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PRIMARY SIGNET RING CELL ADENOCARCINOMA OF THE PROSTATE. A CASE REPORT AND LITERATURE REVIEW

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We report a rare case of primary signet ring cell adenocarcinoma of the prostate in a 61-year-old male, who died of systemic lymphatic spread. Autopsy ruled out another primary signet ring cell adenocarcinoma outside the prostate. However, immunohistochemically, the tumor stained negatively for prostate-specific antigen. A review of the literature revealed only 15 case reports, including our case.

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Key words: Prostatic cancer, Signet ring cell adenocarcinoma, Prostate-specific antigen, Carcino-embryonic antigen

INTRODUCTION

Primary signet ring cell adenocarcinoma of the prostate is a rare entity. Here, we present the 15th case reported to date.

CASE REPORT

A 61-year-old Japanese presented complaining of miction pain and pollakisuria of a 1-month' duration. The urinary sediment showed no hematuria or pyuria. Digital rectal examination revealed a non-movable stony hard prostate of about 5 cm in diameter. All laboratory values were within the normal limits. Neither prostate-specific antigen (PSA) nor prostatic acid phosphatase (PAP) was elevated. There was no abnormality of the bladder mucosa, but irregular protrusion of the prostate was observed on cystoscopic examination. Transurethral resection of the prostate was performed.

Pathological studies of resected specimens revealed a signet ring cell adenocarcinoma (Fig. 1).

Endoscopic and roentgenographic studies of the gastrointestinal tract did not reveal any abnormalities. The prostate was clearly distinct from the surrounding tissues on a pelvic CT scan (Fig. 2). Thorough systemic examinations, including chest films, bone scintigraphy and CT

scans, demonstrated neither distant metastases nor lymph node involvement.

Clinically, the diagnosis was a primary signet ring cell adenocarcinoma of the prostate, stage C.

He received a course of radiation therapy in a total dose of 60 Gy to the prostate region. At the same time, he underwent hormonal manipulation with 2,500 mg of parenteral diethylstilbestrol diphosphate (250 mg \times 10 days). Subsequently, he was orally administered 560 mg of estramustine phosphate and 300 mg of 5-FU per day.

No local progression was noticed for 21 months before he was rehospitalized due to peritonitis carcinomatosa. Intra-abdominal Mitomycin C instillation therapy reduced the ascites transiently, but he died of systemic disease 26 months after the initial diagnosis.

Serum PSA, PAP, carcinoembryonic antigen (CEA) and CA-19-9 did not increase at any time during the clinical course. However, CEA and CA-19-9 in the ascites were markedly elevated, peaking at 402 ng/ml and 309 ng/ml, respectively.

Autopsy was performed. The prostate and adjacent structures, including the bladder and the rectum, were firmly adhered to the pelvic wall, due to the invasion of the prostatic cancer. Metastases were found in the iliac, para-aortic, and medias-

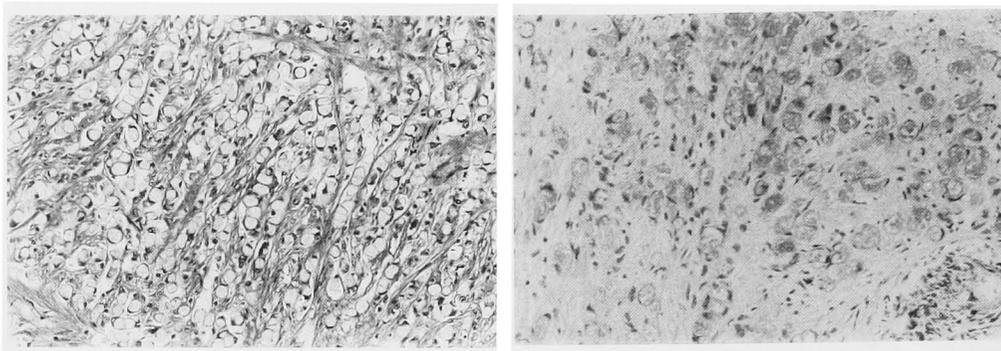


Fig. 1. TUR specimens. Signet ring cells diffusely infiltrate into the stroma of the prostate. (Left). H&E, reduced from $\times 100$. (Right). PAS, reduced from $\times 100$.

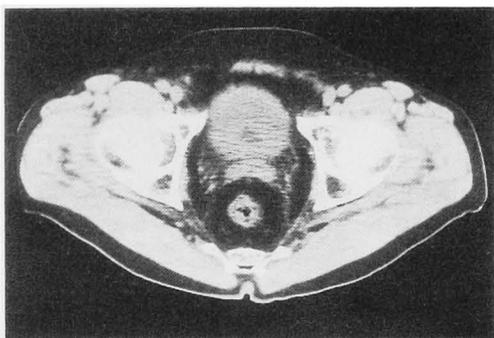


Fig. 2. Pelvic CT scan shows a prostatic enlargement and clear demarcation of the prostate from the rectum.

tinal lymph nodes, and in the left adrenal gland. Peritonitis carcinomatosa with 520 ml of ascites, and left pleuritis carcinomatosa with 1,000 ml of effusion were noted.

No tumor was found in the gastrointestinal tract other than the local invasion of the rectal wall by the prostatic cancer.

The autopsy specimens were fixed in 10 % formalin and embedded in paraffin.

The sections were stained with hematoxylin-eosin (H&E), periodic acid-Schiff (PAS), and mucicarmine. Moreover, immunohistochemical studies were performed using the following antibodies: anti-PSA (Dako, Santa Barbara, CA), anti-PAP (Dako) and anti-CEA (Dako) by the PAP method, and anti-CA-19-9 (CIS bio, Cedex, France) by the ABC method. All of the prostate was diffusely infiltrated by the tumor. Almost all of the tumor consisted of signet ring cells. Small areas of adenocarcinoma with acinar structures were also observed in the primary lesion. The signet ring cells stained positively with routine mucin stains: PAS and mucicarmine. In the immunohistochemical studies, both signet ring cells and acinar cells showed a strongly positive reaction for CEA. Some of the signet ring cells also stained positively for CA-19-9. However, the signet ring cells as well as acinar cells were completely negative for PSA and

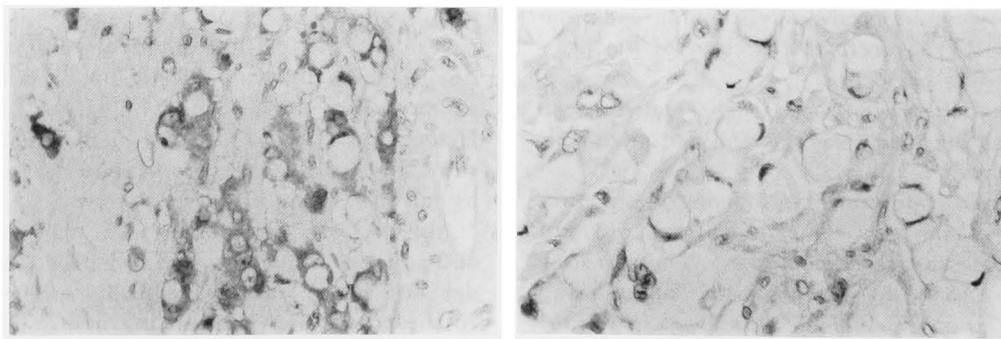


Fig. 3. (Left). Immunohistochemical staining for CEA. Signet ring cells stain positively. (Right). Immunohistochemical staining for PSA. They stain negatively.

PAP (Fig. 3). TUR and autopsy specimens showed the same reactivity immunohistochemically.

DISCUSSION

The term, signet ring cell, is defined as a cell whose nucleus is displaced by a cytoplasmic mass. Traditionally, the term has been used for intracellular retention of mucinous material, but recently, it has also been applied to non-mucinous lesions, that is, lymphoma, thyroid tumor, oligodendroglioma and smooth muscle tumor⁶⁾. In the prostate, the occurrence of signet ring cells is extremely rare⁸⁻¹¹⁾, and some authors even claim that the absence of signet ring cells is one of the specific features of prostatic mucinous adenocarcinoma^{12,13)}.

Signet ring cell adenocarcinoma (SRCA) is defined as a cancer composed mainly of signet ring cells, and it is well known in the stomach, colon, pancreas, and breast. In the genitourinary tract, SRCA of the bladder was reported first¹⁴⁾. In 1981, Giltman described the first case of SRCA in the prostate¹⁾. Since then, only 14 cases of prostatic SRCA have been reported in the literature²⁻⁷⁾, including two latent cancers^{3,6)} and one occult cancer⁷⁾.

The patients' ages ranged from 50 to 80 years (mean: 66.5 years). The symptoms and signs did not differ from those of ordinary prostatic cancers, except for two patients who were diagnosed with swelling of the supraclavicular lymph nodes^{4,5)}. Distant metastases were seen in the lymph nodes (8 patients), bone (6 patients), lung (2 patients), brain, liver, and adrenal gland. Hormonal therapy, irradiation or both were adopted as the therapeutic means, but the tumor responded poorly to these therapies. Of the 12 patients with follow-up, 10 patients died of disease between 1 and 60 months after diagnosis. Two patients were alive with disease at 6 and 12 months, respectively. Mean survival after diagnosis was about 30 months.

For a diagnosis of primary prostatic origin, either of the following criteria has been adopted in the reports to date. (1) Autopsy rules out another primary SRCA

outside the prostate^{1,3,4,6,7)} (2) The cancer stains positively for PSA and/or PAP immunohistochemically^{3,5-7)}. The presence of prostatic cancer structures other than SRCA is also helpful for the diagnosis.

Of nine cases in which immunohistochemical studies were conducted, seven cases showed a positive reaction for PSA. In our case, autopsy proved that the tumor originated in the prostate, but immunohistochemical stains demonstrated a negative reaction for PSA and PAP. Remmele and associates reported another prostatic SRCA which showed negative reaction for PSA⁴⁾. In their case, autopsy revealed systemic lymphatic spread of the cancer, as was seen in our case.

Interestingly, in terms of the reactivity to immunohistochemical stains, primary SRCA of the prostate can be classified into two groups. When the tumor is positive for PSA, it is negative for CEA, and conversely, PSA-negative tumors are CEA-positive. These immunohistochemical findings may present some clues to the understanding of primary prostatic SRCA in the future. It is not clear whether the origin of prostatic SRCAs is different from that of ordinary adenocarcinomas of the prostate. However, it is likely that SRCAs of the prostate behave in a clinical fashion similar to, or worse than, poorly differentiated adenocarcinomas of the prostate.

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和文抄録

前立腺原発印環細胞癌の1例

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清川 岳彦, 笈 善行

前立腺原発の印環細胞癌の1例を報告する。患者は、61歳の男性、頻尿、排尿時痛を主訴に来院した。経尿道的前立腺生検にて印環細胞癌と判明。放射線療法、ホルモン療法、抗癌化学療法に抵抗し、癌性腹膜炎、全身リンパ節転移にて、診断後26カ月で死亡し

た。剖検にて、前立腺原発が確認された。免疫組織化学的には、CA19-9 および CEA に陽性、PAP および PSA に陰性であった。文献上、15例目の報告にあたる。

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