CARCINOMA PROSTATE HISTOPATHOLOGY IN NEEDLE BIOPSIES INCLUDING REVISED GLEASON'S GRADING AND ROLE OF IMMUNOHISTOCHEMICAL MARKERS

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ABSTRACT

BACKGROUND

Adenocarcinoma of prostate is the most common form of cancer in men accounting for 29% of cancers in developed nations and the incidence of prostatic cancer is 6.4% in males of Trivandrum District.

MATERIALS AND METHODS

All prostatic biopsies taken per rectally and stained by haematoxylin and eosin. In suspected cases of malignancy immunohistochemical markers, the AMACR P504S and high molecular weight cytokeratin 34E12 were done.

RESULTS

The total number of cases studied were 142. The final diagnosis with histomorphological features show that maximum cases were prostatic carcinoma constituting 45.5% of the samples received.

CONCLUSION

All prostatic carcinomas were graded by revised Gleason's grade (ISUP 2005) and the use of immunohistochemical markers in arriving at a definite diagnosis in carcinoma prostate was confirmed.

KEYWORDS

Carcinoma Prostate, PSA, Histopathology, 34, AMACR, Immunohistochemistry.

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BACKGROUND

Adenocarcinoma of prostate is the most common form of cancer in men accounting for 29% of cancer in developed nations.[1] The incidence of prostatic carcinoma in Thiruvananthapuram district is 6.4% of all cancers in male. Per rectal needle biopsy of prostate in developed nations where screening for prostatic cancer by regular serum PSA assessment is done the most common indication is a high level of PSA detected in routine screen. In resource depleted nations, many cases are detected at a stage when patients presents with symptoms either due to local spread or metastasis. There is no comprehensive study available commenting on the indications of prostatic biopsy in Kerala, but two indications in our clinical setting are raised PSA values and a hard prostate on digital rectal examination. Epstien J I[2] in his review has observed that patterns favouring malignancy are infiltrative small and crowded glands. At the edge of most adenocarcinomas, scattered neoplastic glands infiltrate widely between larger benign glands. In order to identify limited amounts of cancer on needle biopsy material, one first has to identify the normal nonneoplastic prostate and then look for glands that do not fit in morphologically. Focus of crowded glands, small glands infiltrating between larger nonneoplastic glands, prominent nucleoli with enlargement, hyperchromasia and mitotic figures are in favour of malignancy. Amphophilic cytoplasm with sharp luminal borders is seen malignancy, prostatic crystalloids, glomerulations and collagenous micronodules, are two features along with perineural invasion are pathognomonic of prostate cancer other than metastasis.

At the ISUP (International Society for Urological Pathologist, 2005) conference, it was decided that for needle biopsies, patterns 1 and 2 should be diagnosed rarely, if ever. This decision resulted from the observation that in needle biopsies, it was usually impossible to evaluate the edge of the lesion and as such circumscription of the tumour, which is an important diagnostic feature of these Gleason patterns cannot be assessed in the vast majority of cases. Two distinct patterns were defined for pattern 3 tumours. The most common pattern consists of discrete small acini with variations in size and shape that often infiltrate between benign glands.

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Small cribriform glands with few and irregular bridging cords do not have the aggressive appearance of chains of coalescent acini or large sheets of coalescent glands forming a cribriform sheet. Cribriform glands were considered pattern 3 only if they were well circumscribed, ovoid to round and of similar size to normal glands. There was consensus that most cribriform glands should be classified as pattern.[3]

Cribriform glands larger than benign glands and with an irregular border were classified as pattern 4. This pattern also included small glands with poorly-formed lumens, fused microacini and hypernephroma-like tumours. Grade 5 has been retained as described earlier.

It was also agreed that lower-grade secondary patterns comprising <5% of the tumour area should be ignored, while any proportion of higher secondary pattern, even if <5% of tumour area, should contribute to the score.

If a tertiary pattern was present, then the final score should be derived from the primary pattern with the (higher) tertiary pattern being reassigned as the secondary pattern.

Aims and Objectives

1. To study the histology of all tumours and tumour-like lesions in prostatic needle biopsies received in the department during the study period.
2. To histologically grade all prostatic carcinomas received in such biopsies using the revised Gleason grade (ISUP, 2005).
3. To assess the role of IHC markers (34βE12 and AMACR) in cases of histologically suspicious malignancies of prostate in arriving at a definitive diagnosis.

MATERIALS AND METHODS

Department of Pathology, Thiruvananthapuram Medical College - Histopathology and Immunohistology sections over a period of two years (August 2010 to July 2012). All prostatic needle biopsies taken per rectally received in the department during the study period were included. All specimens were formalin fixed, processed, paraffin embedded in total and thin 3 microns sections were taken and stained by Haematoxylin and Eosin. In cases of atypical proliferation suspected of malignancy, staining for immunohistochemical markers, the AMACR (P504S) and High Molecular Weight cytokeratin (34βE12)[3] was done to further characterise the lesion.

Inclusion Criteria

All per rectal biopsies of prostate in which raised PSA and per rectally hard nodules were selected for biopsy.

Exclusion Criteria

Per rectal biopsies done in prostatic abscess, carcinoma of the rectum, other malignancies infiltrating prostate were excluded.

Technique

All prostate biopsies were taken using prostatic guns and the core biopsy fixed in formalin and stained with haematoxylin and eosin and suspected cases sent for immunohistochemical markers.

RESULTS

The total number of prostatic biopsies received during the study period of two years was 142. The age group included in the study was from 48 to 87 years of age. Four out of these cases had bone metastasis without any urinary symptoms. The rest had nonspecific symptoms related to urinary tract like urinary hesitancy or repeated urinary tract infections. The PSA value were found elevated in 84.5% of cases, a value above 4 ng/mL was suspicious of malignancy and that above 100 ng/mL was more specific for malignancy. The PSA value in ng/mL was categorised into four classes as <4 ng/mL; 4-10 ng/mL; 10-100 nm/mL and above 100 ng/mL. The raised PSA value showed a positive relationship to a diagnosis of cancer. The number of cores received varied from one to four. These were done under digital guidance of hard nodules. 37.3% of case had only two cores in the TruCut and maximum number of four cores was received in 26% of cases. The average number of cores received was 2.7. This is less than that seen in most of the studies done as usually sextant biopsies are advocated for prostate sampling. The lack of availability of transrectal ultrasound and financial constraints are the reason for the above.

Architectural Feature	Frequency (N=142)	%
Stroma only, no glands	7	5.0
Benign glands	79	55.6
Small neoplastic glands	54	38.02
Back-to-back glands	4	2.8
Sheets of neoplastic cells	4	2.8
Lymphoid aggregates	13	9.15
Ductal type glands	1	0.7

Table 1

The most common finding was corpora amylacea seen in 11% of the total biopsies received, but none of these were seen in cases with diagnosis of malignancy. However, James D Christian[4] et al observed that corpora amylacea were located in malignant acini in 0.4% of needle biopsies.

Of the other three intraglandular materials seen in malignancy, crystalloids were most common accounting to 2.1% of all biopsies. This is far less than that described by Del Rosario AD,[5] et al, who observed such crystals in 14 to 36% of cancers.

Varma et al[6] has described presence of faintly basophilic intraluminal mucin in up to 52% of cases, but no such material was demonstrated in the present study probably because of different staining characteristics. The final diagnosis with histomorphological features show that maximum cases were carcinoma constituting 46.5% of the samples received.

Gleason Sum	Number of Cases	Percentage
Score 6	16	24
Score 7	22	33
Score 8	21	32
Score 9	6	9
Score 10	1	2
Total	**66**	**100**

Table 2

A score of 7 and 8 was seen in almost equal proportion, constituting 33% and 32%, a score of 6 was given in 24%.

Grades	Number of Cases	Percentage
Grade (3,5)	7	33.3
Grade (4,4)	11	52.3
Grade (5,3)	3	14.2
Total	**21**	**100**

Table 3

There were five cases diagnosed as atypical glandular hyperplasia. In H and E, these were small glands without appreciable basal cell layer, moderate amount of cytoplasm and mildly enlarged nuclei.

Two immunohistological markers were used, one for staining the basal cell layer (34βE12-HMW CK); the other was P504S (AMACR),[7] which can give cytoplasmic positivity in neoplastic glands.

Two of the five cases showed attenuated basal cells and absent neoplastic cells, hence diagnosed as benign (one crush artifact and other as benign atrophy).

	HMW CK	P504 S	Diagnosis
Case 1	Fragmented	Negative	Same opinion (atypical hyperplasia)
Case 2	Negative	Positive	Possible malignancy
Case 3	Positive	Negative	Normal (crush artifact)
Case 4	Positive	Negative	Normal (atrophic glands)
Case 5	Fragmented	Negative	Same opinion (atypical hyperplasia)

Table 4

DISCUSSION

The use of IHC markers could change the diagnosis into malignancy in prostate 20% of cases; 40% of cases were resolved negative for malignancy by IHC; the rest 40% were left unresolved. Vincent Molinie,[3] et al, describes diagnostic utility of a combination of basal cell and neoplastic marker to resolve up to 89.4% of atypical acinar proliferation.

The number of cases diagnosed as atypical glandular (acinar) hyperplasia in prostatic biopsies by H and E itself is less compared to Western statistics. Also, most of the diagnoses are either malignancy or benign glands. This maybe because majority of patient population are not detected by screening and the biopsies taken are not sonography directed, but hard areas are sampled after manual (digital) palpation. Hence, the biopsied tissue is mostly carcinoma or nodules of benign hyperplasia.

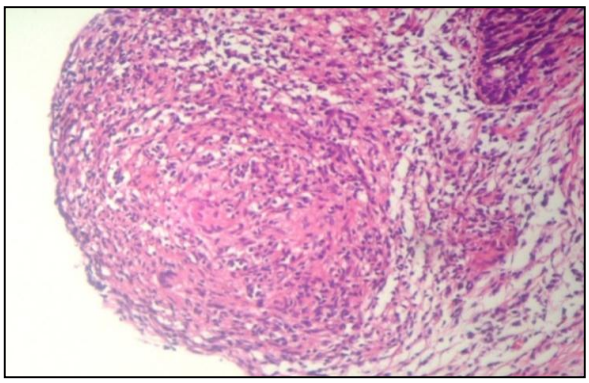

Figure 1. Granulomatous Prostatitis (10X, H and E stain)

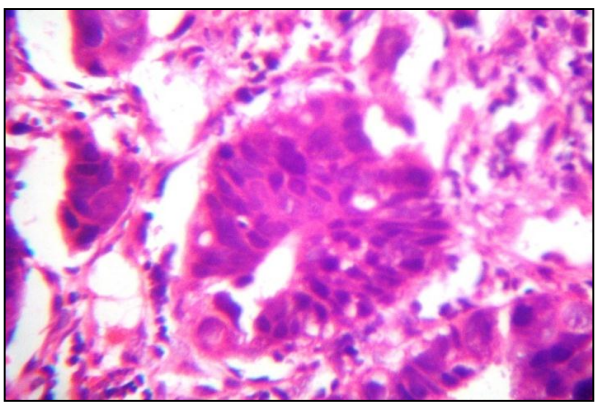

Figure 2. High-Grade Ductal Carcinoma (40X H and E Stain)

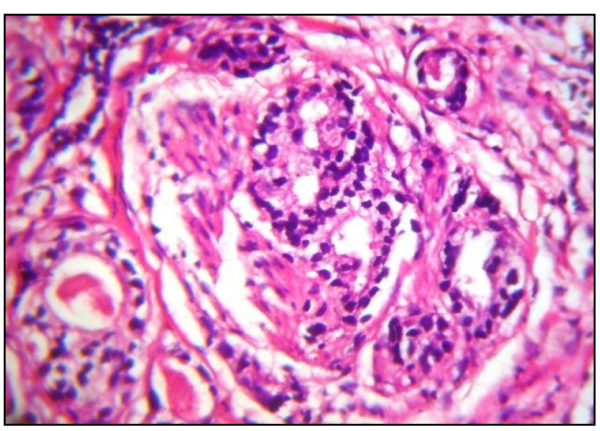

Figure 3. Perineural Invasion (10X, H and E Stain)

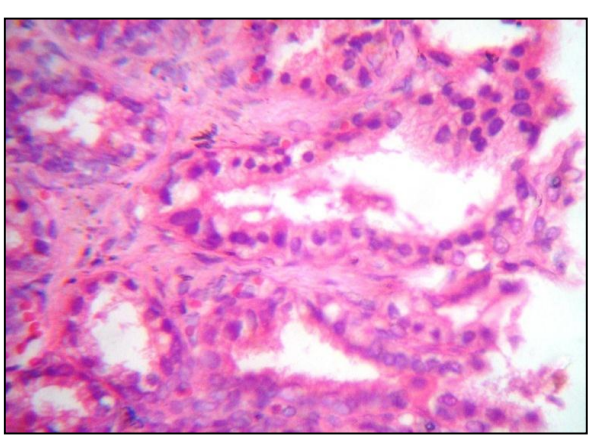

Figure 4. Suspected Atypical Cells on H and E, 40X

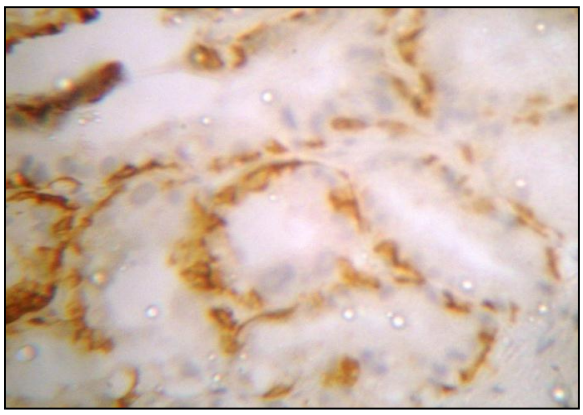

Figure 5. Positivity of Tumour Cells for AMACR (40X)

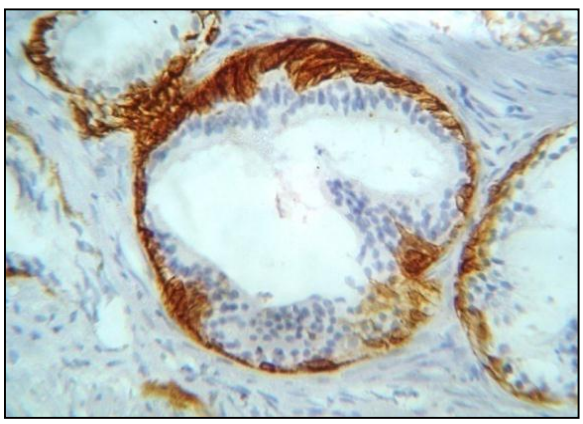

Figure 6. Positivity of Basal Cells in Benign Glands for 34BE12 (10X)

CONCLUSION

To conclude, all prostatic carcinomas were graded by revised Gleason's grade ISUP 2005 and the role and importance of immunohistochemical markers in arriving at a definite diagnosis in suspected cases is definitely more than what is actually being practiced and can go a long way in establishing the diagnosis and prognosis in such lesions.

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