Clinical Outcomes of Local and Metastatic Testicular Sex Cord-Stromal Tumors

Jonathan L. Silberstein,* Wassim M. Bazzi, Emily Vertosick, Brett S. Carver, George J. Bosl, Darren R. Feldman, Dean F. Bajorin, Robert J. Motzer, Hikmat Al-Ahmadie, Victor E. Reuter and Joel Sheinfeld

From the Department of Urology, Tulane University School of Medicine (JLS), New Orleans, Louisiana, and Urology Service, Department of Surgery (WMB, BSC, JS), Department of Epidemiology and Biostatistics (EV), Genitourinary Oncology Service, Department of Medicine (GJB, DRF, DFB, RJM) and Department of Pathology (HA-A, VER), Memorial Sloan-Kettering Cancer Center, New York, New York

Purpose: We evaluated pathological variables of testicular sex cord-stromal tumors, management options and clinical outcomes.

Materials and Methods: We retrospectively reviewed the records of 48 patients with testicular sex cord-stromal tumors treated at Memorial Sloan-Kettering Cancer Center between 1997 and 2012. Clinical outcomes were compared based on treatment and previously described pathological factors associated with metastatic potential.

Results: Of the 48 patients 37 underwent surveillance without retroperitoneal lymph node dissection, including 34 with no high risk feature and 3 with 1. Median followup was 14.5 months (IQR 6.9–32.5). No patient experienced recurrence. Retroperitoneal lymph node dissection was performed in 11 patients, including 6 with clinical stage I disease and 2 or more high risk features who underwent early dissection, 2 with clinical stage IIa disease at diagnosis who underwent early dissection and 3 with clinical stage I disease and 2 or more high risk features who were observed elsewhere but referred to our institution due to retroperitoneal disease. Six patients with clinical stage I disease underwent early dissection, 4 had no evidence of disease at a median followup of 6.6 years and 2 experienced recurrence and died of disease. Neither of the 2 patients with IIa disease at diagnosis experienced relapse. All 3 patients with delayed dissection experienced relapse and 1 died of disease.

Conclusions: Patients with testicular sex cord-stromal tumors and 1 or no high risk feature can be safely observed without retroperitoneal lymph node dissection but longer followup is needed. Given the lack of effective alternative treatments, early retroperitoneal lymph node dissection may be beneficial in those with 2 or more high risk features, or clinical stage IIa disease.

Key Words: testis, sex cord-gonadal stromal tumors, lymph node excision, risk, orchiectomy

Abbreviations and Acronyms

MSKCC = Memorial Sloan-Kettering Cancer Center

RPLND = retroperitoneal lymph node dissection

TSCST = testicular sex cord-stromal tumors

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* Correspondence: Department of Urology, School of Medicine, Tulane University, 1430 Tulane Ave., SL-42, New Orleans, Louisiana 70112-2632 (telephone: 504-988-0768; FAX: 504-988-5059; e-mail: jsilbers@tulane.edu).

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TESTICULAR sex cord-stromal tumors are a rare group of primary testicular neoplasms that arise from the hormone secreting cells of the testis. The most common subtype, accounting for 75% of these tumors, originates from Leydig cells.[1] TSCSTs also include tumors of Sertoli and granulosa cell origin as well as mixed cell types. Most commonly patients present with a painless testicular mass, although symptoms due to excessive hormonal

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secretion such as gynecomastia may also occur.[2] Together these tumors comprise approximately 4% to 5% of all testicular tumors.[3]

While most TSCST are indolent, approximately 10% metastasize, most commonly to the retroperitoneum in a fashion that mimics testicular germ cell tumors.[4] Due to the lack of effective chemotherapeutic or radiation treatment options TSCST metastasis often results in death.[4] For this reason RPLND even in the absence of retroperitoneal disease is believed by some physicians to be critical.[5] However, RPLND would be overtreatment in most patients with clinical stage I disease since most of them are unlikely to experience disease progression.

Kim et al challenged the notion that the only reliable criterion for malignancy is metastasis.[5] They established 6 histopathological criteria predictive of metastatic potential for Leydig cell tumors, including tumor greater than 5 cm, necrosis, moderate or severe nuclear atypia, angiolymphatic invasion, infiltrating margins and greater than 5 mitotic features per 10 high power fields. These criteria were subsequently confirmed and applied to all TSCST subtypes.[3,6] Kim et al advocated orchiectomy alone in patients with none of these features and RPLND when any feature was present.[5] However, due to small cohorts with a limited number of events it remains unclear how to best treat patients with TSCST. Some investigators advocate an aggressive approach by performing RPLND in all patients with TSCST[4,7] and others recommend observation in all patients with clinical stage I disease.[8]

We reviewed our institutional approach to these tumors. We also evaluated primary tumor pathological variables, management options and clinical outcomes in patients with TSCST.

MATERIALS AND METHODS

After receiving institutional review board approval we retrospectively reviewed the records of all patients with TSCST who received care at MSKCC between 1997 and 2012. While not all patients were initially treated at our institution, all pathological specimens were reviewed by genitourinary fellowship trained pathologists at MSKCC. Orchiectomy pathology reports were reviewed for high risk pathological features associated with metastatic potential.[5] At MSKCC we recommend surveillance for patients with 1 or none of these high risk pathological risk features and no evidence of retroperitoneal lymphadenopathy. For patients with 2 or more high risk features, or evidence of retroperitoneal adenopathy on cross-sectional imaging we recommend RPLND. Notably not all patients underwent initial treatment at MSKCC so that not all were treated in this uniform manner.

A total of 48 patients with TSCST were referred to MSKCC for consultation or treatment between 1997 and 2012. Of the 48 patients 37 had 1 or no pathological risk feature with no evidence of retroperitoneal disease on imaging. They were classified as being at low risk and underwent routine surveillance. RPLND was performed in the remaining 11 patients, who were classified as being at high risk due to 2 or more pathological risk features, or retroperitoneal disease on imaging. Patients were characterized and compared based on risk group and indication for RPLND. All patients who underwent RPLND were treated with full bilateral template RPLND as previously described in detail.[9] Time to RPLND was calculated as the time between orchiectomy and RPLND. Time to relapse was calculated as the time between RPLND and the date of post-RPLND relapse. Total followup was calculated as time from orchiectomy to last followup or death. All analysis was done with Stata® 12.0.

RESULTS

All 48 men in this cohort underwent partial or radical orchiectomy for TSCST. In 20 and 26 of these patients the primary tumor was on the left and right side, respectively. Two patients in this group had bilateral synchronous primary tumors. Of these tumors 65% were due to a palpable lesion but 35% were found due to other reasons. A total of 13 men had Sertoli cell tumors, 28 had Leydig cell tumors, 5 had unclassified TSCST and 2 had granulosa cell tumors.

After orchiectomy patients were stratified into 2 groups by risk (table 1). Patients with zero (34) or 1 (3) risk factor and no evidence of retroperitoneal disease on cross-sectional imaging were on surveillance for a median of 14.5 months (IQR 6.9–32.5). None of these 37 patients experienced retroperitoneal recurrence of TSCST. In this group patient age at orchiectomy was 18 to 78 years (median 37, IQR 29–52) (see figure).

The other 11 men in the cohort underwent RPLND because they had 2 or more risk factors, or retroperitoneal disease was found. With a median age at orchiectomy of 48 years (IQR 37–53) these patients were older than those with 1 or no risk factor. Ten of these patients were diagnosed with a palpable testicular mass and 1 was not. Median followup in all patients treated with RPLND was 67 months (IQR 23–112).

Six of these 11 men underwent early RPLND due to high risk features without evidence of radiographic disease (table 2). Metastatic nodal disease (pN2) was identified in 1 of the 6 patients, who subsequently experienced relapse in the lung, pelvis and retroperitoneum. In another patient without pathologically confirmed nodes at RPLND (N0) recurrence developed in the lung and bone. These 2 men died of progressive disease. The remaining 4 patients remained disease free at the most recent followup. Notably the 2 patients who died of

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