Original Article

J Babol Univ Med Sci
23; 2021. P: 60-64

Evaluation of CD10 Expression and Its Relationship with Gleason Score in Prostatic Adenocarcinoma

A. Ghasemi (MD)[1], M. Jalali Nadoushan (MD)*[2], R. Sedaghat (MD)[2]

1.Faculty of Medicine, Shahed University, Tehran, I.R.Iran

2.Department of Pathology, Faculty of Medicine, Shahed University, Tehran, I.R.Iran

J Babol Univ Med Sci; 23; 2021; PP: 60-64

Received: Sep 9th 2019, Revised: Dec 16th 2019, Accepted: Jun 1st 2020.

ABSTRACT

BACKGROUND AND OBJECTIVE: CD10 is a zinc-dependent metalloproteinase that is associated with factors influencing the prognosis of some cancers. Prostatic adenocarcinoma is one of the most common cancers in men and Gleason grading is an important factor in its prognosis. The present study was conducted to investigate the relationship between immunohistochemical expression of CD10 and Gleason score as an indicator of prognosis in prostatic adenocarcinoma.

METHODS: In this cross-sectional study, 60 paraffin blocks of prostatic adenocarcinoma samples from patients referred to Shahid Mostafa Khomeini Hospital in Tehran from 2013 to 2017 were immunohistochemically stained according to CD10 marker. Information about Gleason score was obtained by observing stained slides by hematoxylin and eosin staining method. The percentage of CD10 positive tumor cells was determined by primary and secondary Gleason score and the relationship between CD10 expression and Gleason score was evaluated.

FINDINGS: The mean age of patients was 71±8.79 years. The percentage of CD10 expression varied from 5% to 62% in different samples. The mean percentages of CD10 expression in tumor cells in primary Gleason scores 2 to 5 were 10.75%, 16.16%, 35.20% and 44%, respectively and in secondary Gleason scores 2 to 5 were 10.38%, 17.08%, 38.19% and 53.5%, respectively ($p<0.001$).

CONCLUSION: According to the results of this study, the immunohistochemical marker CD10 has a variable expression in prostatic adenocarcinoma and its increased expression is associated with an increase in the microscopic Gleason score of tumor as a factor influencing the prognosis.

KEY WORDS: *Prostatic Adenocarcinoma, Gleason Grading System, CD10.*

Please cite this article as follows:

Ghasemi A, Jalali Nadoushan M, Sedaghat R. Evaluation of CD10 Expression and Its Relationship with Gleason Score in Prostatic Adenocarcinoma. J Babol Univ Med Sci. 2021;23:60-4.

***Corresponding Author: M. Jalali Nadoushan (MD)**
Address: Department of Pathology, Medical Faculty, Shahed University, Tehran, I.R.Iran
Tel: +98 21 88966131
E-mail: jalali@shahed.ac.ir

[DOR: 20.1001.1.15614107.1400.23.1.9.8]
[DOI: 10.22088/jbums.23.1.60]

Introduction

Prostatic adenocarcinoma is the most common cancer in men and the second leading cause of death after lung cancer in many countries around the world, and accounts for about 20% of all cancers in men in the United States (1). Prostate cancer grading is an important factor in determining the prognosis and choosing the appropriate treatment. One of the histological methods of tumor grading is Gleason grading system. This system is based on the glandular differentiation pattern of the tumor at relatively low magnification and cell characteristics do not play a role in it. There are two patterns including the primary pattern (the pattern that includes most of tumor view) and the secondary pattern (the second dominant view of the tumor), each marked with a score of 1-5 (2).

A high Gleason score has been shown to be a marker of more aggressive biological behavior of tumor and is one of the best predictors of disease outcome in prostate cancer patients which is available today (3). The prostate – specific antigen (PSA) test is the most important and useful biochemical marker in the diagnosis of prostatic adenocarcinoma, but its levels also increase in conditions such as prostatitis, infarction, hyperplasia, and after biopsy and colonoscopy, which reduces the sensitivity and specificity of this test (4, 5). Therefore, studies to identify more specific markers for early detection of prostate cancer can overcome PSA limitations. These markers can provide an opportunity to better define groups of men at high risk for prostate cancer (6).

Immunohistochemical markers are one of the tools used today in the diagnosis and prognosis of various cancers. Markers used to differentiate prostatic adenocarcinoma from benign prostatic lesions include cytokeratins, AMACR, AGR2, endothelin, cyclin D1 and P63 (4). CD10 or neutral endopeptidase is also a zinc-dependent (Zn) enzyme located on the cell surface and its main function is to deactivate a number of messenger peptides (7).

Recent studies have shown that CD10 may be an important and independent predictor of tumor invasion, response to treatment, and overall survival in various cancers (8). Lack of CD10 expression is a common early occurrence in human prostate cancer and is seen in malignancies with lower Gleason scores (6). Several studies have shown that tumors in the early stages show a decrease in CD10 expression and an increase in CD10 expression is seen with higher Gleason scores, which was associated with increased recurrence and lymph node involvement in these patients (3, 9). Another study showed an association between lack of CD10 expression and adverse treatment outcomes and an increased risk of recurrence (10). One study showed that lack of CD10 expression was associated with increased tumor grade (11). Considering the contradictory results and the importance of CD10 expression as an effective marker in the prognosis of different cancers and its application for targeted treatment of prostate cancer, the aim of this study was to investigate CD10 marker expression and its relationship with Gleason score in prostatic adenocarcinoma.

Methods

In this cross-sectional observational study, after the approval of the Ethics Committee of Shahed University (IR.SHAHED.REC.1397.042), 60 archived samples of patients referred to Shahid Mostafa Khomeini Hospital in Tehran from 2013 to 2017 who were admitted with a final diagnosis of prostatic adenocarcinoma and underwent radical prostatectomy were included in the study. Samples included paraffin blocks and slides stained with hematoxylin and eosin (H&E). Information about the characteristics and age of patients was also extracted from their files. In the next step, the slides stained with hematoxylin and eosin were examined and confirmed by a pathologist with the help of a light microscope for the diagnosis of tumor type and Gleason score. Then, paraffin blocks suitable for immunohistochemical staining with sufficient tumor tissue and minimal necrosis were selected for each sample. Then, a 3µ incision was prepared and stained by a microtome machine to study CD10 expression by immunohistochemistry (DAKO, Germany) from each paraffin block related to each tumor. Finally, a pathologist examined the stained slide at X40 magnification in terms of CD10 marker expression in tumor cells. One thousand tumor cells were counted and the number of CD10 positive cells and its percentage were determined in each Gleason score. Data were analyzed using SPSS software version 21 and ANOVA statistical test, while $p<0.05$ was considered significant.

Results

The mean age of patients whose prostatic adenocarcinoma were studied here was 71±8.79 years with a median of 72.5 years, ranging from 53 to 87 years. Immunohistochemical expression of the CD10

[DOR: 20.1001.1.15614107.1400.23.1.9.8]
[DOI: 10.22088/jbums.23.1.60]

marker was observed in all prostatic adenocarcinoma specimens with varying severity. The expression percentage of this marker varied from 5 to 62% in different samples.

The expression percentage of CD10 was determined in each of the primary and secondary Gleason scores and had a normal statistical distribution. After examining the relationship between the mean expression of CD10 marker and primary and secondary Gleason score of prostatic adenocarcinoma samples, a statistically significant relationship was found between percentage of CD10 expression and primary and secondary Gleason score of tumor ($p<0.001$). With increase in Gleason score, the percentage of CD10 expression in tumor cells increased from 10.75±3.86 in primary Gleason score 2 to 44±7.03 in primary Gleason score 5 (Table 1). Furthermore, the CD10 expression percentage increased from 10.38±3.62 in the secondary Gleason score 2 to 53.5±7.28 in the secondary Gleason score 5 (Table 1).

Furthermore, the study of the relationship between the mean expression of CD10 marker and the overall Gleason score of the tumor showed that the expression percentage of CD10 marker in prostatic adenocarcinoma samples had a significant relationship with the Gleason score of this tumor ($p=0.003$). The mean CD10 expression percentage increased from 8.75±3.52 in overall Gleason score 4 to 40±7.86 in overall Gleason score 9 (Table 1).

Table 1. Mean CD10 expression percentage in each of the primary, secondary and overall Gleason scores

Gleason type	Score	Mean CD10 expression percentage	p-value
Primary score	2	10.75±4.55	<0.001
	3	16.19±6.57	
	4	35.2±12.86	
	5	44±9.73	
Secondary score	2	10.38±3.11	<0.001
	3	17.08±6.37	
	4	38.19±7.33	
	5	53.50±6.19	
Overall score	4	8.75±3.52	0.300
	5	13.84±4.02	
	6	20.61±6.98	
	7	26.15±6.67	
	8	34.81±5.57	
	9	40±7.86	

Discussion

The results of the present study showed that the percentage of CD10 expression in prostatic adenocarcinoma tumor samples was associated with the Gleason score of the tumor. Tumors with higher Gleason scores showed a higher percentage of CD10 marker expression. Immunohistochemical expression of the marker CD10 or neutral endopeptidase is also seen in all cases of prostatic adenocarcinoma with variable severity. CD10 expression in our prostate cancer samples was between 5 and 62%. Previous studies have shown that Gleason score in prostatic adenocarcinoma is associated with PSA level, clinical and pathological stage, lymph node and bone metastasis, survival rate and response to treatment (12).

Therefore, considering the important role of Gleason score in the prognosis of prostatic adenocarcinoma, the results of our study suggest the adverse effect of CD10 marker expression on the prognosis of prostatic adenocarcinoma specimens. A study by Dall'Era et al. showed that increased CD10 expression was associated with higher Gleason scores and lower prognosis and lower response to treatment. In patients showing elevated CD10 expression in the primary tumor, lymph node metastases and recurrence were more common (3). The results of a study by Suresh et al. also showed a strong association between CD10 expression and clinical outcome in patients with prostatic adenocarcinoma. In this study, with increase in Gleason score, the expression of CD10 in tumor samples increased (13).

A cohort study by Fleischmann et al. identified CD10 expression as an independent risk factor in prostatic adenocarcinoma and its expression increased with the increase in Gleason score. In this study, CD10 expression was observed in 62% of the samples, which is slightly lower than our study (14). In a study by Singh et al., increase in Gleason score was associated with increase in serum CD10 expression and PSA levels (4). Lack of CD10 expression can be due to promoter hypermethylation of this gene, which leads to non-production of CD10 and consequently reduction or lack of expression in low-grade tumors (15).

Contrary to the above studies, which, similar to our study, have shown an increase in CD10 marker expression as an undesirable factor in patient prognosis, several studies have identified CD10 expression in tumor specimens as a favorable factor or an ineffective factor in prostatic adenocarcinoma prognosis. Of course, the comparability of these studies is somehow limited because they are often cohort studies conducted

[DOR: 20.1001.1.15614107.1400.23.1.9.8]
[DOI: 10.22088/jbums.23.1.60]

in different populations. For example, in the study of Osman et al., in contrast to our study, there was no statistically significant difference in CD10 expression between patients with a Gleason score greater than 7 and patients with a Gleason score less than 7. This study showed that lack of CD10 expression is associated with increased risk of recurrence and progression of localized prostate cancer. However, this study was performed on 223 African-American patients, and racial differences certainly affect the results (10).

In the studies of Kaur et al. and Freedland et al., lack of CD10 expression appeared to be associated with increase in tumor grade in prostate cancer (9, 11). In the study of Zellweger et al., similar to our study, CD10 expression was observed in all cases of prostatic adenocarcinoma, but although the number of CD10-positive cases increased with the increase in Gleason score, this increase was not statistically significant (16).

Considering the expression of CD10 heterogeneity in most prostatic adenocarcinoma specimens, one of the reasons for the differences observed between different studies could be related to differences in sampling and selection of tumor specimens for immunohistochemistry and different interpretation of immunohistochemical results. In this study, we independently assessed CD10 expression for each tumor in each of Gleason components and reported the percentage of expression of this marker in each Gleason component.

Some studies have reported CD10 expression as positive or negative, but definition of positive or negative due to the heterogeneous expression of CD10 and lack of a clear cut-off point for this marker in prostatic adenocarcinoma specimens may lead to erroneous conclusions. In the study of Osman et al., CD10 expression was classified as positive, negative, and heterogeneous (focal) expression (10), which is different from our study and can affect their different results compared to our study. Some studies have suggested that CD10 expression in cancer cells may play a role in proliferation and apoptosis. In addition, the expression of this marker is associated with a higher apoptotic index (17).

CD10 expression in tumors such as breast, pancreas, colorectal, and thyroid cancers has been associated with a poor prognosis and is associated with greater invasiveness and metastasis (18, 19). In addition, some studies have shown that in positive samples of CD10 gene expression, there is a poor therapeutic response to chemotherapy drugs, which can also be justified by changing the direction of CD10 pathway because disruption of this pathway reduces the process of apoptosis and thus creates resistance to chemotherapy (20).

Overall, the results indicate the heterogeneous expression of the CD10 immunohistochemical marker in prostatic adenocarcinoma specimens. Increased CD10 expression in this tumor is associated with an increase in Gleason score as an important factor influencing the prognosis. According to studies in this field, it seems that CD10 marker expression is an influential factor in the progression of prostatic adenocarcinoma.

Acknowledgment

We would like to thank the Vice Chancellor for Research of Shahed University of Tehran for approving and financially supporting the research, as well as the efforts of the staff of Lashgarak Pathobiology Laboratory to perform immunohistochemical tests.

[DOR: 20.1001.1.15614107.1400.23.1.9.8]
[DOI: 10.22088/jbums.23.1.60]

References

1.Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30.

2.Lattouf J-B, Saad F. Gleason score on biopsy: Is it reliable for predicting the final grade on pathology?. BJU Int. 2002;90(7):694-8.

3.Dall'Era MA, True LD, Siegel AF, Porter MP, Sherertz TM, Liu AY. Differential expression of CD10 in prostate cancer and its clinical implication. BMC Urol. 2007;7:3.

4.Singh L, Marwah N, Bhutani N, Pawar D, Kapil R, Sen R. Study the expression of CD10 in prostate carcinoma and its correlation with various clinicopathological parameters. Iran J Pathol. 2019;14(2):135-45.

5.Sirousbakht S, Rezakhaniha B. Effect of colonoscopy on prostate specific antigen; New words about an old subject. Int J Cancer Manag. 2018;11(7):e68919.

6.Cheetan PJ. Markers in prostate cancer. In: Tiwari AK, Whelan P, Graham JD, editors. Prostate cancer: Diagnosis and clinical management, 1st ed. Wiley-Blackwell; 2014.p. 49-71.

7.Wlodek J. Clinical significance of CD10 expression in cancer. Int Clin Pathol J. 2017;5(1):192-4.

8.Mishra D, Singh S, Narayan G. Role of B cell development marker CD10 in cancer progression and prognosis. Mol Biol Int. 2016;2016:4328697.

9.Freedland SJ, Seligson DB, Liu AY, Pantuck AJ, Paik SH, Horvath S, et al. Loss of CD10 (neutral endopeptidase) is a frequent and early event in human prostate cancer. Prostate. 2003;55(1):71-80.

10.Osman I, Yee H, Taneja SS, Levinson B, Zeleniuch-Jacquotte A, Chang C, et al. Neutral endopeptidase protein expression and prognosis in localized prostate cancer. Clin Cancer Res. 2004;10(12 Pt 1):4096-100.

11.Kaur M, Verma S, Gupta R, Pant L, Singh S. CD10 expression pattern in prostatic adenocarcinoma: Elucidation of differences between Gleason's grades. Malays J Pathol. 2018;40(1):57-60.

12.McKenney JK. Prostate and seminal vesicles. In: Goldblum JR, Lamps LW, McKenney JK, Myers JL,editors. Rosai and Ackerman surgical pathology, 11st ed. Philadelphia: Elsevier; 2017.p. 1104-19.

13.Suresh MJ, Saranya D. Analysis of immunohistochemical expression of CD10 in the malignant lesions of prostate. IOSR J Dent Med Sci. 2017;16(7):78-82.

14.Fleischmann A, Schlomm T, Huland H, Kollermann J, Simon P, Mirlacher M, et al. Distinct subcellular expression patterns of neutral endopeptidase (CD10) in prostate cancer predict diverging clinical courses in surgically treated patients. Clin Cancer Res. 2008;14(23):7838-42.

15.Albrecht M, Mittler A, Wilhelm B, Lundwall Å, Lilja H, Aumüller G, et al. Expression and immunolocalization of neutral endopeptidase in prostate cancer. Eur Urol. 2003;44(4):415-22.

16.Zellweger T, Ninck Ch, Bloch M, Mirlacher M, Koivisto PA, Helin HJ, et al. Expression patterns of potential therapeutic targets in prostate cancer. Int J Cancer. 2005;113(4):619-28.

17.Bilalovic N, Sandstad B, Golouh R, Nesland JM, Selak I, Torlakovic EE. CD10 protein expression in tumor and stromal cells of malignant melanoma is associated with tumor progression. Mod Pathol. 2004;17(10):1251-8.

18.Erhuma M, Kobel M, MustafaT, Wulfänger J, Dralle H, Hoang-Vu C, et al. Expression of neutral endopeptidase (NEP/CD10) on pancreatic tumor cell lines, pancreatitis and pancreatic tumor tissues. Int J Cancer. 2007;120(11):2393-400.

19.Taghizadeh-Kermani A, Jafarian AH, Ashabyamin R, Seilanian-Toosi M, Pourali L, Asadi M, et al. The stromal overexpression of CD10 in invasive breast cancer and its association with clincophathologic factors. Iran J Cancer Prev. 2014;7(1):17-21.

20.Jana SH, Jha BM, Patel C, Jana D, Agarwal A. CD10-a new prognostic stromal marker in breast carcinoma, its utility, limitations and role in breast cancer pathogenesis. Indian J Pathol Microbiol. 2014;57(4):530-6.

[DOR: 20.1001.1.15614107.1400.23.1.9.8]

[DOI: 10.22088/jbums.23.1.60]