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Research Article

ANALYSIS OF CD10 EXPRESSION IN PROSTATE ADENOCARCINOMA AND ITS CORRELATION WITH DIFFERENT CLINICOPATHOLOGICAL PARAMETERS AT RNTMC, UDAIPUR

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ABSTRACT

Objective: The study aimed to analyze the expression of CD10 in prostate adenocarcinoma to aid in early diagnosis and anti-CD10 targeted therapy.

Methods: This was a cross-sectional study conducted in the Histopathology section of the Department of Pathologyat RNTMC, Udaipur, after approval from the ethical committee and institutional review board. This study was conducted on 92 patients suspected to have prostate cancer. The cases were assessed for Gleason score, Gleason Grade, and Serum Prostate Specific Antigen (PSA) levels. We performed IHC detection of CD10 in prostatic specimens and correlated the various patterns of CD10 expression concerning histopathological diagnosis.

Results: In our study, we found membranous expression in low-grade carcinomas with low Gleason score and grade. The high-grade carcinomas with high Gleason score and Grade predominantly showed cytoplasmic expression. The increased CD10 cytoplasmic expression was correlated with serum PSA level.

Conclusion: In our study, CD10 was found to be relevant. The low-grade carcinomas showed membranous positivity and high-grade carcinomas showed cytoplasmic expression. One hypothesis states that cytoplasmic expression is due to the localization of CD10 in the cytoplasm. Our study favors this hypothesis as there is cytoplasmic expression in high-grade tumors. In the future, this could be used as a diagnostic marker.

Keywords: CD10 prostate adenocarcinoma, Gleason score, WHO.

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INTRODUCTION

Prostate adenocarcinoma is the second most common cancer in men worldwide and the sixth leading cause of cancer-related deaths. Over 95% of prostate cancers are adenocarcinomas that originate from the prostate acini [1]. Whether benign or malignant, these lesions primarily present with urinary symptoms, making it difficult to distinguish between the two clinically. Prostate cancer, the most aggressive form of malignant neoplasm, has diverse clinical presentations and often develops without any warning signs in its early stages.

The most commonly used screening test for detecting prostate cancer involves measuring serum prostate specific antigen (PSA) levels, combined with a digital rectal examination for suspected cases. PSA is secreted by both normal and malignant prostatic epithelial cells, leading to significantly elevated serum levels in men with prostate cancer. However, while elevated PSA levels can raise suspicion for an underlying tumor, they are not specific to cancer. Benign conditions such as benign prostatic hyperplasia and prostatitis can also cause increased PSA levels. Therefore, it is crucial to utilize newer markers to identify prostate cancer at an early stage [2].

CD10 (Neutral endopeptidase) may be a prognostic molecular marker in prostate cancer [3]. CD10 plays a part in different cancers, including prostate cancer, where it is involved in the migration, survival, and apoptosis of cancer cells, as well as tumor progression. CD10 can play a role in early diagnosis and targeted anti-CD10 therapy. There may be individual interpretive variations in the evaluation of biopsy specimens, but this marker will help in ascertaining the exact grading.

Aims and objectives

1. To identify and analyze the expression of CD10 in malignant lesions of the prostate
2. To analyze the expression pattern which will help screen and discriminate low-grade v/s aggressive disease.
3. We will aim at specific targeted Anti CD10 for better patient outcomes.
4. To correlate the CD10 expression with age, Gleason grade, Gleason score, and serum PSA levels.

METHODS

Study design

Our cross-sectional study was conducted in the Histopathology section, Department of Pathology, Rabindranath Tagore Medical College, M.B.G. Hospital Udaipur, Rajasthan. Patient consent was obtained wherever required.

Inclusion criteria

- All types of prostatic specimens including transurethral resection of Prostate, needle biopsy, Transrectal ultrasound guided biopsy, and prostatectomy having carcinoma.
- Tissue blocks from already diagnosed prostatic adenocarcinoma patients.

Exclusion criteria

- Inadequate biopsies and poorly preserved prostatic specimens
- Tissue blocks of patients diagnosed with prostatic carcinoma and underwent pre-operative radiotherapy or chemotherapy
- Benign and inflammatory lesions of the prostate.

Table 1: Gleason grade vs. CD10 expression pattern

Gleason grade versus CD 10 expression pattern	Negative	Membranous positivity	Cytoplasmic positivity	Membranous and cytoplasmic positivity	Total
Grade I	11 (84.61%)	2 (6.66%)	0	0	13
Grade II	8 (53.33%)	7 (46.67%)	0	0	15
Grade III	6 (27.27%)	12 (54.54%)	3 (13.63%)	1 (4.54%)	22
Grade IV	1 (5.55%)	4 (22.22%)	4 (22.22%)	9 (50%)	18
Grade V	0	1 (4.16%)	9 (37.5%)	14 (58.33%)	24
Total	26	26	16	24	92

p=<0.001 (HS)

Table 2: Gleason grade versus CD10 expression intensity

Gleason grade versus CD 10 expression intensity	Negative	Focal	Diffuse	Total
Grade I	11 (84.61%)	1 (7.69%)	1 (7.69%)	13
Grade II	7 (46.66%)	8 (53.33%)	0	15
Grade III	6 (27.27%)	7 (31.81%)	9 (40.90%)	22
Grade IV	1 (5.55%)	4 (22.22%)	13 (72.22%)	18
Grade V	0	1 (4.16%)	23 (95.83%)	24
Total	25	21	46	92

p≤0.001 (HS)

A total sample of 92 cases was analyzed according to age, Gleason grade, Gleason score, and serum PSA levels. Immunohistochemical staining was performed on 3–4 μm thick, formalin-fixed, paraffin-embedded tissue sections mounted on suitable albumin-coated slides. The slides were mounted on LEICA BOND MAX PREMIUM IHC STAINING SYSTEM. We performed IHC detection of CD10 in prostatic biopsy specimens and correlated the various patterns of CD10 expression concerning histopathological diagnosis.

Statistical analysis

The whole data were entered into a Microsoft Excel master sheet and analyzed using SPSS v29 software. The results obtained were interpreted and descriptive statistics (mean, standard deviation, range, percentage) were applied wherever appropriate. A p<0.05 was considered statistically significant.

RESULTS

On comparing the age-wise distribution of prostatic carcinoma, we had a maximum number of cases in the age group of 61–70 years contributing 51.08% of total prostatic carcinoma cases. A study by Fleischman *et al*. [3], showed maximum cases in the age range of 60–70 years, contributing 59%.

In our investigation, we explored the expression of CD10 across different grades of prostatic carcinoma. Notably, we observed heterogeneous expression patterns. Our focus was on understanding both the localization and intensity of CD10 expression within the prostatic carcinoma cells. The CD10 expression was seen in 71.73% of the cases of carcinoma prostate.

In our study, we observed that at low-grade Group/Gleason Grade (GG) I and II cytoplasmic and membranous positivity was zero with almost all (84.61%) the cases of Gleason Grade I and more than half (53.33%) of Gleason (Figure 1a and b) Grade II showing negative pattern. As the GG increases to III and IV the negative expression decreases to 27.27% and 5.55%, respectively, with no cases of GG V showing negative expression (Table 1). Simultaneously, as the GG increases from II to III the membranous expression also increases from 46.67% to 54.54%, respectively, and further the cytoplasmic expression increases from 13.63% in GG III to 22.22 in GG IV to 37.5% in GG V. The number of cases showing both cytoplasmic and membranous expression increases from 4.54% in GG III to 58.33% in GG V.

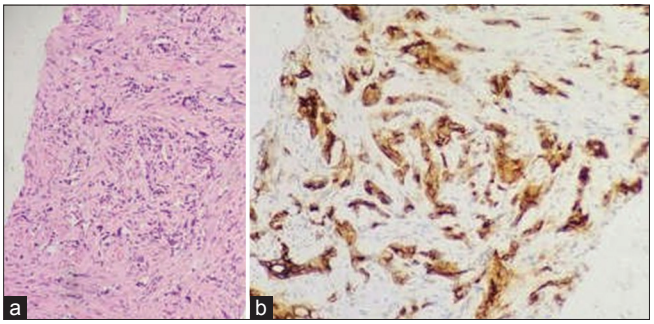

Fig. 1: (a) Photomicrograph showing H and E Gleason score 4+4=8, WHO Grade IV (×100). (b) Photomicrograph showing CD10 membranous positivity (×100)

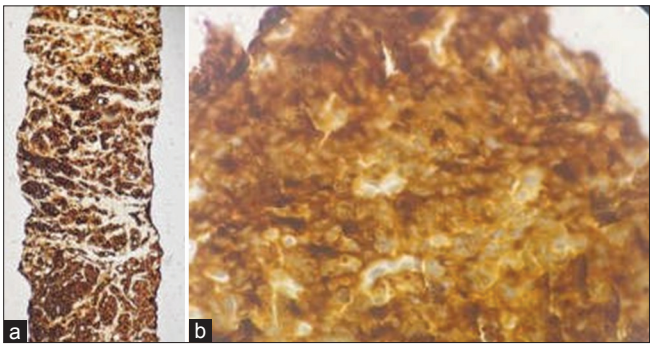

Fig. 2: (a) Photomicrograph showing Diffuse Positivity Gleason score 5+4=9, WHO Grade V (×100). (b) Photomicrograph showing CD10 both membranous and cytoplasmic positivity (×100)

Our study also showed a significant correlation between GG and CD10 expression intensity (p<0.001). The majority of GG I showed negative expression but in GG II almost half showed negative and half showed focal positivity. From GG III onward the majority of cases showed diffuse positivity with 95.83% of cases of GG5 showing diffuse positivity (Table 2 and Figure 2a and b).

In our study, the majority of cases, that is, 84.61% with Gleason Score (GS) 6 had a negative expression for CD10 with none of the cases showing cytoplasmic or both (cytoplasmic+membranous) positivity. As the GS increased half of the cases with GS 9 and all the cases with GS 10 showed both (cytoplasmic+membranous) positivity (Table 3).

In our study, the majority of cases, that is, 84.61% of GS 6 showed negative expression where as 95% of GS 9 and 100% of GS 10 showed diffuse positivity. Also with an increase in Gleason Score, the intensity of expression changed from focally positive to diffusely positive (p<0.001) (Table 4).

According to the serum PSA levels, cases were divided into three groups <10, 11–20, and >20 ng/mL. As the serum PSA levels increased, the intensity of expression changed from focally positive to diffusely positive. A total of 45.56% of cases having serum PSA >20 ng/mL

Table 3: Gleason score versus CD10 expression pattern

Gleason score versus CD 10 expression pattern	Negative	Membranous positivity	Cytoplasmic positivity	Membranous and cytoplasmic positivity	Total
6	11 (84.61%)	2 (18.38%)	0	0	13
7	14 (37.83%)	19 (51.35%)	3 (8.10%)	1 (2.70%)	37
8	1 (5.55%)	4 (22.22%)	4 (22.22%)	9 (50%)	18
9	0	1 (5%)	9 (45%)	10 (50%)	20
10	0	0	0	4 (100%)	4
Total	26	26	16	24	92

p≤0.001 (HS)

Table 4: Gleason score versus CD10 expression intensity

Gleason score versus CD 10 expression pattern	Negative	Focal	Diffuse	Total
6	11 (84.61%)	1 (7.69%)	1 (7.69%)	13
7	13 (35.1%)	15 (40.54%)	9 (24.32%)	37
8	1 (5.55%)	4 (22.22%)	13 (72.22%)	18
9	0	1 (5%)	19 (95%)	20
10	0	0	4 (100%)	4
Total	25	21	46	92

p<0.001 (HS)

Table 5: Serum PS Alevel versus CD10 expression pattern

Serum PSA levels versus CD 10 expression	Negative	Membranous positivity	Cytoplasmic positivity	Membranous and cytoplasmic positivity	Total
<10 ng/mL	1 (50%)	0	0	1 (50%)	2
10–20 ng/mL	1 (9.09%)	4 (36.36)	3 (27.27%)	3 (27.27%)	11
>20 ng/m	24 (30.37%)	22 (27.84%)	13 (16.45)	20 (25.31)	79
Total	26	26	16	24	92

showed diffuse positivity while 25.31% of cases were focally positive. About 81.81% of the cases having PSA 11–20 ng/mL showed diffuse CD10 expression and 9.09% of the cases were focally positive (Table 5).

The pattern of expression also changed from membranous to cytoplasmic to both (membranous + cytoplasmic) types of expression with an increase in PSA levels.

DISCUSSION

Prostate cancer varies widely in its manifestations, treatment responses, and long-term results. Treating the disease poses numerous challenges, with the most formidable being the identification and differentiation of aggressive tumors from those that remain indolent, causing minimal harm to the patient. The latest biomarkers aim to facilitate the selection of tailored treatment strategies for individual patients, detect advanced disease earlier, and predict the likelihood of metastatic cancer and recurrence post-prostatectomy. Numerous studies have shown that both neuropeptides and CD10 play significant roles in the pathogenesis, progression, angiogenesis, and metastatic potential of prostatic adenocarcinoma [1].

CD10 is highly expressed in normal luminal epithelial cells of the prostate and is a natural constituent of human prostasomes [4]. The clinical use of CD10 expression for stratifying prostate cancer could potentially predict the biological behavior of the tumor. Furthermore, CD10 expression in prostate cancer may also have therapeutic implications through the development of CD10 inhibitors [5].

Immunohistochemical markers such as CD10 have become essential tools to confirm the diagnosis in such instances [6]. The PSA test is crucial and valuable for detecting prostatic adenocarcinoma. However, its levels can rise in other conditions, such as prostatitis, infarction, hyperplasia, and post-biopsy and colonoscopy, thereby diminishing the test's sensitivity and specificity. Hence, research aimed at discovering more precise markers for early prostate cancer detection could address the limitations of PSA. These markers may offer a chance to accurately identify high-risk groups of men for prostate cancer [7].

Our study focused on the location and intensity of CD10 expression in prostatic carcinoma cells. Carcinomas with a low Gleason Score of 6 and 7 showed negative or only focal positivity, while high-score tumors (9 and 10) with Grade Group IV and V were diffusely positive in most cases. There was a significant increase in the frequency of CD10 expression with a higher Gleason Score and Grade Group. In carcinomas with a low Gleason Score of 6 and 7, the staining was membranous, but in high-score malignancies, it was either cytoplasmic or both cytoplasmic and membranous.

In line with our study, Singh *et al***.** [1] reported comparable findings. They observed a decrease in negative CD10 expression as the Gleason grade (GG) increased: 88.9% in GG1, 6.7% in GG4, and no cases in GG5. In addition, as the GG increased, the number of cases exhibiting cytoplasmic positivity for CD10 also rose. Notably, an increase in Gleason score correlated with elevated serum CD10 expression and PSA levels.

The distinct pattern of CD10 expression in relation to histological grade has been observed in multiple studies. Tawfic *et al*. [8]. noted similar findings, and Era *et al*. [4]. Reported that tumors predominantly exhibiting pattern 3 had positive CD10 staining in <5–10% of cases, with higher percentages found in tumors with patterns 4 or 5. Saranya [2] found CD10 expression in 26 prostate adenocarcinoma cases, finding that all grade 2 components were devoid of expression. In grade 3 tumors, 76.92% did not show expression, while 71.43% of grade 4 lesions showed cytoplasmic positivity. Especially, all grade 5 cases showed diffuse cytoplasmic positivity. These findings are consistent with the results of our study.

When serum PSA levels were correlated with CD10 expression, it was found that most cases with diffuse CD10 positivity had serum PSA

levels more than 20 ng/mL (78.2%). The intensity of CD10 expression changed from negative to focal and then to diffuse as serum PSA levels increased. In addition, the pattern of expression also changed from membranous to cytoplasmic, and then to both, with higher PSA levels.

The loss of CD10 expression in low-grade tumors might be attributed to hypermethylation of the promoter region, leading to reduced or absent CD10 synthesis and expression [9]. The cytoplasmic localization observed in high-grade tumors may be due to increased binding of CD10 to cytoplasmic heat shock proteins, which may drive the cell along a constant signaling pathway independent of growth factor signaling [10].

CONCLUSION

In our study, CD10 was found to be relevant. In low-grade tumors, we noted membranous expression however in a few cases CD10 was also negative. However, cytoplasmic expression was consistently present in high-grade prostatic tumors. The exact mechanism and role of CD10 in the pathogenesis of prostatic carcinoma are still under investigation. One hypothesis suggests that the observed cytoplasmic positivity is due to the localization of the CD10 molecule within the cytoplasm. Our study supports this hypothesis, as we observed cytoplasmic expression in high-grade tumors. In the future, this marker could potentially be used as a diagnostic tool. Further studies and more markers are needed to differentiate benign or prostatic intraepithelial neoplasia or low-grade prostatic carcinoma.

CONFLICTS OF INTERESTS

None.

AUTHOR OF INTEREST

All authors have contributed equally to the preparation of the manuscript.

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