

Title	A case of prostatic duct adenocarcinoma: its clinical significance in comparison with typical acinar adenocarcinoma
Author(s)	Takazawa, Ryoji; Kawakami, Satoru; Yamamoto, Kohei; Kubo, Yuichi; Kageyama, Yukio; Kihara, Kazunori
Citation	泌尿器科紀要 (2008), 54(3): 243-247
Issue Date	2008-03
URL	<a href="http://hdl.handle.net/2433/71601">http://hdl.handle.net/2433/71601</a>
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

## A CASE OF PROSTATIC DUCT ADENOCARCINOMA : ITS CLINICAL SIGNIFICANCE IN COMPARISON WITH TYPICAL ACINAR ADENOCARCINOMA

Ryoji TAKAZAWA<sup>1</sup>, Satoru KAWAKAMI<sup>1</sup>, Kohei YAMAMOTO<sup>2</sup>,  
Yuichi KUBO<sup>1</sup>, Yukio KAGEYAMA<sup>1</sup> and Kazunori KIHARA<sup>1</sup>

<sup>1</sup>The Department of Urology, Tokyo Medical and Dental University Graduate School

<sup>2</sup>The Division of Comprehensive Pathology, Tokyo Medical and Dental University Graduate School

We report a case of prostatic duct adenocarcinoma treated with radical prostatectomy. Advanced pathological stage (pT3bN1) was beyond the prediction of the favorable preoperative parameters (cT1cN0, PSA 7.64 ng/ml). The main tumor of ductal adenocarcinoma was occupying the transitional zone and surrounded by scattered micro-foci of acinar adenocarcinoma. We identified coexistence of ductal and acinar adenocarcinoma cells side by side in the same gland. Pure ductal cancer cells were detected in the metastasized lymph node without acinar cancer cells. Strong staining of PSA and loss of p63 expression by both types of adenocarcinoma cells were confirmed immunohistochemically. We discuss the clinical significance of prostatic duct adenocarcinoma in comparison with typical acinar adenocarcinoma.

(Hinyokika Kyo 54 : 243-247, 2008)

**Key words :** Prostate, Ductal adenocarcinoma, p63, Immunohistochemistry

### INTRODUCTION

Ductal adenocarcinoma of the prostate is uncommon<sup>1)</sup>. Pathologically, whether ductal adenocarcinoma is distinct from typical acinar adenocarcinoma is still debatable<sup>2)</sup>. Clinically, however, ductal adenocarcinoma has been characterized in several essential aspects including small increment of PSA elevation relative to the tumor volume, difficulty to be diagnosed as a palpable tumor and difficulty to be detected by routine prostate biopsy<sup>3)</sup>.

The p63 is essential for normal prostatic development and a marker of normal prostatic basal cells<sup>4)</sup>. Because p63 is not expressed in typical acinar adenocarcinoma<sup>5)</sup>, p63 immunohistochemistry is a valuable tool for the differential diagnosis of benign versus malignant prostatic lesions. There have not been published figures demonstrating the loss of p63 expression in prostatic duct adenocarcinoma.

### CASE REPORT

A 76-year-old Japanese man presented with a 6-month history of bladder outlet obstruction. Digital rectal examination revealed a moderately enlarged prostate without findings suspicious for malignancy. The serum PSA level was 7.64 ng/ml (Tandem R). Extended 26-core prostate biopsy revealed papillary fronds of adenocarcinoma that consisted of elongated and pseudostratified cells with prominent nucleoli, compatible with a prostatic ductal adenocarcinoma, in 18 cores<sup>6)</sup>. Small foci of cribriform acinar adenocarcinoma of Gleason grade 4 were also found in 2 cores. Computed tomography and bone scintigraphy demonstrated no apparent metastasis. The exophytic

growing tumor around the verumontanum was not detected by cystoscopy.

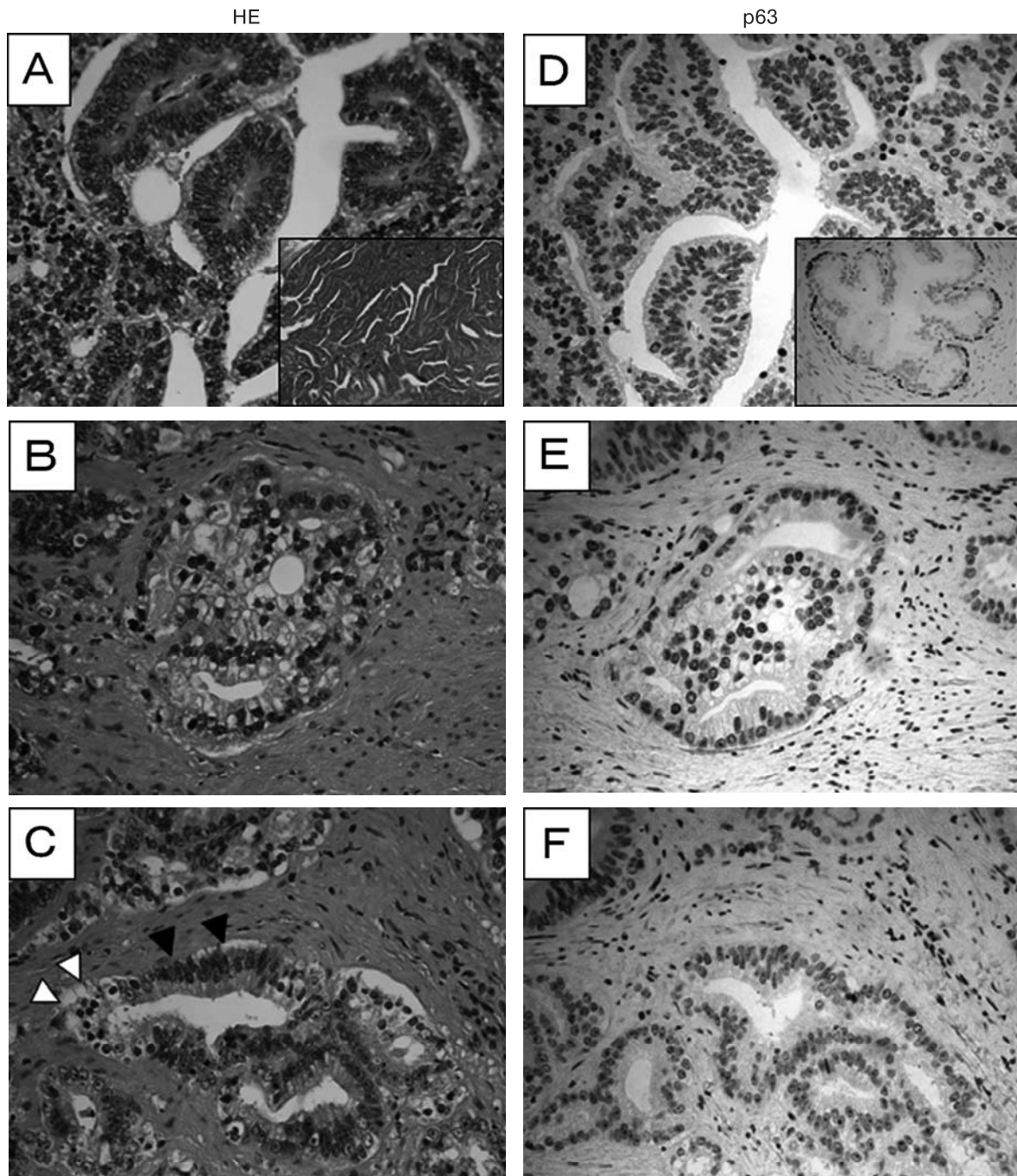
The patient underwent radical prostatectomy with limited pelvic lymph node dissection. Pathological evaluation of the prostatectomy specimen revealed a prostatic ductal adenocarcinoma invading to the right seminal vesicle and metastasized to a right pelvic lymph node, but without capsular penetration (pT3bN1). A 36 cc main tumor, ductal adenocarcinoma, was located in the transitional zone and surrounded with scattered micro-foci of acinar adenocarcinoma. We identified several glands where cuboidal acinar cancer cells and tall columnar ductal cancer cells coexisted side by side. Ductal adenocarcinoma cells were strongly positive for PSA, but completely negative for 34β12E and p63 (Fig. 1). Pure ductal cancer cells were detected in the metastasized lymph node without acinar cancer cells (Fig. 2).

Since postoperative PSA failed to fall to an undetectable level (0.473 ng/ml at the nadir), androgen ablation therapy with luteinizing hormone-releasing hormone analog was commenced. Disease has not progressed for 4 years.

### DISCUSSION

We herein report a case of prostatic duct adenocarcinoma diagnosed by needle biopsy preoperatively and treated with radical prostatectomy. We identified centrally located ductal adenocarcinoma with a peripherally located small acinar adenocarcinoma. Strong staining of PSA and loss of p63 expression by both types of adenocarcinoma cells were confirmed immunohistochemically.

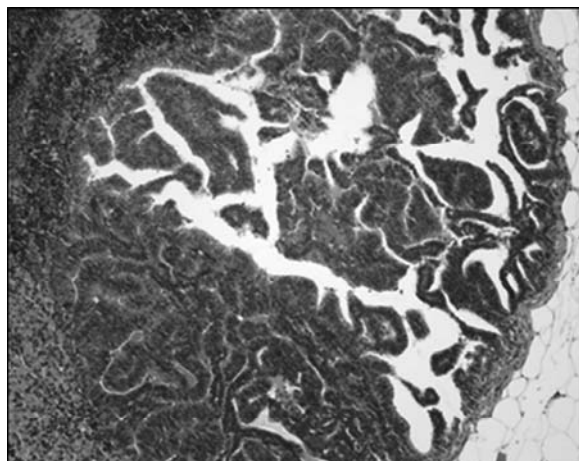
If ductal adenocarcinomas are equivalent to Gleason



**Fig. 1.** HE staining of the prostatectomy specimen. (A) Ductal adenocarcinoma with irregular chromatin and prominent nucleoli. Low power view in the inset ( $\times 40$ ). (B) Small foci of cribriform acinar adenocarcinoma of Gleason grade 4. (C) Coexistence of cuboidal acinar cancer cells (white arrowheads) and tall columnar ductal cancer cells (black arrowheads) in a same gland. p63 immunohistochemistry using a mouse antihuman p63 monoclonal antibody 4A4 on the serial sections of A, B and C. Basal cells of normal glands were p63 positive, serving as a positive control (the inset of panel D). p63 expression was completely lost in ductal adenocarcinoma (D), as well as acinar adenocarcinoma (E). (F) Both acinar and ductal adenocarcinoma cells shared loss of p63 expression. Original magnifications:  $\times 200$ .

score  $4 + 4 = 8$ , Partin nomogram (cT1c, PSA 6.1–10 ng/ml, biopsy Gleason score 8–10) predicts 34% extraprostatic extension, 12% seminal vesicle invasion and 3% lymph node metastasis<sup>7)</sup>. Despite this predicted pathological stage, the present case turned out to be advanced pT3bN1 disease, suggesting that the extent of ductal adenocarcinoma is hard to be estimated

from digital examination and serum PSA level. Prostatic duct adenocarcinoma should not be adapted to nomograms based on the data on typical acinar adenocarcinoma. This was consistent with the largest series reported to date by Epstein and his colleagues, in which 93% capsular penetration, 40% seminal vesicle invasion and 27% pelvic lymph node metastasis was



**Fig. 2.** HE staining of the metastasized lymph node specimen. Purely ductal cancer cells were detected without acinar cancer cells. Original magnifications :  $\times 100$ .

noted in 15 cases of ductal adenocarcinoma treated with radical prostatectomy<sup>8)</sup>. This study demonstrated that ductal adenocarcinomas have advanced in stage by the time of presentation and have a much higher short-term failure rate after radical prostatectomy compared to acinar carcinomas.

In most cases, the two components, acinar and ductal features, are intimately co-mingled. There was a well-known conflict whether prostatic duct adenocarcinoma is assumed as the sole component. Bock and Bostwick presented a series of peripheral zone cancers displaying ductal adenocarcinoma features<sup>2)</sup>. They reviewed 338 prostatectomy specimens with typical clinical and pathological features of acinar adenocarcinomas and identified ductal features in 17 specimens (5% of cases) in the peripheral zone without involving the periurethral region. They concluded that ductal adenocarcinoma results from spread of typical acinar adenocarcinoma into the large flexible periurethral ducts and stroma, having no unique histological features other than site of growth. However, this opinion may not be convincing enough to explain the fact that both two types of carcinoma are also seen in the metastasized lymph nodes. Epstein group reported that four of the 15 cases had pelvic lymph node metastases, in which two cases were a mixture of ductal and acinar carcinoma and two others were purely acinar and acinar pattern dominating<sup>8)</sup>. In the present case, purely ductal cancer cells metastasized to the pelvic lymph node. Therefore, prostatic duct adenocarcinoma may be the sole component that expresses an architectural pattern different from typical acinar adenocarcinoma, although they share several pathological characteristics as demonstrated in the previous and current cases. If an immunohistochemical technique which can distinguish periurethral duct and peripheral glands is explored, the conflict may be solved.

In the present case, we diagnosed by needle biopsy as

ductal adenocarcinoma occupying a larger proportion of the prostate than acinar adenocarcinoma of Gleason grade 4 preoperatively. The significance of ductal cancer features found on needle biopsies has been under discussion. Another study by the Epstein group reviewed 58 prostate needle biopsy cases with ductal adenocarcinoma<sup>9)</sup>. Cribriform or papillary structures or a mixture of the two patterns were seen in 86% of cases, while in the remaining cases discrete glands composed of tall columnar cells were present. Stromal fibrosis accompanied the ductal carcinoma in 67% of the cases. A coexisting acinar carcinoma component was identified in 48% of the biopsies. Six (10% of cases) had metastases at the time of diagnosis. Of the 20 tumors treated by radical prostatectomy, 63% had extraprostatic spread of tumor and 20% had positive margins. Two cases showed seminal vesicle invasion, but none had lymph node metastases. A shortened average time to progression was observed relative to a previous study group of men with acinar carcinoma. Consequently, prostatic duct adenocarcinoma seen on needle biopsy implies more advanced cancer with a shortened time to progression, so that careful clinical management should be demonstrated.

#### REFERENCES

- 1) Yang XJ, Cheng L, Helpap B, et al. : Ductal adenocarcinoma. In: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Edited by Eble JN, Sauter G, Epstein JI, et al. pp 199–201, IARC Press, Lyon, 2004
- 2) Bock BJ and Bostwick DG : Does prostatic ductal adenocarcinoma exist? *Am J Surg Pathol* **23** : 781–785, 1999
- 3) Millar EKA, Sharma NK and Lessells AM : Ductal (endometrioid) adenocarcinoma of the prostate: a clinicopathological study of 16 cases. *Histopathology* **29** : 11–19, 1996
- 4) Signoretti S, Waltregny D, Dilks J, et al. : p63 is a prostate basal cell marker and is required for prostate development. *Am J Pathol* **157** : 1769–1775, 2000
- 5) Parsons JK, Gage WR, Nelson WG, et al. : p63 protein expression is rare in prostate adenocarcinoma: implications for cancer diagnosis and carcinogenesis. *Urology* **58** : 619–624, 2001
- 6) Kawakami S, Hyochi N, Yonese J, et al. : Three-dimensional combination of transrectal and transperineal biopsies for efficient detection of stage T1c prostate cancer. *Int J Clin Oncol* **11** : 127–132, 2006
- 7) Makarov DV, Trock BJ, Humphreys EB, et al. : Updated nomogram to predict pathologic stage of prostate cancer given prostate specific antigen level, clinical stage, and biopsy Gleason score (Partin Tables) based on cases from 2000 to 2005. *Urology* **69** : 1095–1101, 2007

- 8) Christensen WN, Steinberg G, Walsh PC, et al. :  
Prostatic duct adenocarcinoma : findings at radical  
prostatectomy. *Cancer* **67** : 2118-2124, 1991
- 9) Brinker DA, Potter SR and Epstein JI : Ductal  
adenocarcinoma of the prostate diagnosed on needle  
biopsy : correlation with clinical and radical  
prostatectomy findings and progression. *Am J  
Surg Pathol* **23** : 1471-1479, 1999

(Received on May 16, 2006)  
(Accepted on August 16, 2007)

## 和文抄録

前立腺導管癌の1例：通常型腺癌とは区別する  
臨床的意義に関する考察高沢 亮治<sup>1</sup>, 川上 理<sup>1</sup>, 山本 浩平<sup>2</sup>久保 雄一<sup>1</sup>, 影山 幸雄<sup>1</sup>, 木原 和徳<sup>1</sup><sup>1</sup>東京医科歯科大学泌尿器科学教室, <sup>2</sup>同包括病理学教室

根治的前立腺全摘除術を施行した前立腺導管癌の1例を報告する。病理学的病期 (pT3bN1) は術前の臨床パラメータ (cT1cN0, PSA 7.64 ng/ml) に基づく予測よりも進行していた。主病変の導管型腺癌は移行領域を占拠し、その周囲に通常型腺癌の小病変が散在していた。また導管型腺癌細胞と通常型腺癌細胞とが隣接して同一腺管の中に共存する部位も認められた。リン

パ節転移部位には導管型腺癌細胞のみが認められた。さらに両型の腺癌細胞において PSA 蛋白の強発現と p63 蛋白の消失がみられることを免疫組織化学的に確認した。前立腺導管癌を通常型腺癌と区別する臨床的意義について考察した。

(泌尿紀要 54 : 243-247, 2008)