Adenosquamous Carcinoma of the Prostate

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Abstract

An unusual adenosquamous carcinoma originating in the prostate of a 73-year-old man is described. The histological finding showed a well differentiated squamous cell carcinoma admixed in an adenocarcinomatous area. A transitional area of 2 carcinomatous elements was also noted. Seven months prior to the development of this lesion, a diagnosis of adenocarcinoma had been established by transurethral resection of the prostate and the patient had been treated with bilateral orchiectomy. This is the first case of adenosquamous carcinoma of the prostate reported in Korea. The pathogenesis and previous reports of this lesion will be discussed.

Key Words: Prostate, adenosquamous carcinoma

INTRODUCTION

Carcinoma of the prostate gland is the most common malignant tumor affecting adult males in the United States. In 1996, 317,000 new cases were diagnosed and approximately 40,400 Americans died of this disease.¹ Conventional adenocarcinoma represents the large majority of tumors (as much as 95%), however a small number of mixed carcinoma, which incorporates at least 2 malignant epithelial cell components, have also been reported. The majority are cases of mixed adenocarcinoma and transitional cell carcinoma. Adenosquamous carcinoma of the prostate is an extremely rare neoplasm and to our knowledge only 6 well-established cases have been reported.²⁻⁷ Recognition of adenosquamous carcinomas is important because of their general refractories to hormonal manipulation.⁸

We experienced a case of adenosquamous carcinoma of the prostate in which we undertook pathological and immunohistochemical studies. The pathogenesis of this tumor is discussed and the literature is also reviewed.

CASE REPORT

A 73-year-old Korean man was admitted to Kyung Hee University Medical Center due to obstructive urinary symptoms in April 1998. Ten days prior to admission, he had been diagnosed prostatic adenocarcinoma by needle biopsy and bone metastasis at an other hospital. At the time of admission, the patient's general condition was good and his prostate-specific antigen (PSA) level was elevated (30.3 ng/mL, normal: 0–4 ng/mL). Transrectal ultrasonogram showed hypoechoic lesions in both peripheral zones with papillary mass in the bladder base. Clinically the patient was felt to be stage D2. A transurethral resection of the prostate (TURP) and bilateral orchiectomy was done. Tissues from the prostate and papillary mass in the bladder base revealed Gleason score 8 (4+4) prostatic adenocarcinoma, without evidence of squamous differentiation (Fig. 1). In November 1998, the patient was readmitted for a voiding difficulty. Digital rectal examination disclosed a hard consistency without a definite nodule. Transrectal ultrasonogram and cystoscopy revealed enlarged right lateral lobe and papillary mass in the bladder neck portion. Bone scan revealed multiple metastatic foci of the cervical and lumbar spine. Laboratory data were all within normal limits, including PSA level (0.27 ng/mL). The patient underwent a repeat TURP for relief of obstruction. The histological finding showed adenosquamous carcinoma mainly composed of malignant squa-
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Fig. 1. Section of prostate showing adenocarcinoma, Gleason grade 4 (H&E, ×40).

Fig. 2. Section of prostate showing well differentiated squamous cell carcinoma (H&E, ×100).

Fig. 3. Section of prostate showing admixture of adenocarcinoma and squamous cell carcinoma (H&E, ×100).

Fig. 4. Immunohistochemical stain for high molecular weight cytokeratin showing positive staining in the squamous cell carcinoma area and negative staining in the adenocarcinoma area (ABC method, ×40).

Adenosquamous carcinoma of the prostate is an extremely unusual neoplasm and data from 6 well-documented cases in addition to the present case have been collected (Table 1). No definitive conclusions can be drawn from these cases; nonetheless, certain features are noteworthy. In all 7 cases including ours, an initial pathological diagnosis of ordinary prostatic adenocarcinoma was made and treatment, which included radiotherapy or hormonal therapy, was instituted. After varying periods of time, an adenosquamous carcinoma appeared. The duration between diagnosis of conventional adenocarcinoma and subse-

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Table 1. Reported Cases of Adenosquamous Carcinoma of the Prostate

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<tbody>
<tr>
<td>Age at diagnosis (yr)</td>
<td>58</td>
<td>68</td>
<td>77</td>
<td>70</td>
<td>60</td>
<td>56</td>
<td>73</td>
</tr>
<tr>
<td>Clinical symptom</td>
<td>Bone pain</td>
<td>Urinary frequency</td>
<td>Urinary obstruction</td>
<td>Urinary obstruction</td>
<td>Urinary obstruction</td>
<td>Urinary obstruction</td>
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<tr>
<td>Stage of disease</td>
<td>D2</td>
<td>C</td>
<td>D2</td>
<td>BD1</td>
<td>N/A</td>
<td>D2</td>
<td></td>
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<tr>
<td>Serum PAP</td>
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<td>Normal</td>
<td>Elevated</td>
<td>Normal</td>
<td>Elevated</td>
<td>N/A</td>
<td>N/D</td>
</tr>
<tr>
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<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Elevated</td>
<td>Elevated</td>
<td>Elevated</td>
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<tr>
<td>Radiotherapy</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
</tr>
<tr>
<td>Surgery</td>
<td>None</td>
<td>TURP</td>
<td>TURP</td>
<td>TURP</td>
<td>Radical prostatectomy</td>
<td>Radical prostatectomy</td>
<td>TURP</td>
</tr>
<tr>
<td>Interval (biopsy diagnosis to final diagnosis)</td>
<td>4 yr</td>
<td>4 yr</td>
<td>10 yr</td>
<td>8 yr</td>
<td>1 mo</td>
<td>3 mo</td>
<td>7 mo</td>
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<tr>
<td>Follow-up</td>
<td>N/A</td>
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<td>5 mo; alive</td>
<td>9 mo; alive</td>
<td>1 yr; DOD</td>
<td>N/A</td>
<td>5 mo; alive</td>
</tr>
</tbody>
</table>

N/A, not available; N/D, not done; TURP, transurethral resection of prostate; DOD, dead of disease.

quent adenosquamous carcinoma ranged from 1 month to 10 years. However, there was 1 case report showing de novo adenosquamous carcinoma without previous therapy. Gurtuso et al. suggested the possibility that the squamous component was present in the primary tumor but was absent in the biopsy specimen because of the small sample size. In all 7 cases, there is no difference in the conventional prostatic adenocarcinoma in terms of the age group affected, clinical symptomatology, as well as the mode of tumor spreading. Prostatic acid phosphatase was normal in 2 cases, elevated in 3 and not done in 2. Serum PSA was elevated in 3 cases including the 1 described here, while the others were not done. The stage of disease at presentation ranged from stage B to stage D2. The response to estrogen therapy was poor in all cases when it was administered. Histologically, adenosquamous carcinoma showed an intimate association of acinar adenocarcinoma with unequivocal squamous carcinoma. The adenocarcinoma was usually high grade and the squamous component usually showed keratinization and/or intercellular bridges.

There are several possible theories to explain the histogenesis of adenosquamous carcinoma of the prostate: 1) there is a metaplastic transformation of adenocarcinoma cells; 2) it is a collision-type tumor, with the squamous component developing from metaplastic foci after radiation or hormonal therapy; or 3) there is a possible deviation from pluripotent stem cells capable of multidirectional differentiation.

Benign squamous metaplasia in the prostate following infarction or estrogen therapy has been well documented. However, when one considers the large number of patients with prostatic adenocarcinoma treated with radiation and/or hormone therapy, as well as the rarity of adenosquamous carcinoma, it is very difficult to accept any single pathogenetic mechanism. It is likely, as Bennet and Edgerton hypothesized, that the adenosquamous carcinoma may be a collision tumor made up of an adenocarcinomatous component and prostatic ductal elements with squamous metaplasia resulting from radiation or hormonal therapy. This suggestion is also reasonable for the other reported cases, including the present case. However, a recent case showed evidence of de novo adenosquamous carcinoma without previous therapy.

Many types of cancer may develop in the prostate gland, including mucinous, transitional, squamous, signet ring cell, or small cell carcinoma, so it is possible that a pluripotent stem cell capable of multidirectional differentiation may give rise to these various types of cancer. Moyana et al. proposed that adenosquamous carcinoma is derived from resident pluripotent stem cells capable of multidirectional differentiation. Devaney et al. described a case that supported the existence of pluripotent stem cells that, following appropriate stimuli (such as irradiation or estrogen therapy), altered their line of differentiation. The altered differentiation may account for the lack.
of expression of normal prostatic antigens in the metaplastic and malignant squamous cells. The squamous component in their case, although appearing well differentiated by light microscopy, shows no specific ultrastructural features of either an adenocarcinoma or a squamous cell carcinoma. The radiation or hormone therapy used in all reported cases as well as in the present case may alter the differentiation of the pluripotent stem cells. Guttuso et al. supposed that 2 types of epithelia could arise concurrently, which was what may have happened in their case. This finding would support the concept that the glandular and squamous components of adenosquamous carcinoma of the prostate might arise de novo from pluripotential stem cells.

The data describing the histological changes seen in cases of relapsed prostatic adenocarcinoma are rather sparse. This may stem from the perception that the rebiopsy of these patients in the face of a previous positive tissue diagnosis is unwarranted, especially when the stage of disease is advanced and the age of the patient is elderly. In this way, adenosquamous carcinoma may occur more commonly than is currently reported. A more accurate understanding of the incidence of this neoplasm can, however, only be determined by the pathological evaluation of additional tissue taken from subjects with prostatic adenocarcinoma, in particular the estrogen-refractory group with a previous record of radiotherapy.

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REFERENCES