Int J Clin Exp Pathol (2009) 2, 104-107
www.ijcep.com/IJCEP804003

Case Report

Metastatic Prostatic Carcinoma to Testis: Histological Features Mimicking Lymphoma

Bisong Haupt, Jae Y. Ro, Alberto G. Ayala and Jim Zhai

Department of Pathology, The Methodist Hospital, Weill College of Medicine of Cornell University, 6565 Fannin Street, Houston, TX

Received 30 April 2008; Accepted and available online 10 May 2008

Abstract: We report a case of prostatic carcinoma with testicular metastasis, which mimicked malignant lymphoma of the testis. The patient was a 71 year-old man with a history of prostate adenocarcinoma of Gleason score 9 (4+5) diagnosed in 2001 for which he received hormonal therapy. Four years later, the patient developed multiple osteoblastic bone metastases. Radiotherapy of the bone metastases was given with subsequently bilateral orchiectomy for hormonal deprivation therapy in May 2005. Grossly, one of the testes had a subcapsular rubbery 0.9 cm nodule. Microscopically, the nodule was composed of malignant discohesive cells predominantly infiltrating in the interstitium with an appearance of malignant lymphoma. However, immunohistochemical stains were positive for prostate-specific antigen and prostate acid phosphatase and negative for leukocyte common antigen, which confirmed the diagnosis of metastatic prostate adenocarcinoma.
Key Words: prostate cancer, metastasis, testis, lymphoma

Introduction

The most common metastatic sites of prostate carcinoma are bone, lung, and liver. Testicular metastases are very rare, and most of them are incidental findings in 2-4% of orchiectomy specimens performed for hormonal management of advanced prostate carcinoma. Most of these patients are older than 60 years of age. Since the histologic diagnosis of prostatic testicular metastases can be challenging, we report one such a case of unilateral testicular metastasis with morphology mimicking malignant lymphoma.

Case Report

The patient was a 71 year-old man who was diagnosed with prostate adenocarcinoma, Gleason score 9(5+4) in 2001 by transurethral biopsy of prostate. Microscopically, the majority of prostate biopsies had a high grade prostate carcinoma with cribriform pattern and focal necrosis (**Figure 1A**). Small amounts of glandular areas were also present, but solid tumor nests or single isolated tumor cells were not observed. Based on the high Gleason score and the patient age, the patient was elected to receive Lupron 22.5 mg and Trenantone 11.25 mg for hormonal therapy. Four years later, he developed multiple osteoblastic bone metastases. Radiotherapy of bone metastases was given. A bilateral orchiectomy for hormonal deprivation therapy was subsequently done in May 2005.

Pathology

The two testes weighed 24 and 30 grams respectively. Grossly the smaller testicle had an indurated, rubbery, firm subtunical parenchymal nodule measuring 0.9 cm in greatest dimension. No other lesion was seen in the remainder of the testicular parenchyma as well as the other testis.

Microscopically, the testis showed malignant round tumor cells within the interstitium of the testicular parenchyma beneath the capsule (**Figure 1B**). These cells infiltrated among the seminiferous tubules and presented in a discohesive pattern. The tumor cells were large with relatively large round to oval, sometimes vesicular nuclei, large and

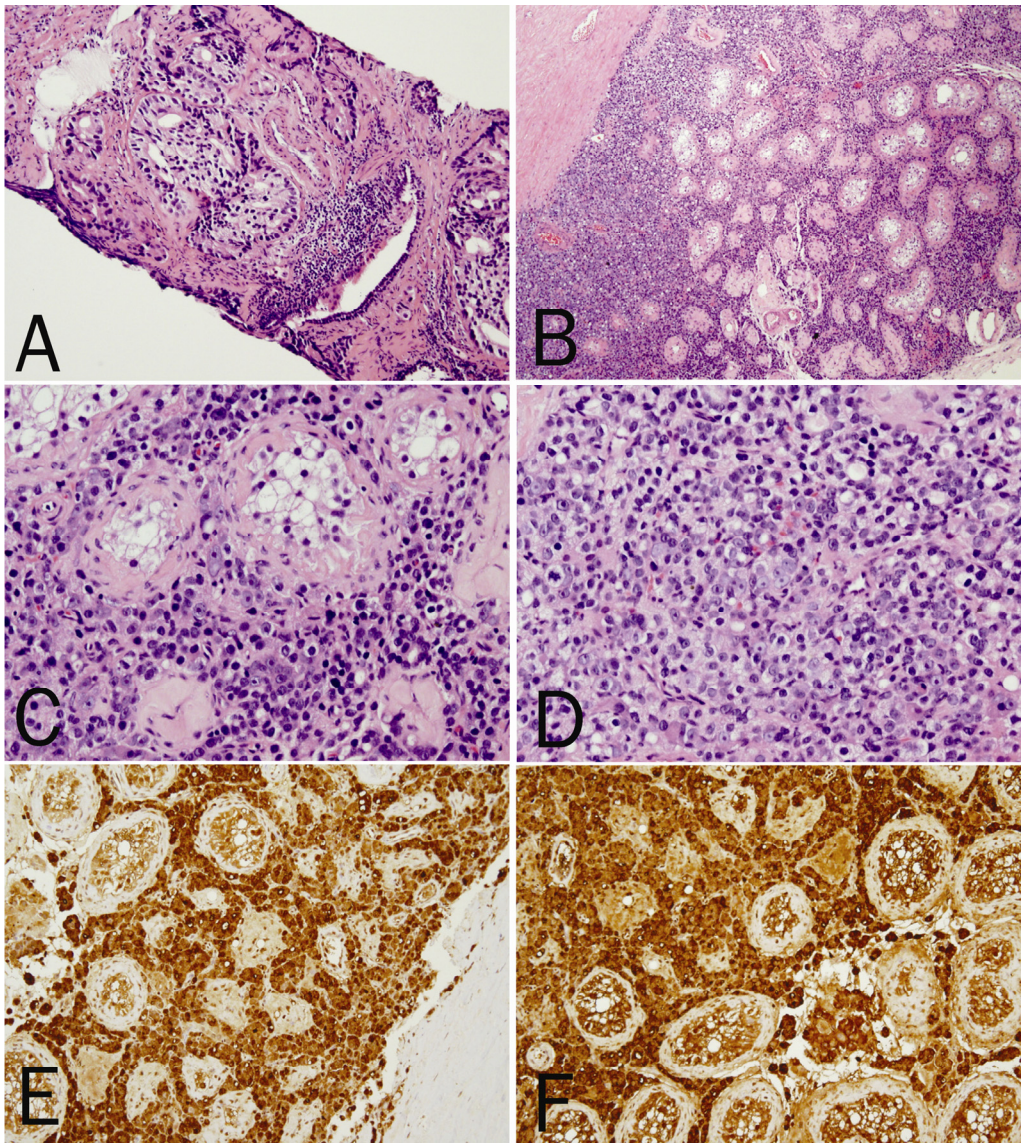

Figure 1 Majority of tumor have a cribriform growth pattern (**A**, H and E stain). Malignant round cells are present in the interstitium of the testicular parenchyma beneath the tunica albuginea (**B**, H and E stain). Tumor cells are large with relatively large round to oval, sometimes vesicular nuclei and small amount of amphophilic cytoplasm (**C**, H and E stain). Tumor cells are present around sclerotic seminiferous tubules (**D**, H and E stain). Malignant cells are strongly immunoreactive for PSA (**E**) and PAP (**F**).

prominent nucleoli and small amount of amphophilic cytoplasm. In some areas, these cells invaded the sclerotic seminiferous tubules (**Figures 1C** and **1D**). The differential diagnosis included large cell lymphoma, metastatic prostate carcinoma, melanoma and less likely seminoma. Immunohistochemical staining with CD20, CD3, OCT3/4 and inhibin were negative, but PSA and PAP (**Figures 1E** and **1F**) were positive, which confirmed the diagnosis of metastatic prostate carcinoma.

Discussion

Testis is a rare organ for metastatic neoplasm. It was reported that the main reason for relatively low incidence of metastases to the testis would be an unfavorable condition for establishment of metastatic tumors with relatively low temperature of scrotum [1]. In a study by Lior and Biggard in 1993 of 85 testicular tumors, 10% of testicular tumors were secondary tumors from extragonadal

sites [2]. On the other hand, in 738 autopsies of adult males with solid malignant extragonadal neoplasms, five (0.68%) of them was found to have metastatic deposits within the testis. These were metastases from bronchial carcinoma (three cases), melanoma (one case), and pancreatic endocrine carcinoma (one case) [3]. In another prospective autopsy study of male subjects with malignant neoplasms, six were shown to have metastatic deposits within the testis (2.5%). These were metastases from carcinoma of the prostate (two cases), melanoma (two cases), bronchial carcinoma (one case) and pleural mesothelioma (one case). In a study from M.D. Anderson Cancer Center in 1971, of 22 cases of secondary carcinoma of testis, the primary tumors were malignant melanoma in 9 cases, lung cancer in 3 cases and prostate cancer in 2 cases [10]. In a few more recent studies for the cases of metastatic carcinomas to the testis, the most frequent primary sites were prostate, followed by lung, kidney, colon and stomach [4, 5]. The detection of high metastatic rate of prostate cancer to the testis was probably due to the therapeutic orchiectomy done in these patients.

The most common cancer expected to occur in men in USA is prostate cancer, 33% of all cancers, followed by lung/bronchus and colon/rectum. The estimated death of prostate cancer is 9%, the third most common cancer death, followed by lung/bronchus and colon/rectum according to American cancer society in 2006 [11]. The low fatality means that many patients survive a long period time following the diagnosis of prostate cancer. Metastatic spread of prostate cancer begins when carcinoma invades into lymphovascular spaces. The most common sites are regional pelvic lymph nodes and bone. A testis metastasis of prostatic adenocarcinoma is uncommon and unilateral involvement of testis is more common than bilateral involvement [6].

There are reported cases of prostatic cancer patients with primary testicular lymphoma [12]. The differential diagnosis of primary testicular lymphoma vs metastatic prostatic carcinoma to the testis in these patients is important, since there are differences in treatments as well as clinical staging. Secondary involvement of testis by lymphoma is more common than primary testicular lymphoma. Tiltman reported that metastatic lymphoma was seen in four of 29 leukaemic patients and in six of 28 with non-Hodgkin lymphoma [13].

The unusual histological features of our case brought lymphoma and melanoma into the differential diagnosis. Primary testicular lymphomas as well as secondary lymphomas are more common in older patients. Primary testicular lymphomas account for up to 2% of all testicular neoplasms and are the most common primary testicular tumor in older male patients (mean age of 60-80 years), 70-80% of which are diffuse B-cell type. It usually presents as unilateral enlargement or swelling of scrotum. Compared with seminoma, lymphoma more often invades the epididymis and spermatic cord. Microscopically, the neoplastic cells infiltrate around seminiferous tubules, cause arrest of spermatogenesis, and tubular hyalinization. Immunohistochemical stains with T and B cell markers (CD20, CD3, CD5, and CD30) confirm the origin of hemotopoietic cells. The prognosis of primary testicular lymphoma is poor with 5-year survival rate of 35-48%.

Malignant melanoma is known to metastasize widely and presents as a variety of morphology. Metastatic malignant melanoma has an ability to imitate all kinds of neoplasms. A few cases of testicular metastasis from malignant melanoma have been reported. In an earlier report from M.D. Anderson Cancer Center of 22 cases of metastatic testicular tumors, nine cases were from malignant melanoma, which may reflect that the large number of patients with malignant melanoma was treated at that hospital during that period of time [10]. When dealing with high grade tumor, metastatic malignant melanoma should always be in the differential. In addition to other markers, immunohistochemical staining for melanoma markers including S-100, HMB 45, and Melanin A can confirm a melanocytic origin.

Primary testicular seminoma is the most common testicular tumor, accounting up to 45-55% of all testicular tumors and occurs more commonly in younger men (about 35-45 years old) than older men (more than 50 year old) [7-9]. Histologically seminoma cells have clear to lightly eosinophilic granular cytoplasm

and central nuclei. These cells are closely apposed, with well-defined cytoplasmic border arranging in sheets or dividing by fine fibrous trabeculae associated with lymphocytic infiltrate. Rarely seminomas presented predominantly with intertubular growth with differential diagnosis of Metastatic carcinoma or lymphoma. Immunochemically, the tumor cells are positive for PLAP, CD117, and OCT3/4, but negative for lymphoma markers and frequently negative for cytokeratin.

In summary, prostate cancer presents a wide range of growth patterns as depicted in the Gleason diagram. The metastatic prostate carcinoma offers different morphologic presentations, especially when original prostate carcinoma has a high Gleason score as seen in the current case. Since most patients are above 60 years of age, lymphoma, primary or secondary and metastatic diseases such as malignant melanoma enter in the differential diagnosis. For pathologists, when examining testicular specimens of patients with history of prostate carcinoma, metastatic prostate carcinoma should be kept in mind, even if the morphology is not typical for prostate carcinoma. Immunohistochemical study generally helps us to arrive at the correct diagnosis.

Please address all correspondences to Jim Zhai, MD, Department of Pathology, The Methodist Hospital, Weill College of Medicine of Cornell University, 6565 Fannin Street, Houston TX 77030. Tel: 713-441-6409; Fax: 713-793-1603; Email: qzhai@tmhs.org

Reference

[1] Smallman LA and Odedra JK. Primary carcinoma of sigmoid colon metastasizing to epididymis. *Urology* 1984;23:598-599.

[2] Lioe T and Biggard JD. Tumors of the spermatic chord and paratesticular tissue. A clinicopathological study. *Br J Urol* 1993; 71:600-606.

[3] Garcia-Gonzalea R, Pinto J and Val-Bernal JF. Testicular metastases from solid tumors: an autopsy study. *Ann Diag Pathol* 2000;4:59-64.

[4] Patel SR, Richardson RL and Kvols L. Metastatic cancer to the testes. A report of 20 cases and review of the literature. *J Urol* 1989; 142:1003-1005.

[5] Haupt HM, Mann RB, Trump DL and Abeloff MD. Metastatic carcinoma involving the testis. *Cancer* 1984;54:709-714.

[6] Giannakopoulos X, Bai M, Grammeniatis E, Stefanou D and Agnanti N. [Bilateral testicular metastasis of an adenocarinoma of the prostate]. *Ann Urol (Paris)* 1994;28:274-276.

[7] Chung PW, Bayley AJ, Sweet J, Jewett MA, Tew-George B, Gospodarowicz MK and Warde PR. Spermatocytic Seminoma: A Review *Eur Urol* 2004;45:495-498.

[8] Krag Jacobsen G, Barkebo H, Oslen J, Schultz HP, Starklint H, Sogaard H and Vaeth M. Testicular germ cell tumors in Denmark 1976-1980. Pathology of 1058 consecutive cases. *Acta Radiol Oncol* 1984;23:239-247.

[9] Pendlebury S, Horwich A, Dearnaley DP, Nicholls J and Fisher C. Spermatocytic seminoma: a clinicopathological review of ten patients. *Clin Oncol (R Coll Radio)* 1996;8:316-318.

[10] Johnson DE, Jackson L and Ayala AG. Secondary carcinoma of the testis. *South Med J* 1971;64:1128-1130.

[11] Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C and Thun MJ. Cancer statistics, 2006. *CA Cancer J Clin* 2006;56:106-130.

[12] Amat CM, Pomero PP and Sevilla CFI. Lymphomas of the urogenital systems. Review of the entirety and report of 2 cases with testicular localization. *Arch Esp Urol* 1994;47: 992-997.

[13] Tilman AJ. Metastatic tumors in the testis. *Histopathology* 1979;3:31-37.