

Mixed primary prostatic carcinoma with acinar, neuroendocrine and ductal components

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INTRODUCTION

Carcinoma of the prostate is the most common form of cancer in men and the second leading cause of cancer-related deaths (1). Morphologically, most of the prostate cancers are acinar, microacinar, or conventional adenocarcinomas (1, 2). However, mixed tumors in the prostate gland have been less frequently described; they are primarily originated in the gland or are the product of metastatic compromise (2, 3). Mixed primary epithelial carcinomas of the prostate are very rare, they display multiple types of epithelial differentiation originated in the prostate gland (2, 4). Other primary mixed tumors described in the prostate are the sarcomatoid carcinoma, which displays both epithelial, and mesenchymal components, and the primary mixed mesenchymal tumors that display features of different stromal origin (5). The more frequent reported mixed epithelial tumor is the coexistence of conventional adenocarcinomas and transitional cell (urothelial) carcinomas (6).

There is considerable controversy in the literature regarding nomenclature and histogenesis of these tumors. Some authors prefer to use the terms differentiation and other collision when these neoplasms are named, however the use of these terms are better restricted when homologous or heterologous components are proved respectively (2, 3, 7, 8). The most recent World Health Organization classification of urinary system and male genital organs does not distinguish between all these lesions (9).

Previous reports of mixed epithelial tumors are described by the coexistence of conventional adenocarcinoma, along with mucinous adenocarcinoma (10), urothelial carcinoma (6, 11), and squamous cell carcinoma (12). Also even rare subtypes raised in metaplastic epithelial changes have been described such as: Paneth cell-like changes (13), endometrioid (2), and others (2). The recognition of these rare histological variants is important because some types are associated with a different clinical outcome and might need a different therapeutic approach (1, 14).

Here we report the case of a 72-year-old man with histopathologic findings of primary prostate mixed carcinoma,

showing characteristics of acinar, ductal and neuroendocrine adenocarcinoma. We also discuss the clinical, diagnostic, and therapeutic aspects of these uncommon mixed tumors.

CASE REPORT

Our patient was a 72-year-old man, who presented for 3 months with a history of urinary obstructive symptoms (poor urinary stream, hesitancy, terminal dribbling and incomplete voiding) and dysuria. He presented previous pathologic history of arterial hypertension in treatment and controlled it with captopril plus metoprolol, other relevant history, symptoms and signs were negative. In the physical exam an indurate irregular prostate increased in size was palpated (approximately 90 grams). A serological prostatic specific antigen (PSA) of 9.8 mg/mL was documented and a trans-rectal biopsy guided by ultrasound was performed. The histopathology was positive for prostatic adenocarcinoma Gleason 4 +5. A radical prostatectomy was executed; in the histopathologic study a mixed malignant epithelial neoplasm with three components was identified. In multiple areas (60% of the tumor area) irregular acine lining by atypical cells (Figure 1A) positives for PSA (Figure 2A), prostatic acid phosphatase (PAP), Alpha MethylAcyl Coenzyme A Racemase (AMACR), and low molecular weight cytokeratin, with negativity for P63, chromogranin, synaptophysin and CDx2 was observed. The second component (35%) was composed by small clear cells, with indented nucleus and fine chromatin which were disposed alone or forming solid nests and glandular formations (Figure 1A, 1B, 1C); in this component, cells were positive for chromogranin (Figure 2B), synaptophysin, CD57, PSA, AMACR and PAP. Finally the third component (5%) was composed by cribriform and papillary glands lined by atypical tall-pseudostratified epithelium with abundant, amphophilic cytoplasm and pleomorphic nucleus (Figure 1B, 1D), positive to AMACR (Figure 2C), PSA and PAP and negative to chromogranin, synaptophysin, P63, CD57, CDx2 and *β*-catenin. All three components exhibited a high number of

mitosis (> 15 in 10 high power fields) and high ki67 labeling index (Figure 2D, 2E and 2F). Peri-neural, and lymphovascular and capsular invasion were identified. Orchiectomy was practiced additionally after the identi-

fication of spine metastasis 2 months later in addition to conventional chemotherapy with taxotere, estramustine and cisplatinium. The patient had a survival of 9 months and died after respiratory insufficiency.

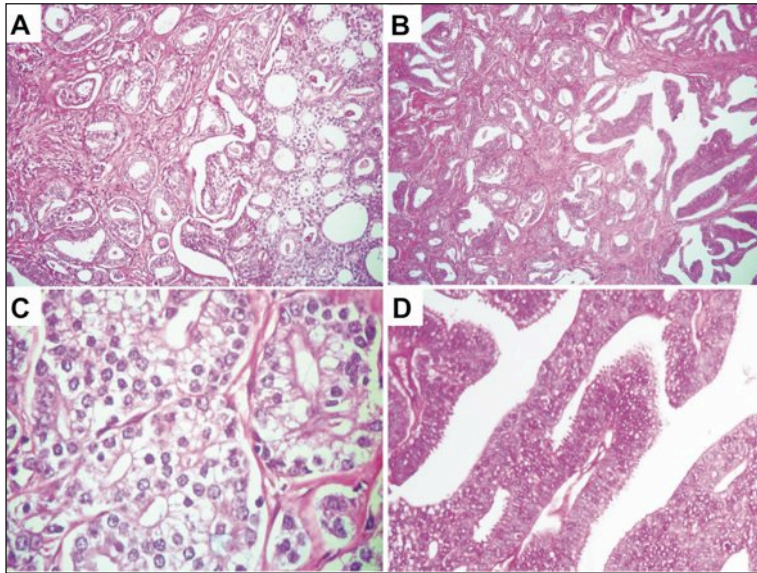


Figure 1.

In the histopathologic analysis, we observed a mixed carcinoma composed by irregular acines lining by atypical hyper-chromatic cells distributed in a fibromuscular stroma (Figure 1A, HE 4x) accompanied by glandular, solid and cribriform formations of small clear cells (Figure 1A, HE 4x), with indented nucleus and fine chromatin which were disposed also alone (Figure 1C, HE 40x). In other areas we identified papillary glands lined by atypical tall-pseudostratified epithelium with abundant, amphophilic cytoplasm and pleomorphic nuclei (Figure 1B, HE 4x and 1D, HE 40x).

Abbreviations: HE: hematoxilin and eosin.

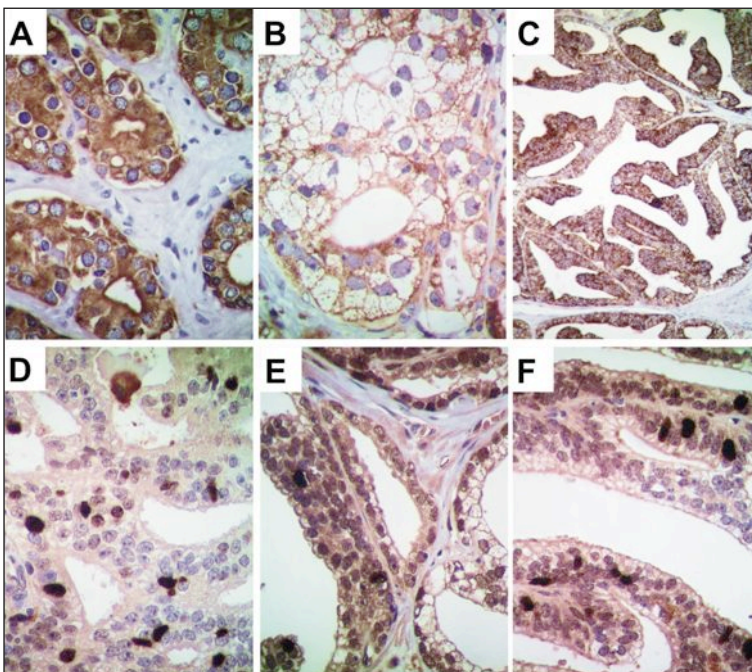


Figure 2.

We observed positivity for PSA (Figure 2A, acinar component, 40x) and AMACR (Figure 2C, ductal component, 20x) in all components, and chromogranine in the neuroendocrine areas (Figure 2B, 10x). In all three components, a high ki67-labeling index (Figure 2D, 2E and 2F) was identified.

Abbreviations: PSA: prostatic specific antigen, AMACR: Alpha MethylAcyl Coenzyme A Racemase.