

METACHRONOUS TESTICULAR SEMINOMA-16 YEARS LATER: EARLY DETECTION AND MANAGEMENT /CASE REPORT/

Ludmil M. Veltchev¹, Manol A. Kalniev², Todor A. Todorov³,

1) Fellow, Master's Program in Hepatobiliary Pancreatic Surgery, Henri Bismuth Hepatobiliary Institute, 12-14, avenue Paul Vaillant-Couturier, 94804 Villejuif Cedex

2) Department of Anatomy, Cytology and Histology, University of Medicine, Sofia, Bulgaria

3) Department of Pathology, University of Medicine, Sofia, Bulgaria

ABSTRACT:

A 28-year-old male presented at a regional hospital with a pulling sensation and feeling of unusual heaviness in the right scrotum. Pain and discomfort appeared two weeks ago.

The patient had no previous medical history.

Physical examination, US and CT confirmed 26 mm mass, localized centrally in the right testis without metastatic process and patient was treated with right inguinal orchiectomy, followed by 25 Gy radiotherapy. After 16 years and 3 months the same symptomatology started in the left side and US discovered two masses: 15 and 21 mm in left testis. Investigation included tumor marker assessment, scrotal US, CT and biopsy. Diagnosis metachronous testicular seminoma, stage T1N1M0.

Biopsy, radical orchiectomy, androgen substitution and follow-up were performed.

Key words: seminoma, bilateral, metachronous, germ-cell tumor.

THE CASE:

A 28-year-old male presented at a regional hospital with a sensation and feeling of unusual heaviness in the right scrotum. Pain and discomfort appeared two weeks ago. The patient had no previous medical history. US imaging showed a right side mass, measuring 28x20 mm and normal left testis. A CT scan revealed no evidence of infiltration of spermatic cord or the inguinal and paraaortic lymph nodes. Blood serum tumor markers of human chorionic gonadotropin (HCG), α -fetoprotein (AFP), and lactate dehydrogenase (LDH) were in referent levels. After consultation with anesthesiologist, right inguinal high orchiectomy was made. Histology demonstrated a seminoma, without infiltrating tunica albuginea-stage pT1N0M0 tumor according UICC (Union International Against Cancer).

One month after operation, the patient was presented to the hospital multidisciplinary oncology group and started

radiotherapy in dose of 25Gy to the periaortic lymph nodes. Patient was accepted as disease free and according the protocol was followed up every 4 months the first two years with chest X-ray, CT, physical examination and tumor marker assessment.

In May 2009, 16 years and 3 months after the first orchiectomy, the patient complained in a medical office of enlarged left testis, firm in consistency and with a sensation for heaviness. Scrotal ultrasonography revealed two hypoechoic left-testicular masses measuring 19x12 mm and 13x7 mm (Fig. 1).

Patient was referred to a specialized urologic clinic, where repeated physical and imaging study revealed no evidence of metastases, and serum concentrations of testosterone, β -HCG, LDH, and AFP were all within normal ranges. No suspicions for spread on CT of chest and abdomen.

In elective plan left inguinal exploration and frozen section biopsy with confirmation of germ cell tumor-pure seminoma was made (Fig. 2).

The tumors measured 12 mm and 10 mm in greatest dimension, respectively, and were confined to the testis. One lymph node was detected 2 cm in the spermatic cord but negative for neoplastic invasion. Second pT1N0M0 was found. Daily topical testosterone replacement therapy was administered, beginning on the first postoperative day-in the form of a hydroalcoholic gel containing 1% testosterone (10 mg/g). In his first month follow-up the patient reported good physical status, maintenance of his libido and improvement of his fatigue and hot waves. His serum testosterone level had increased to 11.9 nmol/l and serum LH level had fallen to 12 IU/l.

DISCUSSION

Diagnosis

The incidence of testis cancer has been steadily increasing over the last 40 years (1). It appears to be most

common in northern European populations with age standardized incidence rates between 4 and 10 per 100 000. The peak incidence is between the ages of 15 to 35 years. Five year survival rates have increased significantly over the last 30 years from about 63% to more than 90% (2). Second testicular cancer arising in the contralateral testis is relatively common: the incidence of metachronous testicular tumors has been reported to be in the range of 2–5% among men followed up for 4–15 years after testicular cancer. The mean time to diagnosis of the second testicular tumor is 6 years (3, 4). Approximately 17% of bilateral tumors occur synchronously, and the remaining 83% are metachronous. About 40-45% of all tumors are pure seminomas. The rest of the tumours are a mixture of the non seminomas.

Seminomas are associated with significant excesses of total second tumors in each follow-up interval after 5 or more years, and risk increases with time since initial diagnosis. Risks are significantly elevated among patients treated initially with radiotherapy alone, but not chemotherapy. The incidence of second tumor correlates positively with the presence of atrophic testis and negatively with age. Approximately 2% of men with a history of cryptorchidism will have germ cell neoplasia (5).

Differential diagnosis

Metachronous testis tumor is defined as such, when the interval between occurrence of first and second is longer than six months and genital ultrasound, CT and physical examinations are negative for neoplasm in contralateral. The mean age of patients with metachronous tumors is 28 years at the diagnosis of the first tumor and 35 years at the diagnosis of the second tumor (6, 7).

Studies have reported that 67% of metachronous tumors are diagnosed within 5 years of the first tumor (8). Three markers of testicular tumors are measured: α fetoprotein, β human chorionic gonadotrophin and lactate dehydrogenase. They were found to be normal at the time of diagnosis of the first and second tumors in this case, which was suggestive of a seminoma rather than a nonseminomatous germ-cell tumor. Serum AFP does not show an increase in seminomas, and increased HCG is found in only 6–10% of pure seminomas. Increased LDH values are noted in 8% of patients with stage I seminoma, compared with approximately 80% of advanced seminomas. Patients with a history of testicular tumors treated with orchietomy and chemotherapy tend to have reduced levels of testosterone and increased levels of FSH and LH. These patients should undergo screening for hypogonadism by

measurement of serum testosterone, LH and FSH levels at 6-12 month intervals. Timely identification of the need for testosterone replacement facilitates the initiation of treatment to maintain or restore sexual function, libido, and wellbeing, and to prevent depression, osteoporosis, and probably also heart disease.

Treatment and management

Radical orchidectomy is the method of choice for testicular cancer. It removes the primary tumors and provides the histological diagnosis. The testis and the spermatic cord are excised through an inguinal incision.

Postoperatively, the most common follow-up program after administration of retroperitoneal radiotherapy for a stage T1N0M0S0 seminoma involves carrying out a physical examination, X-ray, and assessment of tumor markers every 4 months for the first 2 years, every 6 months for years 3–5, and yearly thereafter. Ultrasound can detect lesions in the testis itself. Hypoechoic lesions of the testis frequently indicate the presence of malignancy (9). Some of these tumors may not be palpable. Rarely testicular tumors can grow so fast in the testis that it outstrips its own blood supply. In this situation the primary tumor dies and forms a scar. This scar is called an Azzopardi scar. It is possible to identify these lesions by ultrasound.

A β -FP, β -HCG and LDH are measured serially post orchidectomy. If they were raised pre operatively and the levels fall quickly post operatively then it is likely that all the cancer has been removed by the orchidectomy.

After bilateral orchietomy, the implantation of testicular prostheses and androgen substitution therapy can help in the sexual, psychological and social rehabilitation of the patient.

Topical testosterone gels have good tolerability and a lower incidence of skin irritation than testosterone-containing patches and are met with high levels of patient acceptance.

SUMMARY

The second, metachronous testicular tumor is discovered either during regular follow-up by the physician or by imaging examination during the first 2-3 years and most rarely after patient's complaints of discomfort and unusual heaviness. Statistically, second testicular primary cancer appears between 5 and 6 years, but recent reports suggest extension of this interval to 15 to 20 years after the first operation (in our case 16 years 3 months). The early detection of the new tumor in a contralateral testis leads to radical treatment and long-term survival.

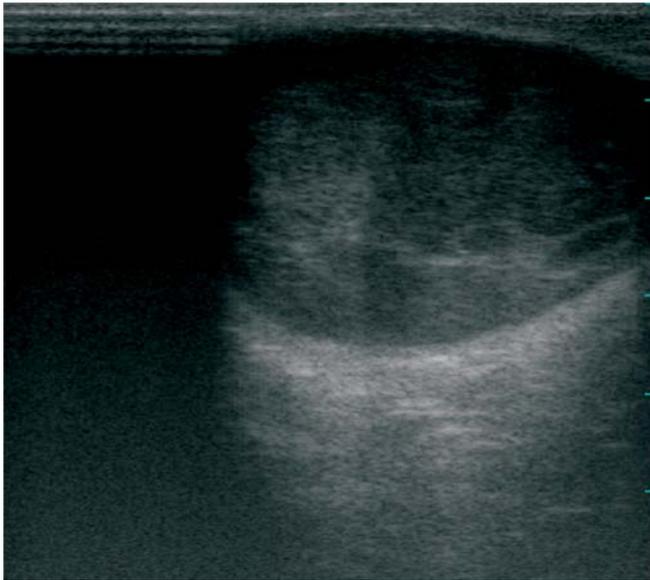


Fig. 1. US of left testis

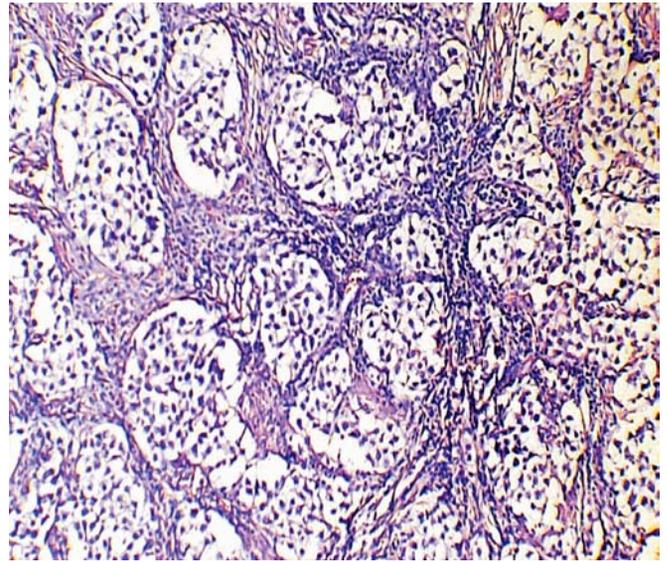


Fig. 2. Histological findings on biopsy samples from the atrophic left testis of the case patient, who had previously undergone right orchiectomy for a stage I seminoma.

REFERENCES:

1. Huyghe E., Matsuda T., Thonneau P. Increasing incidence of testicular cancer worldwide: a review. *J Urol* 2003; 170:5-11.
2. Garner M. J., Turner M. C., Ghadirian P., et al. Epidemiology of testicular cancer: an overview. *Int J Cancer* 2005; 116:331-9.
3. Fordham MV *et al.* Management of the contralateral testis in patients with testicular germ cell cancer. *Br J Urol* 1990; 65: 290-293.
4. Fossa SD *et al.* Risk of contralateral testicular cancer: a population-based study of 29,515 US men. *J Natl Cancer Inst* 2005;97: 1056-1066.
5. Harland S. J. *et al.* Intratubular germ cell neoplasia of the contralateral testis in testicular cancer: defining a high risk group. *J Urol* 1998; 160: 1353-1357.
6. Gűczi *et al.* The incidence, prognosis, clinical and histological characteristics, treatment, and outcome of patients with bilateral germ cell testicular cancer in Hungary. *J Cancer Res Clin Oncol* 2003; 129: 309-315.
7. Holzbeierlein J. M. *et al.* Histology and clinical outcomes in patients with bilateral testicular germ cell tumors: the Memorial Sloan Kettering Cancer Center experience 1950 to 2001. *J Urol* 2003; 169: 2122-2125
8. Patel R. S. *et al.* Synchronous and metachronous bilateral testicular tumors. Mayo Clinic experience. *Cancer* 1990; 65: 1-4
9. Hindley R. G. *et al.* Impalpable testis cancer. *BJU Int* 2003; 92: 572-574

Corresponding author:

Ludmil Marinov Veltchev, MD PhD
 Mobile: +359 876 259 685
 E-mail: drlmarinov@yahoo.com