CASE REPORT

Primary signet-ring cell carcinoma of the prostate

Yoh Matsuoka, MD,[1,3] Gaku Arai, MD,[1] Hisashi Ishimaru, MD,[1]
Kentaro Takagi, MD,[1] Yuji Ito, MD[2]

[1]Department of Urology, Tokyo Metropolitan Tama Geriatric Hospital, Tokyo, Japan
[2]Department of Pathology, Tokyo Metropolitan Tama Geriatric Hospital, Tokyo, Japan
[3]Department of Urology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

MATSUOKA Y, ARAI G, ISHIMARU H, TAKAGI K, ITO Y. Primary signet-ring cell carcinoma of the prostate. The Canadian Journal of Urology. 2007;14(6):3764-3766.

We report a rare case of primary signet-ring cell carcinoma of the prostate in an advanced stage. A 62-year-old man with serum level of prostate-specific antigen at 364.70 ng/ml was diagnosed as having cT4N1M1c prostatic signet-ring cell carcinoma of Gleason score 5 + 4 = 9. Immunohistochemical examination demonstrated cytoplasmic immunoreactivity to prostate-specific antigen in signet-ring cancer cells. The intracytoplasmic vacuoles in the signet-ring cells showed mucin production with a positive staining with periodic acid-Schiff. Although the patient received hormonal therapy, the disease progressed and lead to death 15 months after the diagnosis. The clinical and immunohistochemical characteristics of this malignancy are also reviewed.

Key Words: immunohistochemistry, mucin, prostate cancer, prostate-specific antigen, signet-ring cell carcinoma

Introduction

Signet-ring cell carcinoma (SRCC) has been reported to originate in various organs such as the stomach, colon, breast, and urinary bladder.[1] In the prostate, primary SRCC is a very rare variant of high-grade adenocarcinoma with Gleason pattern 5. In diagnosis, imaging and endoscopic examinations throughout the body are indispensable for distinguishing the primary site, especially in cases with metastatic or invasive SRCC. Herein, we report a case of primary prostatic SRCC in an advanced stage and discuss the clinical and immunohistological features of this neoplasm, with literature review.

Accepted for publication October 2007

Address correspondence to Dr. Yoh Matsuoka, Department of Urology, Graduate School, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan

Case report

A 62-year-old man presented to our hospital with difficulty of urination. The prostate gland was hard and huge on digital rectal examination. The serum level of prostate-specific antigen (PSA; Tandem R) was elevated at 364.70 ng/ml (normal, < 4 ng/ml). Radiological examinations demonstrated that an irregularly enlarged prostate (10 cm x 8 cm x 9 cm) involved the seminal

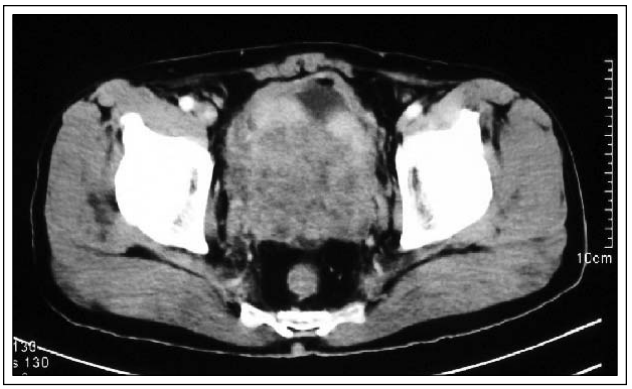

Figure 1. Computed tomography demonstrates a huge invasive prostate tumor protruding into the bladder lumen.

vesicles, bladder trigone, and right ureter, causing right hydronephrosis, Figure 1. Pathological examination of prostate biopsy specimen revealed carcinoma of Gleason score 5 + 4 = 9, composed primarily of signet-ring cell cancer accompanied with poorly differentiated acinar adenocarcinoma, Figure 2. In immunohistochemical study, the cytoplasm of each histological element other than the intracytoplasmic vacuoles in signet-ring cells showed a positive staining with PSA, Figure 3a. Both elements were stained negatively for synaptophysin, chromogranin, and neuron-specific enolase. The vacuoles in signet-ring cells showed mucin production, with a positive staining with periodic acid Schiff, Figure 3b. Multiple metastases were observed in the lung, bones and pelvic lymph nodes. No other lesion

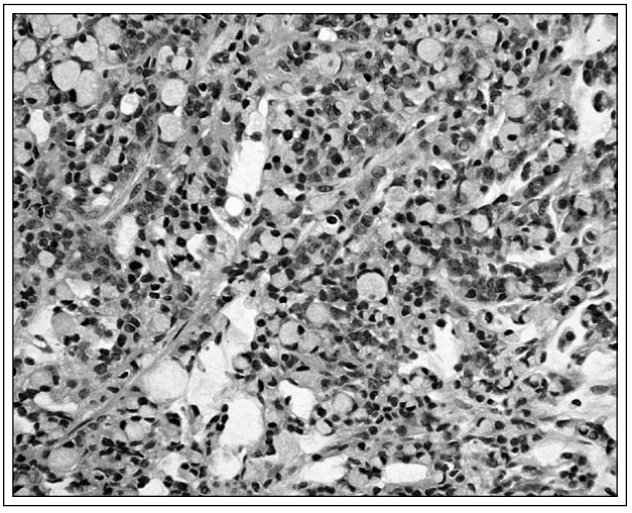

Figure 2. Histological appearance of prostate biopsy specimen showing signet-ring cell carcinoma. Hematoxylin-eosin staining, reduced from x100.

was detected in the urinary bladder and gastrointestinal tract endoscopically. The patient was diagnosed with primary SRCC of the prostate clinically staged as T4N1M1c.

The patient received combined androgen blockade composed of leuprorelin acetate (3.75 mg/4 weeks) and bicalutamide (80 mg/day). Although the serum PSA level decreased after the hormonal therapy, the patient ultimately entered a hormone-refractory state with the serum PSA elevation 3 months after the treatment. Estrogen preparation was minimally effective. Lymphangiosis carcinomatosa developed

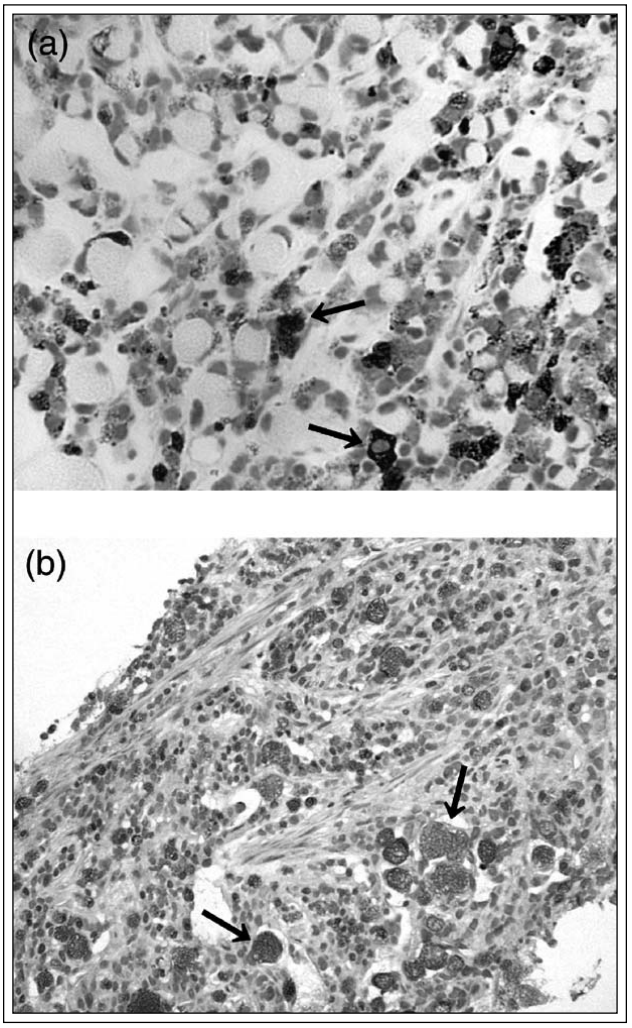

Figure 3. Cytoplasmic immunoreactivity in the prostate cancer cells. Arrows indicate positively stained sites. (a) Anti-prostate-specific antigen immunostain. The cytoplasm other than intracytoplasmic vacuoles was stained positively (x200). (b) Anti-periodic acid-Schiff immunostain. The vacuoles were stained positively (x100).

TABLE 1. **Review of cytoplasmic immunoreactivity**

	PSA	PAS	Alcian blue
Number of cases with positive staining (%)	36/39 (92%)	24/41 (59%)	17/36 (47%)

PSA = prostate-specific antigen; PAS = periodic acid-Schiff

rapidly and lead to respiratory failure. Chemotherapy was unable to be performed due to his poor condition. The patient died 15 months after the diagnosis.

Comment

The term "signet-ring cell" was traditionally used to describe mucin-producing cancer cells that have morphologic features characterized by clear cytoplasm and nuclear displacement. Recently, this term has been applied to tumors derived from a variety of organs with or without cytoplasmic mucous collection.[1] Although mucin is not found in the cytoplasm of usual prostatic cancer cells,[2] about a half of recent cases with prostatic SRCC were reported to be positive for intracellular mucin.[3,4] Ultrastructural examinations demonstrate intracytoplasmic vacuoles and occasional microvilli.[2] It is suggested that 25% or more of the tumor should be composed of signet-ring cells for the diagnosis of prostatic SRCC.[5]

Examinations of the gastrointestinal and urinary tracts are necessary to distinguish the primary site of advanced SRCC. Secondary prostatic SRCC derived from the stomach and urinary bladder has been occasionally reported.[6,7] Prostatic SRCC invading the urinary bladder, like the present case, has to be distinguished from primary SRCC of the bladder. The association with concurrent conventional acinar carcinoma of the prostate is helpful information to diagnose the SRCC as a prostatic origin. To our knowledge, 44 cases with primary prostatic SRCC have been reported in English literature. Table 1 showed the review of immunohistochemical staining of primary SRCC of the prostate. PSA immunostaining is useful in the diagnosis of primary prostatic SRCC. In the majority of the cases with primary prostatic SRCC, positive staining with PSA was found in signet-ring cell components as well as in areas of typical acinar adenocarcinoma. No other apparent lesion was found to be as a primary site in cases with negative PSA immunoreactivity. In some cases with primary SRCC of the bladder and stomach, PSA immunostaining can be weakly positive, but usually negative.[3]

The clinical symptoms and metastatic pattern of primary prostatic SRCC are similar to those of typical prostatic carcinoma. Of the 36 cases available for staging analyses, 27 cases (75%) were in local advanced or metastasized diseases at the diagnosis, with extremely poor prognosis. These results indicate that advanced-stage disease at presentation is the rule in contrast to conventional prostatic carcinoma and that the response to hormonal therapy is poor. Fujita et al[8] reported that an overall survival rate of primary prostatic SRCC in all clinical stages was 11.7% at 5 years. Only a few cases with localized disease were reported to have long survival after radical prostatectomy.[9] Early detection is essential for radical treatment of this aggressive malignancy. □

References

1. Catton PA, Hartwick RW, Srigley JR. Prostate cancer presenting with malignant ascites: signet-ring cell variant of prostatic adenocarcinoma. *Urology* 1992;39:495-497.
2. Ro JY, el-Naggar A, Ayala AG, Mody DR, Ordonez NG. Signet-ring-cell carcinoma of the prostate. Electron-microscopic and immunohistochemical studies of eight cases. *Am J Surg Pathol* 1988;12:453-460.
3. Torbenson M, Dhir R, Nangia A, Becich MJ, Kapadia SB. Prostatic carcinoma with signet ring cells: a clinicopathologic and immunohistochemical analysis of 12 cases, with review of the literature. *Mod Pathol* 1998;11:552-559.
4. Kuroda N, Yamasaki I, Nakayama H, Tamura K, Yamamoto Y, Miyazaki E et al. Prostatic signet-ring cell carcinoma: case report and literature review. *Pathol Int* 1999;49:457-461.
5. Randolph TL, Amin MB, Ro JY, Ayala AG. Histologic variants of adenocarcinoma and other carcinomas of prostate: pathologic criteria and clinical significance. *Mod Pathol* 1997;10:612-629.
6. Amano T, Fukuda M, Imao T, Takemae K. A case of ileus as a late complication of an ileal conduit in a patient with primary signet ring cell carcinoma of the bladder. *Hinyokika Kiyo* 2000;46:811-814.
7. Cobo Dols M, Munoz Gallardo S, Pelaez Angulo J, Algarra Garcia R, Fuente Lupianez C, Gil Calle S et al. Secondary signet-ring cell tumour of the prostate derived from a primary gastric malignancy. *Clin Transl Oncol* 2005;7:409-412.
8. Fujita K, Sugao H, Gotoh T, Yokomizo S, Itoh Y. Primary signet ring cell carcinoma of the prostate: report and review of 42 cases. *Int J Urol* 2004;11:178-181.
9. Kanematsu A, Hiura M. Primary signet ring cell adenocarcinoma of the prostate treated by radical prostatectomy after preoperative androgen deprivation. *Int J Urol* 1997;4:522-523.