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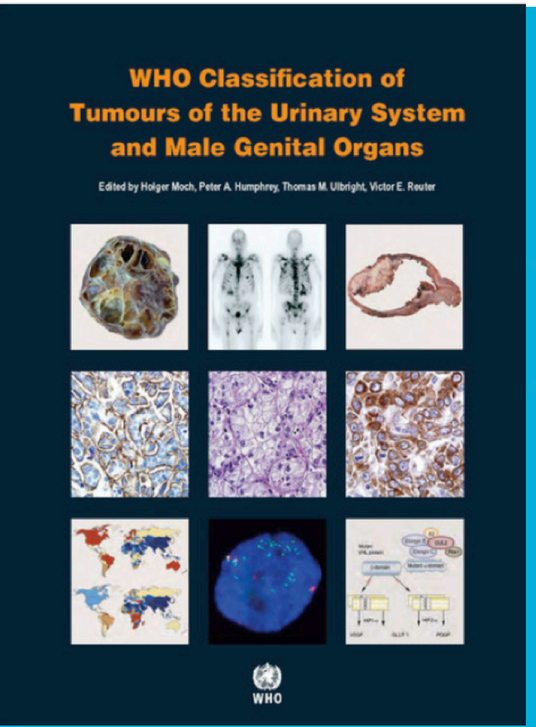
西京医院 XIJING HOSPITAL

PATH 第四军医大学病理学教研室 DEPARTMENT OF PATHOLOGY FOURTH MILITARY MEDICAL UNIVERSITY

Carcinoma In Situ With Plasmacytoid Features

A Clinicopathologic Study of 23 Cases

Ankur R. Sangoi, MD, Sara M. Falzarano, MD, PhD,† Marlo Nicolas, MD,‡ and Jesse K. McKenney, MD‡*



汇报人：徐梦微

西京医院病理科

Journal Club

INTRODUCTION

非浸润性尿路上皮肿瘤（Non-invasive urothelial carcinoma）(WHO 2016)

➢**Flat lesions 平坦型病变**

✓ Urothelial reactive (inflammatory) atypia 反应性(炎症性)不典型

✓ Urothelial atypia of unknown significance 意义不明的不典型增生

✓ Urothelal dysplasia 尿路上皮异型增生

✓ Urothelal carcinoma in situ 尿路上皮原位癌

➢**Papillary lesions 乳头状病变**

✓Urothelial papilloma 乳头状瘤

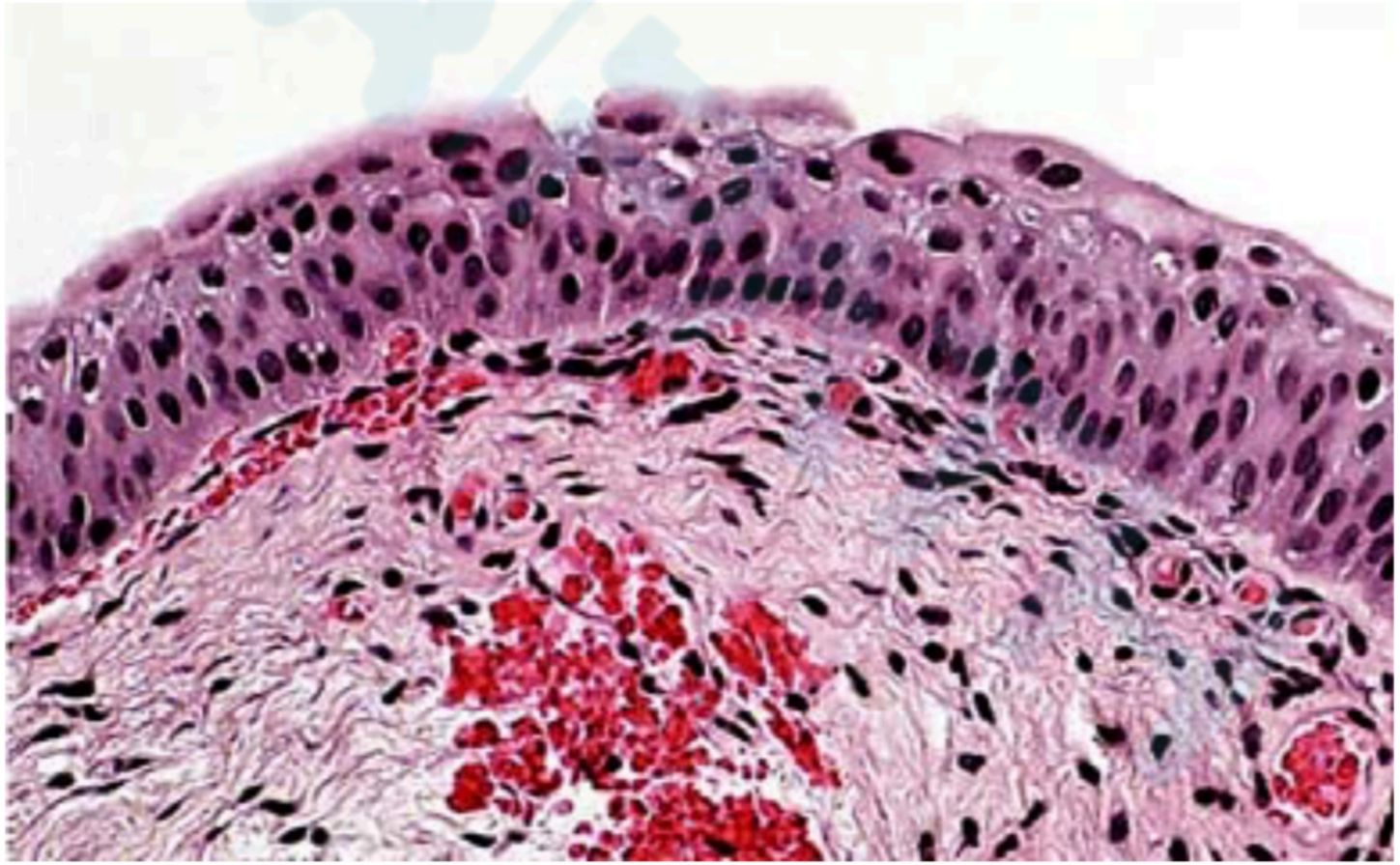
✓Urothelial inverted papilloma 内翻性乳头状瘤

✓Urothelial papillary neoplasm of low malignant potential 低度恶性潜能的乳头状尿路上皮肿瘤

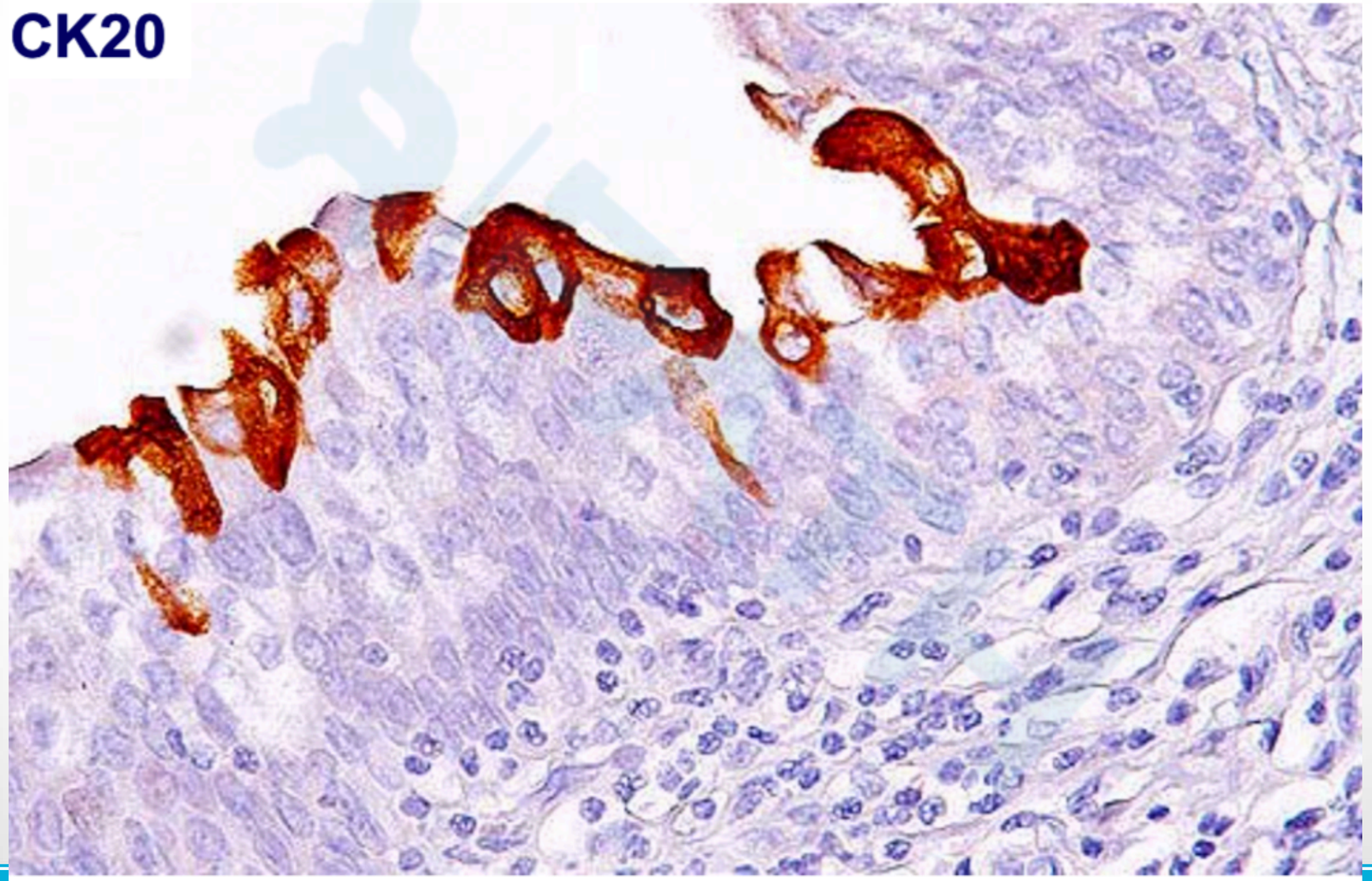
✓Papillary urothelial carcinoma, low grade 乳头状尿路上皮癌，低级别

✓Papillary urothelial carcinoma, high grade 乳头状尿路上皮癌, 高级别

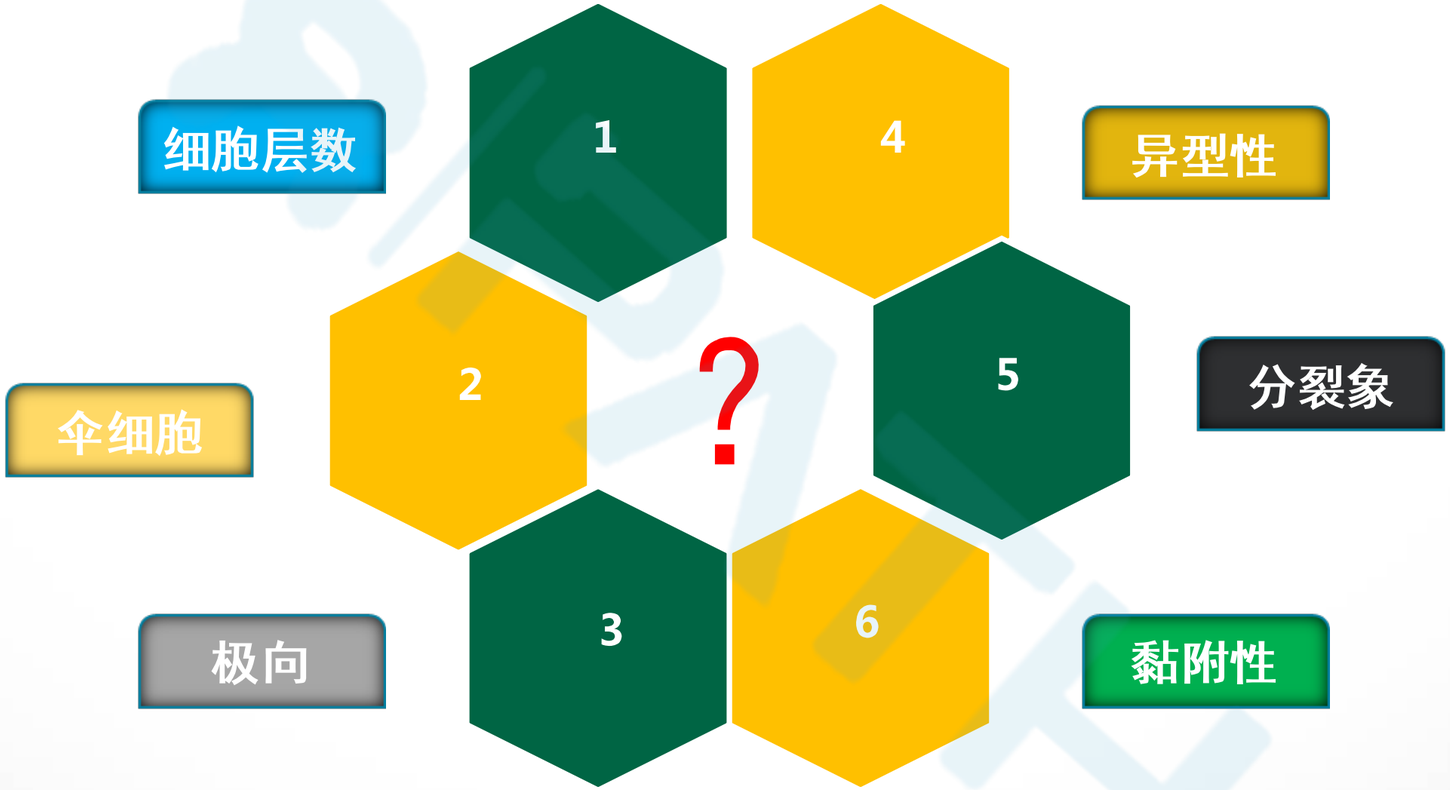
层数　极向　形态



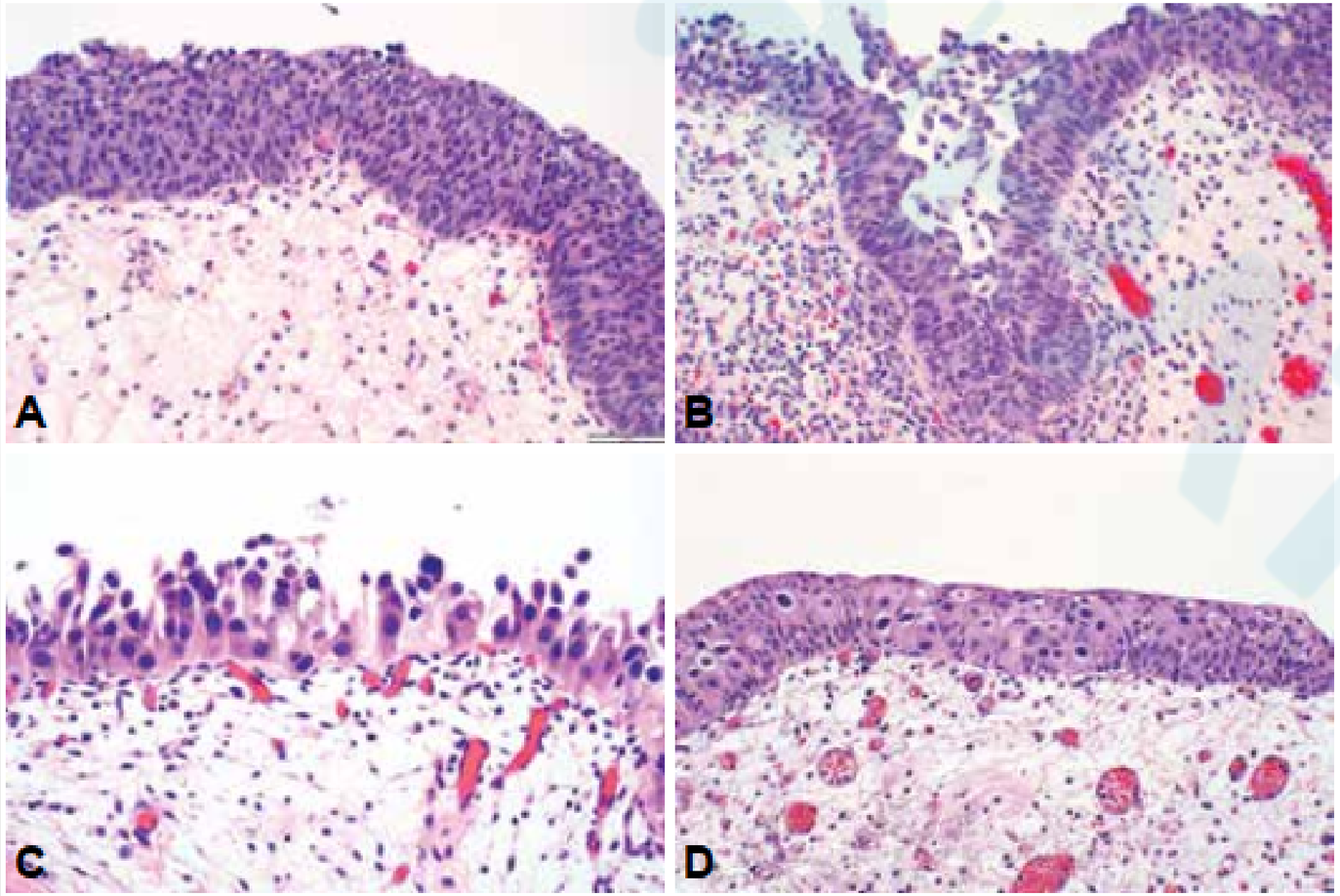
INTRODUCTION



INTRODUCTION



尿路上皮原位癌
Urothelial carcinoma in situ



- **高级别上皮内瘤变**
- 累及/不累及上皮全层
- 极向消失 & 黏附性↓
- **恶性细胞**: 核/浆↑，核多形,染色质↑，明显核仁,病理性核分裂象

INTRODUCTION

原位癌变异型

- 大细胞性
- 小细胞性
- 剥脱性&黏附性
- Paget样&底蚀性
- 伴鳞状分化
- 伴腺样分化
- 微乳头
- 微浸润

McKenney JK, *et al*.(2001). *Am J Surg Pathol.*

尿路上皮原位癌
Urothelial carcinoma in situ

➢流行病学

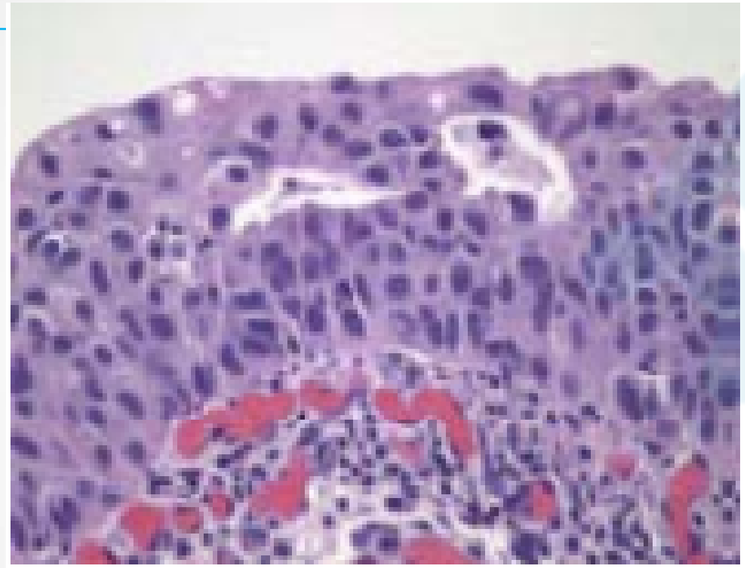
- 原发性: <3%尿路上皮肿瘤
- 同时伴发浸润性尿路上皮癌: ~45%
- 继发性尿路上皮癌(随访患者): ~90%

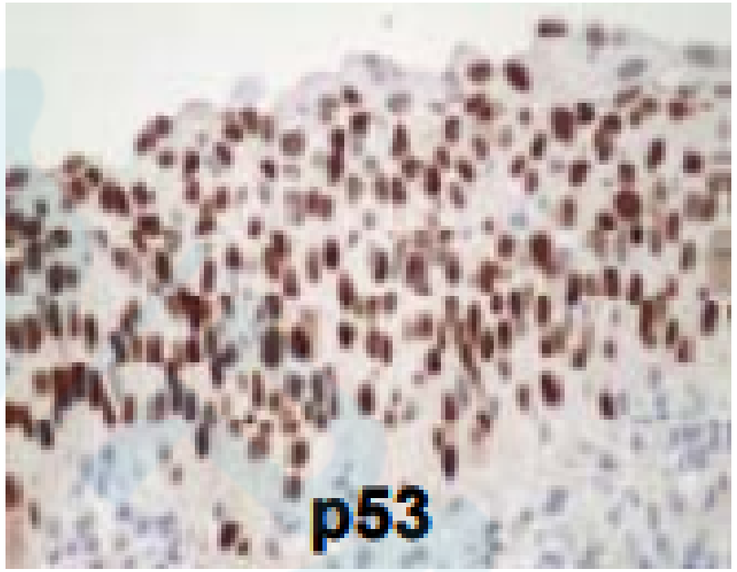
➢影响预后指标: 多灶性, 累及前列腺尿道部, 对BCG反应情况

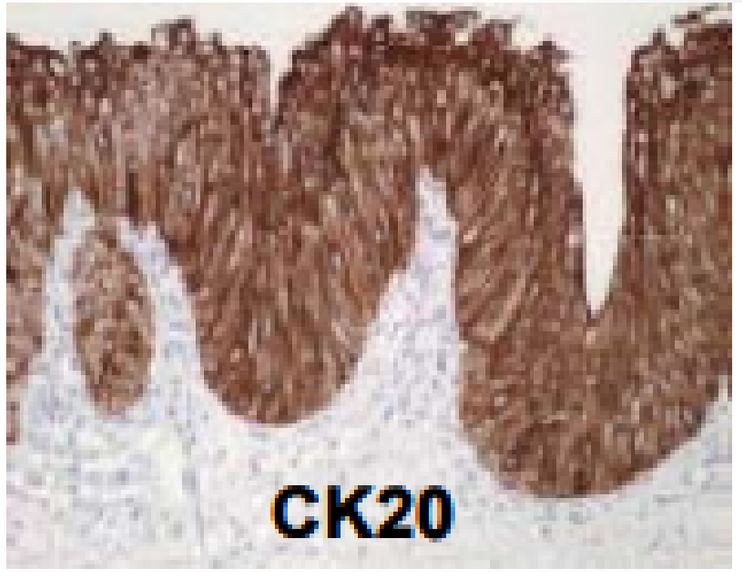
INTRODUCTION

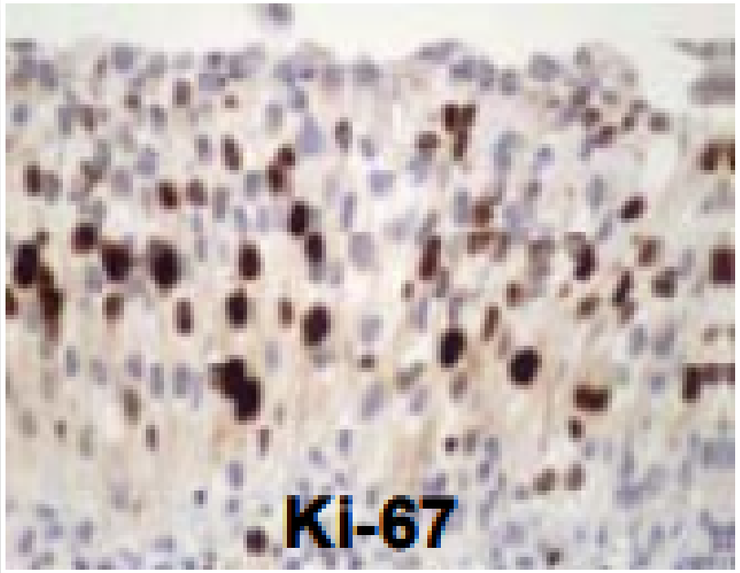
	CK20	CD44	P53	P16
正常	伞细胞+	基底细胞+	常-	-
原位癌	全层细胞+	-	+	+

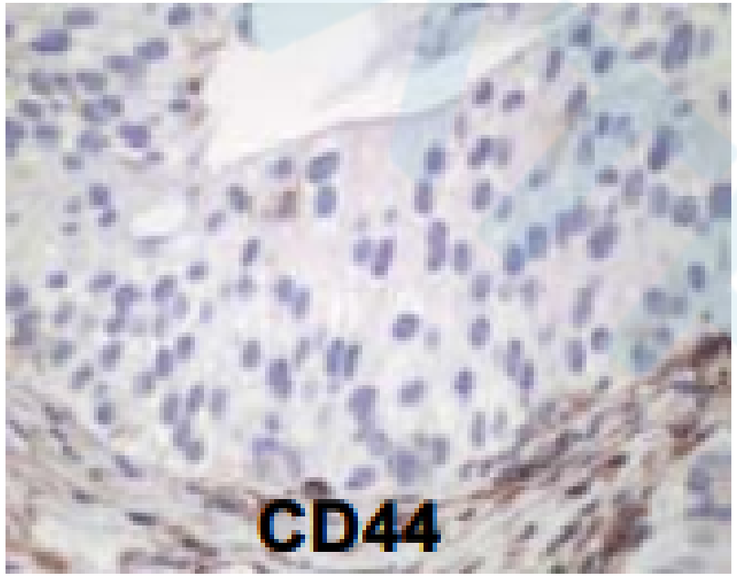
Cheng L, *et al* (2015). *Bladder Pathology*, Wiley-blackwell Publisher.

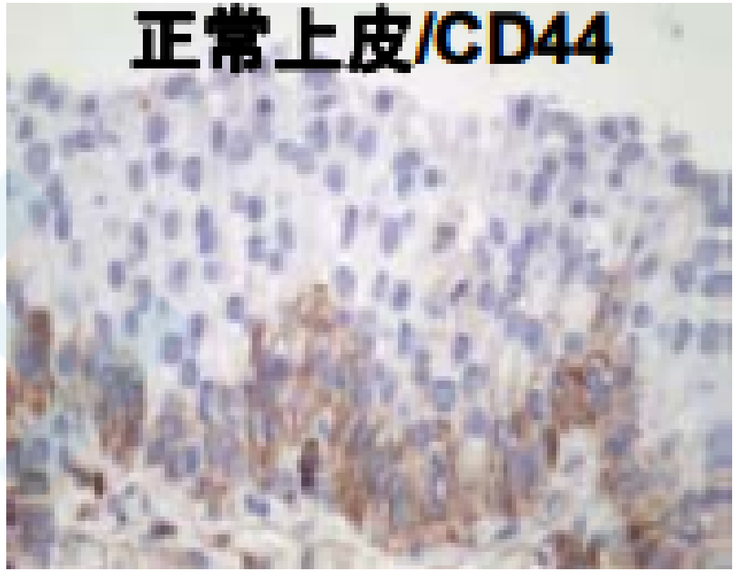



p53


CK20


Ki-67


CD44


正常上皮/CD44

OBJECTIVE

- The authers have encountered another distinct pattern of CIS showing polarized nuclei and cytoplasmic eosinophilia that resembles plasmacytoid differentiation to varying levels.
- Given the anecdotal experience with these flat lesions we regard as an unusual pattern of CIS, the authers sought to formally examine their histology, immunophenotype, and association with other forms of urothelial neoplasia.

MATERIALS AND METHODS

病例

bladder biopsies： 40 cases （ 2009 ~2018）

morphologic features

(1) abnormal architecture with cellular rounding

(2) moderately enlarged nuclei with eccentric nuclear localization

(3) dense eosinophilic (globular) cytoplasm

25 biopsies (from 23 patients) → plasmacytoid carcinoma in in situ (P-CIS)

MATERIALS AND METHODS

免疫组织化学

- **CK20** (Leica; clone PW31)
- **p53** (Leica; clone DO-1)
- **CD44** (Leica; clone MRQ-13)
- **e-cadherin** (Leica; clone 36B5)

Results

TABLE 1. Clinicopathologic Features of 23 Cases of P-CIS

Case No.	Sex	Age (y)	Prior Neoplasm	Concomitant Neoplasm	Therapy	Subsequent Neoplasm	Status (mo)
1	Male	63	None	None	BCG	P-CIS; pT1 nested on cystectomy	AWD (49)
2	Female	67	None	None	BCG	HG pTa	AWD (29)
3	Female	68	None	None	BCG	Typical CIS	AWD (28)
4	Male	73	None	None	BCG	Typical CIS and LG pTa	AWD (56)
5	Male	58	LG pTa; AUS	None	Mitomycin	Multiple LG pTa	ANED (66)
6	Male	64	None	HG pTa	BCG	None	ANED (40)
7	Male	64	HG pTa	None	BCG	None	ANED (49)
8	Male	66	pT2N1 renal pelvis; typical CIS	None	BCG	None	ANED (52)
9	Male	67	None	pT4a on TURP	BCG	pT4aN0 on cystectomy	AWD (41)
10	Male	69	Remote history pTa NOS	HG pTa; dysplasia	Mitomycin	positive urine cytology	AWD (26)
11	Male	69	Typical CIS	Typical CIS	BCG and mitomycin	P-CIS	ANED (26)
12	Male	73	None	pT2	BCG	pT2N0 at cystectomy; liver metastasis	AWD (115)
13	Male	73	Typical CIS	None	BCG	HG pTa; typical CIS; pT2N1 at cystectomy	AWD (16)
14	Male	74	LG pTa	None	BCG	None	ANED (15)
15	Male	75	HG urine cytology	Typical CIS	BCG	Positive urine cytology	ANED (7)
16	Male	76	LG pTa; HG urine cytology	None	BCG	Typical CIS	ANED (61)
17	Male	82	LG pTa	None	BCG	None	ANED (52)
18	Male	83	HG urine cytology; HG pTa	None	BCG	Atypical urine cytology	ANED (11)
19	Female	86	HG pT3 renal pelvis	None	BCG	Liver metastasis	DOD (29)
20	Male	86	HG and LG pTa	None	BCG	Typical CIS	ANED (28)
21	Male	87	Typical CIS; HG pT1	None	BCG	AUS	ANED (7)
22	Male	90	HG pTa	HG pTa	Surveillance	None	DUC; NED (24)
23	Male	91	HG pT1 and pTa; typical CIS	None	Surveillance	None	DUC; NED (39)

De novo P-CIS: cases 1–4.

ANED indicates alive no evidence of disease; AUS, atypia of uncertain significance; AWD, alive with disease; DOD, dead of disease; DUC, died unrelated cause; HG, high grade; LG, low grade; NED, no evidence of disease; TURP, transurethral resection of the prostate.

Patients

Total 23

mean age **74.1 years** (range: 58 to 91 y)

Sex 20 male / 3 female

- 13 prior urothelial neoplasia
- 6 hematuria
- 2 atypical urine cytology
- 2 bladder tumor

No patients had a prior history of bladder/prostate radiation therapy or BK viral infection.

RESULTS

➢ Prior Neoplasm

- Seven of the 23 patients (39%) had no prior urothelial neoplasia diagnosis, whereas the other 16 had a wide spectrum of prior urothelial neoplasms.
- 4 patients had a history of a traditional pattern of CIS in the urinary bladder

➢ Therapy

21 of 23 patients were subsequently treated with intravesical therapy --

18 BCG

3 mitomyci

RESULTS

➢ Subsequent Neoplasm

✓ 12 of 23 patients (52%) had subsequent recurrence/new occurrence:

3 progressed to metastatic disease

2 progressed to invasive disease without metastases

1 developed pTa high-grade disease

1 developed pTa low-grade disease

1 had pTa low-grade disease and conventional pattern CIS

3 had conventional pattern CIS, and 1 had only recurrent P-CIS

✓ the remaining 11 patients

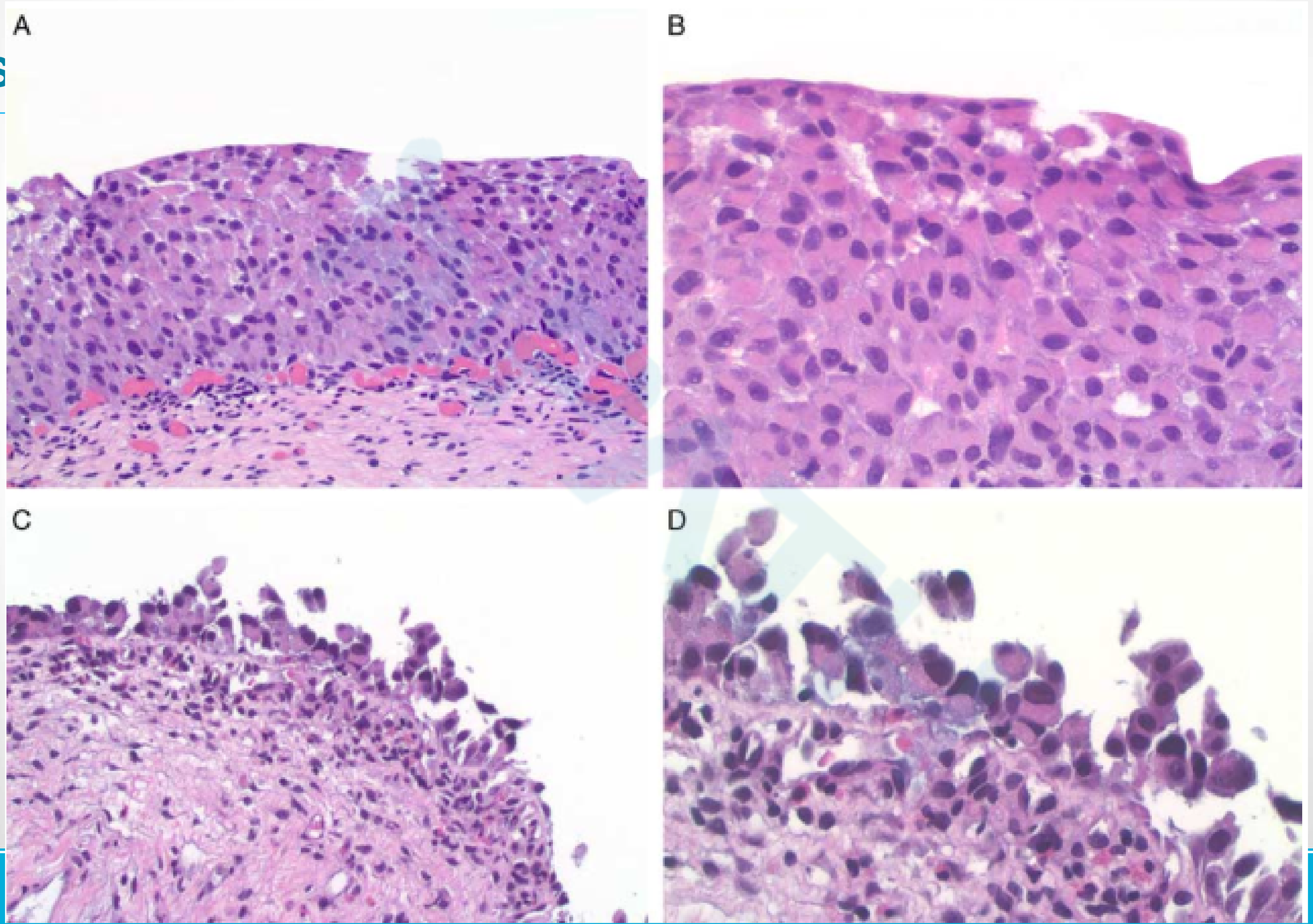
1 had urothelial atypia of uncertain significance on subsequent biopsy

3 patients had abnormal urine cytology alone at follow-up: 2 “positive for carcinoma” and 1 “atypical urothelial cells.”

RESULTS

- **Histology --“abnormal architecture”**
  - varying degrees of cellular disarray
  - loss of perpendicular nuclear orientation to the basement membrane
  - Admixed fibrovascular cores or areas of thickened heaped-up urothelium overlying early fibrovascular core formation (tenting) were absent.
  - These cytoplasmic globules lacked vacuolization, mucin, or lumen formation. All cases lacked significant admixed inflammatory cells.

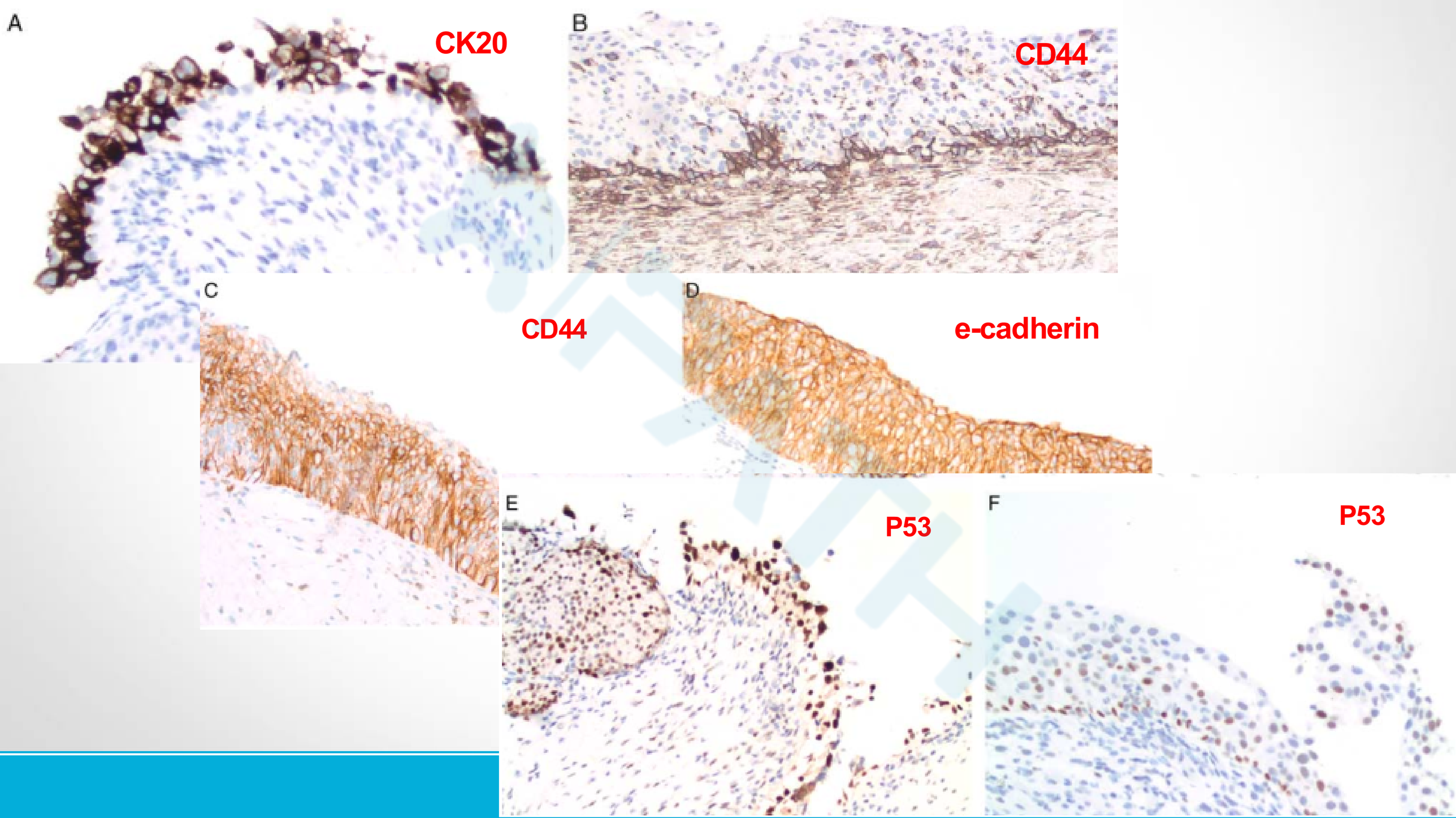
RES



RESULTS

➢ Immunohistochemistry

- CK20 was positive in 23 of 24 (96%) cases .
- An abnormal P53 reactivity pattern (positive or “null phenotype”) was seen in 7 of 19 (37%) cases.
- Absence of CD44 staining in the lesional cells was identified in 15 of 24 (63%) cases.
- Of the 9 cases that showed at least some CD44 staining in the lesional cell population, 89% (8/9) had concurrent CK20 reactivity.
- All tested cases (18/18) showed retained membranous e-cadherin staining.


A
CK20
B
CD44
C
CD44
D
e-cadherin
E
P53
F
P53

DISCUSSION

- resembling plasmacytoid differentiation
- characterized by abnormal architecture with cellular rounding
- moderately enlarged nuclei with eccentric nuclear localization
- dense eosinophilic (globular) cytoplasm

Histology

P-CIS

- CK20 has a similar sensitivity compared with conventional patterns of CIS.
  CK20 appears to be the most sensitive and specific marker when considering P-CIS.

immunohistochemistry

DISCUSSION

- Many non-neoplastic lesions should be considered
  - ✓ Intravesical BCG or mitomycin therapy can cause urothelial alterations.
  - ✓ Radiation can also cause changes overlapping with P-CIS
  - ✓ Viral cytopathic effect
- The nuclear enlargement of P-CIS is at the lower end of the reported range reported for CIS relative to lymphocytes nuclei,therefore, it overlaps significantly more with urothelial dysplasia and reactive atypia.

CONCLUSION

- The histologic features, the immunophenotype, the association with other forms of urothelial neoplasia,and the risk of recurrence and progression in de novo lesions support that the flat urothelial lesions described herein represent a novel pattern of CIS .
- These histologic features may be more subtle than in other patterns of CIS and should be carefully distinguished from therapy-related/reactive changes.

Thanks for your attention