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Primary testicular lymphoma—A single center experience and review of literature

Wei-Jen Chen [a], Junne-Yih Kuo [a, b, c, *], Chih-Chieh Lin [a, b, c], Hsiao-Jen Chung [a, b, c], William J.S. Huang [a, b, c], Howard H.H. Wu [a, b, c], Yen-Hwa Chang [a, b, c], Alex T.L. Lin [a, b, c], Kuang-Kuo Chen [a, b, c]

[a] Department of Urology, Taipei Veterans General Hospital, Taipei, Taiwan
[b] Department of Urology, School of Medicine, National Yang-Ming University, Taipei, Taiwan
[c] Shu-Tien Urological Science Research Center, National Yang-Ming University, Taipei, Taiwan

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ABSTRACT

Objective: The purpose of this study is to evaluate the clinical characteristics, pathology, treatment outcomes, and survival of primary testicular lymphoma (PTL) patients treated at our hospital after 1990. Related literature was reviewed.

Materials and methods: We retrospectively enrolled patients diagnosed with PTL between January 1990 and September 2013 in our institute. Clinical features, pathology, and overall survival were analyzed.

Results: 24 patients were enrolled. They had a mean age at diagnosis of 65.0 years (range 10–84 y), mean follow-up duration 57.0 months (range 3–182 mo), and median overall survival of 38 months (range 4.0–184.7 mo). The most common pathology subtype was diffuse large B-cell lymphoma ($n = 21$, 87.5%). Fourteen patients (58.3%) achieved complete remission of disease and five patients (20.8%) achieved partial remission after treatment. Three patients had a relapse of disease after complete remission: one in the brain parenchyma, one in the pelvis soft tissue and omentum, and one in the left pyriform muscle. Three patients had metastasis after partial remission of disease: two in the brain parenchyma and one in the cauda equina. By univariate analysis, the factors significantly associated with superior overall survival were primary tumor diameter < 7.5 cm, serum lactate dehydrogenase ≤ 250 U/L, Ann-Arbor Stage IE/II, and International Prognostic Index (IPI) ≤ 1 ($p < 0.05$). Rituximab-containing treatment did not show overall survival benefits in our series. By multivariate analysis, IPI ≤ 1 showed statistical significance ($p = 0.019$), suggesting a potential prognostic value of IPI in evaluating PTL patients.

Conclusions: The overall survival of PTL patients is poor, especially those with extensive disease (Stage III/IV). The IPI have a prognostic role in PTL. The use of rituximab in the treatment regimen of PTL does not seem to improve survival in our series.

1. Introduction

Primary testicular lymphoma (PTL) is a rare but aggressive malignant tumor. It constitutes only 1–2% of non-Hodgkin lymphoma, and population-based studies have estimated the incidence at 0.09–0.26/100,000 per year.[1] However, lymphoma remains the most common testicular neoplasm in men > 60 years of age. The usual presentation is a painless testis mass which grows slowly over weeks or months, with either unilateral or bilateral involvement. Typically, PTL is diagnosed after radical orchiectomy, and the most frequent histological subtype is diffuse large B-cell lymphoma (DLBCL), although other histological subtypes have been described.[2]

Currently, there are no gold standard treatment guidelines for PTL. The available data to date are from nonrandomized studies or retrospective series. Generally, the common treatment strategies include radical orchiectomy, followed by chemotherapy and/or radiotherapy. Rituximab, a chimeric monoclonal antibody against

* Corresponding author. Department of Urology, Taipei Veterans General Hospital, Number 201, Section 2, Shipai Road, Taipei City 11217, Taiwan.
E-mail address: jykuotpe@gmail.com (J.-Y. Kuo).

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the protein CD20, has proven therapeutic effects in nodal DLBCL. However, its impact on outcomes in PTL remains unclear, and may be less definitive than in nodal DLBCL.[1]

In this retrospective study, we evaluated the clinical characteristics, pathology, and treatment outcomes of 24 PTL patients treated at our hospital after 1990. Related literature was also reviewed for a better understanding of this rare malignancy.

2. Materials and methods

We retrospectively enrolled patients diagnosed with PTL between January 1990 and September 2013 in our institute (Taipei Veterans General Hospital, Taiwan). The diagnosis of PTL was made if the testes were the primary site of the disease or at least the main site of involvement, without or with only minor nodal involvement.[3] Patients with a lymphoma history and those lost to follow-up were excluded. All patients underwent computed tomography (CT) scan from the neck to pelvis, whole-body bone scan, and bone marrow biopsy for staging. Potential prognostic factors, including age, primary tumor diameter, serum lactate dehydrogenase (LDH), Ann-Arbor stage, International Prognostic Index (IPI) score, and the use of rituximab-containing regimen, were evaluated. IPI is a clinical tool developed by oncologists to aid in predicting the prognosis of patients with aggressive non-Hodgkin lymphoma. One point is assigned for each of the following risk factors: age > 60 years, Stage III/IV disease, elevated serum LDH, Eastern Cooperative Oncology Group (ECOG) performance status > 1, and more than one extranodal site. Based on IPI scores, patients could be classified into low-risk group (IPI $\leq$ 1) or intermediate–high-risk group (IPI $\geq$ 2). The Ann-Arbor staging is the staging system for lymphomas. Stage I indicated lymphoma involving only a single lymph node (Stage I) or a single extralymphatic organ (Stage IE); Stage II indicated lymphoma involving two separate regions, with both the affected areas being confined to one side of the diaphragm; Stage III indicated that lymphoma has spread to both sides of the diaphragm; and Stage IV indicated diffuse or disseminated involvement of one or more extralymphatic organs, including any involvement of the liver, bone marrow, or lung. Patients received further treatment including chemotherapy with or without rituximab, intrathecal chemotherapy, and radiotherapy to the contralateral testis. The standard chemotherapy regimen is CHOP before the rituximab era and R-CHOP after the rituximab era. The standard R-CHOP regimen is as follows: rituximab 700 mg, cyclophosphamide 750 mg/m^2, doxorubicin 50 mg/m^2, oncovin 1.4 mg/m^2, and prednisolone 40mg by mouth twice daily from Days 2 to 5; the regimen was given every 3 weeks. Doxorubicin may be replaced by etoposide 50 mg/m^2 if the patient's cardiac function is poor. The standard intrathecal chemotherapy includes methotrexate 15 mg, cytarabine 50 mg, and dexamethasone 5 mg. The standard dosage of contralateral testis radiotherapy is 30 Gy. The overall survival (OS) was calculated from the date of diagnosis to the time of mortality, or the time of last follow-up for survivors. The Kaplan–Meier survival curve was plotted for patients of each group, and the differences between the curves were examined using the log-rank test. Statistical analyses were performed using SPSS version 19.0 (SPSS, Chicago, IL, USA).

3. Results

From January 1990 to September 2013, 24 patients with PTL were diagnosed and treated in our institute. Their mean age at diagnosis was 65.0 years (range 10–84 y), mean follow-up duration was 57.0 months (range 3–182 mo), and median OS was 38 months (range 4.0–184.7 mo). Radical orchiectomy was performed in 23 patients, and only one patient received open testis biopsy for diagnosis. The most common pathology subtype is DLBCL (n = 21, 87.5%). Patient's clinical characteristics are summarized in Table 1.

3.1. Treatment response

The treatment modalities and outcomes are summarized in Table 2. Of the 24 patients, two (Cases 13 and 22) did not receive further treatment due to poor performance status and rapid disease progression resulting in mortality. The remaining 22 patients received further systemic chemotherapy, with or without intrathecal central nervous system (CNS) prophylaxis or contralateral testis prophylactic irradiation. Fourteen patients (58.3%) had complete remission of disease, but three patients had disease relapse, including one with brain metastasis after 7 years, one with left pyriform muscle metastasis at 11 months, and one with metastasis to the pelvis soft tissue and omentum at 16 months. Five patients (20.8%) had partial remission of disease, with three patients had disease progression, including two with brain metastasis at 9 months and 13 months, respectively, and one with cauda equina metastasis at 6 months.

3.2. Prognostic factors

Patients were grouped according to age, primary tumor diameter, serum LDH level, Ann-Arbor stage, IPI scores, and rituximab-containing regimen. Based on the Ann-Arbor staging system, patients were separated into those with limited disease (Stage IE/II) or extensive disease (Stage III/IV). According to IPI scores, patients could be classified into low-risk group (IPI $\leq$ 1) or intermediate–high-risk group (IPI $\geq$ 2). The statistical results are summarized in Table 3 and Figure 1. By univariate analysis, the factors significantly associated with a superior OS were primary tumor diameter < 7.5 cm, serum LDH $\leq$ 250 U/L, and limited and low-risk disease ($p < 0.05$). Treatment with rituximab-containing regimen did not show OS benefit in our series. By multivariate analysis, only those with low-risk disease (IPI $\leq$ 1) showed significance ($p = 0.019$), suggesting that IPI score had prognostic value in evaluating patients with PTL.

Table 1
Patient characteristics.

Characteristics	Patient number (%)
Age (y)	
> 60	16 (66.7)
≤ 60	8 (33.3)
Location	
Left	11 (45.8)
Right	11 (45.8)
Bilateral	2 (8.3)
Histology	
DLBCL	21 (87.5)
T-cell lymphoma	1 (4.2)
Burkitt's lymphoma	2 (8.3)
Ann-Arbor stage	
IE	10 (41.7)
II	7 (29.1)
III	1 (4.2)
IV	6 (25.0)
IPI	
Low (0–1)	10 (41.7)
Low–intermediate (2)	5 (8.3)
High–intermediate (3)	6 (25.0)
High (4–5)	3 (12.5)

DLBCL = diffuse large B-cell lymphoma; IPI = International Prognostic Index.