Resection of retroperitoneal residual mass after chemotherapy in patients with nonseminomatous testicular cancer

AHMET ÖZET1, ALİ AYDIN YAVUZ2, MURAT BEYZADEOĞLU3, YAŞAR ÖZGÖK4, BEKİR ÖZTÜRK1, FİKRET ARpacı1, ŞEREF KÖMÜRCÜ1, LEVENT YAMANEL2, TEOMAN DOĞRU3

Departments of 1Medical Oncology, 2Internal Medicine, 3Radiation Oncology and 4Urology, Gülhane Military Medicine Academy, Ankara-Turkey

Retroperitoneal lymph node dissection followed by chemotherapy for the treatment of nonseminomatous testis cancer is reserved for partial remissions. One hundred and sixty seven patients with nonseminomatous testis cancer were admitted to Gülhane Military Medical Academy between the years of 1992-1999. Retroperitoneal residual masses determined radiologically were resected in 12 patients (9 teratocarcinoma, 3 embryonal carcinoma) with stage-B after cisplatin-based therapy (PVB in 8 and PEB in 4 patients). Alpha-fetoprotein (AFP) and beta subunit of human chorionic gonadotropin (β-HCG) levels in all patients were normal before resection. The pathologic evaluation of removed retroperitoneal masses showed residual malignancy in 6 patients, mature teratoma in 5 patients and necrosis in 1 patient. Patients with malignant residual tumor (n=6) received chemotherapy, and the others (n=6) were followed by surveillance only. Our data presented herein imply that surgical removal of all post-chemotherapy residual masses is required before suggesting routine salvage chemotherapy. [Turk J Cancer 2001;31(2):57-62]

Key words: Testicular cancer, chemotherapy, lymph node dissection

Testicular cancer has become the model for a curable neoplasm (1). In treatment of nonseminomatous germ cell testicular tumors (NSGCTT), there have been great improvements in the last 25 years. Multi-drug chemotherapy protocols based on cisplatin have greatest role in these improvements (2). Even though the serum tumor marker (β-hCG and AFP) values are normal after the chemotherapy, the residual masses over 2.5 cm detected by radiological techniques must be removed immediately to constitute the treatment integrity (3). Nearly, 80% of the patients can be cured by surgery removing the residual masses after the cisplatin-based chemotherapy (4). Of the patients requiring
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resections of residual disease after primary chemotherapy, approximately 90% will have either necrosis or teratoma in their resected specimens. This number drops to 50% in patients resected after salvage chemotherapy (4). If the histological findings of removed residual masses resected after the primary chemotherapy are necrosis or teratoma, additional chemotherapy is not intensively used (5). On the other hand, if there are viable malignant tumor cells in the specimen, there is need for new salvage chemotherapy protocols (6,7).

We present a limited series of 12 patients with NSGCTT who underwent retroperitoneal lymph node dissection (RPLND) after chemotherapy for residual masses. Attention is paid to indications and outcome.

Patients and Methods

One hundred and sixty-seven patients with NSGCTT have been treated at the Gülhane Military Medical Academy, Department of Medical Oncology between 1992-1999. In 12 of them, retroperitoneal residual masses more than 2.5 cm transverse diameter after primary chemotherapy were determined by abdominal computerized tomography (CT). The median age was 26 years (range: 22-28). Neither family history nor cryptorchidism was present in all patients. Primary histopathology of the tumors detected after the inguinal orchiectomies were teratocarcinoma in nine patients and embryonal carcinoma in three patients. Modified RPLND has been done covering the nodal tissues on the ipsilateral tumor site of inferior mesenteric artery’s lower level, protecting contralateral sympathetic fibres resulting in ejaculation preservation. All of the 12 patients were treated with at least four cycles cisplatin based chemotherapy for B1-B3 NSGCTT (according to the American Urological Classification System). After the removal of these masses the residual tumors were assessed as to viable malignant tumor, mature teratoma or necrosis for further treatment decision.

Results

The histological status of the primary testicular tumor and post-chemotherapy operative specimens for all patients is listed in the table 1. Of the 12 primary tumors, 3 were classified as embryonal carcinoma and 9 as teratocarcinoma. Four patients were treated with four cycle PEB; cisplatin (20 mg/m^2/d i.v. infusion on days 1 to 5), etoposide (100 mg/m^2/d i.v. infusion on days 1 to 5), bleomycin (15 U/m^2 i.v. infusion), others were treated with four cycles PVB; cisplatin (20 mg/m^2/d i.v. infusion on days 1 to 5), vinblastine (6 mg/m^2/d i.v. infusion days 1 and 2), bleomycin (15 U/m^2 i.v. infusion). Histological examination of specimens from the initial post-chemotherapy operation demonstrated malignant tumor (embryonal or teratocarcinoma) in 6, while mature teratoma and complete necrosis were found in 5 and 1, respectively. No major postoperative complications occurred in patients.

Overall 10 of the 12 patients are alive with non-evident disease (mean follow-up after RPLND was 44 months, with a range of 12 to 76 months). All of the six patients with malignant disease after first RPLND have responded to further treatment (salvage chemotherapy in five patient and high dose...
chemotherapy and autologous peripheral blood transplantation in one patient). One patient died thirty-seven months after RPLND due to multiple pulmonary metastases (patient 4, Table 1). The second death occurred twenty-eight months postoperatively because of locoregional progressive disease (patient 9).

Table 1
Primary tumor characteristics and the results of residual retroperitoneal lymph node dissections in 12 patients

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Primary Tumor Histology</th>
<th>Clinical Stage</th>
<th>Primary Chemotherapy Protocols</th>
<th>Histology of Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Teratocarcinoma</td>
<td>B₂</td>
<td>4 cycle PEB</td>
<td>Teratocarcinoma</td>
</tr>
<tr>
<td>2</td>
<td>Embryonal Ca</td>
<td>B₁</td>
<td>4 cycle PEB</td>
<td>Embryonal Ca</td>
</tr>
<tr>
<td>3</td>
<td>Embryonal Ca</td>
<td>B₃</td>
<td>4 cycle PVB</td>
<td>Mature teratoma</td>
</tr>
<tr>
<td>4</td>
<td>Embryonal Ca</td>
<td>B₂</td>
<td>6 cycle PVB</td>
<td>Embryonal Ca</td>
</tr>
<tr>
<td>5</td>
<td>Teratocarcinoma</td>
<td>B₁</td>
<td>4 cycle PVB</td>
<td>Necrosis</td>
</tr>
<tr>
<td>6</td>
<td>Teratocarcinoma</td>
<td>B₃</td>
<td>4 cycle PVB</td>
<td>Teratocarcinoma</td>
</tr>
<tr>
<td>7</td>
<td>Teratocarcinoma</td>
<td>B₂</td>
<td>4 cycle PVB</td>
<td>Mature teratoma</td>
</tr>
<tr>
<td>8</td>
<td>Teratocarcinoma</td>
<td>B₁</td>
<td>4 cycle PVB</td>
<td>Mature teratoma</td>
</tr>
<tr>
<td>9</td>
<td>Teratocarcinoma</td>
<td>B₃</td>
<td>4 cycle PVB</td>
<td>Teratocarcinoma</td>
</tr>
<tr>
<td>10</td>
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<td>B₂</td>
<td>4 cycle PVB</td>
<td>Teratocarcinoma</td>
</tr>
<tr>
<td>11</td>
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<td>B₂</td>
<td>4 cycle PEB</td>
<td>Mature teratoma</td>
</tr>
<tr>
<td>12</td>
<td>Teratocarcinoma</td>
<td>B₂</td>
<td>4 cycle PEB</td>
<td>Mature teratoma</td>
</tr>
</tbody>
</table>

Discussion

During the last two decades the survival for patients with disseminated NSGCTT has improved considerably due to the introduction of multimodal therapy (cisplatin-based combination chemotherapy followed by resection of residual tumor) (6-8). Randomized trials for patients with NSGCTT have demonstrated 56-74% complete response rate with primary chemotherapy, and an additional 10-25% of patients have been rendered disease-free with postchemotherapy resection of residual radiologic abnormalities (1,2). The specimens of retroperitoneal residual mass after chemotherapy show no evidence for malignancy in 10% to 25% (9,10). The finding of viable NSGCTT in postchemotherapy resection specimens has been associated with a high risk of relapse. In 1981 Einhorn et al. (9) reported on 22 patients with cancer in their postresection specimens. Of these 22 patients, only 2 were long-term survivors. However, only four patients received postoperative cisplatin-based chemotherapy, and both long-term survivors were in that group. Other
investigations have noted similar findings (5,7,12,15). As a result, it became standard practice to give two courses of postoperative chemotherapy identical to the induction chemotherapy in such patients. This approach has also been advocated for those patients resected after salvage therapy, in whom the frequency of viable NSGCT is substantially greater (4,9,10). Our series shows that in 50% of the RPLNDs done after primary chemotherapy, the histologic finding is viable NSGCT, which has historically been associated with a poor prognosis.

Histopathological examination of removed residual masses is important for further treatment decision. In 70 to 80% of all cases the histological status of the tumor has shifted towards mature teratoma, or complete necrosis or fibrosis (3-7). If completely necrotic or fibrotic masses are present, probably no benefit is gained from surgical removal. However, if mature teratoma is present complete removal seems to be indicated, since mature teratoma may have the potential for tumor recurrence, as also seen in 5 of our cases (5). Resection of residual malignant tumor may have therapeutic value in some cases, or it assists in defining the optimal subsequent treatment strategy in others. We found residual malignant tumor or mature teratoma in 11 of the 12 patients. This result is higher than in most previous studies (3,5,13,15). The exact percentage of malignant tumor or mature teratoma may depend on the clinical stage of the disease, intensity of chemotherapy and indications for a post-chemotherapy operation (2,5,7,10).

Researches are mainly focused on non-operative techniques, which are capable to distinguish the residual tumor histology. The CT appearance of the masses, that is the size, density and changes noted during the course of treatment, has been ruled insufficient to exclude the presence of residual malignancy or teratoma (16). Although the interpretation with magnetic resonance imaging is more correlated with histopathology, it is not effective when using alone (16).

The histology may be more useful for prediction of the prognosis. Absence of teratomatous elements in the primary tumor histology (undifferentiated malignant teratoma) may represent a favorable prognostic feature, although this finding alone is not an adequate criterion, since approximately 25% of such patients have been reported to have residual malignant tumor or mature teratoma in the resected tissue (15,16). In our series, 1 of 3 patients with absence of teratomatous elements in the testicular tumor had mature teratoma in the residual masses. We believe that the distinction of residual retroperitoneal masses for prediction of prognosis is hard to detect at preoperative period and resection of postchemotherapy residual masses and histological diagnosis of them is a valid approach still used today.

We observed malignant tumor in 6, mature teratoma in 5 and only necrosis in one patient in the resection specimens. Number of our patients and histopathological distribution of them is fairly comparable to other series published in the literature: Mark and Edward (13) has indicated 9 nonseminomatous testicular cancer patients and found embryonal carcinoma in 3 of them, teratoma in 4 of them and necrotic tissue in 2 of them when they applied lymph dissection after the chemotherapy. Qwist et al (12) has seen 12 residual malignant tumors or mature teratomas in 15 cases. Fossa et al (14,15)
has seen malign tumor or mature teratoma in half of the cases. In 6 of 12 patients the histological status of the initial operative specimen differed from that of the second specimen. A similar variable response to chemotherapy at different metastatic sites also has been reported previously (3,12). Possible explanation for this situation is the neoplasms, which are composed of heterogeneous subpopulations, differing with regard to morphological type, biological activity, pattern of spread and therapeutic response. Even though the percentage of patients with necrosis or fibrosis in the residual mass appears to be elevated in certain subgroups with stage B NSGCTT, we believe that the high frequency of residual cancer or mature teratoma demands surgical removal of all post-chemotherapy residual masses, since presently there is no precise method to define the nature of these masses before surgical removal.

Our experience indicating resection of retroperitoneal residual mass after chemotherapy is an uncommon but integral component of NSGCTT management. If surgical resection of residual disease reveals fibrosis or teratoma, no further treatment is required. If surgical resection reveals carcinoma, two more cycles of cisplatin and etoposide therapy are given. In conclusion, we stress that these patients must be closely followed-up after primary chemotherapy, when the residual mass is detected radiologically, dissection of the retroperitoneal lymph nodes must be done and additional platinum-based chemotherapy must be started in the situation of detecting any viable cells in the specimen.

References