Am J Surg Pathol 2018;42:958–970

Primary Vaginal Gastric-type Adenocarcinoma and Vaginal Adenosis Exhibiting Gastric Differentiation

Report of a Series With Detailed Immunohistochemical Analysis

指导老师：徐红

汇报人：吴建锋

阴道肿瘤 WHO 分类

1.2 腺细胞肿瘤

腺癌

- 子宫内膜样腺癌 8380/3
- 透明细胞癌 8310/3
- 黏液性癌 8480/3
- 中肾管癌 9110/3

良性腺细胞病变

- 管状绒毛状腺瘤 8263/0
- 绒毛状腺瘤 8261/0
- 苗勒上皮乳头状瘤
- 腺病
- 子宫内膜异位
- 子宫颈管内膜异位症
- 囊肿

WHO Classification of Tumours of Female Reproductive Organs. Lyon: International Agency for Research on Cancer; 2014.

Int J Gynecol Pathol. 2012 Mar;31(2):184-191

Case Report

Primary Vaginal Mucinous Adenocarcinoma of Gastric Type Arising in Adenosis: A Report of 2 Cases, 1 Associated With Uterus Didelphys

Karen L. Talia, F.R.C.P.A., James Scurry, F.R.C.P.A., Thomas Manolitsas, F.R.A.N.Z.C.O.G., and W. Glenn McCluggage, F.R.C.Path.

宫颈胃型-黏液腺癌
Mucinous carcinoma, gastric-type

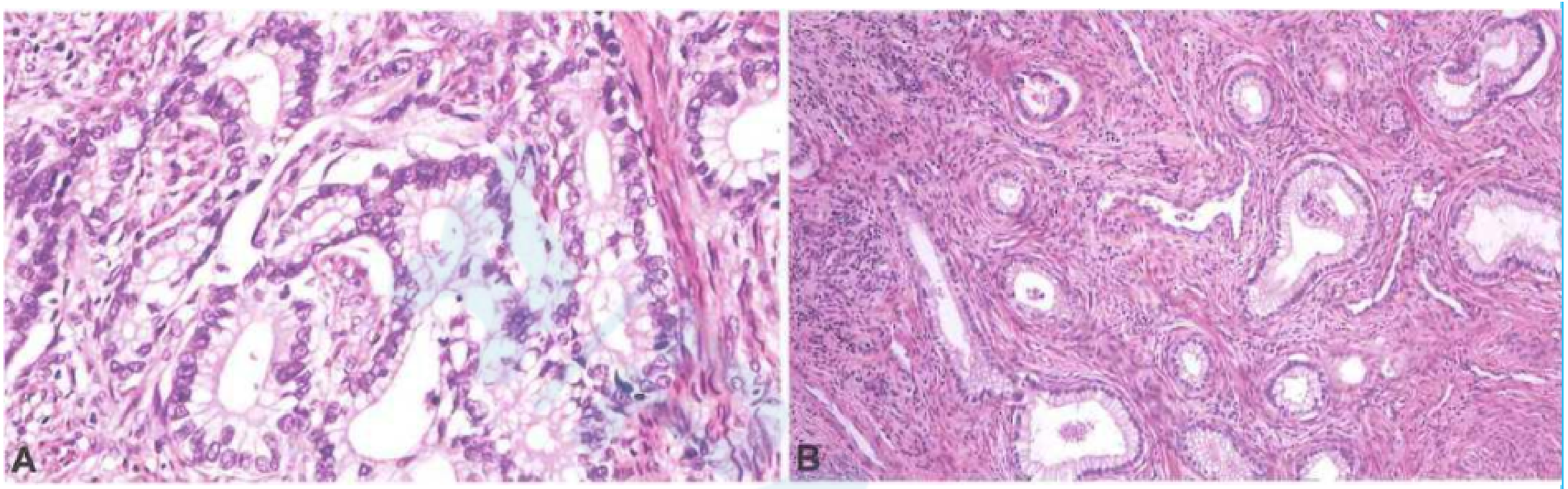
◇组织病理学

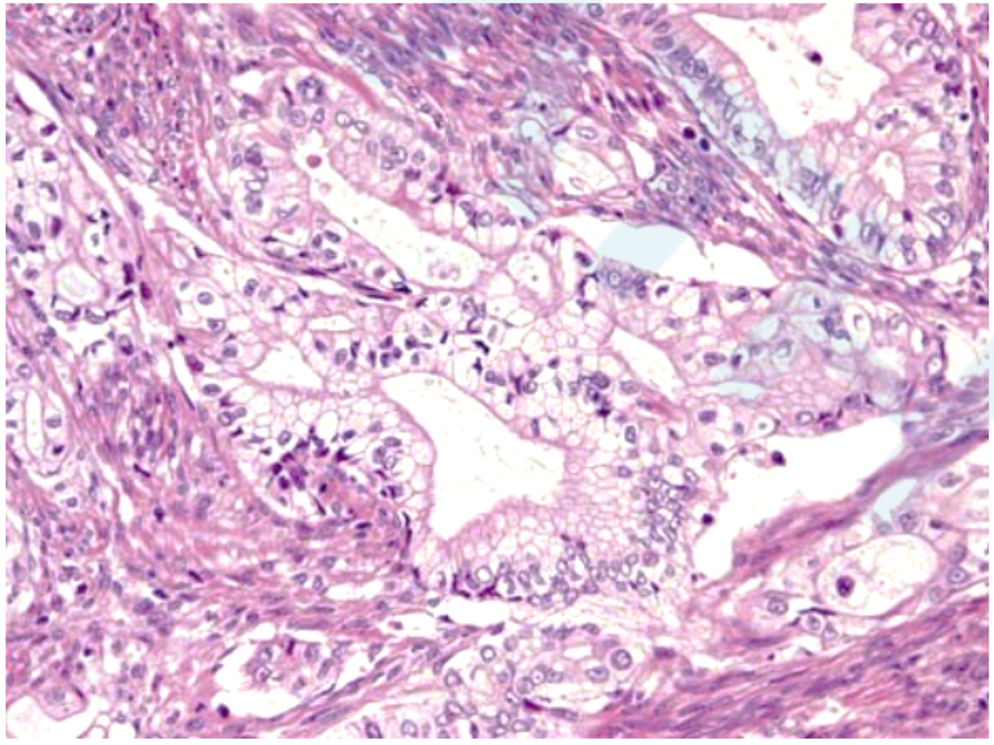
黏液腺体：形状不规则、扩张，也可融合或呈筛状

周围间质可见促纤维增生，或仅有轻微间质反应

细胞胞浆丰富、嗜酸/透明，细胞边界清楚

核增大、不规则、深染，可见核分裂象


A
B



Am J Surg Pathol 2016;40:636–644

A Detailed Immunohistochemical Analysis of a Large Series of Cervical and Vaginal Gastric-type Adenocarcinomas

Claire Carleton, MD, Lien Hoang, MD,† Shatrughan Sah, FRCPath,‡ Takako Kiyokawa, MD,§ Yevgeniy S. Karamurzin, MD,‖ Karen L. Talia, MD,¶ Kay J. Park, MD,† and W. Glenn McCluggage, FRCPath**

免疫表型

阳性：pyloric gland mucin、MUC6、HIK1083、CK7、CEA

CDX2、CA19.9、PAX8、CA125、CK20，P53

阴性：ER、PR、P16

阴道正常组织学

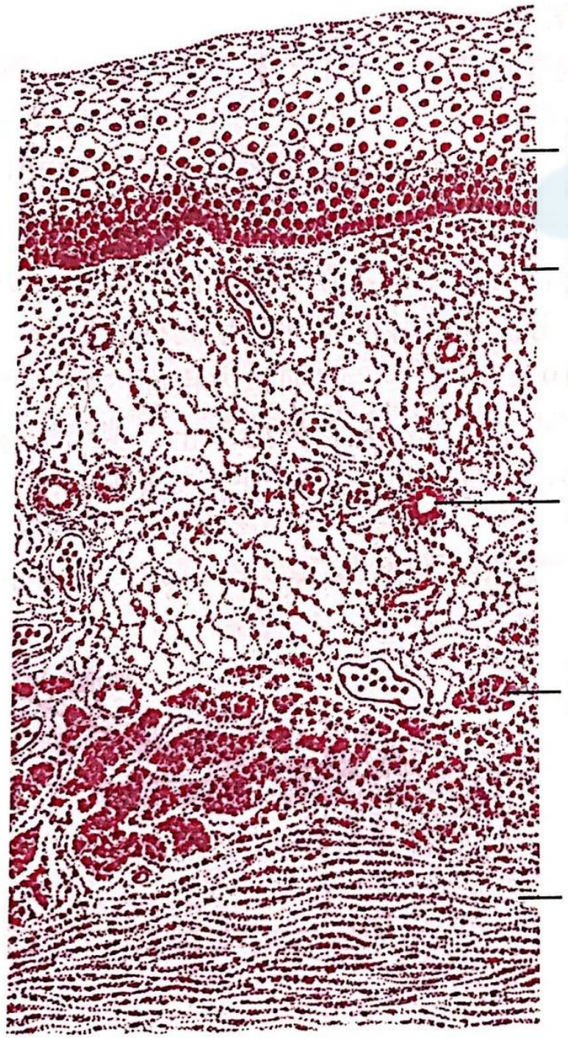


图 19-16　阴道壁切面图
Fig. 19-16 Section of vagina

无腺体

阴道腺病
Vaginal adenosis, VA

◇定义

阴道内存在腺体结构

◇流行病学

30%己烯雌酚(DES)暴露史的女性发生阴道腺病

仅有8%VA患者无DES暴露史

阴道腺病
Vaginal adenosis, VA

◇组织病理学

黏液型——阴道上部

输卵管—子宫内膜型——阴道下部

不成熟胚胎型

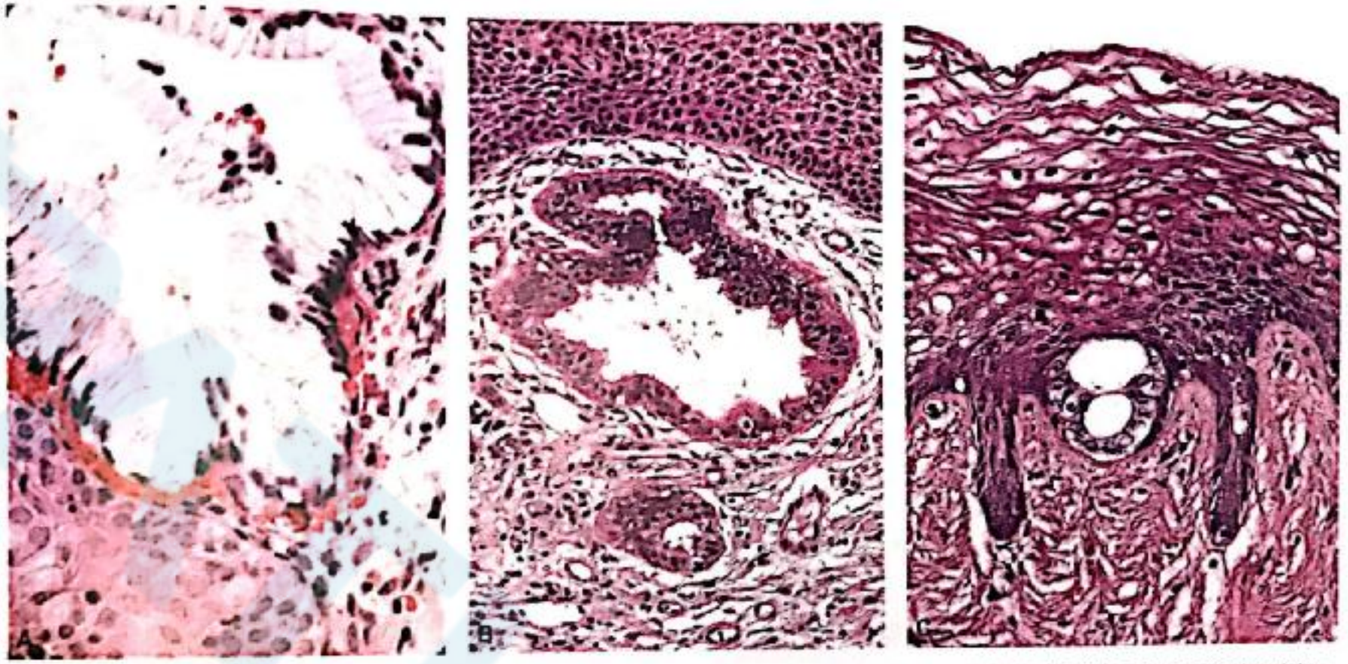
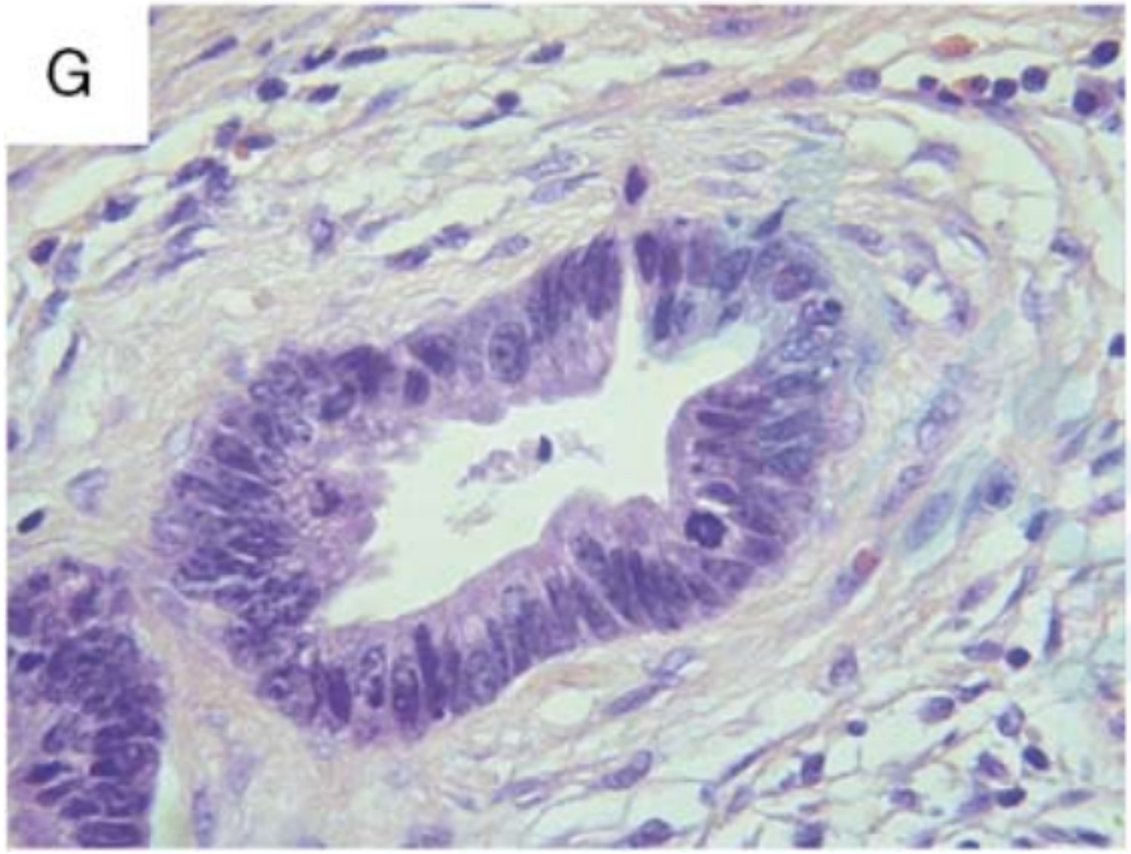


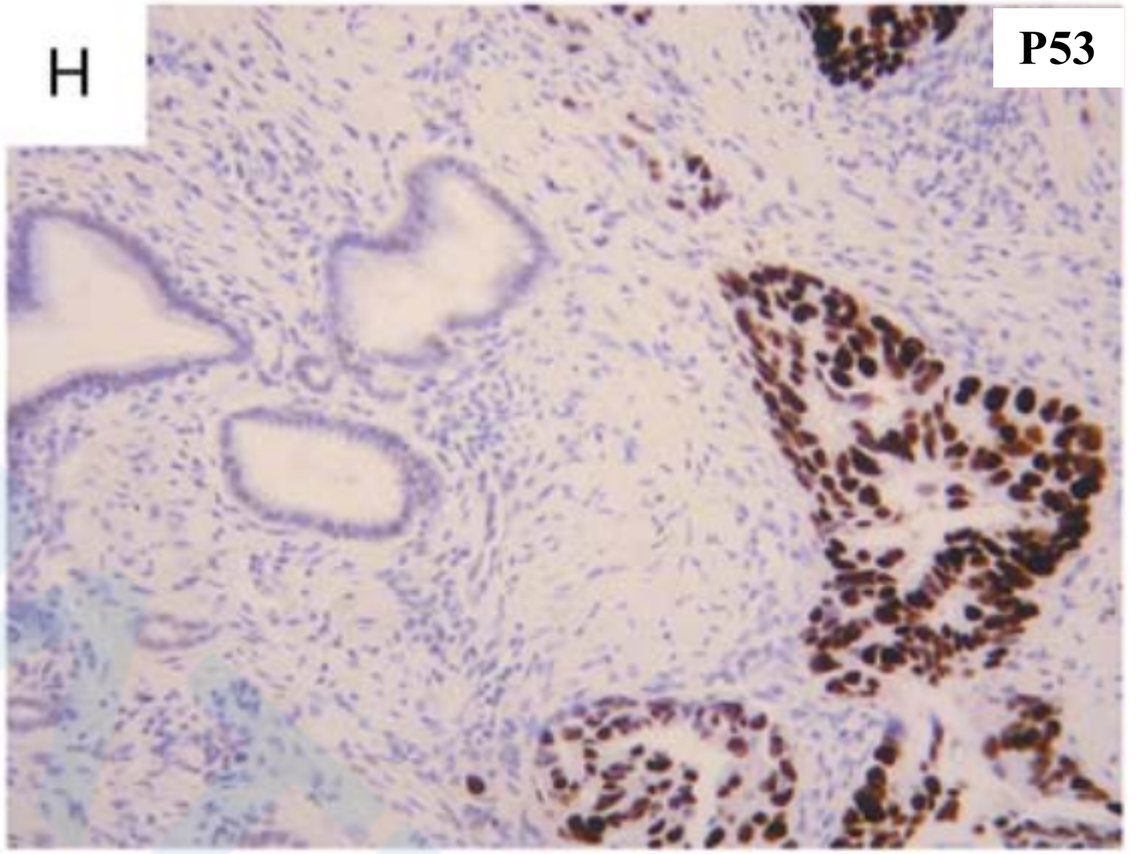
图 40.15 阴道腺病，腺上皮可为黏液性（A）、输卵管子宫内膜样（B）、或不成熟胚胎型（C）（经允许引自：Robboy SJ，Ellington KS.Pathology of the Female Genital Tract in Kodachrome Slides. 2nd ed.Durham，NC：Gyn-Path Associates；1996.）

◇组织起源

妊娠21周前，服用DES抑制正常鳞状上皮向

上迁移，先前存在的苗勒管上皮发展而来





非典型腺病：

核深染、拉长，形态不规则

可见大核仁

Int J Gynecol Pathol Vol. 31, No. 2, March 2012

研究目的

阐述具有胃型分化的阴道腺上皮病变的谱系（良性腺病→非典型腺病→腺癌），通过类比宫颈胃型黏液腺癌的发生推测阴道胃型腺癌的发生机制

MATERIALS AND METHODS

材料与方法

◈病例来源

Belfast Health and Social Care Trust——5例胃型腺癌；6例腺病

◈入选标准

胃型分化：瘤细胞具有丰富的透亮、淡嗜酸性胞浆，细胞边界清楚；

排除其他部位原发肿瘤

◈免疫组化

P16、P53、HER2

MUC6、ER、PAX8、CK7、CK20、CDX2、HNF1β、Napsin A、CA19.9、CEA、CA125、Cga

RESULTS & DISCUSSION

TABLE 1. Clinical Features of Vaginal Adenocarcinomas and Adenosis Exhibiting Gastric Differentiation

Cases	Age (y)	Presentation	Location	Gross Appearance	Operative Procedures	Outcome
Vaginal adenocarcinomas (cases 1-5)						
1	69	Urinary retention; vaginal mass associated with vagino-urethral fistula	Anterior vaginal wall and periurethral	Thickening and nodularity of vaginal wall	Anterior exenteration and pelvic lymph node dissection	DOD within 1 y
2	54	Mucoid vaginal discharge; vaginal mass	Upper right	Polypoid	TAHBSO, vaginal wall resection, and pelvic lymph node dissection	NA
3	59	Abnormal cervical smears (glandular abnormality)	Right vaginal vault	Thickening and nodular	Vaginal biopsies	AWD 1 y
4	41	Abnormal cervical smear (glandular abnormality); vaginal mass	NA	Circumscribed pale mass in vaginal wall	Excision of vaginal mass and pelvic lymph node dissection	DOD 3 y
5	56	Vaginal mass	Right anterolateral wall of lower vagina	NA	Partial vaginectomy and inguinal lymph node dissection	Vulvar recurrence; DOD 3 y
Pure vaginal adenosis with gastric differentiation (cases 6-11)						
6	49	Abnormal cervical smears	Upper vagina	NA	TAHBSO and partial vaginectomy	Alive and asymptomatic at 4 y
7	33	Watery vaginal discharge; history of unsuitable cervical smears	NA	Irregular thickened vaginal wall	Vaginal biopsies	Symptomatic with mass effect on left side of vagina at 4 y
8	62	Cervical stenosis	NA	NA	Vaginal biopsies	NA
9	47	Abnormal cervical smears	NA	NA	Vaginal biopsies; TLH/BS	NA
10	41	Abnormal cervical smears	NA	Desquamation and ulceration	Vaginal biopsies	NA
11	44	Watery vaginal discharge since adolescence	Anterior, posterior and lateral vaginal wall	Thickened firm vaginal wall with intramural cystic structures	TAHBSO and total vaginectomy	NA

TABLE 2. Pathologic Features of Vaginal Adenocarcinomas With Gastric Differentiation

Cases	Size (cm)	Lymphovascular Invasion	Lymph Node Metastasis	Other Pathologic Findings
1	3.7	Present	Absent	Infiltration of periurethral adipose tissue and base of bladder; perineural invasion
2	At least 3	Present	Present (iliac)	Involvement of right ureter wall
3	2.8 (by MRI)	NA*	NA*	Nil
4	3.8	Present	Present (vaginal mural and pelvic)	Nil
5	4	Present	Present (bilateral inguinal)	Nil

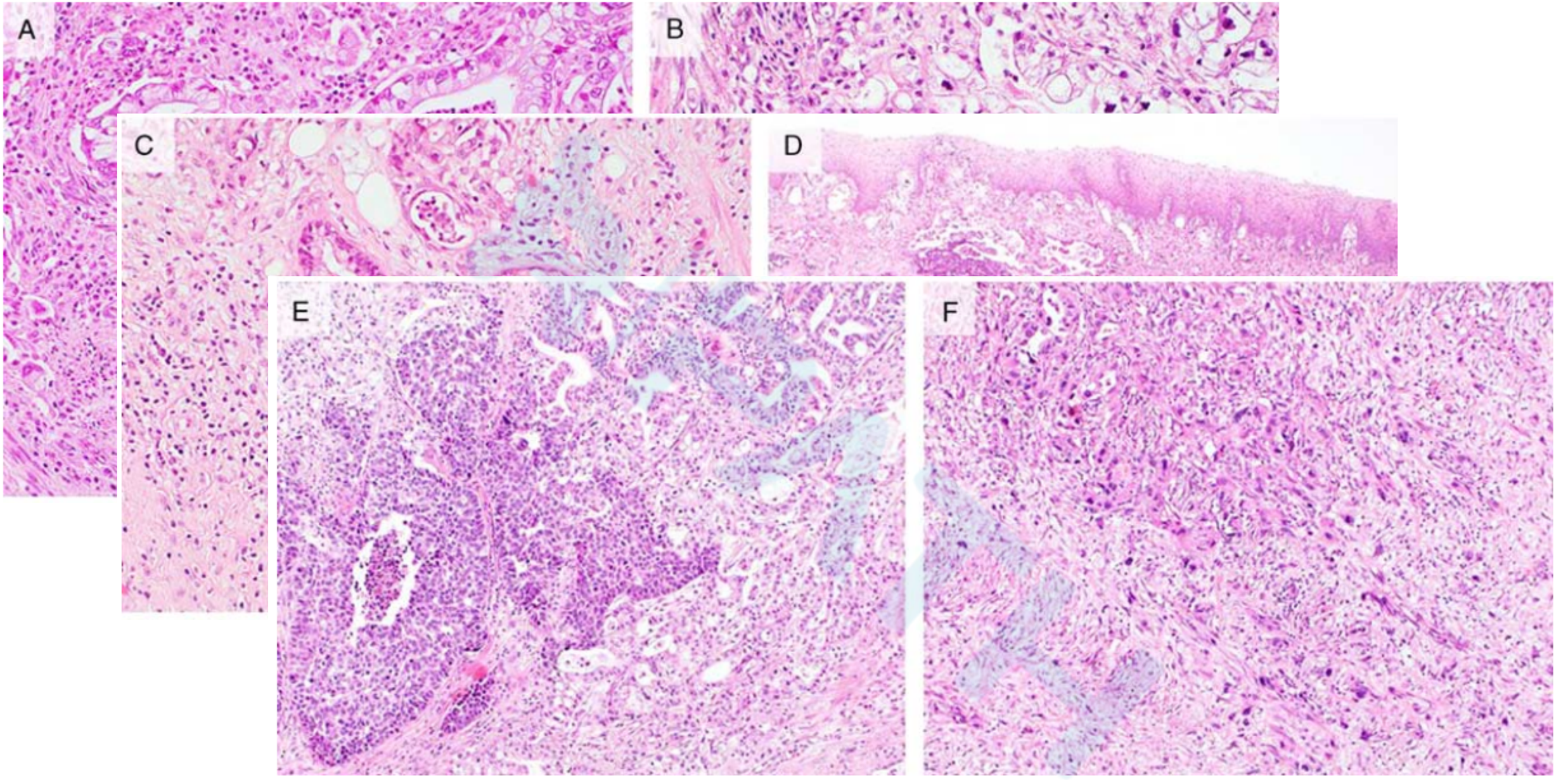


FIGURE 1. Histologic features of vaginal adenocarcinomas exhibiting gastric differentiation. Gastric-type adenocarcinomas composed of glands with pale eosinophilic and foamy cytoplasm (A) and voluminous clear cytoplasm with distinct cell borders (B). C, Goblet cells may be focally present. In case 2, the tumor displayed an admixture of glandular and basaloid patterns underlying the vaginal squamous epithelium (D and E), while elsewhere a sarcomatoid component was present (F).

TABLE 3. Pathologic Features of Vaginal Adenosis

Cases	Type of Adenosis (Mucinous/ Tuboendometrial)	Gastric-type Morphology	Intestinal/Neuroendocrine Features	Cytologic Atypia in Adenosis	Lobular Architecture
Vaginal adenosis associated with gastric-type adenocarcinoma (cases 1-5)					
1	Tuboendometrial	Absent	Absent	Absent	Absent
2	Mucinous	Present	Absent	Present	Absent
3	Mucinous	Present	Goblet cells	Present	Absent
4	Mucinous and tuboendometrial	Present	Absent	Present	Present
5	Mucinous	Present	Absent	Present	Absent
Pure vaginal adenosis with gastric differentiation (cases 6-11)					
6	Mucinous and tuboendometrial	Present	Goblet cells and NE cells	Present	Present
7	Mucinous	Present	Goblet cells	Present	Present
8	Mucinous	Present	Goblet cells	Present	Absent
9	Mucinous	Present	Goblet cells	Absent	Present
10	Mucinous and tuboendometrial	Present	Goblet cells and NE cells	Absent	Absent
11	Mucinous	Present	Goblet cells and NE cells	Present	Absent

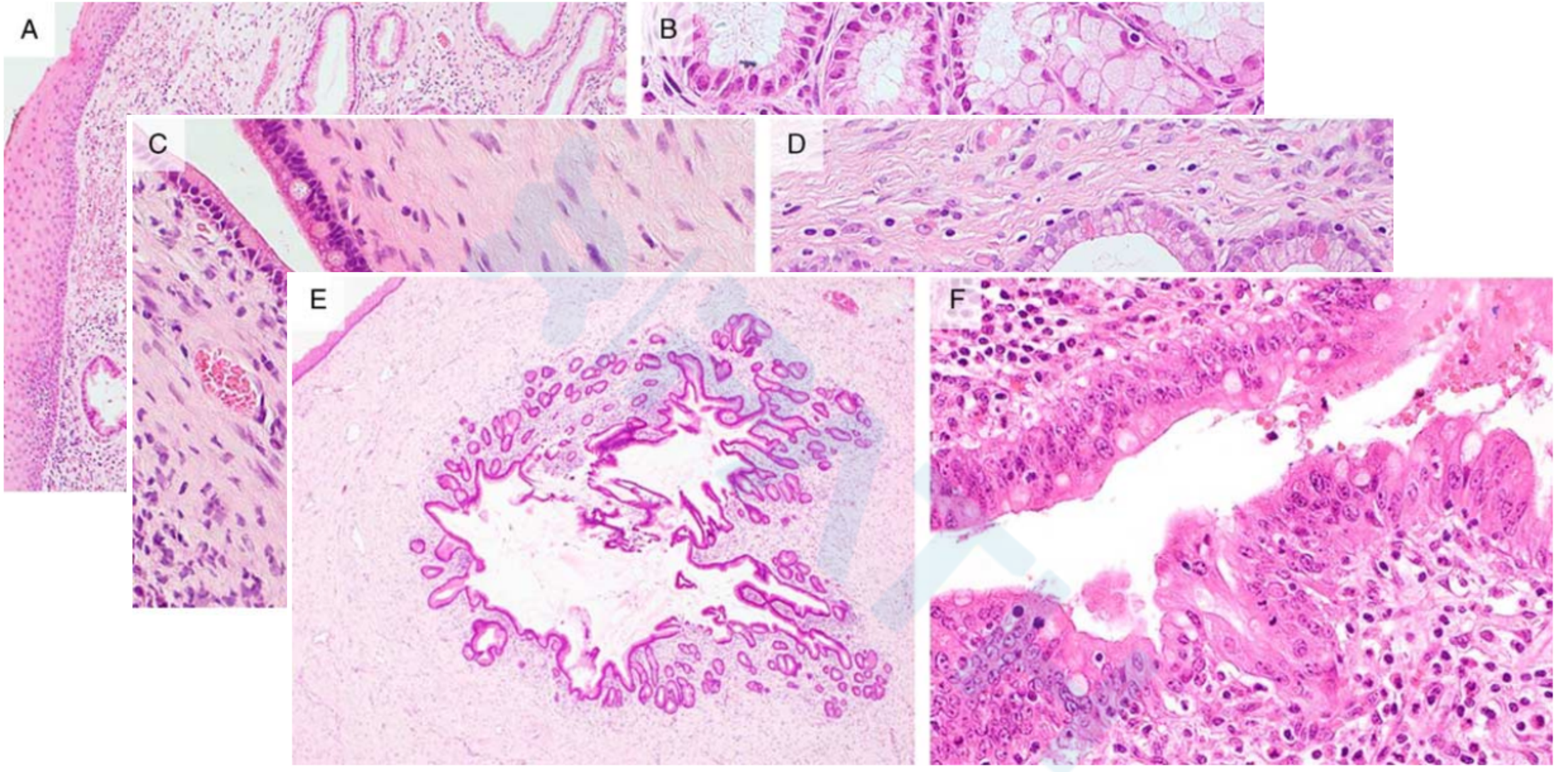


FIGURE 2. Histologic features of pure vaginal adenosis exhibiting gastric differentiation. A, Mucinous glands are present underlying the vaginal squamous epithelium. B, Gastric-type morphology featuring foamy cytoplasm and distinct cell borders. Intestinal differentiation with goblet cells (C) and neuroendocrine cells with eosinophilic cytoplasmic granules (D). E, Foci resembling LEGH are sometimes seen. F, Case showing cytologic atypia with nuclear enlargement and distinct nucleoli.

TABLE 4. Immunohistochemical Findings in Vaginal Adenocarcinoma and Adenosis With Gastric Differentiation

	Vaginal Adenocarcinoma (Cases 1-5)				Vaginal Adenosis (Cases 2-11)			
Antibody	**Diffusely Positive (≥50%)**	**Focally Positive (<50%)**	**Negative**	**Percentage of Cases With Positive Staining**	**Diffusely Positive (≥50%)**	**Focally Positive (<50%)**	**Negative**	**Percentage of Cases With Positive Staining**
MUC6	1/5	3/5	1/5	80	6/10	4/10	0	100
ER	0	0	5/5	0	1/10	4/10	5/10	50
PAX8	1/5	2/5	2/5	60	4/10	4/10	2/10	80
CK7	3/5	2/5	0	100	8/9	1/9	0	100
CK20	1/5	0	4/5	20	0	2/9	7/9	22
CDX2	1/5	4/5	0	100	1/9	4/9	4/9	56
HNF1β	3/5	2/5	0	100	9/10	1/10	0	100
Napsin A	0	0	5/5	0	0	1/10	9/10	10
CA19.9	3/5	2/5	0	100	8/9	0	1/9	89
CEA	2/5	2/5	1/5	80	1/9	5/9	3/9	67
CA125	1/5	4/5	0	100	3/9	3/9	4/9	67
p53	Mutation-type (diffuse positive) in 3/5 cases Wild-type in 2/5 cases			Mutation-type: 60% Wild-type: 40%	Wild-type in 10/10 cases			Mutation-type: 0% Wild-type: 100%
p16	Negative in 5/5 cases			Negative: 100%	Negative in 9/9 cases			Negative: 100%
HER2	Equivocal (2+) in 1/5 cases Negative (0 or 1+) in 4/5 cases			HER2 positive: 0% HER2 equivocal: 20% HER2 negative: 80%	Negative (0 or 1+) in 4/4 cases (for cases associated with adenocarcinoma only)			HER2 positive: 0% HER2 equivocal: 0% HER2 negative: 100%
Chromogranin	Focally positive in 1/4 cases Negative in 3/4 cases			Focally positive: 25% Negative: 75%	Scattered individual chromogranin-positive cells in 5/8 cases (all positive cases were of pure adenosis) Negative in 3/8 cases (all from cases associated with adenocarcinoma)			Scattered individual chromogranin-positive cells: 62.5% Negative: 37.5%

腺病与腺癌的免疫表型区别

免疫表型	腺病	腺癌
ER	+	-
PAX8	+	-
P53	Wild-type	Mutation-type
CDX2、CA19.9、CEA、CA125	-	+

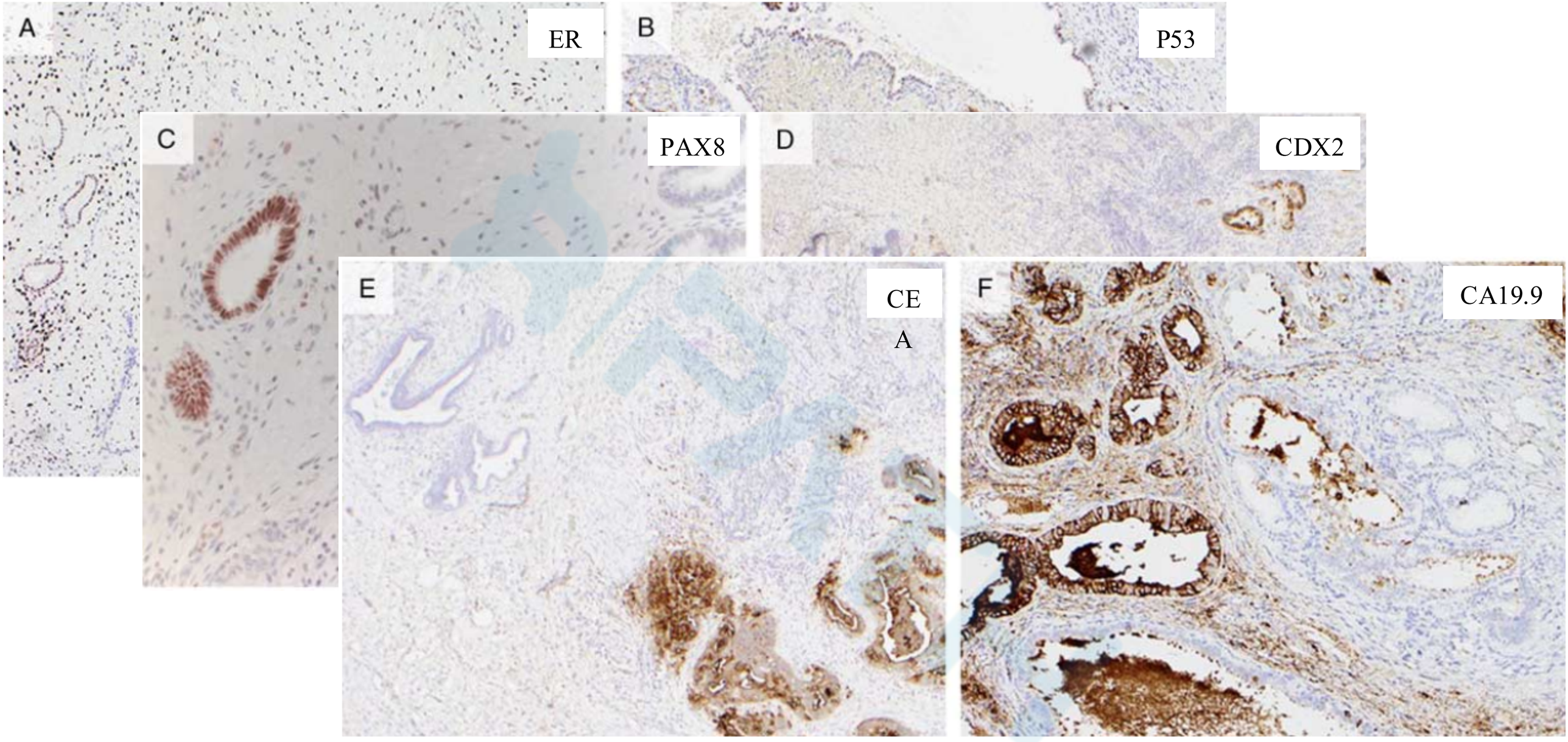


FIGURE 5. Immunohistochemistry of adenosis component in vaginal adenocarcinoma exhibiting gastric differentiation. Upon transition from adenosis to adenocarcinoma, accompanying changes in immunoreactivity may include loss of ER expression (A), p53 switching from "wild-type" to "mutation-type" (B), loss of PAX8 expression (C), and acquisition of expression of CDX2 (D), CEA (E), and CA19.9 (F).

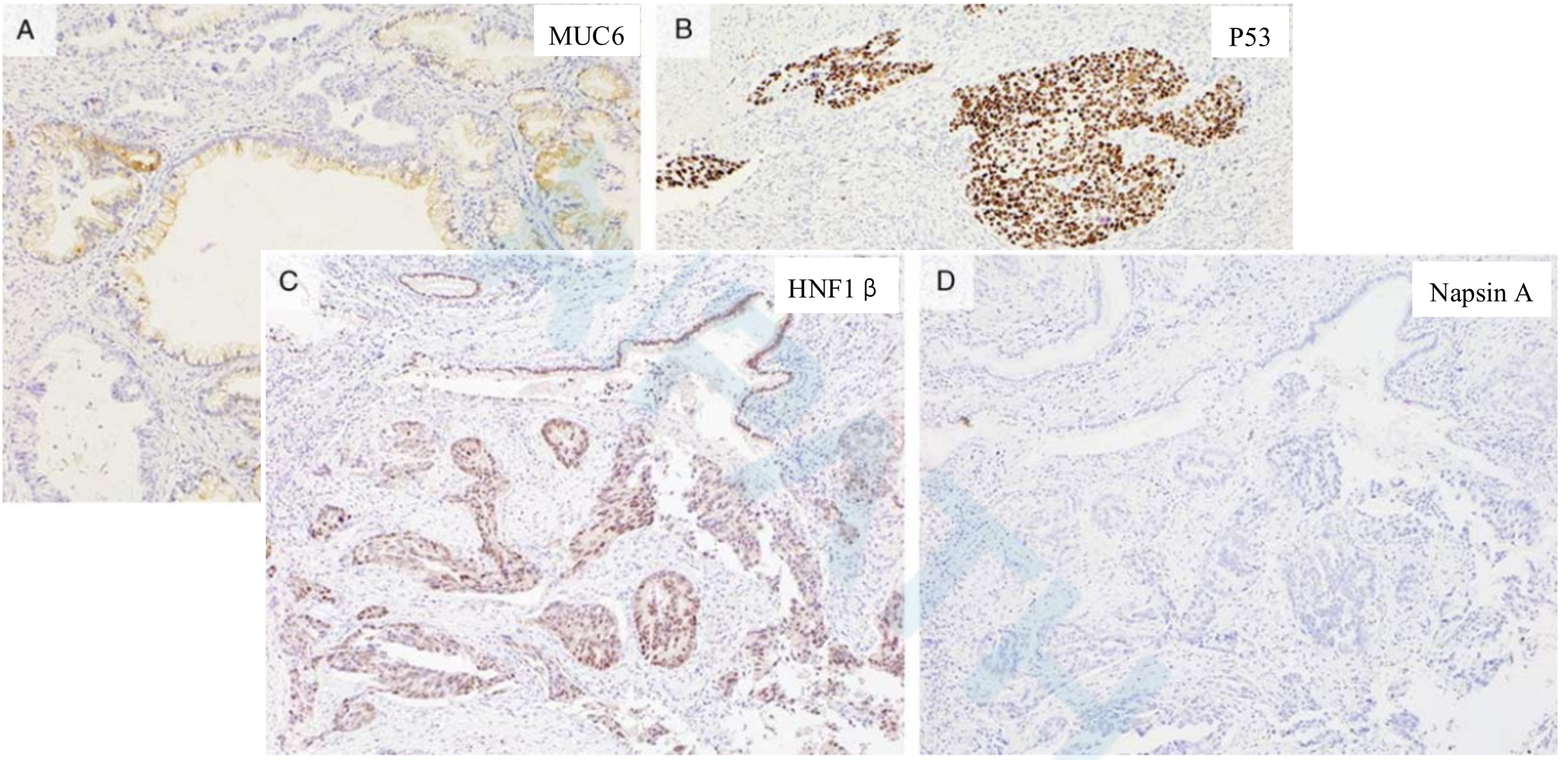


FIGURE 3. Immunohistochemistry of vaginal adenocarcinomas exhibiting gastric differentiation. A, MUC6 commonly shows positive staining. B, Diffuse positive (mutation-type) staining for p53 was seen in several cases, including the glandular and basaloid components of case 2. HNF1β typically shows diffuse positivity in both adenosis and adenocarcinoma components (C), whereas the same area is totally negative for Napsin A (D).

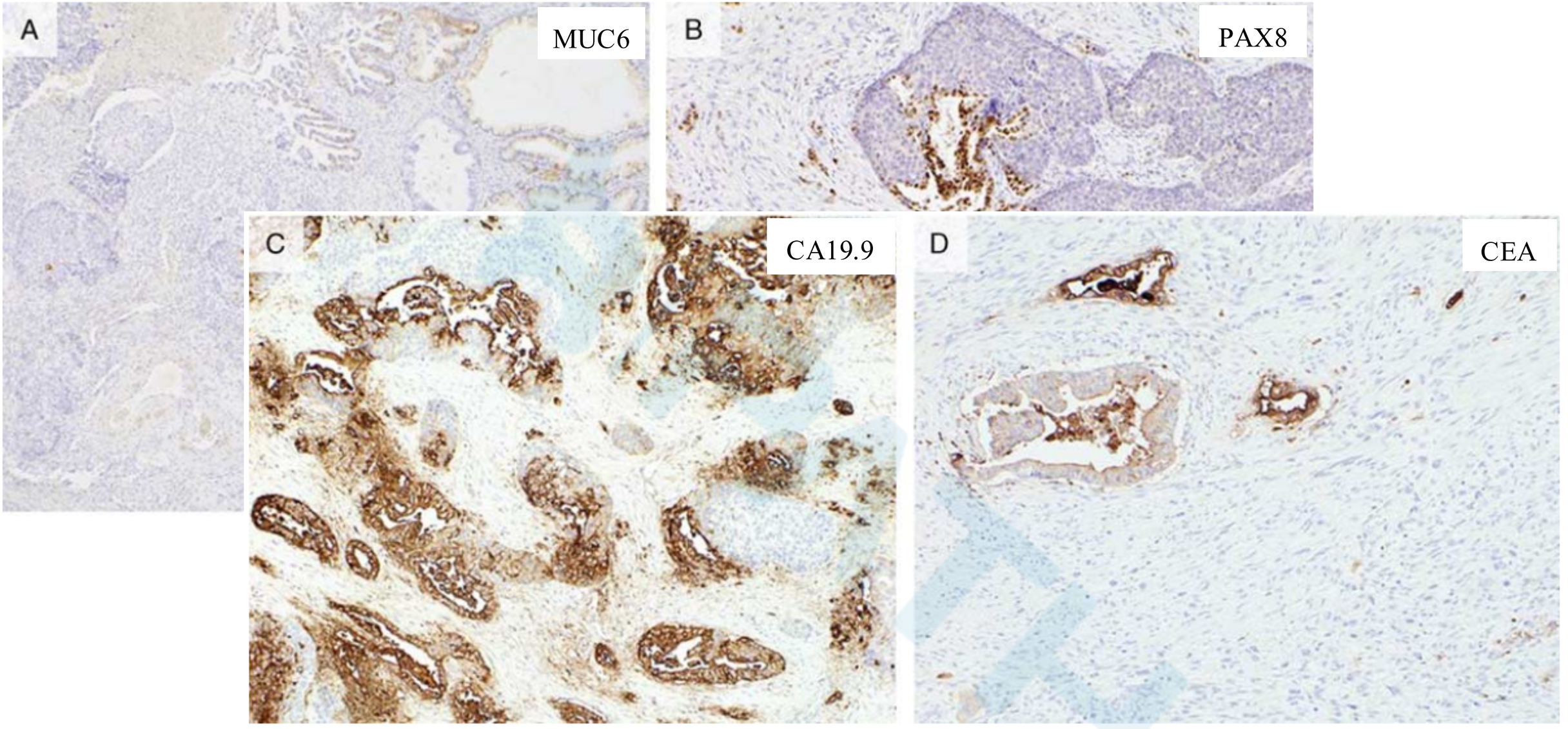


FIGURE 4. Immunohistochemistry of morphologically distinct tumor components in case 2. A, MUC6 is positive in the glandular component but negative in the basaloid component. B, PAX8 shows abrupt transition between the negative basaloid component and the positive glandular component. C, CA19.9 is diffusely positive in the glandular component but only focally positive in the basaloid component. D, CEA is positive in the glandular component but negative in the sarcomatoid component at lower right corner.

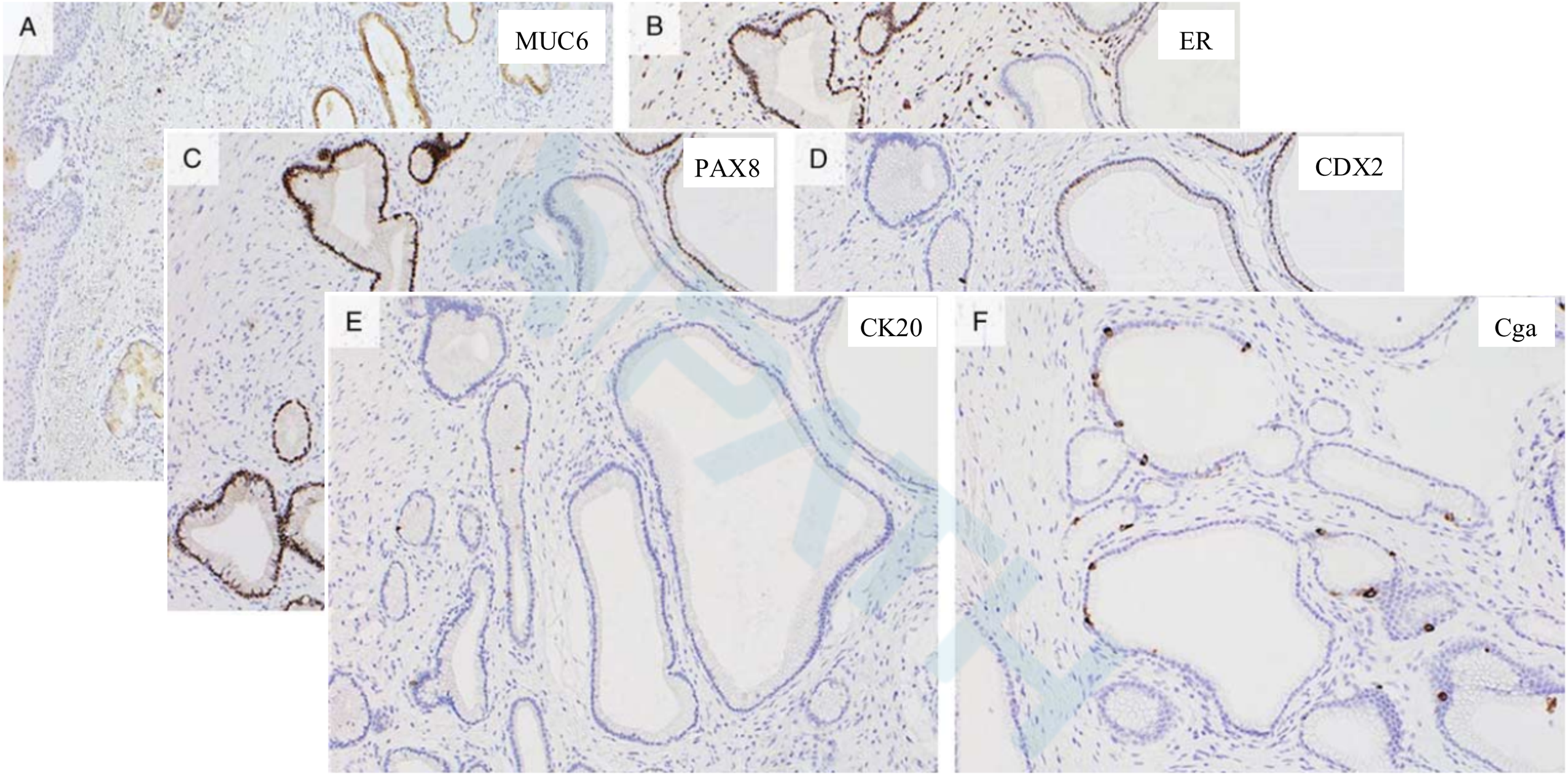


FIGURE 6. Immunohistochemistry of vaginal adenosis exhibiting gastric differentiation. A, MUC6 positivity is commonly seen. ER and PAX8 demonstrate positive staining in some of the glands but are completely negative in others (B and C, respectively). D, CDX2 shows positive staining in the glands negative for ER and PAX8. E, CK20 is largely negative in these glands with only isolated positive cells. F, Scattered individual chromogranin-positive neuroendocrine cells.

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HNF1β	3/5	2/5	0	100	9/10	1/10	0	100
Napsin A	0	0	5/5	0	0	1/10	9/10	10
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鉴别诊断

1、胰胆管系统转移性癌

- 仔细寻找病变周围是否存在良性腺病及非典型腺病成分
- 不表达PAX8

2、阴道透明细胞癌

- 病变周围存在良性腺病及非典型腺病成分
- 表达Naspsin A
- CK20、CDX2阳性更支持胃型腺癌

鉴别诊断

3、阴道肠型腺癌

◈形态更像结直肠癌，并常能见到类似结肠腺瘤形态

◈CK20、CDX2弥漫阳性，CK7阴性或局灶阳性

4、阴道子宫内膜样癌

◈寻找典型的子宫内膜样癌区域

◈ER表达

5、HPV相关腺癌

◈P16阳性

◈HPV杂交

SUMMARY

SUMMARY

- 首次报道阴道腺病伴胃型分化
- 阴道腺病→非典型腺病→阴道胃型腺癌
- 阴道透明细胞癌与胃型腺癌都可能从腺病发展而来，其发生机制类似于宫颈腺癌
- 由于阴道胃型腺癌具有更侵袭的生物学行为，应将其独立分类
- 阴道标本中应重点关注是否存在腺病及非典型腺病
- 本文病例受限，将来需要更多的研究揭示其发病机制

THANK YOU

Any questions?

Q&A