

## Malignant lymphomas of the testis

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**Background.** The aim of the study was to analyse 10 patients with malignant lymphomas of the testis, and to discuss the necessity of immunocytochemical staining to confirm the histologic diagnosis and an effective treatment policy.

**Patients and methods.** Ten patients with malignant lymphomas of the testis were reviewed in order to identify and study the incidence, histologic findings, the type of treatment administered and the overall outcome.

**Results.** Testicular malignant lymphomas were identified ten times between 1984 and 1999. Bilateral tumours occurred simultaneously in 4 patients, and a metachronous malignancy and testicular relapses developed in 2 patients. Of the remaining patients 4 had unilateral testicular involvement. None had elevated AFP and  $\beta$ -HCG or a history of undecided testis. Eight of patients were younger than 50 years. Five of the lymphomas were high grade, 3 were intermediate and 2 were low grade diffuse non-Hodgkin's lymphoma. All patients were initially treated with radical orchietomy and were, according to their clinical stage, treated with chemotherapy and/or radiotherapy. Five of 10 patients were alive with no evidence of disease with follow-up ranging from 9 to 62 months. The remaining 5 patients died between 3 and 42 months respectively.

**Conclusions.** Testicular lymphomas are similar to those of testicular germ cell tumours and account for approximately 5% of all testis tumours and represents 1% of all lymphomas. Testicular lymphomas differ from germ cell tumours of the testis by following points: (1) Testicular lymphomas tend to occur in the middle ages, (2) tumour markers AFP and  $\beta$ -HCG are in normal limits, (3) a development in cryptorchid testis is extremely rare, (4) an early systemic therapy is indicated and watchful waiting policy can not be performed, (5) the prognosis is poor. The recognition of histologic diagnosis with immunocytochemical staining for leukocyte common antigen (LCA) is essential and should help the future treatment policy.

**Key words:** testicular neoplasms, lymphoma; germinoma; lymphoma, non-Hodgkin

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### Introduction

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The average incidence of testis tumours is in the range of 2.1 to 2.3 per 100 000 males and remains the most common solid cancer in men between the ages of 20 and 34 years.<sup>1-3</sup>

Testicular lymphomas account for approximately 5% of testis tumours and constitute the most frequent of all testicular tumours in patients over 50 years of age. The median age of occurrence is about 60 years. Primary lymphoma of the testis rarely occurs in children.<sup>4,7</sup> Testicular involvement by lymphoma may be a manifestation of primary extranodal disease, an initial manifestation of clinically nodal disease or a later manifestation of disseminated nodal lymphoma. The most common histologic pattern is a diffuse histiocytic lymphoma and testicular lymphomas are sometimes misdiagnosed as spermatocytic or anaplastic seminomas. The prognosis is poor within one year after the diagnosis if a disseminated disease is evident.<sup>5,6,9</sup>

The aim of this paper was to analyse a group of patients with malignant lymphomas of the testis and to discuss the necessity of performing leukocyte common antigen (LCA) in pathologically reported anaplastic or spermatocytic seminomas in order to confirm the histologic diagnosis.

### **Patients and methods**

From 1984 to 1996, 1201 patients, 17 to 73 years of age were treated for a testicular tumours in Ankara Oncology Education and Research Hospital. We reviewed medical records of these patients to identify and study lymphomas in the testis with respect to their incidence, histologic findings, the type of treatment administered and the overall outcome.

### **Results**

Malignant lymphomas of the testis were identified in 10 patients. The information recorded for each patients included age, date of diagnosis, initial symptoms and physical findings, initial haematologic data, clinical stage,

histology, mode of therapy, response to therapy, survival time in months and the patient's condition to the last date of follow-up. The data are summarised in Table 1.

The common clinical presentation was a painless enlargement of the testis. Of 10 patients 7 had generalized constitutional symptoms including anaemia (3 patients), anorexia (6 patients), weakness and weight loss (2 patients). The investigation included a complete blood count, peripheral smears, chest radiographs, ultrasonography and/or computerised tomography of abdomen, ultrasound of testes, tumour markers AFP and  $\beta$ -HCG. None of patients had elevated AFP and  $\beta$ -HCG. Bilateral tumours were identified in six patients (60%). The tumours occurred simultaneously in 4 patients, and metachronous tumours plus testicular relapses developed in 2 patients after one and 6 months of the diagnosis.

Initially, all patients were treated with radical orchiectomy. Five of the testicular lymphomas were high grade, 3 were intermediate and 2 were low grade diffuse non-Hodgkin's lymphoma.

### **Discussion**

Cancer of the testis accounts for less than 3 % of all malignant tumours in males. Most of these malignancies are of germinal cell origin.<sup>1-3</sup> To date, approximately 100 % of germ cell tumours can be cured.

The involvement of the testis by lymphomas accounts for almost 5 % of testicular tumours and 50% of patients with bilateral tumours have lymphoma.<sup>3,7,8,10</sup> Testicular lymphomas differ from germ cell tumours in regard to age, incidence, relation to cryptorchidism, frequency of bilateral involvement, normal tumour marker levels of AFP and  $\beta$ -HCG, and prognosis. Despite reports that the median age of occurrence is about 60 years, in our series the age ranged from 32 to

73 years with a median of 49. In contrast, 8 of 10 patients were younger than 50 years at diagnosis. Risk factors, like cryptorchidism, have been reported to range between 7 and 35 % of the total number of patients with testicular germ cell cancer.<sup>11-13</sup> In the medical literature, to our knowledge, testicular lymphoma arising in cryptorchid testis was reported only once.<sup>5</sup> None of our patients had a history of cryptorchidism.

In principle, bilateral tumours can occur synchronously or metachronously and bilateral testicular involvement is reported to be a more common feature of malignant lymphomas of the testis than of germ cell tumours.<sup>14-16</sup> The relative incidence of bilateral testis tumours, reported in the literature from 1981 to 1995, can be calculated as 2.38 %.<sup>17-22</sup> Our study doesn't confirm this, bilateral testis tumours comprise 1.17 %, and lymphoma of the testis comprises 60 % of the total incidence of bilateral testicular carcinomas.

Four of 10 patients had radical inguinal orchietomy in different hospitals. Tissue specimens of all patients were reviewed in our pathology department to confirm the pathologic diagnosis, because testicular lymphomas are sometimes pathologically misdi-

agnosed as spermatocytic or anaplastic seminomas. Our study confirms this in 2 of 10 patients (20 %). There were 2 patients initially misdiagnosed as spermatocytic seminoma. In order not only to prevent misdiagnosis but also for further evaluation and treatment, we recommended to perform immunocytochemical staining with LCA if the levels of  $\beta$ -HCG and AFP are normal in the sera, especially in the clinical stages to IIC to IV seminomas.

Until several years ago, the traditional treatment for testicular lymphoma was radiation therapy for the localized and regional spread and chemotherapy for distant metastasis. To date multiagent chemotherapy, the combined modality treatment has become more frequently used as the initial one.<sup>23</sup> Irradiation of contra lateral testicle as a prophylactic treatment for patients with testicular lymphoma is controversial.<sup>6,24,25</sup> Even though, prophylaxis for the normal opposite testis can be performed safely to the elder patients, the need to preserve testicular function may be vital for young cases. Most previous reports have also indicated a poor prognosis for patients with testicular lymphoma, especially in patients with bilateral disease and there were no 5-year survivors. In centres cumulating a sufficient number of cases, even

**Table 1.** Patients' data presenting with testicular lymphomas

Patients	Age (months)	Laterality	Clinical stage	Treatment	Disease free interval (months)	Status
1	32	Right	III	Chemo	24	Alive with NED
2	38	Right	I	XRT	11	DD
3	38	Left	IV	Chemo	42	DD
4	43	Bilateral, M	I	Chemo+XRT	52	Alive with NED
5	36	Bilateral, M	IV	Chemo	10	DD
6	48	Bilateral, S	I	XRT	62	Alive with NED
7	48	Bilateral, S	I	XRT	18	Alive with NED
8	58	Left	IV	Chemo	9	Alive with NED
9	70	Bilateral, S	IV	Chemo	6	DD
10	73	Bilateral, S	IV	Chemo	3	DD

S = simultaneously; M = metachronous; Chemo = chemotherapy; XRT = radiotherapy; NED = no evidence of disease; DD = died of disease

in patients with low-stage tumours, a 5-year survival rate has been documented as 30 %.<sup>6,12,13,26-29</sup> Thus, even patients whose disease seems to be limited to the testis may have a relatively short survival time. In patients with lymphoma at other sites and who later experience testicular relapses a poor prognostic factor exists.<sup>5,6,9</sup> The reported incidence of relapse in the contra lateral testicle is 0 to 35 % for patients with testicular lymphoma.<sup>13,24,26,27,30</sup> Testicular relapse was occurred in our 2 cases (20 %). Disease free mean survival times in reported series ranges between 16 months to 30 months.<sup>4,6</sup> Five of our cases were alive with no evidence of disease with follow-up ranging from 9 to 62 months. The remaining 5 patients died of disseminated disease, with survival ranging 3 - 42 months. Even though we treated our patients with combine modality, we did not obtain good results.

### Conclusions

Testicular tumours of germ cell origin reach their peak incidence in the age group 20 and 34 years. Malignant lymphomas of the testis account for almost 5% of all testis tumours. The common clinical presentation, initial treatment and the pattern of dissemination of testicular lymphomas are similar to those of testicular germ cell tumours. In contrast, by the following points testicular lymphomas differs from germ cell tumours: (1) Lymphoma of the testis tends to occur in the middle ages; (2) The levels of AFP and  $\beta$ -HCG are in normal limits; (3) Development of testicular lymphoma in cryptorchid testis is extremely rare; (4) In view of aggressive behaviour, an early systemic chemotherapy is indicated and a watchful waiting policy is contraindicated; (5) Patients with disease apparently confined to the testis and who have no clinical evidence of generalised disease 1 year after therapy may or may not have a high

probability of cure; (6) Survival is poor especially with bilateral disease, and later experiencing a testicular relapse.

Since testicular lymphomas are sometimes misdiagnosed as spermatocytic and anaplastic seminomas, immunocytochemical staining for LCA should be performed in order to confirm the histologic diagnosis. The recognition of histologic diagnosis in testicular lymphoma is essential and should help the future treatment policy.

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