

CLINICAL CASE

Primary signet-ring cell carcinoma of the prostate

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Summary

We report on an uncommon case of primary prostatic signet-ring cell carcinoma (SRCC) in a 78-year-old man. His prostatic specific antigen (PSA) level at presentation was 9.8 ng/ml. Histologically the tumor had a signet-ring morphology. Detailed immunohistochemical studies con-

firmed the prostatic origin of this neoplasm. All mucin stains were negative.

This aggressive tumor is a distinct variant of primary prostatic carcinoma which should be distinguished from artefactual vacuolation of the tumor and metastatic disease.

Key words: carcinoma, primary, prostate, signet-ring cell

Introduction

Signet-ring cell carcinoma of the prostate is an uncommon and extremely rare variant of prostate cancer [1]. Since Giltman [2] described this type of prostatic carcinoma in 1981, only 42 cases have been reported in the relevant english literature [3]. We describe an additional example of this tumor and analyse the findings reported in the literature.

Case presentation

A 78-year-old man presented with microhematuria and irritative voiding symptoms. Serum PSA was 9.8 ng/ml (normal 0-3 ng/ml).

Sextant ultrasound-guided transrectal needle biopsy of the prostate was carried out.

For light microscopy, sections of formalin-fixed paraplast-embedded prostatic tissue were stained with hematoxylin and eosin (H&E). Alcian blue (pH 2.7), periodic acid-Schiff (PAS) with or without diastase predigestion and mucicarmine stains were performed on additional sections.

Immunohistochemical stains were performed from paraplast blocks of the formalin-fixed material and included PSA, prostatic acid phosphatase (PAP), cytokeratin 34 β E12, cytokeratins 7, 20 and CEA, using the standard avidin-biotin-peroxidase (ABC) technique.

Histological findings

On the needle core biopsy specimen large areas of fibromuscular stroma of the left lobe of the prostate contained typical signet-ring cells characterized by abundant clear cytoplasmic vacuoles displacing and compressing the nuclei (Figure 1a,1b). The tumor cells infiltrated the prostatic stroma as single cells or variously-sized small clusters estimated to represent >40% of the entire tumor. In addition to the SRC component, transition patterns were identified between the SRC component and the poorly differentiated adenocarcinoma, most commonly of the acinar type.

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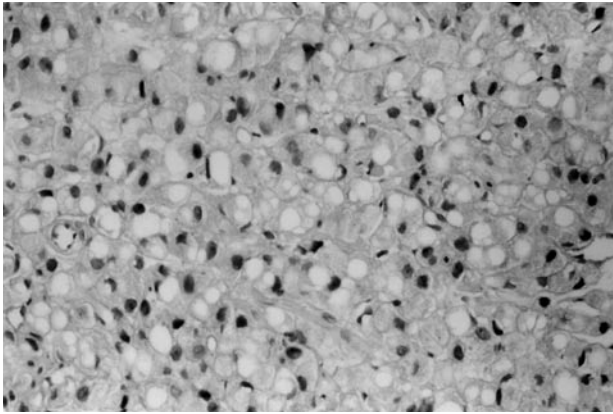


Figure 1a. Signet-ring cells with large cytoplasmic vacuoles displacing and compressing nuclei (H&E $\times 100$).

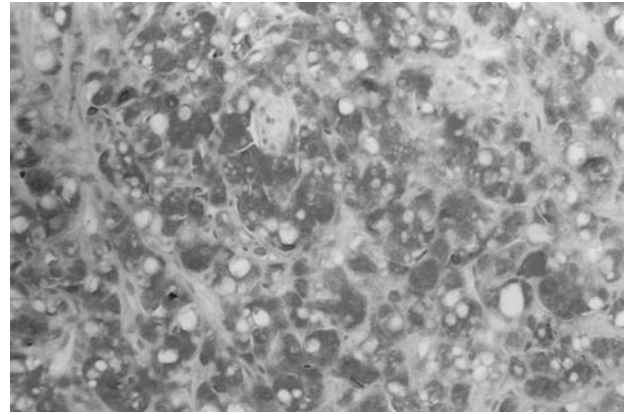


Figure 2. Prostate-specific antigen immunostaining shows immunoreactivity in signet-ring cells (ABC $\times 250$).

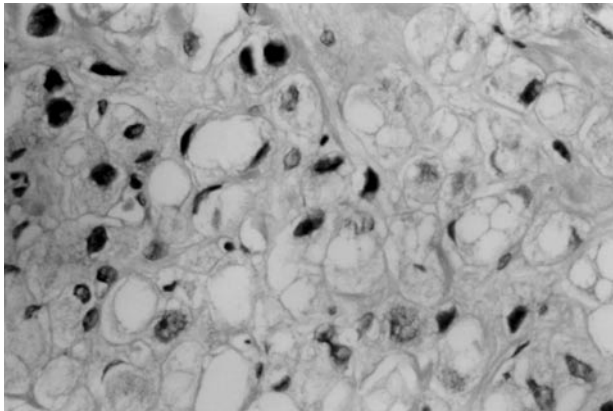


Figure 1b. At a higher power the development of intracytoplasmic lumen is seen (H&E $\times 400$).

Immunohistochemical examinations of the tumor showed a positive reaction for PSA (Figure 2) and PAP. The staining was predominantly intracytoplasmic. Cytokeratin 34 β E12 was positive in the basal layer of normal prostate but was uniformly negative in both the areas of the usual prostate adenocarcinoma and the SRC component. Cytokeratins 7, 20 and CEA were negative.

The intracytoplasmic vacuoles showed negative staining for mucin with alcian blue and PAS.

The patient initially underwent androgen deprivation therapy with Zoladex[®] 10.8 mg every 3 months for one year, along with zoledronic acid 4 mg i.v. This manipulation was necessary, because the bone mineral density of the femoral neck of the patient was 57% (T-Score -3.5).

The patient is alive with no evidence of disease 9 months after initiation of therapy.

Discussion

The term “signet-ring cell” is used to describe cells that have their nuclei displaced by an intracytoplasmic vacuole. SRCs are present in 2.5% of acinar carcinoma [4], but rarely in sufficient numbers to be considered SRCC. The diagnosis of SRCC of the prostate requires that 25% or more of the tumor be composed of SRCs, although some investigators require 50% [5,6]. Other authors suggested restricting the definition of SRCC of the prostate to those cases that have characteristic morphological features with a cytoplasmic vacuole displacing and compressing the nucleus and cytoplasmic mucin positivity [7].

However, the combined results from previously reported cases indicate that the content of SRCs would be mucinous material, PSA or lipids [8-10].

Ro et al. [11] reported that SRCC of the prostate was a variant of poorly differentiated adenocarcinoma of the prostate. Artificial vacuolar changes mimicking SRCs have been described in transurethral prostatic resection specimens, but also in needle biopsy specimens [12]. These were ruled out in our case.

The differential diagnosis of SRCC of the prostate included metastatic SRCC from the stomach and colon as well as local extension of SRCC from the urinary bladder. Positive staining for cytokeratin 20 (CK20) in the face of negative CK7 is seen in gastrointestinal carcinomas but usually not in prostatic cancer [13-15]. Both these cytokeratins were absent in our patient. The coexpression of CK7 and CK20 [13] in carcinomas of the urinary bladder is useful in those cases where the nature of the SRC is unclear. Bladder carcinomas with SRC components can show some PSA positivity [16]. In our case PSA and PAP were positive. Also adjacent foci of more typical prostatic adenocarcinoma strongly

Table 1. Special and immunohistochemical staining of SRCC of the prostate

	<i>PAS</i>	<i>Alcian blue</i>	<i>PSA</i>	<i>PAP</i>	<i>CEA</i>	<i>Keratin</i>
Positive	22/39	17/36	35/38	17/20	7/19	6/8
%	56.41	47.22	92.10	85	36.84	75

PSA: prostate specific antigen; PAP: prostate acid phosphatase; PAS: periodic acid-Schiff; CEA: carcinoembryonic antigen

supported its prostatic origin. Most studies reported in the literature showed positive PSA and PAP staining [3] but two cases of SRCC of the prostate were negative for PSA [17,18].

In searching the relevant english literature we found 42 cases of primary SRCC of the prostate. Table 1 shows the results of immunohistochemical and histochemical staining of 43 cases.

The age of the patients in these cases ranged from 50 to 84 years with an average of 69.8 years.

In male patients with metastatic SRC adenocarcinoma, it may be prudent to stain the tumor for both mucins and prostate-specific immunohistochemical markers [17].

In the presence of SRCs within the prostatic tissue with or without mucin production, primary SRCC should only be considered after the exclusion of benign conditions, traumatic artefact and metastatic disease.

SRCC of the prostate is considered an aggressive tumor with poor prognosis, comparable to the prognosis of high-grade adenocarcinoma [3,7,9,11,14]. Our patient underwent a treatment combining hormone therapy and zoledronic acid for non-metastatic prostate cancer. This kind of treatment increases bone mineral density in the hip and spine during androgen deprivation therapy [19].

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