epithelial and sarcoma-like)	2
Mixed	31
Cytology (n = 32)	
Cuboidal-columnar cells	22
Columnar cells	3
Large polygonal cells	9
Spindle cells*	4
Cytoplasm (n = 16)	
Eosinophilic	6
Eosinophilic-clear	7
Granular	5
Stroma (n = 14)	
Fibrous	4
Desmoplastic	3
Hyalinized	7
Necrosis (n = 45)	12
Calcification (n = 45)	4 (3 with psammomatous calcification)

*See Supplementary Table (Supplemental Digital Content 1, http://links.lww.com/PAS/A722) for individual case details and references.

- Microscopically, the transition between tumor and normal rete testis epithelium, serves as an important diagnostic clue;
- 69% of cases showed mixed growth patterns;
- Cuboidal to columnar lesional cells are most frequently described in the literature;

TABLE 6. A Summary of the Immunohistochemical Features of Rete Adenocarcinoma in the Literature, Including this Series*

Immunohistochemical Staining Panel	Positive Cases (n/N [%])
AE1/AE3 Ab	22/23 (96)
Ber-EP4 Ab	7/8 (87)
EMA	16/19 (84)
CK7	10/12 (83)
Vimentin	17/21 (81)
MOC-31 Ab	4/5 (80)
PAX-8	4/6 (67)
CK5/6	4/7 (57)
WT-1	4/9 (44)
Calretinin	4/12 (33)
CK20	2/10 (20)
PSA	0/9 (0)
Inhibin	0/8 (0)
S100-P	0/7 (0)
CD30	0/5 (0)
Oct-4	0/5 (0)
SALL4	0/4 (0)
NKX3.1	0/4 (0)

*See Supplementary Table (Supplemental Digital Content 1, http://links.lww.com/PAS/A722) for individual case details and references.

Ab indicates antibody.

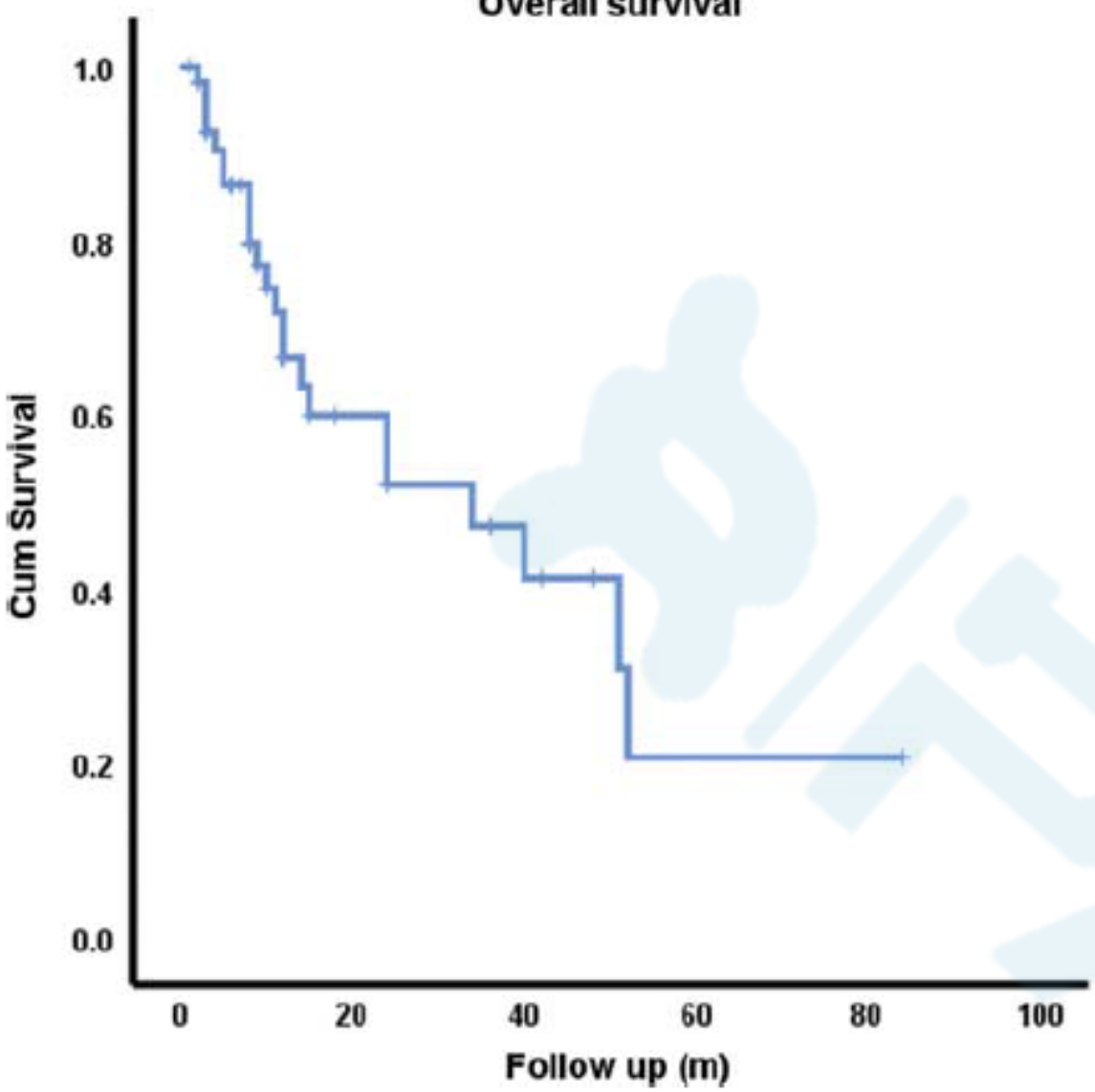


FIGURE 6. Kaplan-Meier disease-free survival curve for all reported cases, including those in this study.

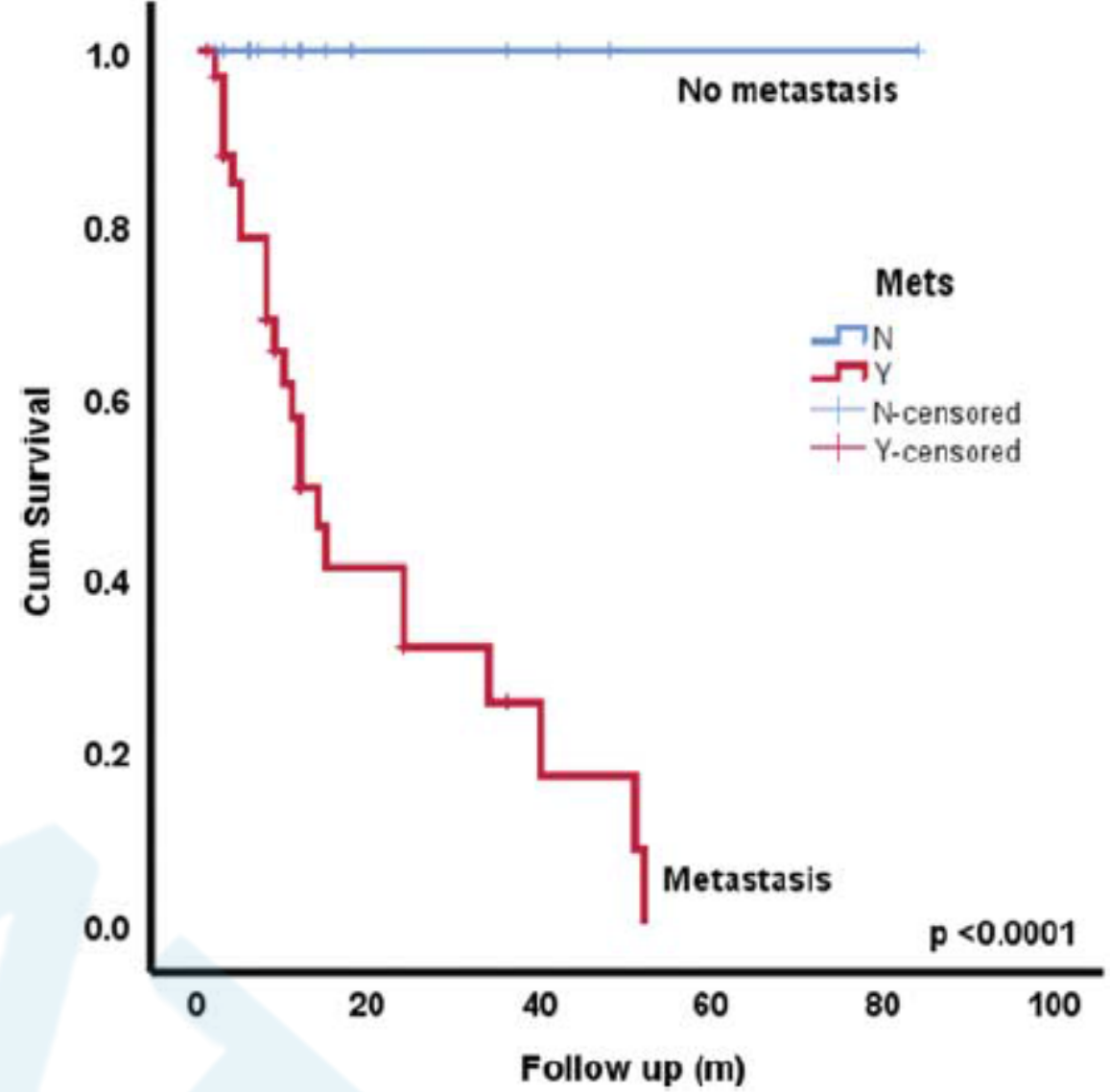


FIGURE 7. Kaplan-Meier curve showing survival of patients with and without metastasis (log rank, $P < 0.0001$).

FIGURE 6 Analysis of the data available shows a median survival time of 33 months. The 3- and 5-year survivals were 45% and 20%, respectively；

DISCUSSION

- **Diagnostic criteria** of adenocarcinoma of the rete testis

A. absence of histologically similar extra-scrotal tumor that could be the primary site;

B. tumor centered in the hilum of the testis;

C. morphology incompatible with any other type of testicular or paratesticular tumor;

D. immunohistochemical exclusion of other possibilities.

Differential Diagnosis

- **Mesothelioma**

a) Mesothelioma grossly involves the tunica;

b) there is usually less nuclear pleomorphism and more uniformly round to oval nuclei

c) An adjacent surface of atypical mesothelial cells is occasionally seen and may be helpful in this differential diagnosis.

- Adenocarcinoma markers: BerEP4 、 MOC31

➢ Germ cell tumors

a) The typically occur in younger patients and often have associated serum marker elevations.

b) In difficult cases, immunohistochemica stains (SALL4 and OCT3/4) should help identify germ cell origin.

- Adenocarcinoma of the rete testis has a poor prognosis and is resistant to conventional chemotherapy or radiation.
- A significant difference in survival was noted between patients with and without metastasis (log rank, P<0.001) (Fig. 7).
- The hilar localization, with its proximity to lymphatic drainage, and the low-intermediate proliferative index, as reflected by mitotic rate and Ki-67 index, are potential reasons for metastasis and resistance to chemotherapy or radiation.

谢谢!