Original Research

Study of CD10 Expression Pattern in Prostatic Adenocarcinoma and Its Correlation with Gleason's Grade

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Abstract

Benign prostatic hyperplasia and carcinoma of the prostate are increasingly prevalent with advancing age. CD10, a 100-kDa transmembrane glycoprotein, plays a role in the cleavage and inactivation of specific peptide hormones essential for signal transduction. This zinc-dependent enzyme is widely expressed in the epithelial cells of the kidney, breast, lung, intestine, and prostate. The aim of our study is to evaluate the CD10 expression pattern in benign and malignant prostatic lesions by immunohistochemistry and to correlate it with Gleason grade group and pre-treatment PSA levels in prostatic adenocarcinoma.

Immunohistochemical staining for CD10 was performed on 56 cases of paraffin-embedded tissue from transurethral resected and core biopsy specimens of the prostate. Our study found that CD10 positivity was higher in prostatic adenocarcinoma patients compared to BPH patients, with a significant p-value of 0.003. Additionally, we identified a positive linear correlation between CD10 positivity and both Gleason grade group and PSA levels, with significant p-values of 0.0016 and 0.0083, respectively.

In conclusion, high CD10 expression may help accurately distinguish prostatic adenocarcinoma from BPH, thereby enhancing diagnostic accuracy.

Keywords: CD10, Prostatic adenocarcinoma, Benign prostatic hyperplasia, Gleason grade group, PSA.

Introduction

Prostate cancer predominantly affects older individuals, with over three-quarters of cases appearing in men aged 65 and above. In recent decades, it has emerged as a significant global health concern. Research indicates that prostate cancer ranks as the second most commonly diagnosed cancer in men globally and the fifth most prevalent cancer overall.(1) Prostate cancer stands as the sixth

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leading cause of cancer-related fatalities among men. [2] Research has demonstrated that the prevalence of benign prostatic hyperplasia (BPH) escalates from 25% in the 40-79 age bracket to 80% in individuals aged 70-79.[3] India boasts a rich tapestry of diversity, encompassing differences in religion, culture, environment, literacy rates, and dietary habits from region to region. These diverse factors may significantly influence the occurrence of prostate cancer across the nation. Several risk factors have been associated with the development of prostate cancer, including a positive family history, diabetes mellitus,[4] height, weight, obesity,[5] smoking, level of physical activity, [6]body mass index (BMI),[7] and history of vasectomy.[8] In India, research exploring the precise influence of these risk factors on the development of prostate cancer is sparse. Prostate cancer is a common malignancy among men, and current screening methods rely on serum levels of prostate-specific antigen (PSA). However, the serum PSA test can yield a false-positive rate as high as 70%, resulting in numerous unnecessary biopsies. [9] Histological grading through Gleason's grading system and assessment of PSA levels demonstrate relatively effective performance in predicting disease prognosis for many patients.[10] Yet, this assertion does not hold for a significant portion of patients. Cluster of differentiation (CD) antigens are cell surface molecules found to be expressed by various human cell types in both normal and pathological conditions. Immunophenotyping of human prostate using CD antigens has been conducted, revealing distinctions between cancerous and normal prostatic tissue. [11] CD10, a 100-kDa transmembrane glycoprotein, plays a role in cleaving and deactivating specific peptide hormones crucial for signal transduction. This zinc-dependent enzyme exhibits widespread expression in epithelial cells found in the kidney, breast, lung, intestine, and prostate.[12] An early reduction in CD10 expression has been observed in a significant proportion of prostate tumors.[13] However, studies assessing the prognostic value of CD10 in prostate cancer have produced inconsistent results, likely due to variations in the cohorts evaluated, which complicates direct comparisons.[14][15] Prostate-specific antigen (PSA) is secreted by both normal and malignant prostatic epithelial cells, leading to significantly elevated serum levels in men with prostate cancer. Although elevated PSA levels can indicate an underlying tumor, PSA is not a specific marker, as benign conditions like benign prostatic hyperplasia and prostatitis can also increase serum PSA levels. Therefore, identifying a more specific marker for early-stage prostate cancer is of utmost importance. CD10 is consistently expressed on the apical luminal surface of normal prostatic epithelial cells. However, its expression pattern varies in different prostatic lesions, ranging from altered expression to complete loss of expression. This study aims to investigate the relationship between CD10 expression in prostatic adenocarcinoma and its significant correlation with Gleason grades.

Methodology

We conducted a single-institution observational study at NRSMCH from January 2021 to July 2022 on biopsy-proven BPH and prostatic adenocarcinoma patients.

Inclusion criteria: Histopathologically confirmed cases of BPH or prostatic adenocarcinoma, with adequate biopsy tissue for histopathological and IHC analysis, available pre-operative PSA levels, and no prior treatment for prostatic adenocarcinoma. Patients must be able to provide informed consent and have follow-up availability.

Exclusion criteria: Inadequate biopsy samples, prior prostate cancer treatment, metastasis, history of other malignancies, lack of pre-operative PSA levels, incomplete data, inability to provide consent, or loss to follow-up. These criteria ensure consistent and reliable data for the study.

Diagnoses were confirmed by two pathologists, with adenocarcinoma cases reclassified by Gleason grade and PSA levels. Both groups were tested for CD10 expression, categorized as negative, apical membranous, diffuse membranous, cytoplasmic positivity or both.

The study was approved by the institutional ethics committee, and informed consent was obtained. (IEC certificate Ref no. No/NMC/287 dated 20/01/2021)

Immunohistochemical staining was performed on 5-mm thick, formalin-fixed, paraffin-embedded sections, deparaffinized and rehydrated, followed by heat-induced antigen retrieval using citrate

buffer. CD10 (mouse monoclonal) antibody was applied, followed by Poly excel HRP and DAB chromogen detection. CD10 expression patterns were categorized, and statistical analysis using chi-square and Fisher's exact tests was performed. A p-value of <0.05 was considered statistically significant.

Results

We initially recruited 60 patients, but 2 were lost to follow-up, and 2 withdrew consent, resulting in a final sample size of 56, consisting of 27 BPH cases and 29 adenocarcinomas.

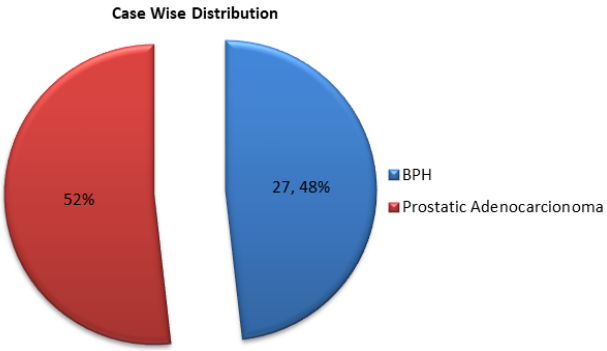

Figure 1: Pie Chart showing Case Distribution Pattern in BPH & Prostatic Adenocarcinoma

Age Wise Distribution of prostatic neoplasms

The median age of patients diagnosed with benign prostatic hyperplasia (BPH) was 68 years, ranging from 56 to 84 years, while the median age of those with prostatic adenocarcinoma was 69 years, ranging from 63 to 76 years.

Gleason grade group and prostatic adenocarcinoma

In our study, all cases of prostatic adenocarcinoma were graded from grade group 1 to grade group 5. Grade 1 indicates the most well-differentiated tumors, while grade 5 represents the most poorly differentiated ones. The distribution of these grade groups in our study was as follows:

Table 1: Gleason Grade Group Distribution with Prostatic Adenocarcinoma

Grade Group	No. of Prostatic Adenocarcinoma Cases	Percentage
1	8	27.5
2	7	24.13
3	6	20.68
4	6	20.68
5	2	6.89

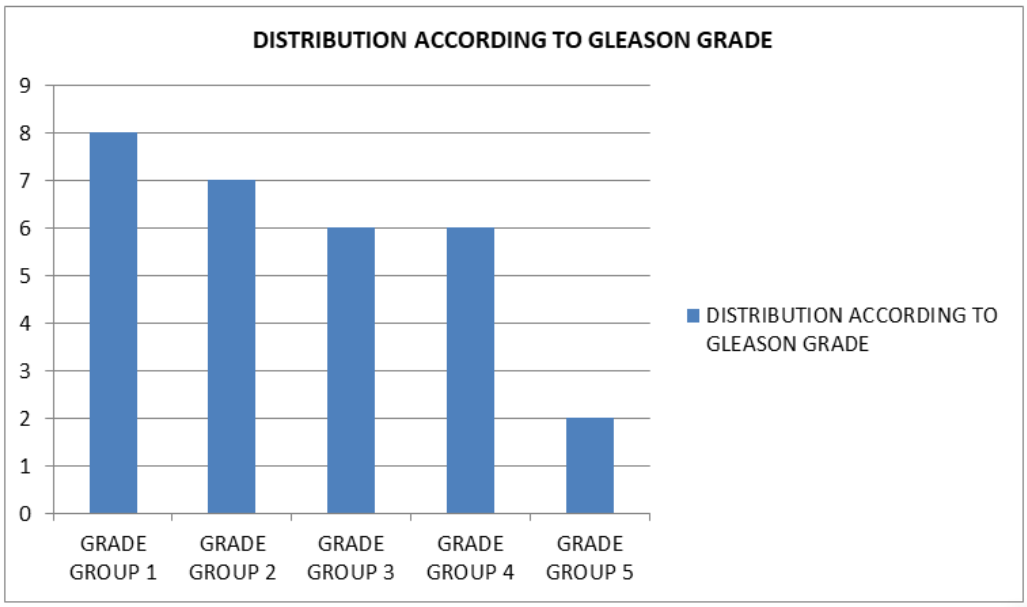

Figure 2: Bar Chart showing Gleason Grade Group Distribution Pattern in Prostatic Adenocarcinoma

Serum PSA level and Prostatic Adenocarcinoma-

We collected serum PSA levels from patients with prostatic adenocarcinoma and categorized them as <10 ng/ml, 10-20 ng/ml, and >20 ng/ml. The distribution of these categories was as follows:

Table 2: Serum PSA Distribution among Prostatic Adenocarcinoma cases

Serum PSA levels	Prostatic Adenocarcinoma	Percentage
<10ng/ml	10	34.48
10-20ng/ml	11	37.93
>20ng/ml	8	27.58
Total	29	100

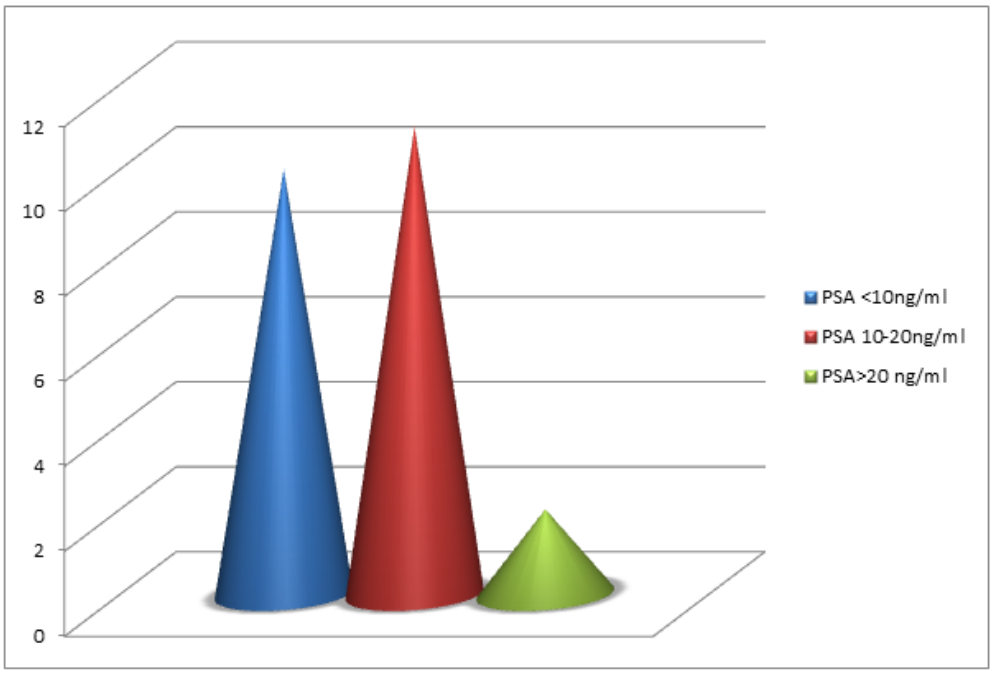

Figure 3: PSA Distribution Pattern in Prostatic Adenocarcinoma

Relationship between Serum PSA level & Gleason Grade

We categorized patients into two distinct groups based on Gleason grade. The low-risk and intermediate-risk group comprised Gleason grades 1, 2, and 3, while the high-risk and very high-risk group comprised Gleason grades 4 and 5. The distribution of these groups according to PSA values, categorized as less than 20 ng/ml and more than 20 ng/ml, is as follows:

Table 3: Serum PSA distribution according to Gleason Grade Grouping in Prostatic Adenocarcinoma Cases

Serum PSA levels	Gleason Grade 1,2 & 3	Gleason Grade 4&5
<20ng/ml	20	1
>20ng/ml	1	7
p Value (Fisher Exact Test)	0.00003	

The data presented in the table indicates a linear increase in PSA value with higher Gleason grades.

Immunohistochemical expression of CD10 in BPH Lesions

In the case of benign prostatic hyperplasia, out of 27 patients, 10 exhibited CD10 positivity, while 17 showed CD10 negativity. Among the 10 CD10-positive patients, 5 showed apical membranous positivity, 3 exhibited diffuse membranous positivity, and 2 displayed cytoplasmic positivity.

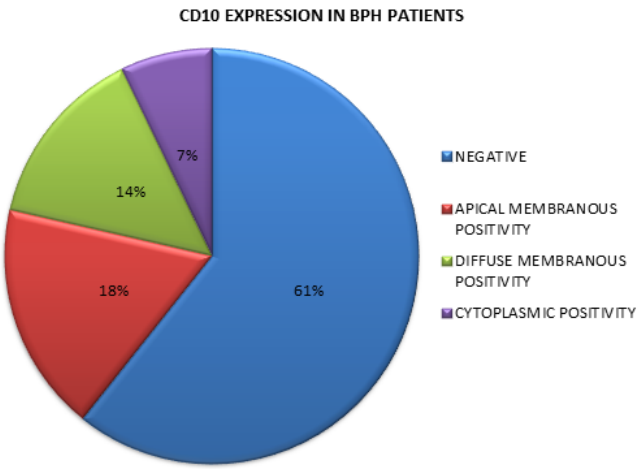

Figure 4: Pie Chart showing CD10 Expression Pattern in BPH

Immunohistochemical expression of CD10 in Prostatic Adenocarcinoma Lesions-

In the case of prostatic adenocarcinoma, 23 out of 29 patients exhibited immunohistochemical positivity for CD10, while 6 patients showed CD10 negativity. Among the 23 CD10-positive patients, 8 displayed only apical membranous positivity, 7 showed only diffuse membranous positivity, 2 exhibited only cytoplasmic positivity, 1 presented both apical membranous positivity and cytoplasmic positivity, and 5 displayed both diffuse membranous positivity and cytoplasmic positivity.

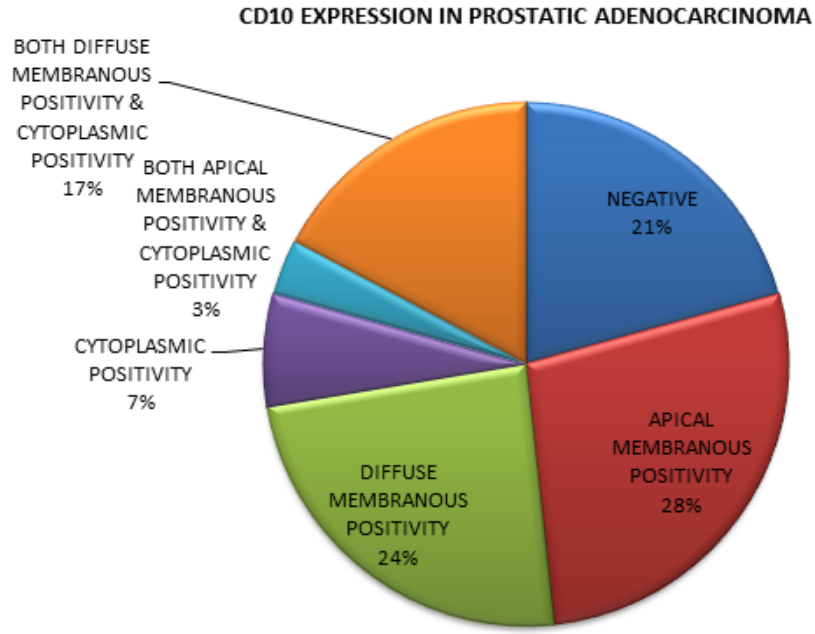

Figure 5: Pie Chart showing CD10 Expression Pattern in Prostatic Adenocarcinoma

Differences in immunohistochemical expression positivity of CD10 between patients with benign prostatic hyperplasia (BPH) and prostatic adenocarcinoma:

In the series of patients with benign prostatic hyperplasia (BPH), 17 exhibited immunohistochemical positivity for CD10, while 10 showed CD10 negativity. In contrast, among patients with prostatic adenocarcinoma, 23 displayed CD10 positivity, while 6 demonstrated CD10 negativity.

Table 4: CD10 Positivity Comparison between BPH & Prostatic Adenocarcinoma Cases

	IHC expression of CD10 Positive	IHC expression of CD10 Negative	Total
BPH	10 (37.04%)	17(62.96%)	27(100%)
Prostatic Adenocarcinoma	23(79.31%)	6(20.69%)	29(100%)
p Value (Chi square test)		0.003	

The data from the table indicates a higher prevalence of CD10 positivity in immunohistochemistry among patients with prostatic adenocarcinoma compared to those with benign prostatic hyperplasia (BPH), with a statistically significant p-value of 0.003.

Gleason grade & CD10 expression

All prostatic adenocarcinoma patients were graded according to the Gleason grade, and the corresponding patterns of CD10 positivity were quantified.

Table 5: Pattern of CD10 Staining in Different Gleason Grade Grouping in Prostatic Adenocarcinoma Cases

Gleason grade group	Negative staining of CD10	Positive staining of CD10				
		Apical membranous positivity	Diffuse membranous positivity	Cytoplasmic positivity	Both Apical membranous & cytoplasmic Positivity	Both Diffuse membranous & cytoplasmic Positivity
Grade 1 &2 (n=15)	6 (40%)	6 (40%)	3 (20%)	0 (0%)	0 (0%)	0 (0%)
Grade 3,4 & 5 (n=14)	0 (0%)	2 (14.3%)	4 (28.6%)	2 (14.3%)	1 (7.1%)	5 (35.7%)
p Value (Fisher Exact Test)			0.0016			

The data from the table indicates that as the grade increases, there is a higher prevalence of cases exhibiting cytoplasmic positivity, with a statistically significant p-value of 0.0016.

PSA & CD10 expression

All prostatic adenocarcinoma patients were stratified based on their PSA levels into two distinct groups: one with values <20 ng/ml and the other with values >20 ng/ml. The corresponding patterns of CD10 positivity were quantified for each group.

Table 6: Pattern of CD10 Staining in according to Serum PSA levels in Prostatic Adenocarcinoma Cases

PSA Value	Negative staining of CD10	Positive staining of CD10				
		Apical membranous positivity	Diffuse membranous positivity	Cytoplasmic positivity	Both apical membranous & cytoplasmic positivity	Both diffuse membranous & cytoplasmic positivity
<20ng/ml (n=21)	6 (28.5%)	7 (33.3%)	6 (28.6%)	1 (4.8%)	0 (0%)	1 (4.8%)
>20ng/ml (n=8)	0 (0%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	1 (12.5%)	4 (50%)
p Value (Fisher exact test)			0.0083			

The data from the above table reveals that as the grade increases, there is a higher incidence of cytoplasmic positivity, with a statistically significant p-value of 0.0083.

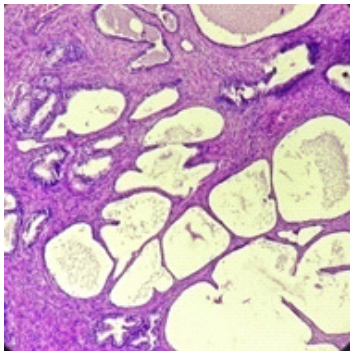

FIGURE 6: H&E of BPH (10X)

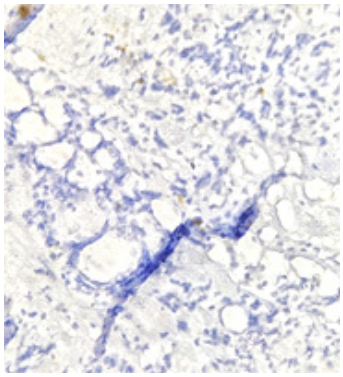

FIGURE 7: IHC CD10 Negative in BPH(40X)

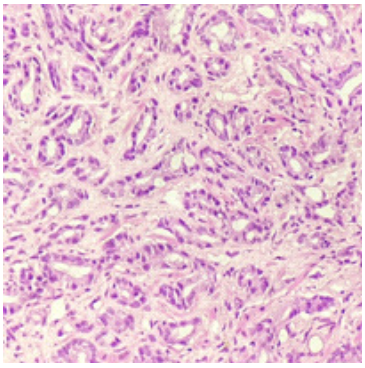

FIGURE 8: H&E of Prostatic adenocarcinoma Gleason grade group 2(40X)

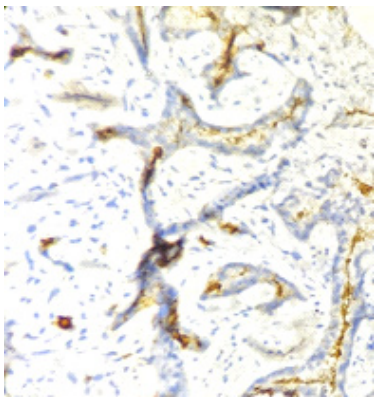

FIGURE 9: IHC CD10 Apical positive in Prostatic adenocarcinoma Gleason grade group 2(40X)

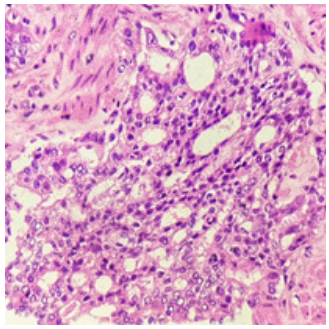

FIGURE 10: H&E of Prostatic adenocarcinoma Gleason grade group 3(40X)

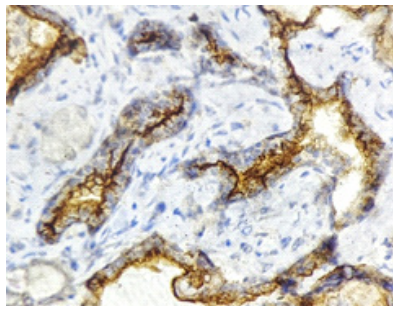

FIGURE 11: IHC CD10 Diffuse membranous positive in Prostatic adenocarcinoma Gleason grade group 3(40X)

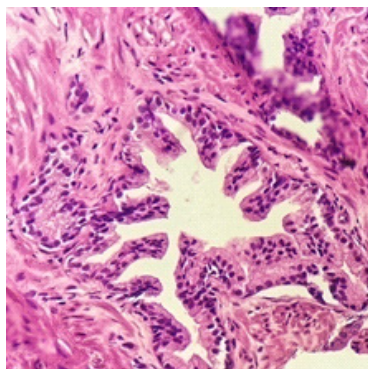

FIGURE 12: H&E of Prostatic adenocarcinoma Gleason grade group 4(40X)

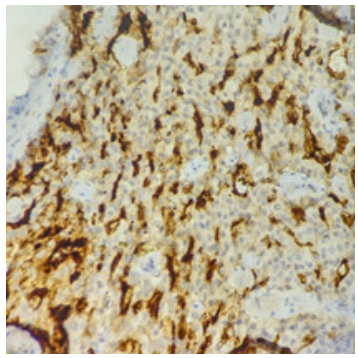

FIGURE 13: IHC CD10 Diffuse membranous & Cytoplasmic positive in Prostatic adenocarcinoma Gleason grade group 4(40X)

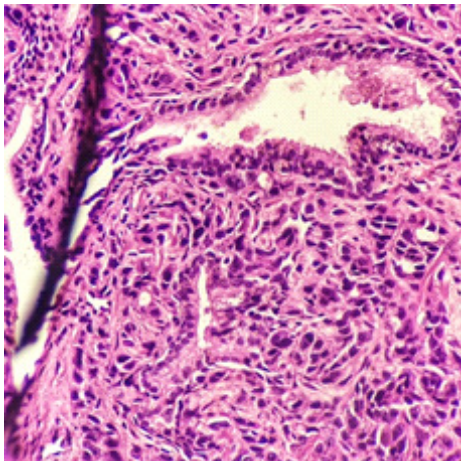

FIGURE 14: H&E of Prostatic adenocarcinoma Gleason grade group 5(40X)

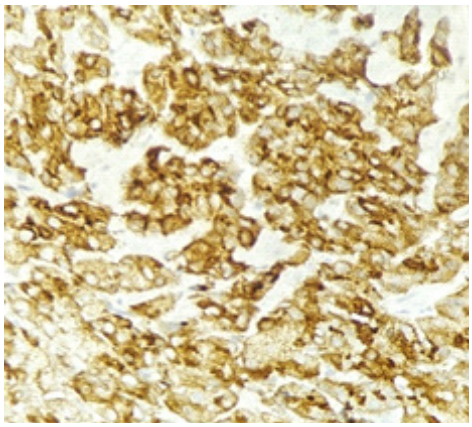

FIGURE 15: IHC CD10 Diffuse Membranous & Cytoplasamic positive in Prostatic adenocarcinoma Gleason grade group 5 (40X)

Discussion & Review of Literature

Prostatic lesions significantly affect male health. This study evaluates CD10 expression in benign and malignant prostatic lesions, examining its potential role in prostate cancer diagnosis.

The comparison between the review of literature and our study results highlights several important correlations between CD10 expression, prostate cancer grade, and PSA levels.

CD10 Expression and Tumor Grade:

- Review of Literature:
  - Kaur Mandeep et al. (2018): Found that CD10 expression decreased with increasing tumor grade. [16]
  - DaII'Era Marc A et al. (2007): Demonstrated that higher Gleason grades and more advanced stages of prostate cancer correlated with increased CD10 expression.[17]
  - Singh Lalit et al. (2019): Observed that as the Gleason score increased, CD10 expression shifted from membranous to cytoplasmic and mixed expression patterns. [18]
- Study Results:
  - Our study showed that CD10 positivity was significantly higher in prostatic adenocarcinoma (79.31%) compared to BPH (37.04%), with a p-value of 0.003, indicating that CD10 expression correlates with malignancy.
  - CD10 expression increased with tumor grade, showing a statistically significant increase in cytoplasmic positivity with higher Gleason grades ($p = 0.0016$). This is consistent with Singh Lalit et al., who also noted a shift to cytoplasmic and mixed expression in higher-grade tumors.

Correlation with PSA Levels:

- Review of Literature:
  - DaII'Era Marc A et al. (2007): Found that CD10 expression correlated significantly with PSA levels and advanced tumor stage. [17]
  - Fleischmann Achim et al.: Reported a positive correlation between CD10 expression and elevated PSA levels. [19]
- Study Results:
  - In our study, patients with PSA > 20 ng/ml exhibited significantly more CD10 positivity (50%) with a higher prevalence of both cytoplasmic and diffuse membranous positivity. In contrast, those with PSA < 20 ng/ml had lower positivity (4.8%), indicating a statistically significant association

between higher PSA levels and CD10 expression (p = 0.0083). This finding aligns with the literature, confirming the link between elevated PSA and higher CD10 expression, indicating more aggressive disease.

CD10 Expression Patterns:

- Review of Literature:
  - Tawfic Sherif et al. (2003): Found that normal and hyperplastic tissues exhibited distinct CD10 expression, whereas adenocarcinomas (Gleason patterns 2 or 3) showed a loss of membrane and cytoplasmic staining.[20]
  - Voutsadakis Ioannis A et al. (2012): Showed an inverse relationship between CD10 and NF-kB, indicating that CD10 expression decreased with increasing tumor grade.[21]
  - Wang S et al. (2024): Reported a significant association between CD10 expression and aggressive tumor behavior in prostate cancer. [22]
- Study Results:
  - Our data showed that apical membranous CD10 expression was prevalent in lower-grade tumors, while cytoplasmic and mixed expression became more frequent in higher grades. The shift from membranous to cytoplasmic expression in higher Gleason grades (p = 0.0016) parallels findings from Singh Lalit et al. & also with the more recent studies done by Wang S et al. and partially aligns with Tawfic Sherif et al. who observed CD10 loss in early adenocarcinomas but did not describe higher grades .

Key Similarities and Differences:

- Similarities:
  - Both the literature and our results confirm a positive correlation between CD10 expression and increasing Gleason grade, tumor stage, and PSA levels.
  - The shift from membranous to cytoplasmic CD10 expression with increasing tumor grade is consistently observed.
- Differences:
  - Tawfic Sherif et al. observed the absence of CD10 expression in Gleason patterns 2 or 3, whereas our study reports some CD10 positivity in low-grade tumors (Gleason 1 & 2), suggesting that CD10 might be more variably expressed in early-stage cancers in different cohorts. [20]

Our findings align with current literature, confirming CD10's association with aggressive prostate cancer, indicated by higher Gleason grades and PSA levels. The shift from membranous to cytoplasmic CD10 expression supports CD10's role as a biomarker.

Summary & Conclusions

Prostate cancer, the second most common cancer in men, presents diagnostic challenges due to BPH and elevated PSA levels. Our study in West Bengal found higher CD10 positivity in adenocarcinoma versus BPH (p = 0.003) and noted a shift in CD10 expression patterns with rising Gleason grades (p = 0.0016). Additionally, CD10 correlated with PSA levels (p = 0.0083), supporting its potential as a prognostic marker for prostate cancer.

Drawbacks of our study:

1. Small sample size.
2. Single institutional study.

Source of Funding: Nil

Ethical Clearance: This study was approved by Institutional Ethical Commiteee of NRS Medical College & Hospital, Kolkata . Ref no NMC/287, dated 20/8/2021.

Conflict of Interest: Nil

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