SHORT COMMUNICATION

CD10 expression pattern in prostatic adenocarcinoma: Elucidation of differences between Gleason’s grades

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Abstract

CD10, a transmembrane endopeptidase, has been shown to be lost as an early event in prostate cancer. We aimed at evaluating the pattern of expression of CD10 in various Gleason’s grades of prostatic adenocarcinoma in comparison with nodular hyperplasia of prostate. This retrospective study included 30 cases of nodular hyperplasia and 30 of prostatic adenocarcinoma of various Gleason’s grades. Immunohistochemical staining for CD10 was performed on all cases and positivity evaluated as percentage of cells as well as location (membranous or cytoplasmic or both). Of prostatic adenocarcinomas, grade 3 was seen in 10 foci, grade 4 in 28 and grade 5 in 22 foci. CD10 positivity in carcinoma was lower than in nodular hyperplasia, with the lowest positivity in grade 5. The pattern of expression of CD10 also changed from membranous in grade 3 to cytoplasmic in grade 5. Loss of CD10 expression appears to be associated with increasing tumour grade in carcinoma prostate and this can potentially be useful in stratification of such patients.

Keywords: CD10, immunostaining, carcinoma, prostate, Gleason’s grade

INTRODUCTION

CD10 or neutral endopeptidase is a zinc-dependent metalloendopeptidase expressed in the epithelial cells of a wide range of tissues. CD10 has been shown to be involved in migration, survival and apoptosis of prostate cancer cells as well as tumour progression. However, studies evaluating the prognostic potential of CD10 in prostate cancer have generated conflicting results, possibly due to differences between the evaluated cohorts making comparison difficult. An extensive review of the available indexed English literature did not yield any previous report of CD10 expression in prostate cancer from our country.

The present study, hence, aimed to evaluate the CD10 expression in prostate cancer in this part of the world. Additionally, the pattern of CD10 expression in various Gleason’s grade of prostate cancer was evaluated and compared with nodular hyperplasia.

MATERIALS AND METHODS

Selection of cases
A retrospective search for cases of prostatic adenocarcinoma and nodular hyperplasia of the prostate reported from January 2008 till February 2011 (3 years) was made from the files of the Department of Pathology, Hindu Rao Hospital. A total of 60 cases (30 nodular hyperplasia and 30 adenocarcinomas) were included in the study.

Routine H&E sections of all the cases were evaluated to confirm the diagnosis and select appropriate cases for CD10 immunohistochemical staining. In cases of nodular hyperplasia, sections displaying more glandular tissue than the stromal component were selected. For adenocarcinoma cases, sections with malignant foci were selected and Gleason’s grading (primary and secondary) were performed in a blinded fashion by three pathologists (MK, LP, SS).

Immunohistochemistry for CD10
Immunostaining for CD10 (Dako, Germany) was performed by the avidin-biotin complex technique using heat-based antigen retrieval and DAB as the chromogen. The immunostained sections were evaluated for membranous and cytoplasmic positivity for CD10 and percentage of epithelial cells stained positive were noted in different foci of Gleason patterns (grade).
Appropriate statistical testing (non-parametric Mann-Whitney U test) was applied to the results.

RESULTS
The study included 30 cases of nodular hyperplasia and 30 cases of adenocarcinoma of prostate. Of the latter, Gleason’s grade 3 was noted in 10 foci, grade 4 in 28 and grade 5 in 22 foci, making a total of 60 foci (2 grades in each case).

Nodular hyperplasia of prostate showed various histological patterns, including large glands with corpora amylacea, small glands with corpora, large glands with papillary formation and small glands with marked stromal proliferation.

On immunostaining, all (100%) cases of nodular hyperplasia of prostate showed strong apical and cytoplasmic staining for CD10. The mean percent epithelial positivity was 94.3% in these cases (Fig. 1).

In contrast, the mean CD10 positivity in adenocarcinoma cases was lower. The mean positivity ranged from 58.3% in grade 5 foci to 86.2% in grade 4 and 82.2% in grade 3 foci (Table 1). The staining was heterogeneous in grade 4 with a few tumours showing high positivity and others displaying low positivity.

Additionally, the pattern of expression also varied from membranous in grade 3 to both membranous and cytoplasmic in grade 4 and cytoplasmic in grade 5 foci (Fig. 2).

Non-parametric statistical test (Mann-Whitney U test) was applied for significance of difference between various categories (Table 2). Grades 3 and 5 carcinoma had statistically significant lower CD10 positivity than nodular hyperplasia, the difference being highest for grade 5 foci. The difference was significant for grade 3 vs grade 5 and grade 4 vs grade 5. However, the mean positivity for grade 3 and grade 4 were similar.

DISCUSSION
Prostate cancer is a frequent malignancy in men and patients are currently screened using serum levels of prostate-specific antigen (PSA). However, the false-positive rate of serum PSA can be as high as 70%, leading to many unnecessary biopsies. Histological grading by Gleason’s grading system and PSA level, in addition to the post-surgery clinical staging, show relatively good performance in disease prognosis prediction for many patients. However, for a significant number of patients, this is not true. Hence there is the need for informative biomarkers to identify

![FIG. 1: Photomicrographs showing glandular and stromal components of nodular hyperplasia of prostate (a, H&E x200) and strong membranous positivity for CD10 in the glandular component (b, LSAB x100).](image)

| TABLE 1: Values of mean CD10 positivity in nodular hyperplasia and prostate adenocarcinoma |
|---------------------------------------------|-----------------|----------------|
| Nodular hyperplasia                        | 94.3 (77 - 112) | 5.8            |
| Gleason’s grade 3 carcinoma                | 82.2 (44 - 120) | 12.7           |
| Gleason’s grade 4 carcinoma                | 86.2 (52 - 120) | 11.4           |
| Gleason’s grade 5 carcinoma                | 58.3 (27 - 144) | 28.4           |
patients whose cancer requires treatment. An early and reliable differentiation between patients with good vs poor prognosis cancer could reduce unnecessary interventions.\(^7\)

Cluster designation (CD) antigens are cell surface molecules found to be expressed by a variety of human cell types in normal as well as pathological states. Immunophenotyping by CD antigens of human prostate has been done and differences have been noted between cancer and normal prostatic tissue.\(^8\) Among them is the common acute lymphocytic leukaemia antigen (CALLA) or CD10, also known as neutral endopeptidase (NEP), enkephalinase or membrane metallo-endopeptidase (MME). CD10 is a 100-kDa transmembrane glycoprotein involved in cleavage and inactivation of certain peptide hormones important for signal transduction. This is a zinc-dependent enzyme that is widely expressed in epithelial cells of kidney, breast, lung, intestine and prostate.\(^9\)

Early loss of CD10 expression has been reported in a high percentage of prostate tumours.\(^4,8\) Functional studies using prostate

### Table 2: Statistical analysis of CD10 positivity

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<th>P value</th>
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<tr>
<td>Nodular hyperplasia</td>
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<tr>
<td>vs Grade 3</td>
<td>0.016</td>
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<tr>
<td>vs Grade 4</td>
<td>0.05</td>
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<td>vs Grade 5</td>
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<td>vs Grade 5</td>
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<td>Grade 4</td>
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<td>vs Grade 5</td>
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cancer cell lines showed antitumour effects of CD10, including inhibition of migration, growth and survival of cells.\textsuperscript{1} However, results from single cell lines may not appropriately reflect the \textit{in vivo} findings in hormone-naive patients. Studies on prognostic potential of CD10 in human prostate cancer have yielded conflicting results, describing CD10 expression as favorable, unfavorable and having no effect.\textsuperscript{2-4} The results of these various studies are probably not comparable due to differences between the evaluated cohorts. Loss of CD10 has also been implicated in transition from androgen-dependent prostate cancer to androgen-independent cancer.\textsuperscript{10}

The gene encoding CD10 is transcriptionally activated by androgen and androgen withdrawal results in decreased CD10 expression.\textsuperscript{11}

In the present study, prostate carcinoma showed lower CD10 positivity compared to cases of nodular hyperplasia. Grade 5 foci demonstrated lowest positivity for CD10 among the various Gleason grades. The pattern of CD10 expression also changed from membranous in grade 3 to cytoplasmic in grade 5 foci. Hence, we found progressive loss of expression and change in differential cytoplasmic staining of CD10 with increasing histological grade of prostate carcinoma. Our results are in consonance with earlier studies by Freedland \textit{et al} and Voutsadakis \textit{et al}.\textsuperscript{4,12} However, other authors have shown high CD10 expression in lymph node metastases of prostate cancer.\textsuperscript{8} It has been hypothesised that CD10 allows the malignant cells to escape the prostate to regional lymph nodes and proximal organs.\textsuperscript{7} Extensive review of the available indexed English literature failed to reveal any previous report of CD10 expression in prostate cancer from this subcontinent.

In conclusion, CD10 expression can potentially be utilised clinically for stratifying prostate cancer in an attempt to predict biologic behaviour of the tumour. CD10 expression in prostate cancer may have therapeutic implications as well in the form of CD10 inhibitors. The present study is the first such report from our region. Further studies are required on this subject to validate the existing results.

REFERENCES


