Orbital Lymphomas: A Clinicopathologic Study of a Rare Disease

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ABSTRACT: *Objective:* To evaluate the clinicopathologic features and prognosis of patients with orbital lymphomas. *Methods:* Clinical and pathologic data of 35 patients with biopsy-proven orbital lymphoma diagnosed at a tertiary care hospital from 1992 to 2001 were reviewed. Lymphomas were divided into low-grade and high-grade lymphomas. Survival of patients was compared according to age, gender, disease site, extent of disease, tumor grade, and treatment modality by using log rank test. *Results:* Median patient age was 75 years (23-94) and the male-to-female ratio was 1:2.9. Twenty-three patients (66%) were diagnosed with low-grade lymphoma, and 12 patients (34%) were found to have high-grade lymphoma. Among low-grade lymphomas, marginal zone lymphoma (n = 6), follicle center cell lymphoma (n = 6), and small lymphocytic lymphoma (n = 5) were common entities, whereas diffuse large cell B-cell lymphoma (n = 5) was the most common entity in patients with high-grade lymphoma. Disease was clinically localized in 74% of patients at the time of diagnosis. Radiation alone or with chemotherapy was the primary treatment modality in 83% of patients. All except one patient had an objective response to therapy. Over the median follow-up period of 47 months (range, 1.5-141 months), disease recurred in 37% patients who achieved a complete response. The estimated 5- and 10-year survival rates were 64% and 42%, respectively. Overall, 13 (37%) patients died, 6 with high-grade and 7 with low-grade lymphoma. No clinical variable was found to be prognostically significant with respect to survival. *Conclusions:* Orbital lymphoma is a disease of the elderly with a female preponderance. It tends to be localized to the orbit at the time of diagnosis and responds well to local or systemic therapy. **KEY INDEXING TERMS:** Eye; Orbit; Lymphoma; Orbital lymphoma; Non-Hodgkin lymphoma; Marginal zone lymphoma; Diffuse large cell B cell lymphoma. **[Am J Med Sci 2006;331(2):79–83.]**

Orbital lymphoma is the most common malignant tumor of the eyes. It can occur either as the primary site of disease or rarely as a secondary site of systemic non-Hodgkin lymphoma (NHL) dissemination.[1–3] Although primary lymphoma of ocular adnexa involving orbit, conjunctiva, and eyelids accounted for 5% to 15% of all extranodal NHLs, overall it represents only 1% of all NHLs.[1–3]

Orbital lymphoma typically is a disease of the elderly.[1–3] It is localized to the orbit in a majority of patients at the time of presentation and may be difficult to differentiate from benign reactive lymphoid lesions.[3] With the recent advent of immunophenotype and molecular genetic methods, many new clinicopathologic entities have been identified among NHLs. Many cases of benign lymphoid reactive lesions of the eye that were previously described using the term *pseudolymphoma* in fact are found to have a clonal population of malignant cells.[4] Among different ocular adnexal lymphomas, extranodal marginal zone lymphoma (MZL) is the most common entity.[4–10]

We present here our experience with patients with orbital lymphoma. The aim of our study is to evaluate the clinicopathologic features of orbital lymphoma diagnosed over the past decade at our institution and to identify the prognostic variable that affects the survival of these patients.

Methods

The study protocol was approved by the hospital's Institutional Review Board. Medical records of 35 patients with biopsy-proven orbital lymphomas diagnosed at Long Island Jewish Medical Center, New York from 1992 to 2002 were reviewed. Cases of

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Table 1. Characteristics of Patients with Orbital Lymphoma

Age, y (range)	75 (23–94)
M:F ratio	9:26
Localization, n (%)	
Orbit	22 (63)
Orbit with lacrimal gland involvement	5/22 (23)
Conjunctiva	14 (40)
Eyelid	1 (3)
Symptoms and signs, n (%)	
Visible tumor mass and/or eyelid swelling	12 (34)
Blurred vision and/or diplopia	11 (32)
Tearing and/or redness	11 (32)
Proptosis	6 (17)
Headache	1 (3)
Constitutional symptoms,[a] n (%)	1 (3)
Abnormal LDH, n/n (%)	4/25[b] (16)

[a] *Fever, night sweats, and >10% weights loss.*
[b] *LDH level at diagnosis was available in 25 patients.*

atypical lymphoid hyperplasia that did not have a confirmed monoclonal cell population were excluded. Of 35 cases of orbital lymphoma, pathologic slides from 26 cases were available and were reviewed by a pathologist (AF) and, based on morphology and immunophenotype, classified according to the World Health Organization classification.[11] Clinical staging was performed according to the Ann Arbor classification.[12] Complete staging work-up included computed tomographic scan of chest, abdomen and pelvis, gallium and/or positron emission tomographic scan, and bone marrow examination. Complete clinical response was defined as complete disappearance of the disease for a period of at least 1 month, whereas partial clinical response was defined as 50% or greater reduction in the measurable disease. For study purposes, all lymphomas were divided into two groups, "low-grade lymphoma" and "high-grade lymphoma". Low-grade lymphomas included extranodal MZL, follicle center cell lymphoma (FCL) (grade 1 and 2), small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL), and lymphoplasmacytoid lymphoma. High-grade lymphoma included diffuse large cell B cell lymphoma (DLCL), mantle cell lymphoma, and FCL (grade 3). Survival was estimated from time of the diagnosis of lymphoma to death from any cause. Survival analysis was carried out using the Kaplan-Meier method. Comparison of survival curves according to age (≥65 versus <65), gender, disease site (orbit versus conjunctiva), extent of disease (localized versus systemic), tumor grade (low-grade versus high-grade), and treatment modality (radiation therapy versus other therapies) was done using the log-rank test.

Results

Clinical Features, Histopathology, and Staging of Orbital Lymphoma

The median age of patients with orbital lymphoma was 75 years (range, 23-94 y) and the male-to-female ratio was 9:26. Patients' characteristics are described in Table 1. Three patients had a remote history of NHLs and were in remission at the time of diagnosis. Nineteen (54%) patients had left eye involvement, 15 (43%) had right eye involvement, and 1 (3%) patient had bilateral disease. Vision abnormalities (31%), salmon-colored subconjunctival infiltrate (26%), visible mass (23%), proptosis (17%), eyelid swelling (17%), and tearing (11%) were common presenting signs and symptoms (Table 1). Some patients had more than one symptom. Median duration of symptoms prior to definitive diagnosis was 2.5 months (range, 0.5-13 mo). All lymphomas were of non-Hodgkin histologic type and of B cell origin. Twenty-three (66%) patients were diagnosed with low-grade lymphoma, and 12 (34%) patients were found to have high- grade lymphoma. Histopathology of the tumor is described in Table 2. Complete staging work was preformed in 21 (60%) patients, 14 patients with low-grade lymphoma and 7 patients with high-grade lymphoma. Of 21 patients, 14 (67%) had localized disease. Nine of 14 patients (64%) with low-grade lymphoma and five of seven (71%) with high-grade lymphoma had stage IE disease on complete staging work-up. Of the remaining 14 patients who had a limited staging work-up, 12 patients did not have evidence of systemic disease. Overall, 26 (74%) of 35 patients had localized disease at the time of diagnosis. One patient with SLL/CLL had peripheral blood involvement at the time of diagnosis. Lumber puncture was performed in seven patients (20%), two with low-grade and five with high-grade lymphomas. None had central nervous system (CNS) involvement at the time of diagnosis.

Table 2. Histopathology and Stage of the Disease in Patients with Orbital Lymphoma

Histopathology	All Patients, n	Stage 1, n	Stage 2, n	Stage 3, n	Stage 4, n	Staging not done, n
All lymphomas	35	14	0	3	4	14
Low-grade lymphomas	23	9	0	3	2	9
MZL	6	3	0	1	0	2
FCL (grade 1, 2)	6	3	0	0	0	3
SLL/CLL	5	2	0	1	2	0
Lymphoplasmacytoid	1	0	0	1	0	0
Unspecified low-grade lymphoma	5	1	0	0	0	4
High-grade lymphomas	12	5	0	0	2	5
DLCL	5	3	0	0	1	1
FCL (grade 3)	2	2	0	0	0	0
MCL	1	0	0	0	1	
Unspecified high- or intermediate- grade lymphoma	4	0	0	0	0	4

MCL, mantle cell lymphoma.