# EVALUATION OF PROSTATE BASAL CELL BY CYTOKERATIN 903 STAINING IN PROSTATIC ADENOCARCINOMA GLEASON SCORE 6

<sup>†</sup>Ramlan Nasution, <sup>1</sup>Suwandi Sugandi, <sup>1</sup>Aaron Tigor Sihombing, <sup>2</sup>Anglita Yantisetiasti, <sup>2</sup>Betthy S Hernowo.

<sup>1</sup>Department of Urology, Faculty of Medicine/Padjadjaran University, Hasan Sadikin Hospital, Bandung.

#### **ABSTRACT**

**Objective:** To evaluate the role of prostate basal cell staining in diagnosing Gleason score 6 prostate cancer. **Material & Method:** During research period, we collected 20 medical records and paraffin block specimens of Gleason score 6 prostatic adenocarcinoma patients. Specimens were taken from prostate needle biopsy. Demographic data and PSA level were extracted from medical records. Basal cells were detected by immunohistochemical staining for antikeratin 34 $\beta$ -E12 on paraffin block specimens analyzed by an experienced pathologist. Positive results suggest a benign lesion. **Results:** Mean age is  $70 \pm 6.5$  years. Mean prostate volume and PSA level was  $52\pm17$ cc and  $25\pm21$  ng/ml. Three specimens (15%) showed presence of basal cells on antikeratin  $34\beta$ -E12 staining, which indicated benign lesions. Leucocyturia was found in all patients of this group. There was a significant association between PSA level and antikeratin  $34\beta$ -E12 staining (p=0,03) **Conclusions:** 15 % cases of prostatic cancer Gleason score 6 still showed basal cell existence. Immunohistochemical staining of basal cell should be considered in suspicious cases of prostatic cancer.

**Keywords:** Gleason score 6 prostate cancer, basal cell, antikeratin 34β-E12.

Correspondence: Ramlan Nasution, c/o: Department of Urology, Faculty of Medicine/Padjadjaran University, Hasan Sadikin Hospital. Jl. Pasteur No. 38 Bandung. Phone: 022-2039141.

### INTRODUCTION

Histopathological examination is the gold standard in diagnosis of prostatic adenocarcinoma. Diagnosis of Gleason score 6 prostatic adenocarcinoma by needle biopsy is challenging. Approximately 11% of needle biopsy specimens stained with hematoxylin and eosin were misinterpreted as prostatic adenocarcinoma. Inadequately collected specimens may cause misinterpretation of the nucleus cytoplasm ratio and nucleoli of the prostate cells. Some benign lesions, such as adenosis, basal cell hyperplasia, atrophy, and prostatitis, may also mimic malignant growth. Detection of basal cells using cytokeratin 903 staining in suspicious lesions from needle biopsy is an invaluable method in diagnosing prostatic adenocarcinoma. The absence of basal cells in prostatic acini is an essential characteristic of prostatic adenocarcinoma. 1,2

Shah et al and Acimovic et al (2005) confirmed the existence of prostate basal cell in 1,1% prostate cancer specimens, using antikeratin  $34\beta$ -E12 staining. Therefore, basal cell staining is believed to increase specificity of histopathological evaluation of prostate cancer. <sup>4,5</sup>

#### **OBJECTIVE**

To evaluate the role of prostate basal cell staining in diagnosing Gleason score 6 prostate cancers.

#### **MATERIAL & METHOD**

We collected all specimens of Gleason score 6 prostatic adenocarcinoma taken by needle biopsy, within January 2009 - September 2009. Demographic data, PSA level, and prostate volume was extracted from medical records. Immunohistochemical staining to cytokeratin 903 was performed to all specimens

<sup>&</sup>lt;sup>2</sup>Department of Anatomical Pathology, Faculty of Medicine/Padjadjaran University, Hasan Sadikin Hospital, Bandung.

using antikeratin  $34\beta$ -E12. Positive result suggests a benign lesion. Histopathological evaluation was performed by an uropathologist.

False positive rate was evaluated using a 2x2 table. Mann-Whitney test was used to evaluate the association between PSA level and antikeratin  $34\beta$ -E12 staining. Statistical analysis was performed using SPSS 16.

## **RESULTS**

Mean age was  $70 \pm 6.5$  years. Mean prostate volume and PSA level was  $52 \pm 17$ cc and  $25 \pm 21$  ng/ml. Three specimens stained positive for cytokeratin 903, which indicates benign lesions. All patients also had leucocyturia on urinalysis.

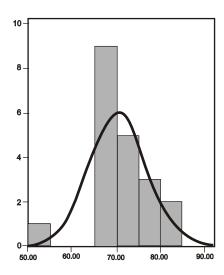


Figure 1. Age distribution.

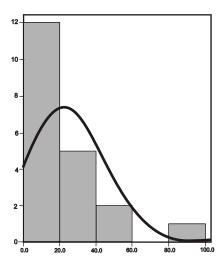


Figure 2. PSA level distribution.

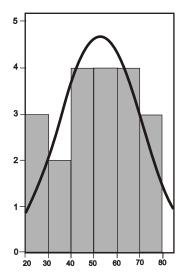


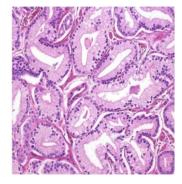
Figure 3. Prostate volume distribution.

A significant association was found between PSA level and antikeratin  $34\beta$ -E12 staining (p=0,04).

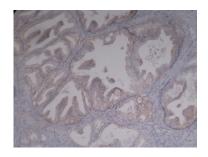
**Table 1.** Association between antikeratin 34β E12 staining and PSA level group.

		PSA group			Total
		ng/ml	10-20 ng/ml	>20 ng/ml	Total
Antikeratin 3β-E 12	(+)	0	0	3	3
		,0%	,0%	100,0%	100,0%
	(?)	2	10	5	17
		11,8%	58,8%	29,4%	100,0%
Total		2	10	8	20
		10,0%	50,0%	40,0%	100,0%

In multivariate analysis, a significant association between age, prostate volume, leucocyturia with antikeratin  $34\beta$ -E12 staining (p>0,05).



**Figure 4.** Gleason score 6 prostatic adenocarcinoma on HE staining.



**Figure 5.** Gleason score 6 prostatic adenocarcinoma on antikeratin 34β-E12 staining (positive staining).



**Figure 6.** Gleason score 6 prostatic adeno-carcinoma on antikeratin 34β-E12 staining (negative staining).

## **DISCUSSION**

Accurate diagnosis of prostatic adenocarcinoma is a crucial part in management. Histopathological appearance of prostate cancer may mimic benign lesions, therefore more specific examination is needed. Imunohistochemical examination can help a pathologist to identify prostate basal cells, an important marker in diagnosis of prostate cancer.

15% (3) cases of needle biopsy specimens were falsely diagnosed as Gleason score 6 prostatic carcinoma on HE staining. All patients had leucocyturia, which may be associated with infection of the urinary tract, including the prostate. Many evidence suggest that infection may mimic prostatic histopathological appearance, which may lead to misdiagnosis. Therefore, immunohistochemical staining of cytokeratin 903 in prostatic basal cell is needed to increase accuracy of Gleason score 6 prostate cancer diagnosis, especially in patients with leucocyturia.

## **CONCLUSION**

Presence of basal cells was demonstrated in 15% cases of Gleason score 6 prostate cancer.

Immunohistochemical staining of basal cell should be considered in suspicious cases of prostate cancer.

## REFERENCES

- 1. Hedrick L, Epstein J. Use of keratin 903 as an adjunct in diagnosis of prostate carcinoma. Am J Surg Pathol 1989; 13 (5): 389-96.
- Shin M, Fujita MQ, Yasunaga Y, Okuyuma A, Aozasa K.
   Utility of immunohistochemical detection of high molecular weight cytokeratin for differential diagnosis of proliferative conditions of the prostate.
- 3. Acimovic M, Govedararevic V, Mitrovic D. Correlation of high-molecular cytokeratin in tissue of prostatic cancer with Gleason score and PSA. Acta Chir Iugosl 2005; 52 (4): 45-9.
- Zhou M, Shah R, Shen R, Rubin MA. Basal cell cocktail (34βE12+p63) improves the detection of prostate basal cells. Am J Surg Pathol 2003; 27 (3): 365-71.
- Kozuka Y, Imai H, Yamanaka M, Kozuka M, Uchida K, Shiraishi T. Histopathological features of prostate cancer. Nippon Rinsho 2005; 63 (2): 231-6.
- Kumar, Abas, Fausto, Mitchell. The male genital system.
   In: Vogelstein B, Kinzler KW, editors. Basic Pathology.
   8<sup>th</sup> ed. New York: Elsevier; 2008. p. 675-700.
- 7. Kirk JW, Epstein J. The utility of basal cell-spesific anticytokeratin antibody in diagnosis of prostate cancer. Am J Surg Pathol 1995; 19 (3): 251-60.
- Oliai BR, Kahane H, Epstein J. Can basal cells be seen in adenocarcinoma of prostate. An immunohistochemical study using high molecular cytokeratin (clone 34βE12) antibody. Am J Surg Pathol 2002; 26 (9): 1151-60.
- 9. Gregor M. Clinical pathology of urologic tumors. India: Replika Press; 2007. p. 98-99.
- 10. Varma M, Jasani B. Diagnostic utility of immunohistochemistry in morphologically difficult prostate cancer: Review literature. Histopathology 2005; 47(1): 1-16
- 11. Hameed O, Humphrey PA. Immunochemistry in diagnostic surgical pathology of the prostate. Semin Diagn Pathol 2005; 22 (1): 88-104.
- 12. Helpap B. Prostatic adenocarcinoma-still a diagnostic problem. Verh Dtsch Ges Pathol 2004; 88: 152-7.
- 13.Zhou M, Magi-Galluzi C, Epstein J. Prostate basal cell lessions can be negative for basal cell keratins: A diagnostic pitfall. Anal Quant Cytol Histol 2006; 28 (3): 125-9.