Mucin Production in Prostatic Adenocarcinoma: A Retrospective Study of 51 Radical Prostatectomy Specimens in Thai Population

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ABSTRACT

Background: Intraluminal and extracellular acid mucin secretion is one of the ancillary findings of prostatic adenocarcinoma and can aid in diagnosis.

Objective: To determine the actual frequency and percentage of acid mucin production in prostatic adenocarcinoma from radical prostatectomy specimens at the Department of Pathology, Siriraj Hospital.

Methods: This is a retrospective study of 51 cases of radical prostatectomy with diagnosis of prostatic adenocarcinoma at the Department of Pathology, Siriraj Hospital from January to March 2008.

Results: Forty-nine cases (96%) of these prostatic adenocarcinomas showed positive mucicarmine stain. Among these, 24 (47.1%) cases were graded as Gleason score (GS) 7; 12 (23.5%) cases as GS 9; 8 (15.7%) cases as GS 6; 4 (7.8%) cases as GS 8, and 1 (1.9%) case as GS 5. Two cases (3.8%) without mucin production were graded as GS 7 and 9.

Conclusion: Intraluminal acid mucin is one of the useful ancillary findings in diagnosing prostatic adenocarcinoma, particularly when combined with other architectural and cytological findings. The high frequency and percentage of actual acid mucin production in prostatic adenocarcinoma studied in radical prostatectomy can be applied to a questionable positive core biopsy with confidence.

Keywords: Prostatic adenocarcinoma, intraluminal and extracellular acid mucin, radical prostatectomy

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Prostatic adenocarcinoma is the most common malignancy and the second leading cause of cancer-related deaths in men in the United States.1 In Thailand it is one of the five most common malignancies in males with an estimated incidence rate of 4.9 per 100,000 and the trend has been increasing gradually during the past decade.2 In Siriraj Hospital, it is the second most common cancer in men.

Generally, the diagnosis of prostatic adenocarcinoma is based on a constellation of architectural, cytological, and ancillary findings.1,4 Well known ancillary histologic features of prostatic adenocarcinoma include perineural invasion, mucinous fibroplasia (collagenous micronodule), glomerulations, mucin production, crystalloids, microvascular invasion, and extra-prostatic extension.1,6 Intraluminal and extracellular mucin secretion in prostatic carcinoma has been observed by many authors.7,10 It is estimated that two-thirds of prostatic carcinomas produce acid mucin which can be visualized in routinely H&E stained sections and can be highlighted by mucicarmine, alcian blue, and colloidal iron stain.11-15 Recently, it has been found that mucin secretion is prostatic carcinomas is helpful in diagnosis and is practical in routine practice.16-17 Although it is shown that acid mucin can also be present in other conditions including atrophic change, basal cell hyperplasia, adenosis, sclerosing adenosis, mucinous metaplasia, prostatic intraepithelial neoplasia (PIN), and nodular hyperplasia,16,21 a combination of acinar atypia and mucin production is adequate to make a diagnosis of prostatic adenocarcinoma.

In Thailand, no study of mucin production in prostatic carcinoma has been carried out. Routinely, mucicarmine stain is not performed in either benign or malignant prostatic lesions. Questionable cases of prostatic carcinoma are diagnosed on the basis that malignant acini possess no basal cell layers which can be
demonstrated by immunohistochemical study, using 34 \( \beta \)E12 antibody clone, and antibody to high-molecular-weight cytokeratin, found only in the basal cells not in acinar cells. This technique is, however, available only in large medical centers, not in regional or provincial hospitals. The objective of this study is to determine the actual frequency and percentage of mucin production in prostatic adenocarcinoma from radical prostatectomy specimens in Thai patients and to implement its presence in the diagnosis of prostatic carcinoma.

MATERIALS AND METHODS

The study included 51 cases of prostatic adenocarcinoma, with any of Gleason’s scores in radical prostatectomy specimens at the Department of Pathology Siriraj Hospital from January to March 2008. All H&E slides were retrieved and reviewed for mucin production. Mucicarmine was applied for confirmation. The Gleason scores and number of mucin positive areas were recorded. Questionable prostatic glands with mucin production were further studied by 34\( \beta \)E12 immunostaining to exclude benign glands. Information was filled in the case record form. The data were analyzed by Z-test statistic.

This study received approval from the Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University [No. Si236/2008].

RESULTS

Forty-nine cases (96%) of these prostatic adenocarcinomas showed positive acid mucin production in both routine H&E and mucicarmine stain. Two cases (4%) showed negative mucin production. No doubtful glands with mucin production that required 34BE12 immunostaining to confirm the absence of basal cell layer were present in the study. The relationship between Gleason score and number of cases with and without mucin production was shown in Table 1. Mucin, intraluminal and extracellular, could be seen in all Gleason scores. The distribution varied from case to case and from area to area.

DISCUSSION

The frequency of intraluminal and extracellular mucin production in prostatic adenocarcinoma in this study was as high as 96%, much higher than many previous studies that showed 25-68% of mucin is prostatic carcinomas. The difference might be due to the numbers of blocks submitted. In our Department, approximately 30-50 blocks are routinely cut in each case of radical prostatectomy. Careful examination of these specimens is very important to detect mucin production. Whether race plays a role in this variation needs further study with larger sample sizes and more different sources of specimens.

We did not find mucin in benign conditions in this study. We performed only mucicarmine stain for mucin detection because of its simplicity in preparing, staining, and interpretation. In a short trial before this study, we found that Alcian blue stain was not specific and provided a high background while colloidal iron stain was difficult to prepare and stain.

Acid mucin is already visualized in routine H&E stained sections. It appears as delicate, threadlike, faintly basophilic (blue-tinged) material (Fig 1A and Fig 2A). In mucicarmine stain, it turns red, quite a contrast to the pale grey background (Fig 1B and 2B). The pattern of distribution of mucin production in prostatic adenocarcinoma is non-homogeneous and multifocal. We also found that prostatic adenocarcinoma with a Gleason score of 9 could still produce mucin but with fewer positive areas. The findings also indicated that tumors with better differentiation (lower Gleason scores) would have a better chance to produce mucin.

<table>
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<tr>
<th>Gleason score</th>
<th>No of cases</th>
<th>No of cases with mucin production</th>
<th>%</th>
<th>No of cases with negative mucin production</th>
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TABLE 1. The relation of Gleason score and number of cases with and without mucin production in prosthetic adenocarcinoma.
It has to be kept in mind that mucin production is only one of the ancillary findings in prostatic adenocarcinoma. Definite diagnosis is still based on the absence of basal cell layers in malignant acini.\textsuperscript{5,6} All doubtful cases should be confirmed by 34βE12 immunostaining.\textsuperscript{22} If only a few atypical acini are present in a core biopsy and no adequate tissue is available for study in subsequently cut sections, a descriptive diagnosis should be made and a repeat biopsy should be encouraged.

CONCLUSION

Intraluminal and extracellular acid mucin is one of the useful ancillary findings in diagnosing prostatic adenocarcinoma, particularly when combined with other architectural and cytological findings. An actual mucin production in prostatic adenocarcinoma in radical prostatectomy specimens is of a relatively high percentage in Thai patients. If mucin is not detected in suspected cores, other ancillary findings and immunohistochemical study are required in diagnosis.

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REFERENCES