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Foamy gland carcinoma in core needle biopsies of the prostate: clinicopathologic and immunohistochemical study of 56 cases☆

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ABSTRACT

Foamy gland carcinoma is a subtype of acinar adenocarcinoma characterized by foamy appearance, large cytoplasm, pyknotic nuclei, inconspicuous nucleoli and infiltrative pattern. In this study, we investigated the histological features and the incidence of foamy gland carcinoma. We compared foamy gland carcinoma with acinar adenocarcinoma according to age, prostate-specific antigen value, Gleason score, peripheral nerve invasion and accompanying high-grade prostatic intraepithelial neoplasia. Besides, we investigated the diagnostic value of immunohistochemical markers in foamy gland carcinoma. A total of 863 TRUS-guided prostate needle core biopsies performed at our hospital pathology clinic between January 1, 2010, and December 31, 2011, were examined, 251 of these were diagnosed acinar type adenocarcinoma. Conventional acinar type adenocarcinoma was present in 195 (78%) cases, and foamy gland carcinoma, in 56 cases (22%). We found that 11 (19%) of the 56 foamy gland carcinoma cases were pure and 45 (81%) cases were mixed with conventional acinar type adenocarcinoma. Single-core localization was present in 7 of 14 pure foamy gland carcinomas, and the number of cases with a Gleason score of 7 and above was 21 (37%). No statistically significant difference was found between foamy gland carcinoma and conventional acinar type adenocarcinoma in terms of age, Gleason score, high-grade prostatic intraepithelial neoplasia, and prostate-specific antigen values. Peripheral nerve invasion was found to be statistically significantly more common in foamy gland carcinoma compared to acinar type adenocarcinoma ($P < .05$). The staining percentage of immunohistochemical markers in foamy gland carcinoma was 90.1% for p63, 90.6% for 34Beta12 and 90.6% for AMACR.

1. Introduction

Prostate cancer is the most common type of cancer in men and ranks second in cancer deaths [1]. Its incidence has been increasing and the age at detection decreasing with the increase of diagnostic methods, use of prostate-specific antigen (PSA) among the routine controls of those over the age of 50 in particular, and increased awareness of prostate cancer.

Most prostate adenocarcinoma cases are conventional acinar type adenocarcinoma. Although less common, there are also many subtypes of prostatic adenocarcinoma. Foamy gland carcinoma was first defined by Epstein and Nelson in 1996 and is one of the subtypes that cause the most difficulty during diagnosis [2]. Foamy gland adenocarcinoma is a subtype of acinar type prostatic adenocarcinoma and consists of cells with abundant foamy cytoplasm and a very low nucleus/cytoplasm ratio. It is more difficult to diagnose because it has a low histological grade and resembles the normal prostate glands in small tumors. There are few studies on foamy gland adenocarcinoma and although there is no difference with conventional acinar type adenocarcinoma in prognostic terms, a Gleason score of 7 has been reported to be more frequent in recent studies [3,4].

The large nuclei, prominent nucleoli and prominent infiltrative pattern that are the typical histological characteristics of classic acinar adenocarcinoma are not usually found in foamy gland carcinoma. This makes it difficult to identify these lesions in needle core biopsy materials especially when they are well differentiated. Immunohistochemical markers are therefore needed in the diagnosis of pure foamy gland carcinoma especially when there is only a small number of glands in only a few cores.

We compared the frequency of the foamy cell *variant* and diagnostic problems of the cases diagnosed with prostate acinar type adenocarcinoma in all transrectal ultrasound (TRUS) biopsy of the prostate materials sent to the pathology laboratory of our hospital between 2010 and 2011 and compared these cases with the conventional type acinar adenocarcinoma in terms of PSA, age,

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Gleason score, high-grade prostatic intraepithelial neoplasia (HGPIN) and peripheral nerve invasion. We also investigated the value of the p63, high-molecular-weight cytokeratin and alpha-methyl acyl CoA racemase (AMACR) immunohistochemical markers in our foamy gland carcinoma cases.

2. Materials and methods

The 251 cases diagnosed with acinar type adenocarcinoma among a total of 863 TRUS-guided prostate needle core biopsies performed at our pathology clinic between January 1, 2010, and December 31, 2011, were examined. Foamy gland carcinoma was searched for in all cases.

Foamy gland carcinoma was diagnosed according to the following criteria: forming at least 10% of the tumor, abundant foamy cytoplasm, and the frequent presence of pyknotic (small, round, hyperchromatic) nuclei and infiltrating features. Grading was performed according to modified Gleason grading criteria [5]. The ratio of cases with a Gleason score of 7 and above was taken into account for the foamy gland carcinoma and acinar adenocarcinomas. The association of foamy gland carcinoma with the pure or classic type acinar adenocarcinoma was investigated and those with single core biopsy were also identified.

In addition, the age, PSA level, Gleason score, HGPIN and peripheral nerve invasion in foamy gland carcinoma and conventional acinar type adenocarcinoma were compared. The immunhistochemical stains p63, high-molecular-weight cytokeratin and AMACR were used in cases diagnosed with foamy gland carcinoma to determine their diagnostic value.

Statistical evaluation: The SPSS for windows 10.0 statistical package program was used for statistical analyses. Student t test, the Mann-Whitney U test, and the χ^2 test were used for the comparison. $P < .05$ was accepted as significant.

3. Results

Conventional acinar type adenocarcinoma was present in 195 (78%) cases and foamy gland carcinoma in 56 cases (22%). We found that 11 (19%) of the 56 foamy gland carcinoma cases were pure and 45 (81%) cases were mixed with conventional acinar type adenocarcinoma (Figs. 1–5). Single-core localization was present in 7 of 14 pure foamy gland carcinomas and the number of cases with a Gleason score of 7 and above was 21 (37%). No statistically significant difference was found between foamy gland carcinoma and conventional acinar type adenocarcinoma in terms of age, Gleason score, HGPIN, and PSA values. The mean age was 68.45 years in foamy gland carcinoma and 67.32 years in conventional adenocarcinoma. The mean PSA was 46.5 ng/mL in foamy gland carcinoma and 31.2 ng/mL in conventional carcinoma with no statistically significant difference although higher in foamy gland carcinoma.

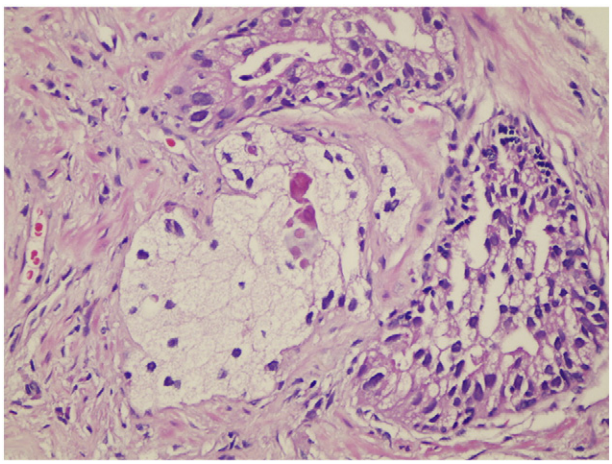

Fig. 1. One foamy gland between two conventional adenocarcinoma glands.

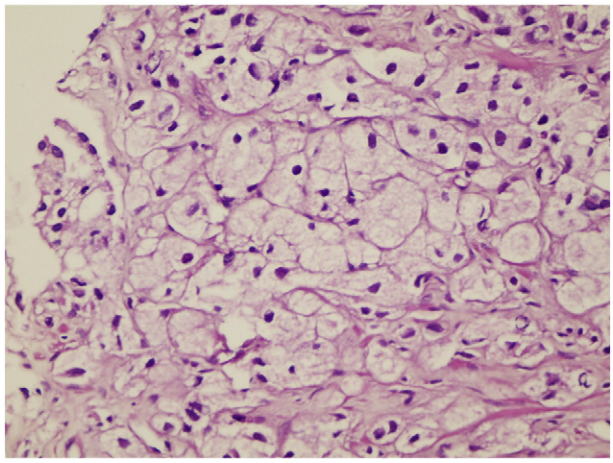

Fig. 2. Foamy gland carcinoma shows abundant foamy cytoplasm in the tumor cells; Gleason score 4 + 4 = 8.

No statistically significant difference was found between the groups in terms of HGPIN positivity ($P > .05$). The number of cases with a Gleason score of 7 and above was 21 (37%) in the foamy gland carcinoma cases and this ratio was 38% in classic acinar adenocarcinoma.

Peripheral nerve invasion was found to be statistically significantly more common in foamy gland carcinoma compared to acinar type adenocarcinoma ($P < .05$) (Fig. 6). The staining percentage for the three immunohistochemical markers was 90.1% for p63 and 90.6% for 34Beta12 and AMACR 90.6% (Fig. 7) in foamy gland carcinoma.

4. Discussion

Acinar type adenocarcinoma is the most commonly seen carcinoma in the prostate and makes up about 90% of the tumors. The tumor is diagnosed by its infiltrating characteristics, small glandular structure, large nucleus, prominent nucleolus, amphophilic staining cytoplasm, flat cytoplasmic luminal border, mucin in the lumen, collagenous micronodules (mucinous fibroplasia) and glomeruloid proliferation in the gland [1]. In addition, malignancy criteria are peripheral nerve, periprostatic soft tissue and angiolymphatic invasion.

Although acinar type adenocarcinoma shows the above mentioned histological features in most cases, many histological subtypes have been defined in the recent World Health Organization classification such as foamy gland variant (carcinoma), atrophic variant, pseudohyperplastic

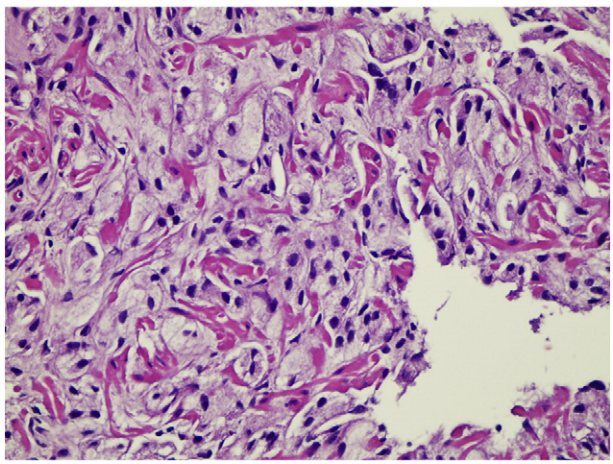

Fig. 3. Foamy gland carcinoma showing small hyperchromatic nuclei and foamy cytoplasm; Gleason score 4 + 4 = 8.