DUCTAL ADENOCARCINOMA OF THE PROSTATE: CASE REPORT AND DIFFERENTIAL DIAGNOSTIC CONSIDERATIONS

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Abstract: *Prostatic ductal adenocarcinoma is a rare subtype of cancer of the prostate. Recognition of this malignant neoplasia is important because of its particularities: diagnosis in advanced stages, normal or low serum prostate specific antigen (PSA) and poor prognosis. It also shows no response to hormonal therapy, such as acinar adenocarcinomas and requires early aggressive treatment. We present the case of a male patient who suffered a transurethral prostatic resection surgery. Histopathological examination revealed a malignant neoplastic proliferation with predominantly papillary architecture composed of conjunctive-vascular cores lined by tall cylindrical epithelium with atypical pleomorphic nuclei and mitoses. Immunohistochemical examination highlighted the primary nature of tumour and origin in the prostatic ducts, excluding several primary or secondary neoplastic lesions.*

INTRODUCTION

Prostatic ductal adenocarcinoma is a poorly differentiated malignant neoplastic lesions representing less than 1% of prostate cancers.(1,2) That arises from the periurethral or peripheral prostatic ducts. Histologically, it is characterized by a variable architecture that can be papillary, cribriform, solid, with comedonecrosis or isolated glands. From the clinical point of view, it is not associated with elevated serum prostate specific antigen (PSA) which can be normal, low or rarely elevated values and it associates with normal digital rectal examination.(3,4)

CASE REPORT

We present the case of a male patient, 73-year-old. He complained of gross hematuria. Digital rectal examination revealed a slightly enlarged prostate. PSA has a value of 550 ng/dl. Patient's medical history was insignificant. The excised material by transurethral prostatic resection surgery in the Department of Urology of Emergency County Hospital of Constanta has identified a ductal prostatic adenocarcinoma, Gleason score 9=4+5. The histopathologycal and immunohistochemical techniques were performed in the Clinical Service of Pathology, Saint Apostle Andrew Emergency County Hospital of Constanta. The specimen was fixed in 10% formalin and included in three blocks. The sections were stained with Hematoxylin-Eosin and monoclonal Mouse Anti-Human Prostate Specific Antigen (PSA), clone ER-PR 8, isotype IgG1, Kappa (DAKO), monoclonal Mouse anti-Human High Molecular Weight Cytokeratin (HMWCK), Clone 34βE12, Isotype IgG1, Kappa (DAKO), monoclonal Mouse Anti-Human Carcinoembryonic antigen (CEA), Clone II-7, Isotype IgG1, Kappa (DAKO), monoclonal Mouse Anti-Human Cytokeratin 7 (CK7), clone OV-TL 12/30, isotype IgG1, Kappa (DAKO), monoclonal Mouse Anti-Human Cytokeratin 20 (CK20) Clone Ks20.8, Isotype IgG2a, kappa (DAKO) and monoclonal Mouse Anti-Human Ki67 antigen clone MIB1 isotype IgG1, Kappa (DAKO) were applied. Microscopic images were taken with a Nikon Camera using a Nikon Eclipse E600 Microscope.

RESULTS

Macroscopic examination revealed the presence of multiple fragments with variable diameters, which measures overall 7/1.5/0.5 cm, weighting 8 grams, gray-yellowish colored, elastic consistency. Histopathological examination revealed a malignant neoplastic proliferation with papillary (figure no. 1) and cribriform architecture (figure no. 2) that affects over 5% of the fragments examined, some of them with comedonecrosis.

Figure no. 1. Ductal adenocarcinoma with papillary architecture, HEx100

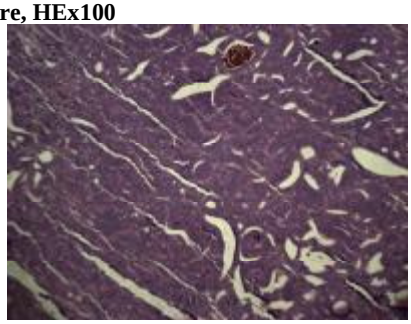
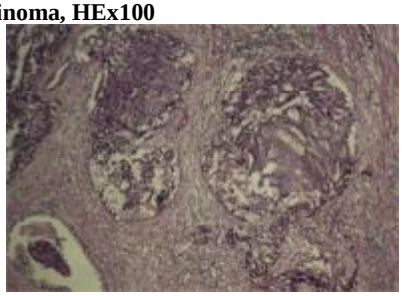


Figure no. 2. Cribriform architecture of ductal adenocarcinoma, HEx100



Gleason score was 9=4+5. Cells were large with abundant eosinophilic or amphophilic cytoplasm and large nuclei with atypia and mitoses (figure no. 3). It was not

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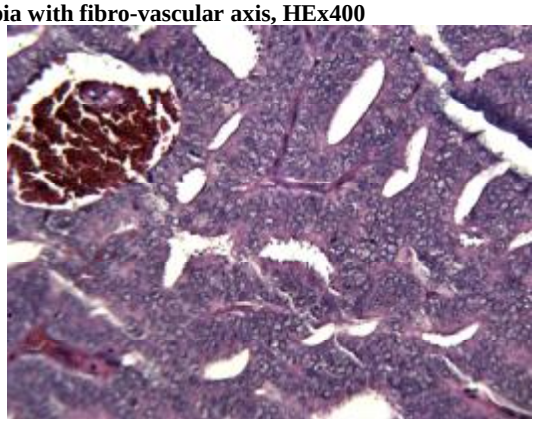
identified any component acinar adenocarcinoma.

Figure no. 3. Tall cylindrical neoplastic cells with nuclear atypia with fibro-vascular axis, HEx400



For the certain diagnosis, the immunohistochemical methods were mandatory. Thus, the application of monoclonal antibodies highlighted the following:

- positive reaction for PSA in all prostatic neoplastic epithelial cell, that reveal the origin from the prostate gland (figures no. 4,5).
- negative immunoreaction for HMWCK (34βE12) in basal cells layers; positive in basall cells of benign glands;
- negative reaction for CEA;
- negative reaction for CK7;
- CK20 weakly positive in neoplastic epithelial cells;
- Ki67 positive a proportion of 30-40% (figure no. 6).

Figure no. 4. PSA positive in malignant neoplastic cells with cribriform appearance, x 400

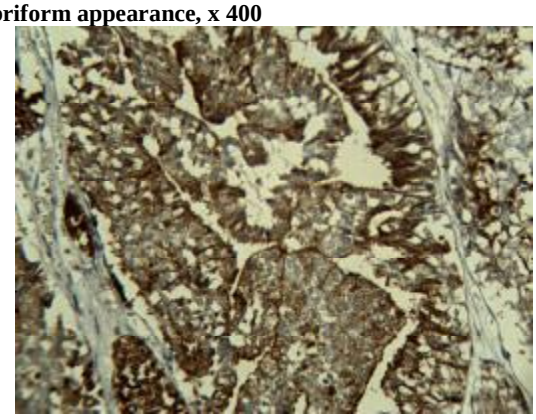


Figure no. 5. Membranes positive for PSA in cancer cells with papillary appearance, x 100

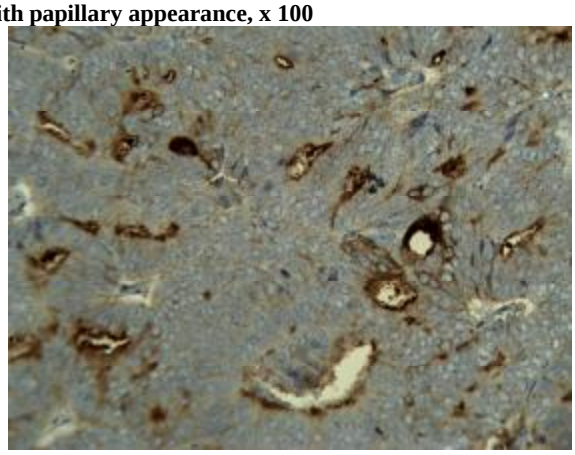
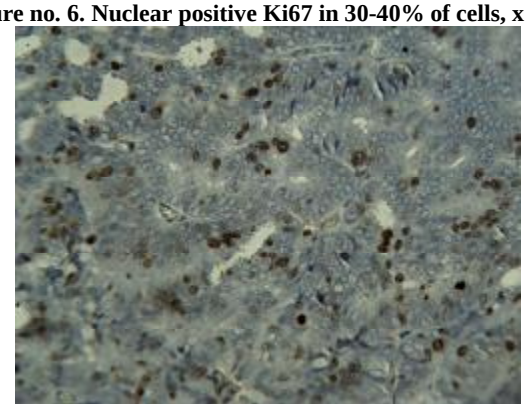


Figure no. 6. Nuclear positive Ki67 in 30-40% of cells, x 200



DISCUSSIONS

Ductal adenocarcinoma was first described in 1967 and was referred as endometrial adenocarcinoma of the prostate due to the appearance of endometrial carcinoma, and it is believed that it develops from prostatic utricle (mullerian vestiges).(5) This term was used until ultrastructural study of prostatic acinus proved prostatic origin by the existence of nonciliate cell (light) and ciliates cell (dark) and these data were combined with immunohistochemistry studies.(6)

According to the specialty literature, the age of diagnosis of the disease varies between 65 and 87 years.(7) Macroscopically, it is presented as an exofitic urethral mass developed in or around verumontanum when arises from periurethral prostatic ducts large and is associated with obstructive symptoms. When the starting point is the peripheral ducts, the tumour may be palpable on digital rectal examination and urethral damage is variable.(8)

From the microscopic point of view, it is characterized by a predominant papillary architecture, but may be cribriform, glandular or solid with cylindrical malignant neoplastic cells with high nucleo-cytoplasmic ratio and increased expression of PSA and prostatic acid phosphatase (PAP).(9) It is necessary to differentiate prostatic ductal carcinoma with acinar adenocarcinoma with cribriform Gleason 4 pattern, high-grade prostatic intraepithelial neoplasia with cribriform appearance, urothelial carcinoma and colon adenocarcinoma metastasis. Cribriform acinar prostatic adenocarcinoma is characterized by a cubic malignant neoplastic epithelial cell proliferation and round lumens while ductal adenocarcinoma presents as tall cylindrical cell prolifereation. Also ductal adenocarcinoma is accompanied by an intense stromal desmoplasia and macrophage filled with hemosiderin. It was also found that the two forms of cancer may be associated in approximately 5% of cases.(10)

High grade prostatic intraepithelial neoplasia (PIN) with cribriform pattern is characterized by the presence of glands similar to those of normal size, the absence of major atypia, absence of comedonecrosis, and presence of micropapilary structures without fibro-vascular cores. In contrast, ductal adenocarcinoma is composed of fibro-vascular papillae and glands are large and placed back to back. Using markers for basal cells showed focal positivity in both lesions, but in the absence of basal cell layer ductal adenocarcinoma is more likely.(11)

Urothelial carcinoma of the prostate is represented by nuclear atypia, marked anaplasia and immunohistochemical tests are negative to PSA, positive to CK7, CK20, high molecular weight cytokeratin Uroplakin or thrombomodulin. In contrast, ductal adenocarcinoma is positive for PSA and negative to urothelial markers.(12,13)

Regarding the differentiation of colon carcinoma

invasion, PSA positivity certifies the origin of prostatic proliferation while CDX2 positivity certifies the colonic origin. Integration in the clinical context and corroboration of data with colonoscopy imaging are also recommended.(14) Although it was considered to cause metastases similar to acinar adenocarcinoma have been described metastases in unusual locations such as testicular, penile or liver.(15,16,17)

Overall, mortality due to prostate ductal adenocarcinoma is higher than that of men diagnosed with acinar type and response to androgen deprivation is not comparable to that of classical form of adenocarcinoma.(18,19,20)

CONCLUSIONS

Prostatic ductal adenocarcinoma is a relatively rare variant of prostate cancer with distinctive morphological features. It is important to recognize this histopathological type of cancer and set it apart from other types of malignancies mainly due to poorly prognosis.

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