

Testicular Metastasis of Prostatic Adenocarcinoma after Ablatherm[®] Treatment

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Abstract

Testicular metastases are rare in prostatic adenocarcinomas. The discovery is often fortuitous, and they are diagnosed with a histological examination. Metastasis is often confused with a primitive testicular tumor. We describe an 86-year-old patient with metastatic prostate adenocarcinoma that affected the left testis. The metastasis was discovered after Ablatherm[®] treatment. A prostatic origin must be suspected in a patient over 50 years old with testicular metastasis. This study highlights the importance of clinicopathological investigation and immunohistochemistry in determining the etiopathogenesis of testicular masses.

Keywords: Adenocarcinoma; Prostate; Metastatic; Testis

Abbreviations HIFU: High Intensity Focus Ultrasound; PC: Prostate Cancer; PSA: Prostate Specific Antigen; LDH: Lactic Dehydrogenase; α FP: Alpha-Fetoprotein; β HCG: Beta Hormone Chorionic Gonadotropin; PSAP: Prostatic Acid Phosphatase; LH-RH: Luteinizing Hormone-Releasing Hormone; MRI: Magnetic Resonance Imaging; CAB: Combined Androgen Blockade; GnRH: Gonadotropin Releasing Hormone

Introduction

Prostate cancer is currently one of the highest health prevalent problems in developed countries. The treatments currently validated for prostate adenocarcinoma include surveillance, radical prostatectomy, external or interstitial radiation therapy, high intensity focused ultrasound (HIFU), hormonal therapy, and chemotherapy, depending on the stage.

The prognosis of prostate cancer is determined by the histologic grade and by the presence or absence of metastasis with pelvic lymph node involvement. The most common site of prostate cancer metastasis is the bone, particularly bones in the axial skeleton and the proximal long bone, which account for more than 90% of distant metastases [1]. Metastases are also found regularly in visceral locations (lung, liver, adrenal glands) [2]. Other locations are rare, and they are typically described in case reports.

Prostate cancer metastases can occur years after the diagnosis and initial treatment of the disease. Both synchronous and metachronous metastases to the testis are currently rare. The incidence was more outstanding previously, when the disease was treated with a bilateral orchiectomy (surgical castration) [3].

Testicular metastasis of prostate adenocarcinoma is recognized as an advanced disease. It is often associated with metastases in other tissues or organs, particularly bones. Only 80 cases of testicular metastasis have been reported in the literature [4].

Here, we describe an 86-year-old patient that presented with a single metastasis in the left testis, 6 years after treatment with HIFU. The patient subsequently presented with a biochemical recurrence. He is currently receiving treatment with hormone therapy. We describe his clinical status 5 years after orchiectomy left.

Clinical Case

A patient, aged 86, with no particularly relevant medical history, was referred in August 2004, due to an elevated PSA (5.2 ng/ml, 17% ratio). Prostatic biopsies revealed prostate adenocarcinoma with a Gleason score of 6 (3+3)-grade I following the 2016 WHO new grading system. The proposed treatment was a transurethral resection of the prostate, followed by treatment with HIFU Ablatherm[®] because the patient was 71 years old and he had a LUTS due to a prostatic enlargement. Pathologic analysis did not reveal any tumoral cell.

Six years later, the clinical and laboratory follow up highlighted a biochemical recurrence (PSA doubling time <1 year). PSA rose from 1.7 in August 2009 to 3.4 ng/ml 7 months later. Clinical (digital rectal and testis examination) and radiologic (Cerebral CT, thoraco-abdominal CT and Total body MRI), assessments were negative. Treatment was then started with anti-androgen (Bicalutamide 150 mg).

One year after the start of anti-androgen treatment, the patient complained of scrotal discomfort and an increase in volume. A clinical control visit revealed left testicular swelling. A testicular ultrasound showed a lesion of 7 mm \times 10 mm \times 12 mm, which appeared hypoechoic, heterogeneous, and vascularized, with micro-calcifications (Figure 1a and 1b). Renal function was normal. Serum tumor markers, including lactate dehydrogenase (LDH), alpha-fetoprotein (α FP), and the beta fraction of chorionic gonadotropin (hCG), were normal. A scrotal exploration was performed via the left inguinal route, followed by a radical orchiectomy.

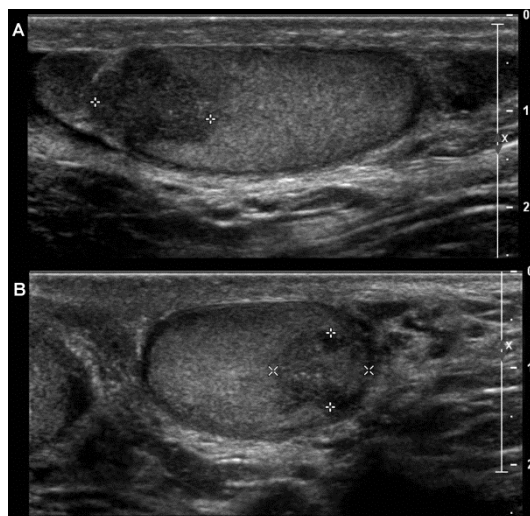


Figure 1: Testicular ultrasound images. (A) sagittal and (B) coronal sections show an injury (indicated with white crosses) of 7 mm × 10 mm × 12 mm, which is hypoechoic, heterogeneous, and vascularized, with calcifications.

Histological analysis showed that the testis was infiltrated by a revamped neoplastic cell population; Gleason 7(4+3) corresponding to a grade 3 according to the 2016 WHO grading system. Neoplasia extended to the rete testis and epididymis. The tumor displayed a massive, cribriform or reticular architecture (Figure 2a). Immunohistochemistry (Figure 2b) showed that the tumor cells were diffusely positive for PSA and prostatic acid phosphatase (PSAP), which confirmed a prostate adenocarcinoma metastasis.

A subsequent work-up, including a MRI centered on the total spine and pelvis and a thoraco-abdominopelvic CT, showed negative results. A new hormonal treatment was initiated, with an LH-RH analog, Triptorelin (Decapeptyl), at 11.25 mg, every 3 months. Two years later, the patient presented a new increase in PSA (0.1 in October 2012 to 0.6 ng/dl six months later). Therefore, we added Bicalutamide (Casodex®) at 50 mg daily, to establish a complete hormonal blockade. Currently, the patient is clinically asymptomatic, without biological relapse (PSA 0.31 ng/ml), and a good quality of life 5 years after orchiectomy.

Written informed consent was obtained from the patient for the publication of this case report and the use of the accompanying images. A copy of the written consent is available for review by Editor-in Chief of this journal.

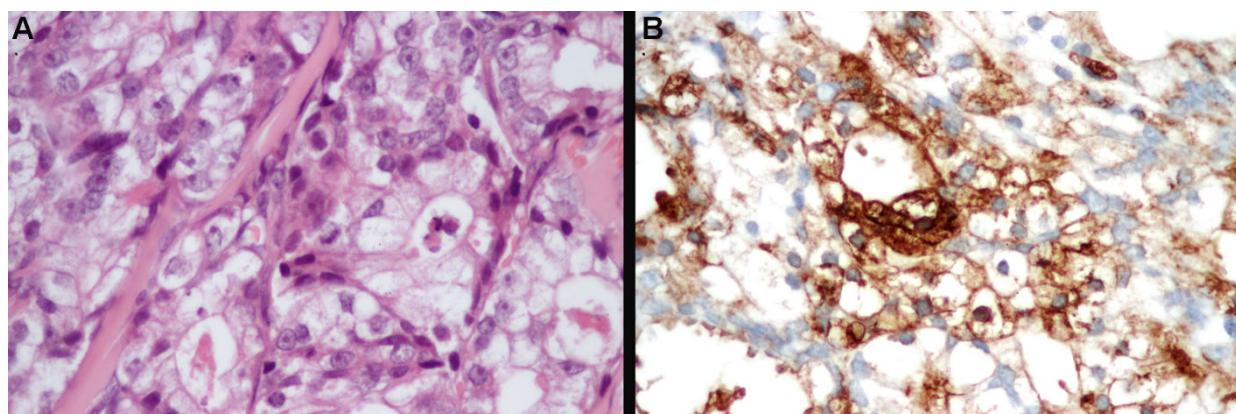


Figure 2: Micrographs of neoplastic cells. (A) Hematoxylin-eosin-stained section shows neoplastic cells, distinguished by a large nucleus and nucleolus (magnification 400X) (B) Testicular tumor sections were treated with immunoperoxidases and DAB detection. Immunohistochemistry results show cells diffusely positive for PSA and tumor cell PSAP; magnification 400X.

Discussion

The choice of Ablatherm treatment was done because of concern about the collateral side effects of radiotherapy and radical prostatectomy. Ablatherm is a minimally invasive treatment for patients more than 70 years old that was considered at that time as a good alternative treatment. In addition, Ablatherm doesn't preclude second line radiotherapy or surgery.

When a testicular lesion occurs in a patient over 50 years old, in the context of an unknown neoplastic hematologic pathology, the etiologic diagnosis is unclear; it could be a primary or secondary tumor. Other studies have shown that prostate cancer rarely metastasizes to the testicles; an autopsy study reported an incidence of about 0.02-2.5 % [3].

Secondary testicular lesions typically originate from, in order of frequency, lymphoma, acute leukemia, prostate, lung, kidney, melanoma, colon tumors, and esophageal cancer [1,5]. In 15% of cases, both testicles are affected [6]. The patient is typically asymptomatic, and the metastasis is often discovered incidentally after therapeutic orchiectomies or during autopsies. The metastatic spread to the testicles can occur in several ways. First, via retrograde migration into the lumen of the vas deferens. Second, it can spread through vascular or lymphatic routes. Third, it may occur as a direct, local extension of the prostate tumor. In the present case, we suspected a vascular spread, because the lesion also permeated the vascular bed in the vas deferens. However, we could not rule out a retrograde invasion, due to the invasion of the rete testis and the epididymis. In this case the absence of other metastatic localization than the testicular one could support

this hypothesis. The rarity of the testis metastases may be related to the relatively low scrotal temperature, which inhibits the growth of tumor cells, and thus, testicular secondary locations [7].

Currently, there has been a relative increase in the frequency of testicular metastases of prostatic origin. This increase may be related to a number of phenomena. First, may be related to the effectiveness of hormonal treatment, which prolongs survival, but favors the appearance of metastases in unusual sites. Second, the increased frequency may be due to the longer life expectancies of current human populations. Furthermore, in most reported cases, the testicular lesion is not isolated. Nevertheless, infrequently, the testes or epididymis are the only site of metastasis [8]. In the present study, our patient presented a single metastatic site after treatment with HIFU.

In previous studies, the interval between the prostate adenocarcinoma diagnosis and the onset of testicular metastasis was 2.5 to 15 years [9]. In our case, it was 7 years. Prostatic testicular metastases are typically asymptomatic. In our case, the patient complained of scrotal discomfort and an increase in volume, which motivated a consultation with a urologist earlier than expected.

Testicular metastasis of prostate adenocarcinoma is challenging to diagnose for pathologists, particularly when the lesion is poorly differentiated. The neoplasia can mimic a primary testicular germ tumor or lymphoma. However, a secondary tumor of prostatic origin can be diagnosed based on the prostate cancer history, serum PSA and PSAP positivity, unconvincing morphology for a germ cell tumor, and negative results from immunolabeling with specific antibodies against alpha-fetoprotein, PLAP, CD117, and CD30 [10,11].

The survival rate after a diagnosis of this type of metastasis is a controversial issue. For some series, it was less than a year [12]. In the present case study, the patient is currently alive. He has survived more than 50 months after the metastasis was treated with a radical orchidectomy and his current PSA is 0.31 ng/ml. In addition, there was no sign of another metastatic lesion. The subsequent follow therapeutic approach was the continuously combined androgen blockade (CAB) similar to the overall management of a classical metastatic prostate cancer.

The medical treatment represents the standard of care. The GnRH agonists and antagonists are the first choice of treatment in both phases of natural history of tumor (locally advanced and metastatic setting) with continuously or intermittent modality [13].

The concept of total androgen blockade has been a subject of great controversy [14,15] But the meta-analysis published by the Prostate Cancer Trialists' Collaborative Group in the *Lancet* in 2000 demonstrated that the use of anti-androgen in conjunction with LHRH agonist results in an approximately 3% improvement in overall survival [16].

Our choice for continuously combined androgen blockade (CAB) was justified by the fact that the evidence-based data of the intermittent modality was not conclusive [14].

Conclusion

Testicular metastases from prostate adenocarcinoma are rare. They should be suspected when any testicular mass is detected in a patient with a history of carcinoma in the prostate. A total radical orchidectomy with histological and immunohistochemical analyses are essential for establishing the precise diagnosis.

Statement of Ethics

Informed consent was provided by the patient for publication of this case and for the dissemination of images. A copy of the written consent is available from the editor of the journal.

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