



Oncology

Incidental Leydig Cell Tumor in Patient with Hormone Resistant Prostate Cancer



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ABSTRACT

We hereby present the case of a 55 years old patient with clinical diagnosis of high-risk prostate cancer T2bN1Mo Gleason 9 (4 + 5) treated with androgen deprivation therapy and external beam radiotherapy. Despite treatment, castration levels were not achieved and clinical progression was evidenced by the appearance of bone metastases and progression of PSA. After several hormonal treatments without any PSA or testosterone response, surgical castration was performed by bilateral orchiectomy. The pathology results showed an incidental Leydig cell tumor in the right testicle.

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Introduction

Leydig cells are located in the testicular interstitial tissue and exhibit the main endogenous secretory activity of male hormones and other nonsteroidal substances. Their activity is controlled by the pituitary gonadotrophin hormone GHRH. It is known that prostate cancer growth is linked to androgens like testosterone or dihydrotestosterone.¹

Case presentation

We report the case of a 55 year old patient with a personal history of hypertension, hyperlipidemia and smoking.

In March 2013 he presented a PSA determination of 10.59 ng/ml, several months later the PSA was 13.28 ng/dl and also at the same time during a DRE a suspicious lesion in the right lobe of the prostate was found, so an ultrasound guided prostate biopsy was performed.

Transrectal ultrasound showed a hypoechoic lesion in the right apex and the right middle lobe (cT2b) without invasion of the prostatic capsule or the seminal vesicles. The pathology tests resulted in prostate adenocarcinoma Gleason 9 (4 + 5) (Group 5 ISUP)

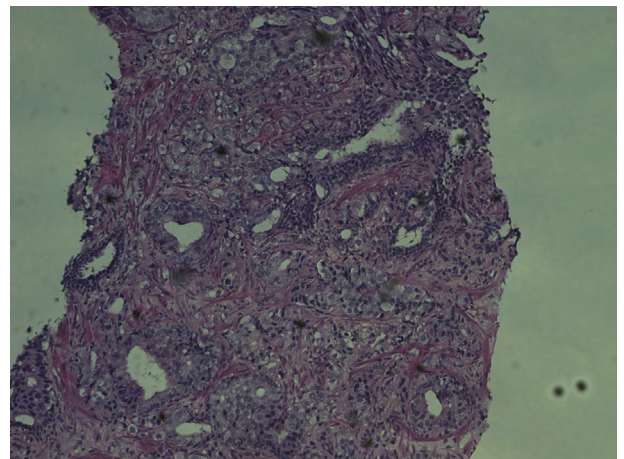


Figure 1. Prostate cancer G 9 (4 + 5) with positive perineural invasion.

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Figure 2. Right testicle.

found in all 12 cylinders with numerous images of perineural invasion (Fig. 1).

Extension study was performed by abdominopelvic CT and bone scan. The CT scan detected the presence of two metastatic lymph nodes of 1.2 cm and 1.1 cm on the right and left external iliac chain respectively. The bone scan showed no lesions. Therefore it was clinically staged as high risk prostatic adenocarcinoma Gleason 9 (4 + 5) T2bN1M0.

Treatment was started with androgen deprivation therapy with bicalutamide 50 mg/day for a month associated with a single dose of triptorelin. In addition the patient received radiotherapy treatment: pelvis 46 Gy to 2 Gy/tx + SIB 64.4 Gy for prostate and VSP 2.8 Gy/tx VMAT technique.

After the second dose of triptorelin, the patient continue with high PSA and testosterone values. Because of the persistence of high PSA values and not-castration levels, the treatment was changed to leuprolide. The analytical control after 3 months revealed a PSA of 12.66 ng/ml with a testosterone 3.10 ng/ml. At this moment we added daily bicalutamide 50 mg and the extension study was updated.

Bone scan showed on the middle third of the right femur a focal increase of activity compatible with the presence of a metastatic lesion. It was confirmed with a simple radiography as a blastic centromedullary asymptomatic bone lesion of 1.6 cm. The CT scan did not show metastatic lymph nodes or changes in the prostate gland compared with previous studies.

The second analytical control after initiation of leuprolide and bicalutamide showed a PSA of 1.17 ng/ml but testosterone remained at 3.70 ng/ml. It was decided to treat with focal radiotherapy on the bone metastases (37.5 Gy) and surgical castration with subalbuginea orchiectomy. During the surgery, a solid node was detected so we decided to change to a bilateral simple orchiectomy.

The pathology exam of the specimen showed on both testicles hipoespermato-genesis and absence of stromal Leydig cells and only in the right testicle a Leydig cells tumor of 16 mm, with immunophenotype: inhibin +, calretinin +, melan A +, chromogranin – and EMA – (Figs. 2 and 3).

After surgery, the patient recovered with no complications and further analytical control presented a PSA value of 0.10 ng/ml and a testosterone level of 0.20 ng/ml.

Discussion

Leydig cell tumors are mostly benign (10% are malignant) and the most frequent in the group of testicular stromal tumors representing 1–2% of all testicular cancer. More than 90% are unilateral and affect adults between 30 and 60 years, with another peak of incidence in childhood between 3 and 9 years.²

Leydig cell tumors usually present as painless palpable mass, about 30% develop gynecomastia and rarely Cushing's syndrome. They have been associated with Klinefelter syndrome, leiomyomatosis and hereditary renal cell carcinoma caused by FH mutations syndrome. Most cases are diagnosed incidentally by ultrasound and accompanied in 80% of cases by endocrine changes. Secretion of testosterone, androstenedione, dehydroepiandrosterone, estrogen and estradiol are described.³

Hormonal androgen deprivation therapy against prostate cancer causes changes in testicular histology by severe atrophy of the seminiferous tubules and Leydig cells.¹ Lower levels (less than 0.5 ng/ml) of circulating testosterone slow the growth of prostate tumor and increase the response to other treatments like radiotherapy.^{2,3} To define a prostate cancer as a castration-resistant two criteria must be met: maintain testosterone levels below 0.5 ng/ml and cancer progresses, either by rising PSA or radiological progression.

Some studies have shown that the probability of distant metastasis is inversely proportional to the density of Leydig cells and consequently to lower testosterone levels could be an increase of distant disease. As a result of endocrine and metabolic disorders caused by chemical castration, which develops prostate cancer by not yet well known mechanisms, it is important to suspect the

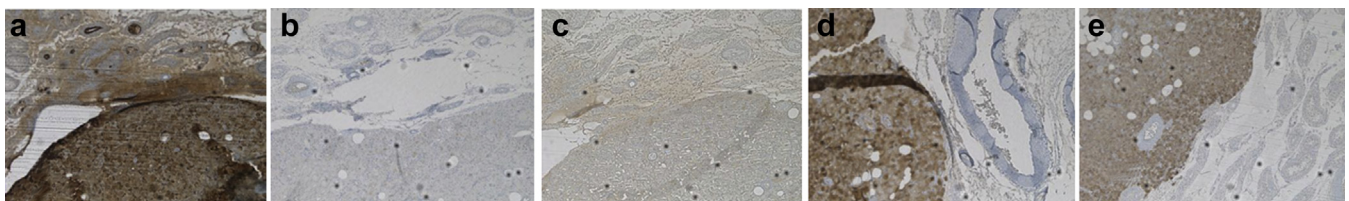


Figure 3. Immunohistology techniques (in order of appearance left to right): a) Calretinine +, b) Cromogranine –, c) EMA –, d) Inhibine +, e) Mart-1 +.

presence of secretory tumors such as Leydig cells in cases where the ADT is not effective.⁴ Most often the lesion is indolent and the diagnosis is usually incidental.⁵

Conclusion

A testicular Leydig cell tumor should be considered in patients with prostate cancer in which hormonal castration levels are over 0.5 ng/ml. Because of the secretory activity of the tumor, this can lead to a false conclusion of failure of androgen deprivation therapy. In case of clinical suspicion, testicular US should be performed before considering other treatment options.

Consent

Yes.

Conflict of interest

No have any potential conflict of interest.

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