Am J Surg Pathol 2018;42:1286–1296

ORIGINAL ARTICLE

Prostatic Adenocarcinoma With Focal Pleomorphic Giant Cell Features

A Series of 30 Cases

Abdullah M. Alharbi, MD, Angelo M. De Marzo, MD, PhD, Jessica L. Hicks, MSc, Tamara L. Lotan, MD, and Jonathan I. Epstein, MD

汇报人：刘灵
指导老师：李侠

2004

Epithelial tumours

Glandular neoplasms

Adenocarcinoma (acinar)	8140/3[1]
Atrophic	
Pseudohyperplastic	
Foamy	
Colloid	8480/3
Signet ring	8490/3
Oncocytic	8290/3
Lymphoepithelioma-like	8082/3
Carcinoma with spindle cell differentiation (carcinosarcoma, sarcomatoid carcinoma)	8572/3
Prostatic intraepithelial neoplasia (PIN)	
Prostatic intraepithelial neoplasia, grade III (PIN III)	8148/2
Ductal adenocarcinoma	8500/3
Cribriform	8201/3
Papillary	8260/3
Solid	8230/3

Urothelial tumours

Urothelial carcinoma	8120/3

Squamous tumours

Adenosquamous carcinoma	8560/3
Squamous cell carcinoma	8070/3

Basal cell tumours

Basal cell adenoma	8147/0
Basal cell carcinoma	8147/3

2016

Epithelial tumours

Glandular neoplasms

Acinar adenocarcinoma	8140/3
Atrophic	
Pseudohyperplastic	
Microcystic	
Foamy gland	
Mucinous (colloid)	8480/3
Signet ring–like cell	8490/3
Pleomorphic giant cell	
Sarcomatoid	8572/3
Prostatic intraepithelial neoplasia, high-grade	8148/2
Intraductal carcinoma	8500/2
Ductal adenocarcinoma	8500/3
Cribriform	8201/3
Papillary	8260/3
Solid	8230/3
Urothelial carcinoma	8120/3

Squamous neoplasms

Adenosquamous carcinoma	8560/3
Squamous cell carcinoma	8070/3
Basal cell carcinoma	8147/3

前列腺腺泡性腺癌　多形性巨细胞变异亚型
Acinar Adenocarcinoma, Pleomorphic Giant Cell Variant

临床特征： 为前列腺癌特别罕见的一种亚型，目前已报道的病例不足10例。患者平均年龄为75岁，大多数患者有普通型腺泡腺癌的激素或放疗治疗史。

组织学特点： 该亚型几乎总是和≥Gleasong 9的经典型腺癌混合存在，局部可见巨大、怪异的间变性瘤细胞，核多形性、核分裂象活跃。

预后： 差，侵袭性强，总体生存率不超过1年。

鉴别诊断： 膀胱尿路上皮癌累及前列腺。
前列腺肉瘤样癌

Arch Pathol Lab Med. 2005;129:683–685

Pleomorphic Giant Cell Carcinoma of the Prostate

Antonio Lopez-Beltran, MD, PhD; John N. Eble, MD; David G. Bostwick, MD

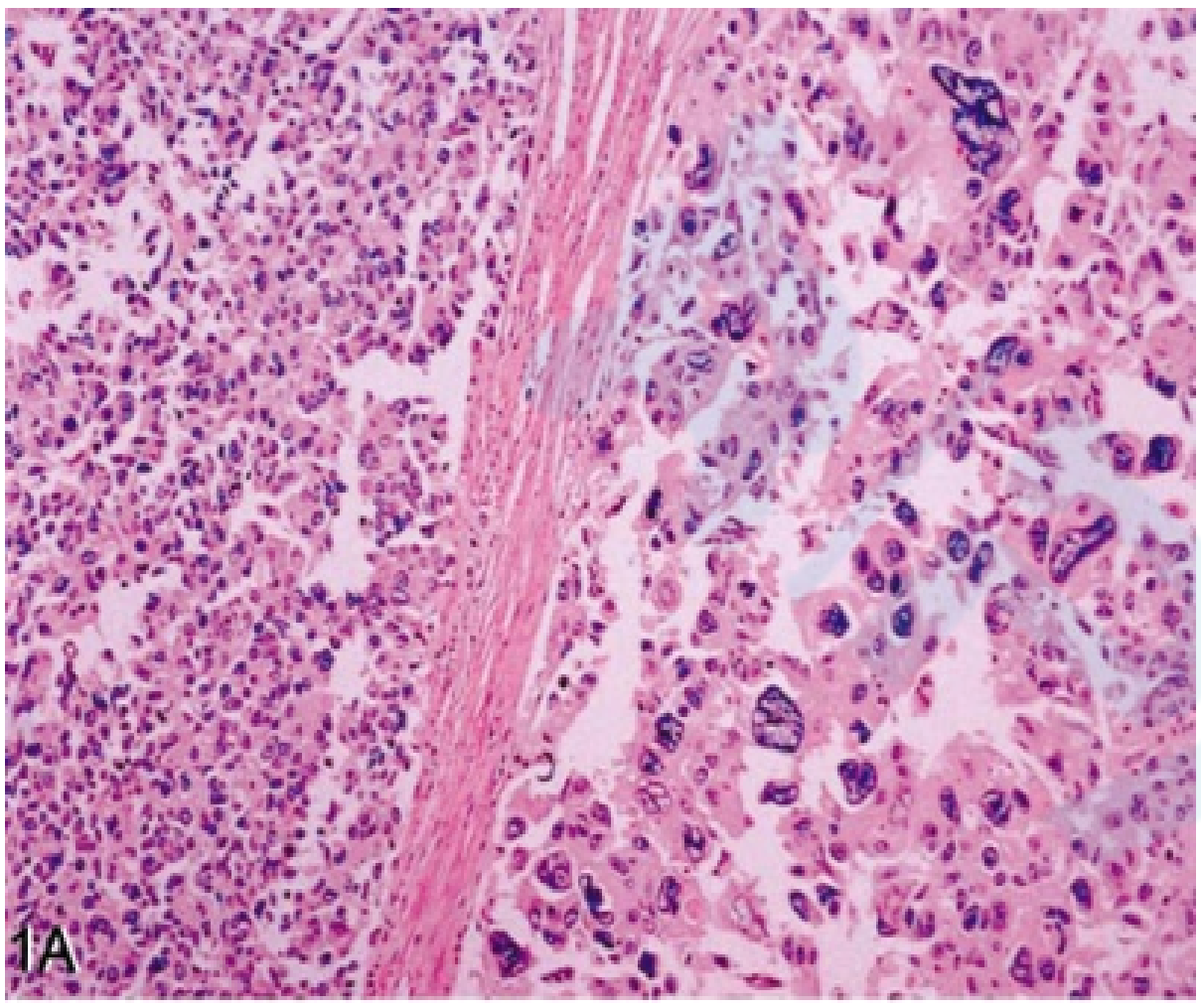
Am J Surg Pathol 2006;30:1254–1259

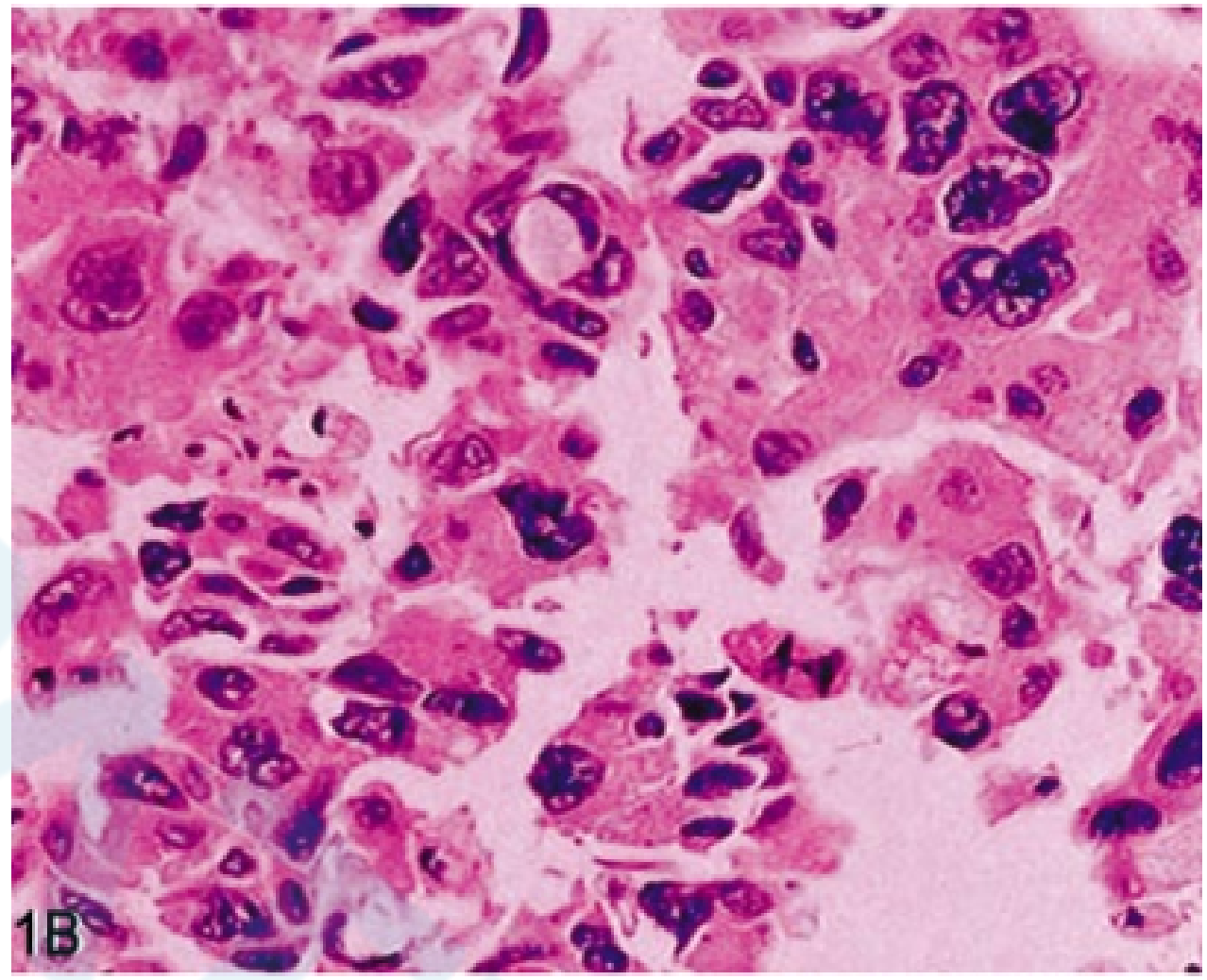
ORIGINAL ARTICLE

Pleomorphic Giant Cell Adenocarcinoma of the Prostate

Report of 6 Cases

Anil V. Parwani, MD, PhD, Mehsati Herawi, MD, PhD,† and Jonathan I. Epstein, MD†*





A, Giant cell carcinoma of the prostate composed of large cells with single or multiple bizarre nuclei and associated ordinary.
B, High-power view of giant cell carcinoma of the prostate.

Virchows Arch (2017) 471:133–136
DOI 10.1007/s00428-017-2134-y

BRIEF REPORT

HOXB13 a useful marker in pleomorphic giant cell adenocarcinoma of the prostate: a case report and review of the literature

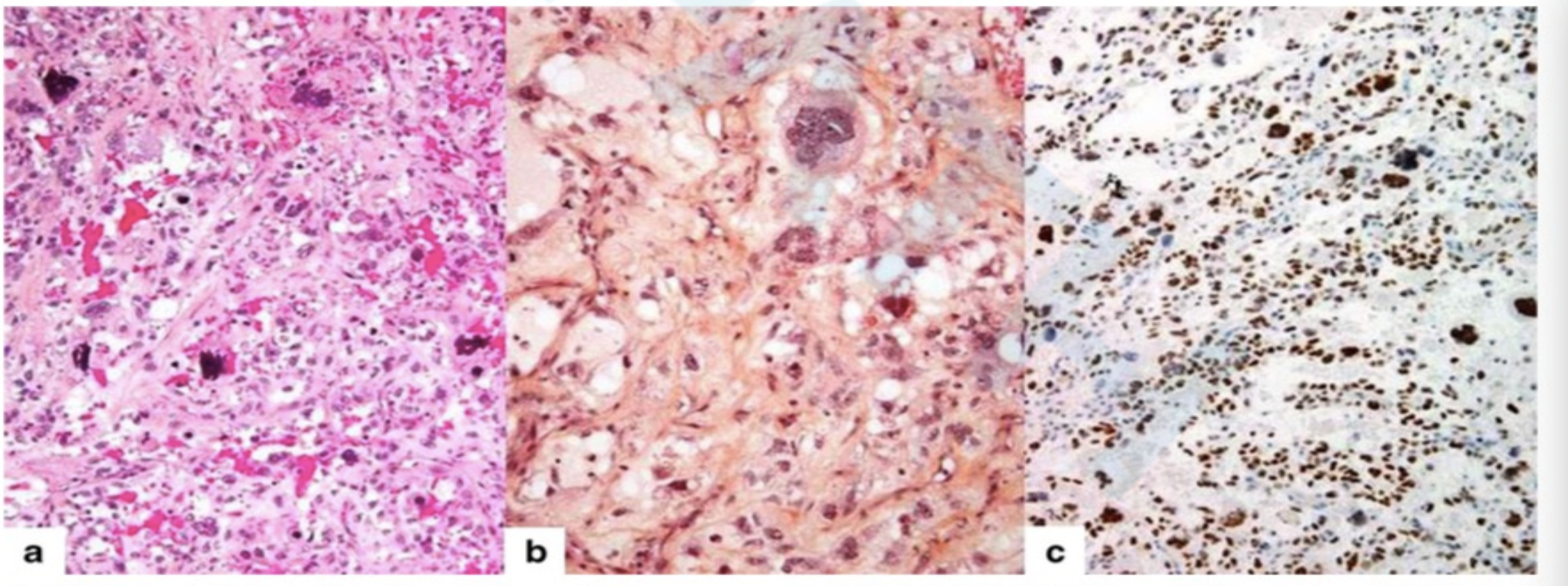


Fig. 1 Microscopic photographies. **a** Pleomorphic prostate cancer, numerous atypical mitosis (HES ×10). **b** Clear cell features with multilobulated giant nuclei (HES ×20). **c** Nuclear expression of HOXB13 in all tumor cells

研究目的

1. 扩大样本量进一步揭示该亚型的临床及病理特点

2. 评估鉴别诊断时抗体的应用及该亚型中的分子标记物的表达情况

材料和方法

- 收集2005-2018年，诊断为前列腺腺泡性腺癌，多形性巨细胞型病例30例，并评估死亡率。

- 其中10例进行免疫组化，评估免组染色阳性肿瘤细胞所占的百分比。

PSA、P501S、NKX3.1、HOXB13、GATA3、Ki-67、p53、PTEN、Cyclin-D1、ERG、AR。

结　果

TABLE 2. Demographic Information

Case	Age (y)	Grade	# Cores With Ca./Total Cores	# Cores Pleo./ Cores Ca.	% Involve of Ca. Cores	% Pleo. Cells in Affected Cores	Additional Features	Specimen	Prior Treatment	F/U (mo)
1.	88	5+5=10	100%	NA	NA	NA	PNI	Needle	None	Died (3)
2.	62	5+5=10	50%	NA	NA	NA		Needle	None	
3.	76	5+4=9	3/3	2/3	90	5	PNI, EPE	Needle	None	Died (8)
4.	73	5+5=10	5+5=10 involving 80% of the specimen	PNI	Needle	None	Died (5)			
5.	78	4+5=9	1/6	1/6	70	<5	PNI, EPE, LVI, ductal features	Needle	None	
6.	90	5+4=9	¼	1	10	5		Needle	None	Died (6)
7.	59	5+5=10	70%	NA	NA	Focal		Needle	None	Died (24)
8.	69	5+5=10	16/16	NA	65		PNI	Needle	None	
9.	61	4+3=7	6/12	5/12	10	1		Needle	None	
10.	83	5+5=10	10/10	10/10	95		PNI	Needle	None	
11.	79	5+5=10	6/9	2/6	55	5		Needle	None	
12.	67	4+5=9	6/12	6/6	55	<5	IDCP	Needle	None	
13.	59	4+5=9	NA	NA	NA			Needle	None	
14.	51	5+5=10		NA	NA	NA	Bladder neck, SVI	TURP	Liver mets. at time of diagnosis	Died (17)
15.	86	5+5=10	55/125	22/55	65	5		TURP	None	
16.	73	5+5=10	100%	NA	100	<5		TURP	H/O PCa. with RT	Died (60)
17.	82	5+5=10	19/37	16/19	90	5		TURP	H/O PCa. With HT	Died (10)
18.	43	4+5=9	96/96	39/96	90	5	PNI	TURP	Recurrent PCa. in bladder	
19.	80	5+5=10	5/5	3/5	70	<5	IDCP	TURP	None	
20.	87	5+5=10	44/45	16/44	95	<5		TURP	None	
21.	86	5+5=10	35/40	12/35	95	5		TURB	Recently misdiagnosed as UC with chemotherapy	Died (23)
22.	79	5+5=10	NA	NA	NA	NA		TURB	H/O PCa. with RT & HT and now bone mets.	Died (4)
23.	79	5+4=9	10/10	6/10	100	5	LVI, Bladder neck	TURB	None	
24.	69	5+5=10	115/120	35/115	95	5	LVI	TURB	None	
25.	70	5+5=10	NA	NA	NA	Rare		Bladder bx.	H/O PCa.	Died (4)
26.	77	5+5=10	NA	NA	NA	NA		Bladder bx.	H/O PCa. with RP and RT	
27.	82	5+5=10	90%	20%	90	20		Bladder bx.	H/O PCa. with mets.	
28.	74	4+5=9	1/15	1	7	1		PU	None	
29.	39	5+5=10	NA	NA	NA	<1	Extensive LVI, + margins, SVI, EPE	RP	None	
30.	75	NA	NA	NA	NA	<5		Orchiectomy	Met. to testis at time of diagnosis	

Bx. indicates biopsy; Ca., carcinoma; EPE, extraprostatic extension; F/U, follow-up; H/O, history of; HT, hormone therapy; IDCP, intraductal carcinoma of the prostate; LVI, lymphovascular invasion; mets., metastases; NA, not applicable; PCa., prostate cancer; Pleo., pleomorphic; PNI, perineural invasion; PU, prostatic urethra; RP, radical prostatectomy; RT, radiation therapy; SVI, seminal vesicle invasion.

TABLE 3. Clinicopathologic Features

			Miscellaneous			
Needle (N = 13)	**TURP (N = 7)**	**Radical Prostatectomy (N = 1)**	**TURB (N = 5)**	**Bladder Bx. (N = 2)**	**PU (N = 1)**	**Orchiectomy (N = 1)**
No. cores/chips involved by cancer						
Mean: 6 cores	Mean: 43.8 chips		Mean: 53.3 chips			
Median: 6 cores	Median: 44 chips	NA	Median: 35 chips	NA	1 core	NA
Range: 1-16 cores	Range: 19-96 chips		Range: 10-115 chips			
Overall extent of carcinoma						
Mean: 55%	Mean: 85%	70%	Mean: 95%	NA	7%	80%
Median: 65%	Median: 90%		Median: 95%			
Range: 10%-95%	Range: 50%-95%		Range: 90%-100%			
% of pleomorphic component						
Mean: 3.2%	Mean: 3%		Mean: 8.75%			
Median: 5%	Median: 5%	1%	Median: 5%	NA	1%	< 5%
Range: 1%-5%	Range: <5%-5%		Range: 5%-20%			
Grade						
5+5 = 10 (n = 7)	5+5 = 10 (n = 6)	5+5 = 10 (n = 1)	5+5 = 10 (n = 4)	5+5 = 10 (n = 2)	4+5 = 9 (n = 1)	5+5 = 10 (n = 1)
5+4 = 9 (n = 2)	4+5 = 9 (n = 1)		5+4 = 9 (n = 1)			
4+5 = 9 (n = 3)						
4+3 = 7 (n = 1)						
Additional features						
PNI (n = 6)	PNI (n = 1)	LVI (n = 1)	LVI (n = 2)			
LVI (n = 1)	SVI (n = 1)	EPE (n = 1)				
EPE (n = 2)	IDCP (n = 1)	SVI (n = 1)				
IDCP (n = 1)		+Margins (n = 1)				
Ductal features (n = 1)						

EPE indicates extraprostatic extension; IDCP, intraductal carcinoma of the prostate; LVI, lymphovascular invasion; NA, not applicable; PNI, perineural invasion; PU, prostate urethra biopsy; SVI, seminal vesicle invasion.

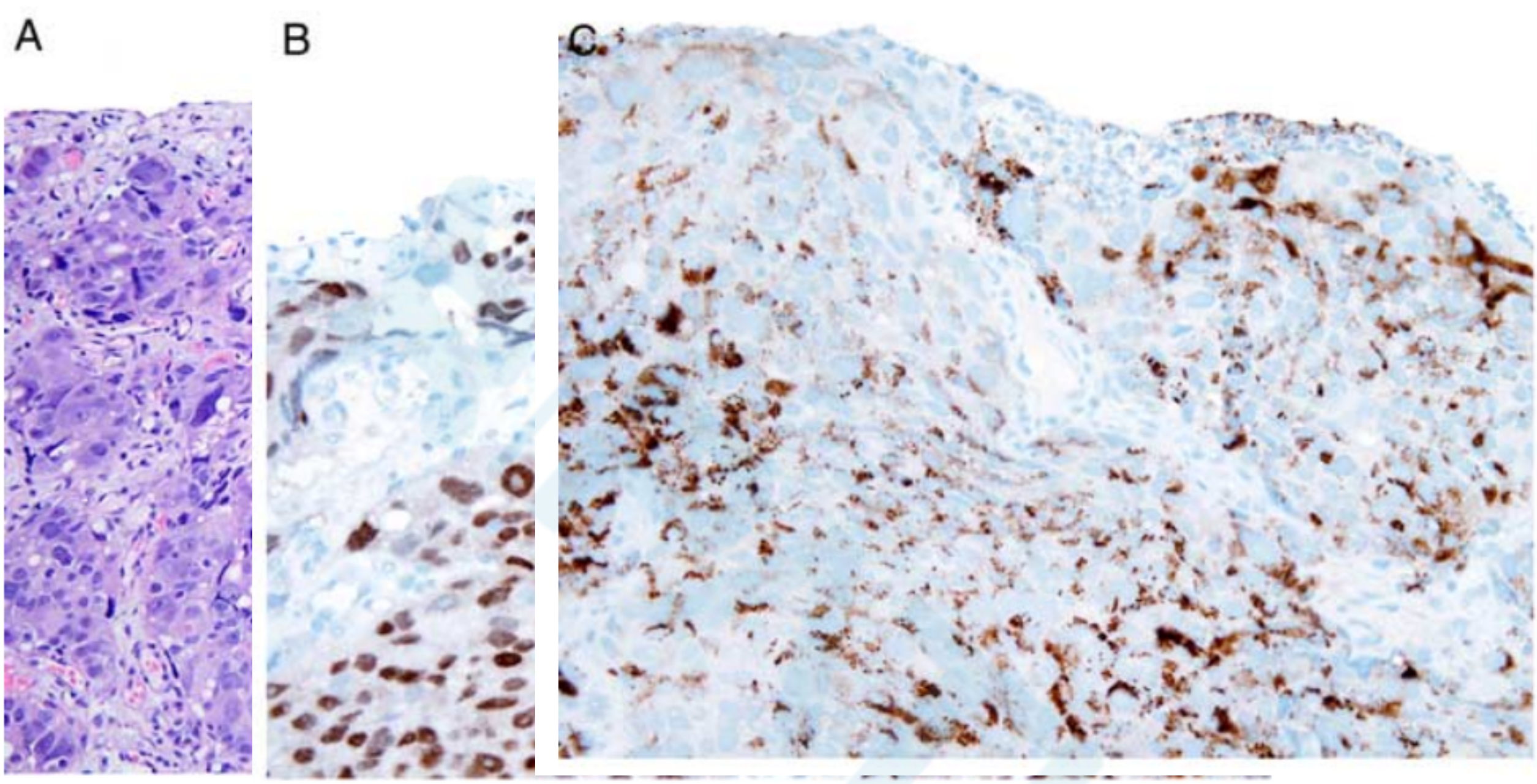


FIGURE 1. A, Typical histology of pleomorphic giant cell adenocarcinoma composed of large cells with single or multiple bizarre nuclei undermining denuded flattened urothelium. B–F, Are from the same case with similar staining in the pleomorphic and usual carcinoma components; diffuse NKX3.1 immunostaining (B); diffuse P501S immunoreactivity (C);

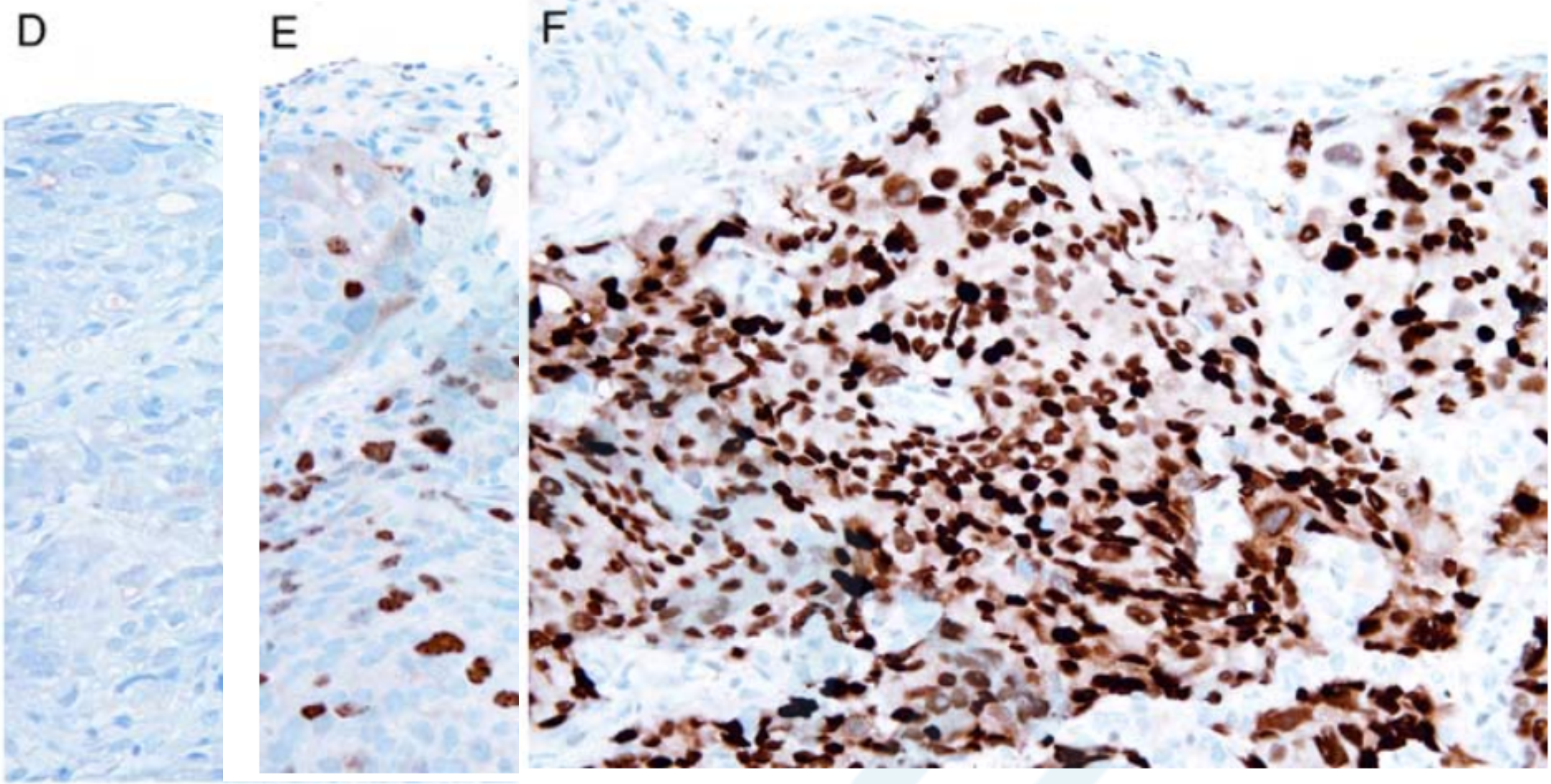


FIGURE 1. focal PSA staining (D); Ki-67proliferation rate of ~ 20% (E);diffuse androgen receptor positivity (F).

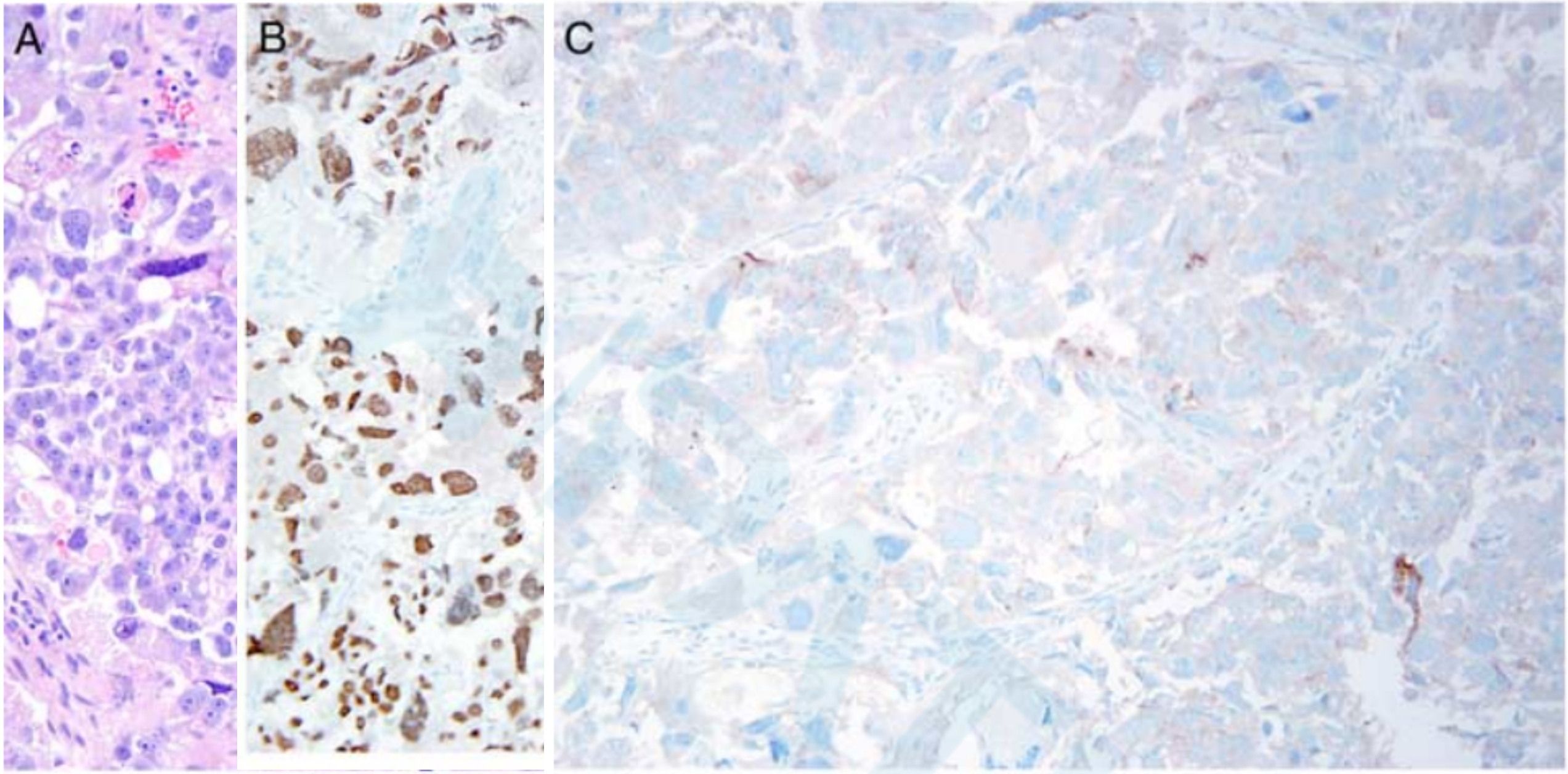


FIGURE 2. A, Pleomorphic giant cell adenocarcinoma with atypical mitotic figure (arrow).
B, Same cases as (A) with NKX3.1 immunoreactivity in 100% of usual and 90% of pleomorphic components.
C, Same case as (A) with 5% staining for p501S in both components. PSA (not shown) revealed immunopositivity in only rare usual and pleomorphic prostate adenocarcinoma cells.

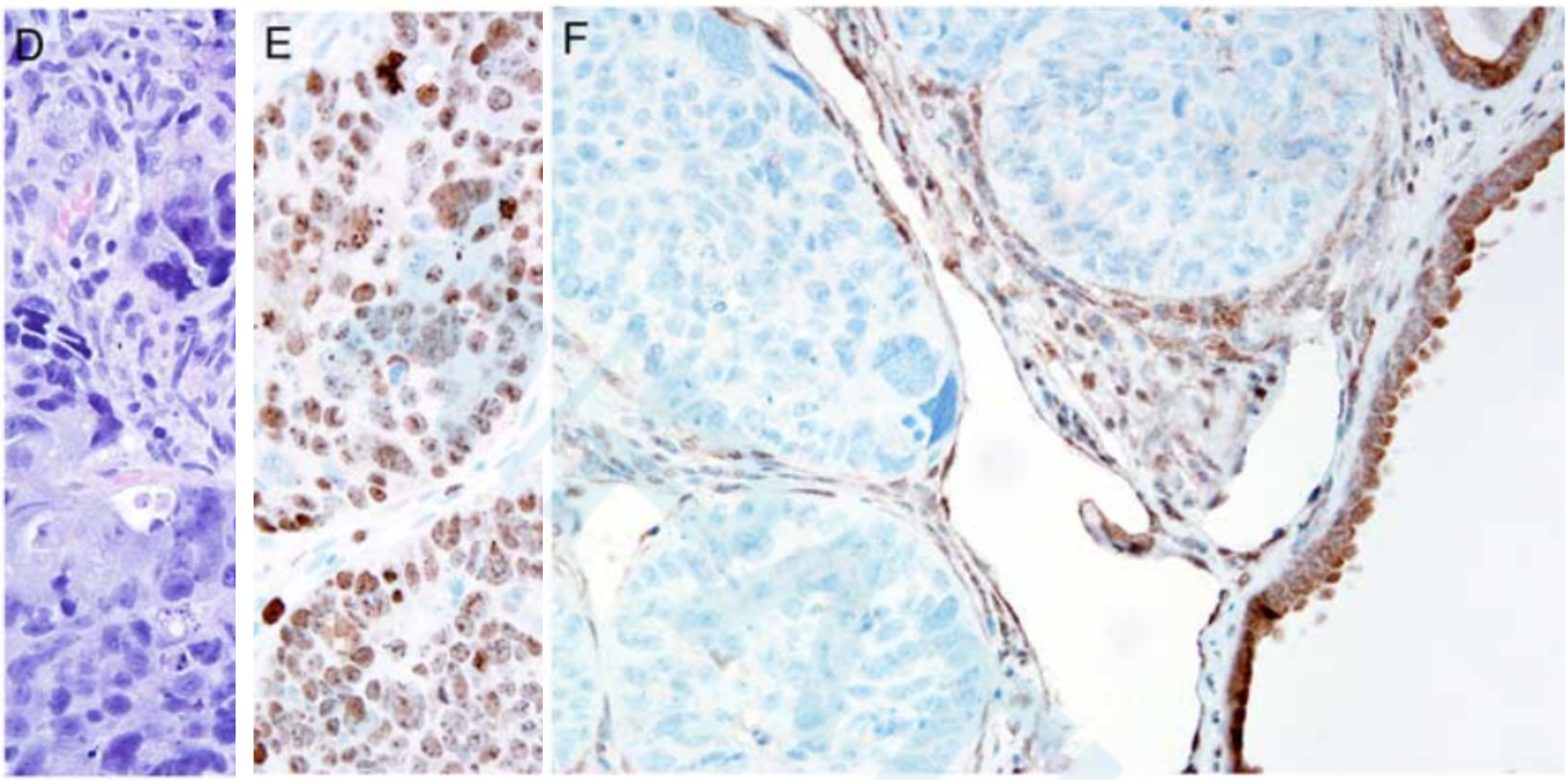


FIGURE 2. D, Pleomorphic giant cell adenocarcinoma.
E, Same case as (D) with Ki-67 in almost all cells including pleomorphic giant cells. This was the case with the highest Ki-67 proliferation rate;
F, same case as (2D) with loss of PTEN immunoreactivity in both usual and pleomorphic components.

TABLE 4. Imunohistochemical Profile of 10 Cases of Pleomorphic Giant Cell Carcinoma

% Positive Tumor	NKX3.1 (%)		PSA (%)		P501S (%)		GATA3		Ki-67 (%)		p53		Cyclin-D1		PTEN		ERG		AR		HOXB13	
Cells/Case	U	P	U	P	U	P	U	P	U	P	U	P	U	P	U	P	U	P	U	P	U	P
1.	30	–	<5	–	<5	–	+	F	20	30	–	–	R	R	R	L	–	–	+	–	30	–
2.	80	50	70	50	60	10	–	–	10	<5	+	+	L	L	L	L	–	–	+	+	80	80
3.	100	50	<5	<5	–	–	–	–	20	20	+	+	R	R	L	L	–	–	+	+	30	30
4.	100	90	R+	R+	<5	<5	–	–	<5	<5	–	–	R	R	L	L	–	–	+	+	50	5
5.	100	100	<10	–	50	5	–	–	30	30	+	+	R	R	L	L	–	–	+	+	80	50
6.	<5	–	<5	–	<5	–	–	–	90	90	–	–	L	L	L	L	–	–	F	–	NA	NA
7.	90	90	80	5	90	90	–	–	20	20	–	–	R	R	L	L	–	–	+	+	80	1
8.	60	90	–	5	–	90	–	–	20	80	–	–	L	L	L	L	–	–	+	+	NA	NA
9.	80	5	–	–	7	1	W	W	70	30	+	+	R	R	L	L	–	–	+	+	70	1
10.	80	80	–	–	–	–	–	-	20	50	–	–	R	R	L	L	–	–	+	+	10	1

– indicates negative; +, positive; F, focal; L, lost; NA, unstained slides and/or blocks not available; P, pleomorphic giant cell component; R, retained; U, usual carcinoma component; W, weak.

TABLE 5. Immunohistochemistry Usual Prostate Adenocarcinoma and Pleomorphic Giant Cell Prostatic Adenocarcinoma

% Positive Tumor Cells/Case	NKX3.1 (%)		PSA (%)		P501S (%)		HOXB13 (%)		Ki-67 (%)	
	U	P	U	P	U	P	U	P	U	P
Mean	72.5	69	25	13.6	40	33	53.7	24	30.5	36
Median	80	85	5	5	50	7.5	60	5	20	30
Range	5-100	5-100	1-80	1-50	1-90	1-90	10-80	1-80	5-90	5-90

P indicates pleomorphic giant cell component; U, usual carcinoma component.

临床随访

- 其中7例都有前列腺癌的病史，并进行了多种治疗的患者，4/7（57%）在诊断复发性前列腺腺癌并伴有多形性巨细胞特征后7个月内死亡.
- 余23例却无相关病史，19例随访＞1年，7/19（37%）在诊断后8个月内死亡.

讨论

- PSA、PSAP是目前最常用的前列腺特异性标志物，在多形性巨细胞型的前列腺腺癌中敏感性降低。

- 在当前研究中，未证实HOXB13在多形性巨细胞型腺癌中较NKX3.1更有优势。

- 本研究显示：NKX3.1是更为敏感和特异的低分化前列腺癌标志物，可以更好的用于鉴别低分化前列腺癌和尿路上皮癌。

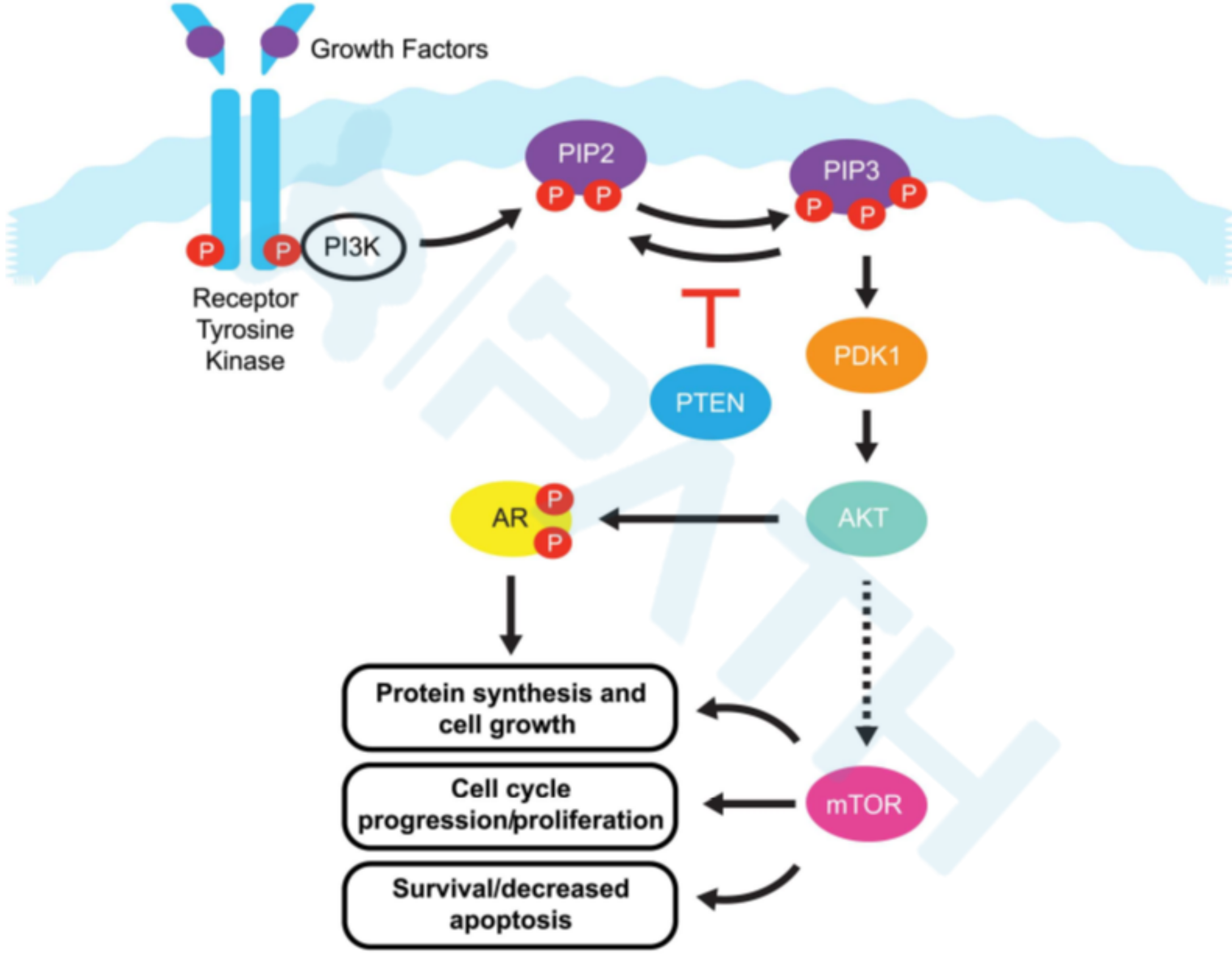
- GATA3在前列腺癌会出现少见的阳性，因此进行一组抗体鉴别高级别尿路上皮癌和低分化前列腺腺癌是十分有必要的。

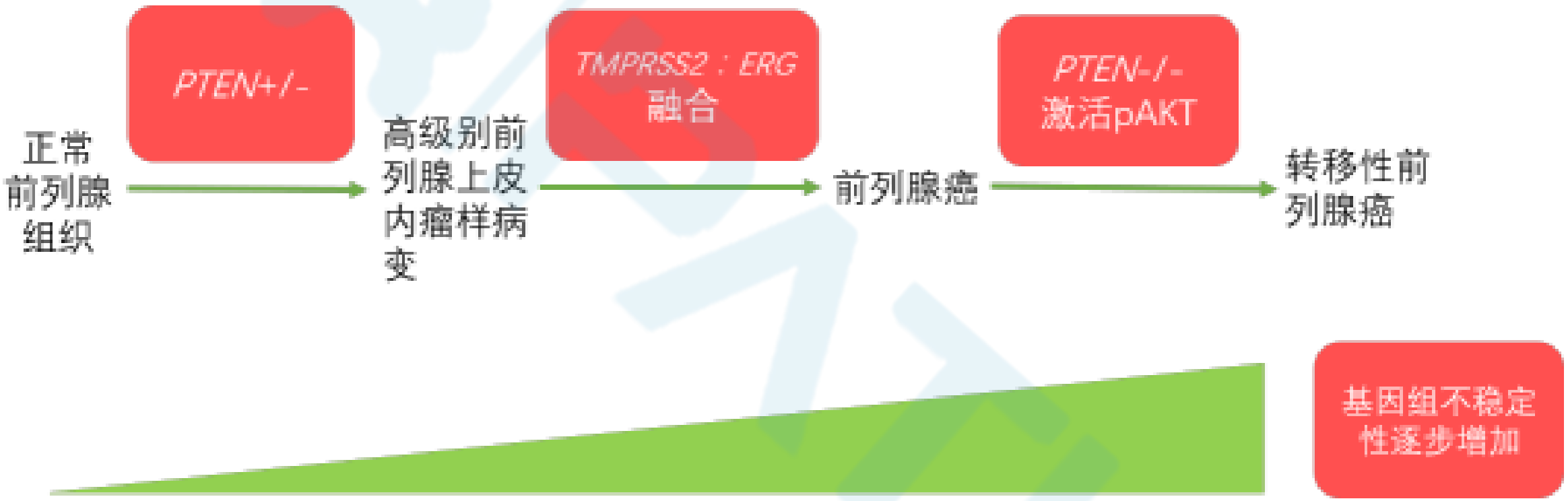
- PTEN的缺失及ERG蛋白的阴性表达，提示不同的基因组驱动途径可能是多形性巨细胞型腺癌发生的基础。并且PTEN的缺失可能是该亚型发生的关键驱动点。

- P53 、PTEN 及cyclin-D1状态在普通型前列腺癌和多形性巨细胞型中状态的一致性，强烈提示两种肿瘤形态起源具有同源性。

- 雄激素受体和NKX3.1在经典型及多形性巨细胞型腺癌中的阳性提示抗雄激素治疗患者可能会获益。

谢 谢！


Growth Factors
P
P
Receptor
Tyrosine
Kinase
PI3K
PIP2
P
P
PIP3
P
P
P
PTEN
PDK1
AR
P
P
AKT
Protein synthesis and
cell growth
Cell cycle
progression/proliferation
Survival/decreased
apoptosis
mTOR


PTEN+/-
TMPRSS2：ERG
融合
PTEN-/-
激活pAKT
正常
前列腺
组织
高级别前
列腺上皮
内瘤样病
变
前列腺癌
转移性前
列腺癌
基因组不稳定
性逐步增加