

SUBCUTANEOUS AND TESTICULAR METASTASIS FROM PROSTATIC ADENOCARCINOMA WITH NEUROENDOCRINE DIFFERENTIATION

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ABSTRACT

The pathological finding of testicular metastasis in cases of disseminated prostatic adenocarcinoma is rare, but was more frequently reported in the past, when bilateral castration was performed more often. The existence of skin and subcutaneous metastasis adds a worse prognosis, because generally it is sign of advanced disease with an average survival time of less than one year. The synchronous occurrence of such metastasis has not been described previously, neither their association to neuroendocrine differentiation. The presence of such differentiation of prostatic adenocarcinoma represents a very unfavorable prognostic factor, as suggested in recent literature. Herein, we discuss the case of a 53 year old man, who presented with macroscopic hematuria and frequency associated to several painless subcutaneous nodules in left axilla and shoulder, as well as in the lower abdominal wall. The right testis was painful, endured and on rectal examination, the prostate was diffusely enlarged. Serum PSA was elevated, reaching 1760 ng/ml and prostatic biopsy disclosed a Gleason 10 prostatic adenocarcinoma with neuroendocrine differentiation. The same pathological pattern was detected in the right testis and in all subcutaneous nodules, documented by positive staining of chromogranin, a marker of neuroendocrine cells. He was submitted to a prostate tunnelization and maximal androgen blockade plus adjuvant chemotherapy, nevertheless, he died 5 months latter.

Key words: prostate; prostatic neoplasms; neoplasm metastasis; testis; subcutaneous; neuroendocrine differentiation

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INTRODUCTION

Advanced prostatic adenocarcinoma with symptomatic testicular metastasis is a rare condition, with only 70 cases presented until 1990 (1). Subcutaneous metastasis is even less frequent, with only 14 cases presented in the literature (2). To our knowledge, this is the first case in which both types of metastasis are synchronously present and neuroendocrine differentiation of the prostatic adenocarcinoma is histologically confirmed, both in the prostate and in the metastatic tissues.

CASE REPORT

A 53 years old patient of African origin presented an isolated episode of painless macro-

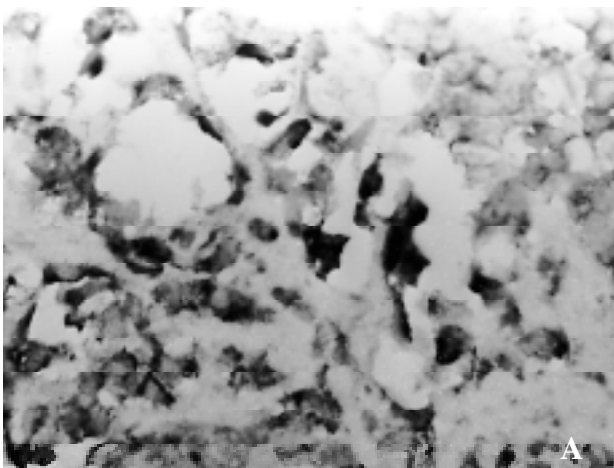
scopic hematuria that ceased spontaneously. The same symptom recurred after one year associated to disuria and frequency, weight loss, fatigue and pain in both upper and lower limbs and painful enlargement of the right testis. Due to the complaints, he was sent to the urologist. On physical examination, he was in adequate general condition, presenting several painless subcutaneous nodules in the left axilla and shoulder, as well as in the lower abdominal wall, with sizes varying from 1 to 2.5 cm in diameter. These nodules were firm in consistency and fixed in the subcutaneous layer. The right testis was endured, swollen and painful on palpation. On rectal examination, the prostate was diffusely enlarged, presenting an irregular surface and increased consistency. Its lateral limits were imprecise. Serum PSA was elevated, reaching 1760

ng/ml and prostatic biopsy disclosed a Gleason 10 prostatic adenocarcinoma in all fragments. A bone scan revealed diffuse metastatic involvement of the vertebral spine and costal arches, while abdominal CT disclosed left bladder wall and lower ureteral infiltration by a large prostatic neoplasm. This exam also demonstrated the subcutaneous abdominal lesion (Figure-1). As urinary symptoms and hema-



Figure 1 - Abdominal CT shows subcutaneous nodule in the left anterior wall.

turia worsened, antiandrogen therapy was initiated, with decrease of PSA. However, due to persistence of urinary symptoms and hematuria, he was submitted to prostatic tunnelization, associated to bi-



lateral orchiectomy and excisional biopsy of 4 abdominal and thoracic subcutaneous lesions. Pathologic examination of the prostatic tissue confirmed the presence of Gleason 10 prostatic adenocarcinoma with areas of neuroendocrine differentiation. Examination of the right testis and all subcutaneous nodules also confirmed the presence of metastatic neuroendocrine tumor, positively stained for chromogranin, a specific marker of neuroendocrine cells (Figure-2). Two months after surgery, he was clinically improved, with significant weight gain and without urinary symptoms or hematuria. The PSA levels dropped to 53 ng/ml, and maximal androgen blockade with cyproterone citrate was initiated, nevertheless he still had generalized pain and adjuvant chemotherapy was initiated, even so, he died 5 months latter.

DISCUSSION

In the past, when antiandrogenic drugs were yet unavailable, orchiectomy was the treatment of choice in advanced adenocarcinoma of the prostate. In many patients, silent microscopic metastatic involvement of the testes was discovered on pathological examination, being described in 2.4 to 4% of the cases reviewed with this specific interest (1). Symptomatic testicular metastases are very rare, signaling to an advanced disease, with undetermined, but gen-

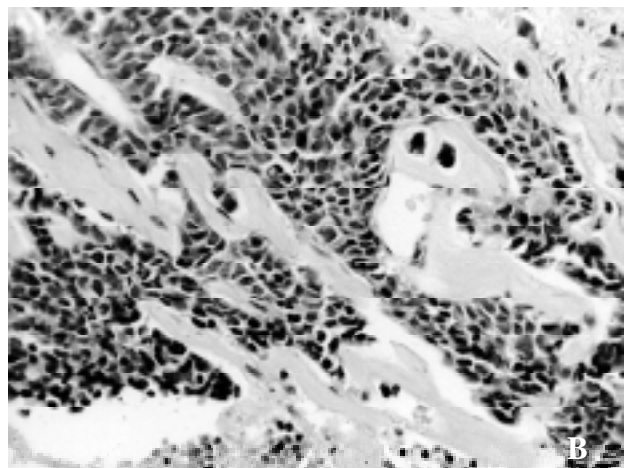


Figure 2 - A)- Neuroendocrine tumor with chromogranin positive in cellular cytoplasm (immunolabeling, X400). B)- Solid groups of cuboidae cells with scanty cytoplasm, nuclei hyperchromatic, grouped in organoid arrangement in microscopic section of the right testis, showing prostatic adenocarcinoma metastasis (HE, X 100).

erally poor prognosis (1). Subcutaneous metastases were previously presented in 14 patients, most of them in terminal stages of the disease, with survival of less than 12 months, despite therapy (2). The synchronous occurrence of such metastases has not been described previously. Moreover, the presence of neuroendocrine differentiation may explain the aggressive behavior of the prostatic adenocarcinoma in this patient, as it is usually associated to a very unfavorable prognosis. Cohen et al., analyzing 17 patients who died of prostatic cancer, disclosed that 15 exhibited neuroendocrine differentiation (3). However, additional studies are needed in order to establish neuroendocrine differentiation as an independent prognostic factor and to evaluate new therapeutic options against these tumors, particularly unresponsive to current modes of therapy.

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