Asynchronous adenoid cystic carcinoma of the prostate and transitional cell carcinoma of the urinary bladder

Luma M. Fayyad, MD, MRCPath, Khalaf M. Al-Jader, MD, Belal A. Al-Hawwari, MD.

ABSTRACT

Histologic variants of prostatic carcinoma are readily recognized. In this report, we describe a rare variant, adenoid cystic carcinoma, in a 75-year-old man previously diagnosed to have transitional cell carcinoma of the urinary bladder. The diagnosis of adenoid cystic carcinoma was made by the characteristic microscopic features of the tumor morphologically and immunohistochemically. Two months later he was found to have metastatic disease. The patient's treatment consisted of chemotherapy in combination with prednisone and hormonal therapy. Five and a half months after diagnosis, he died with metastatic disease. Making this case unique is the asynchronous occurrence of this variant with transitional cell carcinoma of the urinary bladder, which has never been reported in the literature. We discussed the histopathologic and immunohistochemical features of adenoid cystic carcinoma of the prostate with review of literature.

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Adenoid cystic carcinoma of the prostate gland is a rare and distinctive type of prostatic carcinoma. Thirty-one of such cases, have been reported in the English literature; not all of them, however, have been described in details. Cases of synchronous and asynchronous prostatic acinar-type adenocarcinoma, and transitional cell carcinoma of the bladder have been previously described in the literature, however, this is the first case in which the prostatic carcinoma is of the adenoid cystic type.

Case Report. A 75-year-old man diagnosed to have papillary transitional cell carcinoma of the urinary bladder in 1998, developed 6 years later a carcinoma of the prostate, which was of the adenoid cystic type.

The bladder tumor, which had recurred frequently, was treated by pelvic external beam radiation, intravesical bacillus Calmette-Guerin and repeated excision and fulguration of the regrowths. Follow up cystoscopies carried out in the year 2004 revealed no evidence of tumor recurrences. Urinary outflow obstruction due to enlarged prostate gland was found from the onset of the disease. Serum prostate specific antigen (PSA) level, carried out 3 times was normal and a prostatic biopsy from the medial wall revealed benign prostatic tissue. The prostatic obstructive symptoms progressively worsened until the patient underwent transurethral resection of the prostate (TURP) in February 2005. Histopathology revealed an adenoid cystic carcinoma of the prostate. The patient was treated with Taxotere (Docetaxel) 75

From the Departments of Histopathology and Cytology (Fayyad), Department of Urology (Al-Jader), and the Department of Oncology (Al-Hawwari), King Hussein Medical Center, Amman, *Jordan*.

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Address correspondence and reprint request to: Dr. Luma M. Fayyad, PO Box 1, Dahiyet Al-Amir Rashed, Amman 11831, *Jordan*. Tel. +962 (6) 5535957. Fax. +962 (6) 5854462. E-mail. l_fayyad@yahoo.com

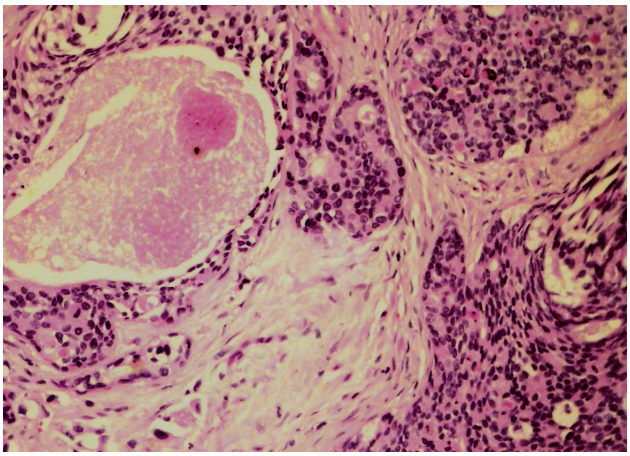

Figure 1 - Tumor nests of adenoid cystic carcinoma showing intraglandular and periglandular hyalinization. Hematoxylin and eosin stain × 100.

Table 1 - Immunohistochemistry: antisera, sources and staining results.

Antibody	Source	Result
Prostate specific antigen	BioGenex, USA	Negative
Cytokeratin 34ßE12 (high molecular weight)	BioGenex, USA	Positive (strong, multifocal)
Cytokeratin 7	BioGenex, USA	Positive (strong, diffuse)
Cytokeratin 20	BioGenex, USA	Negative
Muscle-specific actin	BioGenex, USA	Negative
Chromogranin	BioGenex, USA	Negative
Bcl-2	BioGenex, USA	Positive (weak, multifocal)
S-100 protein	BioGenex, USA	Positive (weak, multifocal)

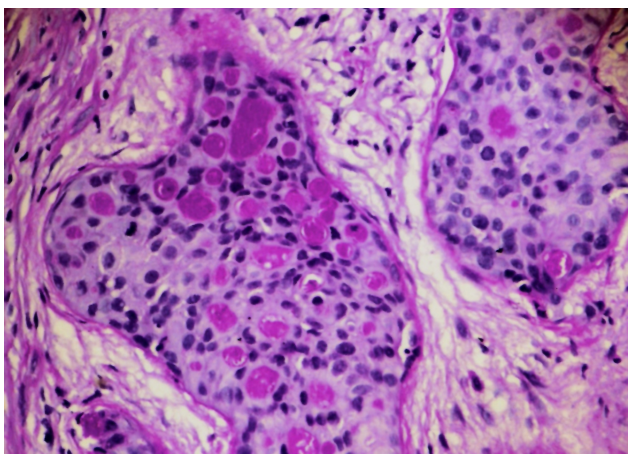

Figure 2 - Periodic acid-Schiff -positive, diastase-resistant material inside the glandular lumina of the cribriform tumor nests. periodic acid-Schiff-diastase stain × 200.

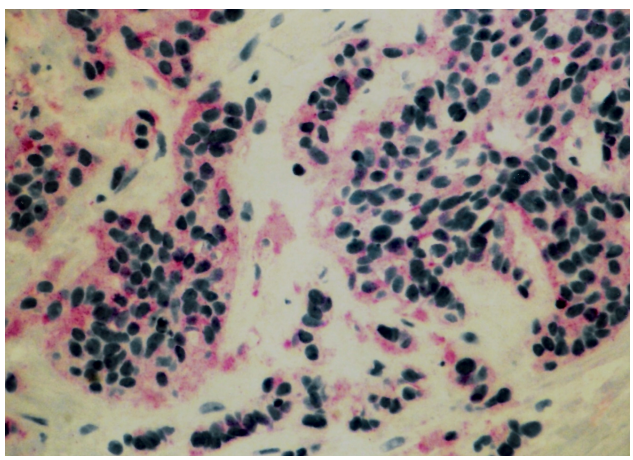

Figure 3 - Positive immunohistochemical stain for high molecular weight cytokeratin (34ßE12) × 200.

mg/m^2 intravenous infusion over one hour every 3 weeks in combination with prednisolone 5 mg tablet twice daily, as well as Decapeptyl SR (Triptorelin) intramuscular injection 11.25 mg every 3 months. Two months following the diagnosis the patient developed local tumor recurrence and on CT scans was found to have multiple metastatic liver lesions, enlarged left lower paraaortic and pelvic lymph nodes, as well as metastasis to L4 vertebral body and pedicle. Two and a half months later the patient died.

Gross and microscopic pathologic findings. Eighteen grams of prostatic chippings were received. They were formalin-fixed, routinely processed and paraffin-embedded. Sections were stained with hematoxylin and eosin, periodic acid-Schiff with and without diastase digestion and Alcian blue at pH 2.5. Microscopy showed prostatic tissue multifocally infiltrated by a tumor, having a predominant cribriform architecture with glandular anastomoses. Intraglandular as well as foci of periglandular hyalinization were present (**Figure 1**). Material within the cribriform spaces stained positively with both periodic acid-Schiff stain after diastase digestion (**Figure 2**) and Alcian blue. Necrotic debris was present in occasional solid nodules. Infiltrating small, poorly differentiated tumor nests were present focally, as well as a desmoplastic reaction. Mitotic figures were frequent in few areas ranging from 4-5 figures/10 high power fields. Perineural invasion and lymphovascular space permeation were prominent. Concurrent findings included basal cell hyperplasia, squamous metaplasia and adenoid cystic-like hyperplasia. No usual form of prostate cancer was noted.

Immunohistochemistry was performed using avidin-biotin-complex method with prediluted antisera. The results are summarized in **Table 1**. The main diagnostic immunohistochemical findings in the tumor cells were strongly positive although multifocal staining with Cytokeratin 34ßE12 (**Figure 3**) and negative staining with PSA.

Discussion. Adenoid cystic carcinoma of the prostate has been classified in the 2004 World Health Organization classification of tumors of the urinary system and male genital organs along with basaloid carcinoma under the diagnostic term basal cell carcinoma.[1] However, separation of true adenoid cystic carcinoma is preferred by some due to its distinctive histologic appearance, which closely mimics an adenoid cystic carcinoma of the salivary glands.[2]

Tumor origin has been postulated to be from periurethral seromucinous glands[3] suggested by the presence of myoepithelial cell differentiation by light microscopy, central location of the tumor and negative immunohistochemical staining for PSA and prostatic acid phosphatase.[4] This was questioned by Cohen et al[5] who by ultrastructural examination, found no evidence of prostatic myoepithelial cell differentiation in humans except for a single focus in an infantile prostate gland. Others, however; found evidence that this tumor originated from basal cells of the prostate.[6] In our case, the positive immunohistochemical staining of tumor cells for high molecular weight cytokeratin and negative staining for PSA support the theory that this is a proliferation of basal cells. Histopathologic features described to separate benign from malignant basal cell proliferations include the following: an infiltrative pattern of tumor growth, stromal desmoplasia, perineural invasion, irregular growth pattern with central necrosis and finally extraprostatic extension.[1] The first 4 features were all present in our case, however, the last one was not demonstrated histologically since the specimen was only a TURP.

Diagnosis of this tumor is usually made on histopathologic study after the patients present with a clinical picture of urinary outflow obstruction. Terris[7] described specific unusual transrectal sonographic features of 2 cases in the form of a monotonous pattern of multiple small cysts of similar size. However, this was not supported by any other report. Serum levels of PSA are not helpful in investigating this tumor since they are usually not elevated. Adenoid cystic carcinoma of the prostate has an uncertain and unpredictable biologic behavior with a wide range of age of occurrence, from 36-83 years. The majority of the reports describe the indolent behavior of this tumor[2-4,7,8] while only few have encountered aggressive behavior with distant metastasis and death.[9] Our patient belongs to the latter group.

Treatment modalities have also varied between centers. These have included TURP alone,[3,8] TURP followed by radical or suprapubic prostatectomy,[2,5,9] or pelvic exentration.[9] Surgery have been followed in some cases by chemotherapy, hormonal therapy, radiation therapy[4] or a combination of these.[2] In our case, the patient received the chemotherapeutic agent Taxotere in combination with prednisolone as well as hormonal therapy Decapeptyl. The occurrence of this tumor asynchronously, following transitional cell carcinoma of the urinary bladder, has never been described before, even though there are reports in which the prostatic carcinoma is of acinar type.[10]It is uncertain if previous pelvic irradiation was a predisposing factor for the development of the second tumor since a literature search yielded no such evidence.

Finally, this tumor appears to have a variable, unpredictable and sometimes aggressive clinical course with a variable response to different types of treatment. More cases need to be studied and investigated with adequate long term follow up. A method of early diagnosis and best modality of treatment of this distinct and uncommon tumor still has to be unveiled.

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