Primary malignant lymphoma of the testis

AMELIA PETRESCU1), CAMELIA DOBREA2), MARIANA VASILICA3), FL. ANDREI2), L. NICULESCU4)

1)Pathology Department, “Prof. dr. Th. Burghele” Hospital, Bucharest
2)“Victor Babes” Institute of Pathology, Bucharest
3)Department of Hematology, “Fundeni” Clinical Institute, Bucharest
4)Pathology Department, “Carol Davila” University of Medicine and Pharmacy, Bucharest

Abstract
Primary testicular lymphomas are rare entities representing 1–2% of non–Hodgkin lymphoma (NHML) and 1–7% of malignant testicular tumors and they are the most common testicular tumors in men older than 50 years of age. This study included 8 cases of inpatients diagnosed by echography and NMR with testicular tumors. The age of patients was between 46 and 81 (with a mean of 52). The tumors were unilateral, with disease limited to testicle and accompanied by pain except 1 case with bone involvement. Orchiectomy was performed as first therapeutic and diagnostic purpose. All patients were clinically staged according to the Ann Arbor criteria in IE and IIID stage and received a doxorubicin based chemotherapy regimen (CHOP, MTX, CVP, and Leukeran). A standard chemotherapy protocol has not been used because of reduced number of patients. Tumor fragments were fixed in 10% formalin, paraffin embedded, sectioned and standard H.E. stained. Immunohistochemistry for L26, Alphafetoprotein, NK1, CD30, and CLA was performed. Microscopy revealed in all cases a stromal proliferation with medium size cells, monomorphic shape and prominent nucleoli. Alphafetoprotein was positive in seminal tubes and negative in tumor, NK1 in small lymphocyte and negative in tumor and L26 diffuse positive in tumor. CLA diffuse positive in tumor. We were able to follow up only four patients. Conclusions: The diagnosis was of NHML in 6 cases and for 2 secondary involvement of hematopoietic malignancy (myeloid sarcoma and leukemia). Lymphoma cases were typed using REAL classification as small and large B-cell lymphoma. Unfavorable evolution with 6 months relapse and one death prove a more aggressive evolution of primitive testicular lymphoma.

Keywords: primary lymphoma, testis, chemotherapy, immunohistochemistry.

Introduction
Primary malignant testicular lymphoma is a rare disease that accounts for only 1% to 7% of all testicular malignancies and represents 1% to 2% of all non–Hodgkin’s lymphomas.

Approximately 85% of patients are older than 60 years age [1, 2].

According to literature data, histopathologically 80 / 90% of primary lymphoma of the testis are of diffuse large-cell type with B-cell immunophenotype [3, 4] and show a tendency to disseminate systematically including the contralateral testis, central nervous system, skin, Wladeyer’s ring, lung, pleura and soft tissue [5–7].

Concerning the treatment, retrospective analyses published until now, have shown that, after locoregional treatment only (orchiectomy and radiation therapy) relapse is high, ranging approximately from 50% to 80% with a third of the patients relapsing in the central nervous system or in the contralateral testis [7, 8].

Recent publications have attempted to define the utility of early treatment with conventional-dose chemotherapy for these patients, but results are controversial [6, 9].

In fact, the rarity of testicular diffuse large-cell lymphoma has prevented the care fully designed prospective trials that would evaluate clinical outcome of specifically targeted treatment programs.

Therefore, clinical approach to the treatment of these cases has generally followed the evaluation of knowledge in the treatment of similar extra testicular lymphoma with variable recommendation for introduction of prophylactic intrathecal chemotherapy or contralateral testicular irradiation.

According to the literature data, 38% of testicular lymphoma cases are bilateral and usually metachrones.

We present the prospective analysis of a series including 8 cases hospitalized and diagnosed at “Prof. dr. Th. Burghele” Hospital between the years 2001-2004, by echography and NMR with testicular tumors. The age of patients was between 46 and 81 with a mean of 52.

The tumors were unilateral with disease limited to testicle and accompanied by pain except 1 case with bone involvement.

All patients were clinically staged according to the Ann Arbor criteria in I-E and III-D stage.

We intend to contribute with our experience in diagnose and treatment to define prognosis and outcome of patients presenting with primary testicular lymphoma.

The treatment was performed at “Fundeni” Haematologic Center with a doxorubicin based chemotherapy regimen (CHOP, MTX, CVP and Leukeran).

Material and methods
The macroscopic examination carried out the removed testicle shows partial or complete replacement of the testicular parenchyma by a fleshy to firm, often lobulated, cream-colored, tan, pale yellow, homogenous in diameter 5-10 cm.

In some cases we have found tumoral focal areas of necrosis (Figure 1).
Usual light microscopy: fragments of the tumor were fixed in formaldehyde 10% included in paraffin and the sections were stained with HE and VG than examined by light microscopy (Nikon Eclipse E600).

Representative photomicrographs were taking using Nikon Plan 20× and 40×.

Immunohistochemistry: was performed on 3 μm thick sections from 10% formalin fixed paraffin – embedded specimens, according to the Avidin-Biotin Complex method of the tissue [10], modified by Bussolatti and Gugliotta [11] and Miller K [12].

Briefly, the procedure was: deparaffinization in xylene and alcohol series, rehydration, washing in phosphate saline buffer (PBS), incubation with normal serum for 20 minutes, incubation with primary antibody overnight, standard labeled streptavidin-antibody biotin (LSAB) kit (DAKO), washing in carbonate buffer and development in 3,3’-DAB hydrochloride/H2O2.

Selected tumoral fragments were tested by the following antibodies: L26, polyclonal, 1:100 (Neomarkers), Alphafetoproteine 1:100 (Neomarkers), NK1 clone NK1, 1:50 (Dako) CD30, clone 3erH2, 1:40 (Dako) CLA, clone 136-4B5, 1:50 (Neomarkers) [13].

All specimens were counterstained with Mayer’s hematoxylin, examined and photographed on a Nikon Eclipse 600 microscope.

Results and discussions

Histologically, at low power, the stromal lymphomatous infiltrate in 6 cases was diffuse. The cytologic composition was variable with predominance of small cells, medium-sized cells and large cells or a mixture of these cell types.

The tumor cell nuclei frequently showed irregular folding and granular chromatin. The larger cells possessed distinct nucleoli. The cytoplasm was unlike most lymphoma cells, have distinct cell membranes, abundant glycogen-rich cytoplasm and rounded central nuclei with prominent nucleoli.

The cells of spermatocytic seminomas are polymorphous and of three distinct types.

Other differential diagnosis included viral and granulomatous orchitis, but the heterogeneous and benign-appearing inflammatory cellular infiltrates of these lesions contrast with the more homogeneous and malignant appearing infiltrate of lymphoma.

Viral orchitis has a patchy rather than diffuse distribution.

Distinction of lymphoma from embryonal carcinoma is rarely a problem except the anaplastic large cell lymphoma [14].

Our experience confirm other data communicated by Tournoutoglou et al., 1995 [9], Crellin et al., 1993 [6], Sasai K et al., 1997 [15], Buzzoni et al., 1993 [16].

The 5-year survival rate for patients with malignant testicular lymphoma was 35 percent, with a medium of 13 month [14].

Three favorable prognosis features were stage I disease, unilateral tumors and sclerosis.

The 5 year survival rate for stage I patients was 60 percent compared to 17 percent for other stages, 40 percent for patients with unilateral disease compared to 0 percent for those with bilateral disease and 72 percent for patients with tumors with sclerosis compared to 16 percent for those whose tumors lacked sclerosis.
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Figure 1 – Tumoral focal areas of necrosis

Figure 2 – Neoplastic cells infiltrate seminiphereous tubes. Small areas of necrosis were found

Figure 3 – Alphafetoproteine was positive in seminal tubes and negative in tumor

Figure 4 – NK1 positive reaction in small lymphocyte and negative in tumor

Figure 5 – CLA diffuse positive reaction in tumor

Figure 6 – L26 diffuse positive reaction in tumor
Conclusions

Our study confirms the literature data concerning the poor prognosis of primary malignant lymphoma of the testis and the prevalent diffuse large B cell phenotype. We consider that, beside orchiectomy and radiotherapy, systemic aggressive chemotherapy is useful to the patients with primary testicular lymphoma because of unfavorable outcome of disease and to decrease the possible occult systemic dissemination or cerebral and counterpart testis metastasis.

Testicular lymphomas represent an entity that should be considered for differential diagnosis with other testicular malignancy.

References


Mailing address
Amelia Petrescu, M. D., Ph. D., “Prof. dr. Th. Burghelae” Hospital, Pathology Department, 20 Panduuri Road, 050653 Bucharest, Romania; Phone: +4021-410 69 10, E-mail: etamy58@yahoo.com

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