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Orbital and Ocular Adnexal Lymphomas: A Retrospective Single Center Study

Orbital ve Oküler Adneksiyal Lenfomalar: Retrospektif Tek Merkezli Çalışma

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ABSTRACT

Aim: To evaluate and present the clinical and histopathologic features of patients with orbital and adnexal lymphoma.
Methods: Eight patients who had histologically proven orbital and adnexal lymphoma between 2011 and 2021 were evaluated retrospectively. The clinical appearance, age, sex, imaging, tumor location, treatment methods, pathologic diagnosis, and systemic features of the patients were obtained from patient files.
Results: The mean age of the patients was 59.1 (range, 42-79) years. Six of the patients were male and two were female. Painless mass and orbital swelling were the most common first signs and symptoms in the patients. The magnetic resonance imaging findings demonstrated unilateral involvement in six patients and bilateral involvement in two patients. Intraorbital location in three patients (behind the orbital septum), lid location in two patients (eyelids in front of the orbital septum), conjunctival involvement in one patient, and lacrimal gland involvement in two patients were detected. All cases were reported as non-Hodgkin B-cell lymphoma [primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue (n=5), diffuse large B-cell lymphoma (n=2), follicular lymphoma (n=1)].
Conclusion: Orbital lymphomas can be seen more frequently among orbital tumors and clinical findings vary according to the location in the orbit. Ophthalmologists should be attentive to orbital swellings and consider orbital and ocular adnexal lymphomas among differential diagnoses.

Keywords: lymphoma; orbital diseases; non-Hodgkin lymphoma

ÖZ

Amaç: Orbital ve adneksiyal lenfomalı hastaların klinik ve histopatolojik özelliklerini değerlendirmek ve sunmak.
Yöntemler: 2011-2021 yılları arasında histolojik olarak orbital ve adneksiyal lenfoma saptanan sekiz hasta retrospektif olarak değerlendirildi. Hastaların klinik görünümü, yaşı, cinsiyeti, görüntülemesi, tümör lokalizasyonu, tedavi yöntemleri, patolojik tanıları ve sistemik özellikleri dosyalardan elde edildi
Bulgular: Hastaların yaş ortalaması 59.1 (dağılım 42-79) idi. Hastaların 6'sı erkek, 2'si kadındı. Hastalarda ağrısız kitle ve orbital şişlik en sık görülen ilk belirti ve bulguydu. Manyetik rezonans görüntüleme bulgularında 6 hastada unilateral, 2 hastada bilateral tutulum gösterdi. 3 hastada intraorbital yerleşim (orbital septum arkası), 2 hastada göz kapağı yerleşimi (göz kapakları orbital septum önünde), 1 hastada konjonktival, 2 hastada gözyaşı bezi tutulumu tespit edildi. Tüm vakalar patolojik incelemede Non-Hodgkin B hücreli lenfoma [Mukoza ile ilişkili lenfoid dokunun primer ekstranodal marjinal lenfoması (5 hasta), diffüz büyük B hücreli lenfoma (2 hasta), foliküler lenfoma (1 hasta)] olarak rapor edildi.
Sonuç: Orbita tümörleri nadir olmakla birlikte bunlar arasında orbital lenfoma daha sık görülebilmekte ve orbitadaki lokalizasyona göre klinik bulgular değişmektedir. Göz hekimleri orbital şişliklere karşı dikkatli olmalı ve ayırıcı tanılar arasında orbital ve oküler adneksiyal lenfomaları düşünmelidir.

Anahtar kelimeler: Lenfoma, orbita hastalıkları, Non-Hodgkin lenfoma.

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Introduction

Orbital and ocular adnexal lymphomas are malignant lymphoid neoplasms that develop as primary or secondary tumors in the orbit, conjunctiva, lacrimal gland, lacrimal sac, and eyelid [1,2]. It is the most common adult orbital malignancy, accounting for approximately 10% of all orbital tumors and 2% of all nodal and extranodal lymphomas [3,4]. Although most orbital lymphomas are B-cell non-Hodgkin lymphomas; T-cell lymphomas, Burkitt lymphoma, and Hodgkin lymphoma have also been reported in the literature [5-8]. Differential diagnoses include inflammatory lesions, vascular tumors, lacrimal gland tumors, neurogenic tumors, myogenic tumors, and metastatic tumors [3-9].

Due to the increasing incidence of lymphomas of the orbit and adnexia and their progression, if not treated appropriately, it is important to investigate the frequency of distribution according to age, diagnosis, and treatment methods. Our study aimed to evaluate and report the clinical and histopathologic findings of patients with orbital and adnexal lymphoma.

Materials and Methods

This retrospective study received approval from the Ethics Committee of Cukurova University and was adherent to the tenets of the Declaration of Helsinki. All cases diagnosed as orbital or adnexal lymphoma in Cukurova University Faculty of Medicine between January 2011 and May 2021 were analyzed retrospectively. The demographic characteristics and clinical and histopathologic findings of eight patients with orbital or ocular adnexal lymphoma were evaluated. Incisional biopsy was performed in all patients after routine eye examinations. Tissue samples were fixed in 4% formalin solution and sent for histopathologic examination. Patients diagnosed as having lymphoma as a result of the biopsy were included in the study.

Magnetic resonance imaging (MRI) and positron emission tomography (PET) scans were evaluated for systemic involvement to determine the location of the tumor. Systemic investigation of the patients was performed by the Internal Medicine-Oncology clinic. In the follow-up of the patients, the clinical appearance, age, sex, imaging, tumor location, treatment methods, pathologic diagnosis, and systemic features were examined, retrospectively.

Results:

The mean age of the patients was 59.1 (range, 42-79) years. Six patients were male and two were female. Painless mass and swelling in the eye were the most common first signs and symptoms in the patients (Figures 1 and 2). In the ophthalmologic examination findings of the patients, proptosis, eyelid lesions, chemosis, salmon patch appearance in the conjunctiva, decreased visual acuity, epiphora, limited eye movements, ptosis, pain, strabismus, and optic nerve compression were observed. The MRI findings demonstrated unilateral involvement in six patients and bilateral involvement in two patients (Figure 3).

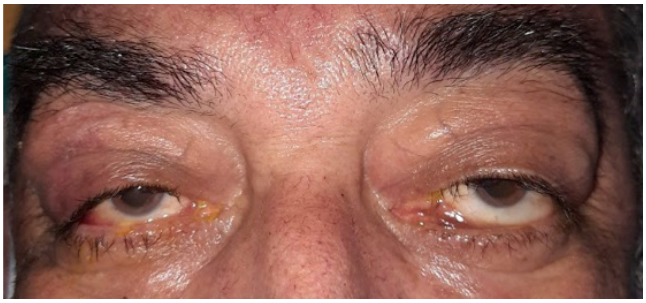

Figure 1. The patient had complaints of mass and swelling in both eyes.

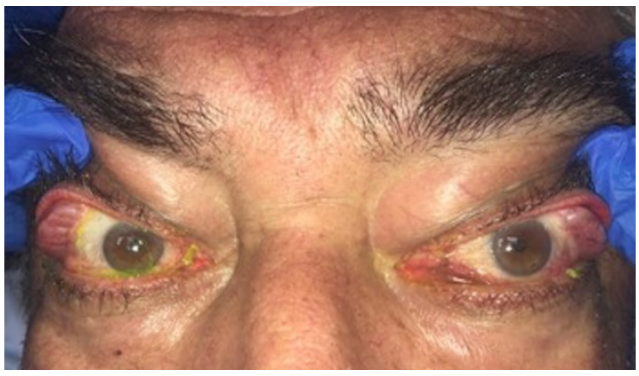

Figure 2. Bilateral lacrimal gland involvement was observed.

The diagnosis was made through incisional biopsies in all patients and evaluating their histopathologic features (Figure 4). All cases were reported as non-Hodgkin B-cell lymphoma; primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue was observed in five patients, diffuse large B-cell lymphoma in two patients, and follicular lymphoma in one patient. Intraorbital location in three of the eight

patients (behind the orbital septum), lid location in two patients (eyelids in front of the orbital septum), conjunctival involvement in one patient, and lacrimal gland involvement in two patients were detected (Table 1). Orbital disease was primarily observed in eight patients. One patient with conjunctival involvement had a salmon patch appearance (Figures 5 and 6). The mean follow-up period of the patients was 15.8 (range, 6-48) months. Complete regression was observed in all patients with chemotherapy and/or radiotherapy, and no recurrence was observed in the follow-up. The treatment protocol was arranged by the Oncology Department according to the subtype and location of the disease (Table 1).

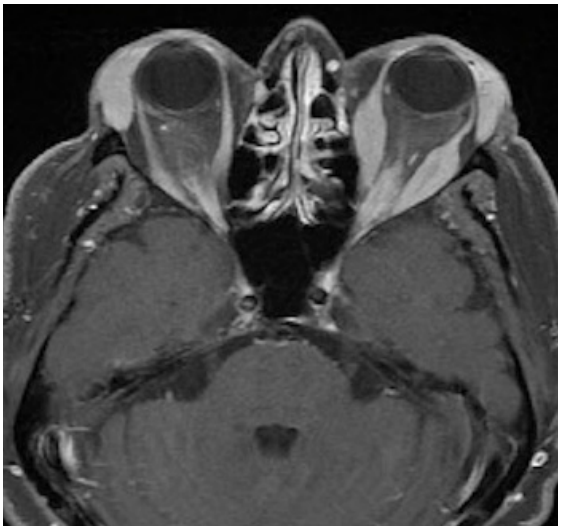

Figure 3. Bilateral symmetrical exophthalmos, hypertrophy in the periorbital muscles, and hypertrophy in the lacrimal glands were observed in magnetic resonance imaging.

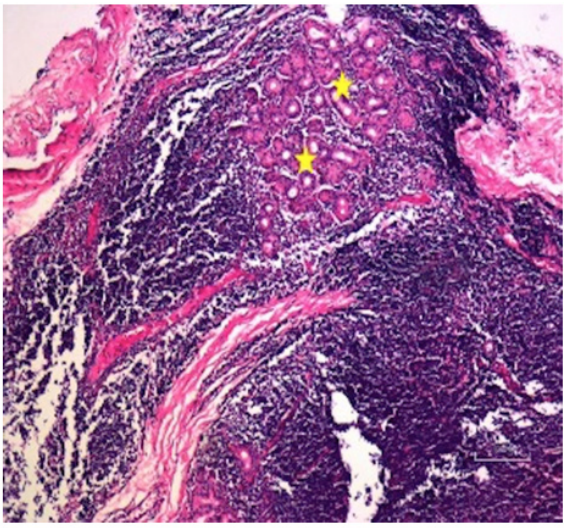

Figure 4. Areas of dense lymphoid infiltration and lacrimal gland ducts with asterisks were visible (hematoxylin-eosin, x100) in the pathological evaluation of the biopsy.

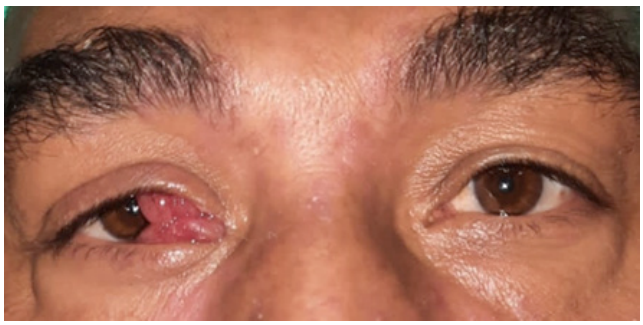

Figure 5. This patient had conjunctival involvement in right eye.

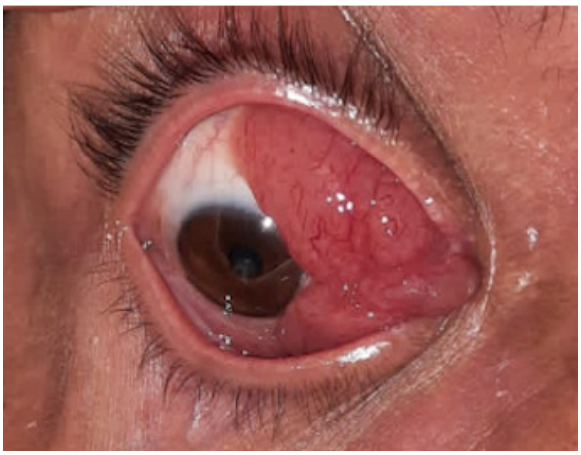

Figure 6. Conjunctival involvement with salmon patch appearance was seen in biomicroscopic evaluation.

Discussion:

Despite the small area of the orbit, follow-ups and treatments are different from one another due to the variations in tumor types [1,2]. Due to the different tissue types involved, many different tumor types can be seen in the orbit. In the approach to orbital tumors, the age of the patient, the location of the tumor, and radiologic findings should be considered [1]. Orbital and ocular adnexal lymphoma is the most common adult orbital malignancy [1-4]. Most orbital and ocular lymphomas are B-cell non-Hodgkin lymphomas; T-cell lymphomas, Burkitt lymphoma, and Hodgkin lymphoma have also been seen [1,2]. According to the Revised European American Lymphoma (REAL) classification, the most common lymphoma subtypes in the ocular adnexia are extranodal marginal zone B-cell lymphoma, diffuse large-cell B-cell lymphoma, and follicular lymphoma, respectively [2,9]. Less common B-cell lymphoma subtypes include lymphoplasmocytic lymphoma/immunocytoma, mantle cell lymphoma, plasmacytoma, and immunoblastic lymphoma

Table 1. Patients and characteristics of orbital lymphoma.

Patient	Sex	Age	Location	Diagnosis	Initial complaint	Unilateral/ bilateral	Chemotherapy	Radiotherapy
1	F	70	Intraorbital location (behind the orbital septum)	NHL; Primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue	Swelling in the left eye, painless mass	Unilateral	Rituximab	(-)
2	M	64	Intraorbital location (behind the orbital septum)	NHL; Primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue	Swelling in the right eye	Unilateral	Rituximab	(+)
3	M	79	Right eyelid (in front of orbital septum)	NHL; Primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue	Painless mass and swelling in the right eyelid	Unilateral	Rituximab	(-)
4	F	58	Left eyelid (in front of orbital septum)	NHL; Follicular lymphoma	Swelling in the left eyelid, ptosis, pain	Unilateral	(-)	(+)
5	M	56	Lacrimal gland involvement	NHL; Primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue	Ptosis, epiphora, proptosis	Bilateral	Rituximab	(-)
6	M	42	Intraorbital location (behind the orbital septum)	NHL; Diffuse large B-cell lymphoma	Bilateral eyelid swellibg and ptosis	Bilateral	Rituximab-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	(-)
7	M	46	Right eye conjunctival involvement	NHL; Primary extranodal marginal lymphoma of the mucosa-associated lymphoid tissue	Chemosis, salmon patch appearance in conjunctiva	Unilateral	Rituximab	(-)
8	M	58	Lacrimal gland involvement	NHL; Diffuse large B-cell lymphoma	Pain, limited eye movements,ptosis, epiphora	Unilateral	Rituximab-CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)	(-)

[9,10]. In the histopathologic evaluation of orbital lymphomas, marginal zone lymphoma is seen most commonly, followed by diffuse large B-cell lymphoma [1,2,9,10]. In our study, the most common marginal zone lymphoma diagnosis was in line with the literature.

Lymphomas in the orbital region can be detected at all ages but are generally seen in 50–70-year-olds [1,2,8-10]. The mean age of 59.1 years of the patients in our study is concordant with the literature. Orbital lymphomas are generally unilaterally observed in the literature, bilateral involvement is rarely witnessed [9-12]. Our study detected unilateral involvement in six patients and bilateral involvement in two patients.

In orbital tumors, the age of the patient, the location of the tumor, and radiologic findings should be considered in the approach [1,13]. A radiologic examination is recommended in terms of localization, spread, and differential diagnosis of the disease before biopsy [11,13]. The definitive diagnosis of the disease is made by histopathologists [13,14]. In the literature, the most common location of lymphomas is stated as the intraorbital region (orbital septum posterior), followed by the eyelids, lacrimal gland involvement, and conjunctival region involvement [8-14]. In our study, the most common involvement was the intraorbital region (behind the orbital septum), followed by the eyelids and lacrimal glands. Depending on the location of the tumor, various findings such as diplopia, vision loss, proptosis, watering, chemosis, decreased visual acuity, and eyelid edema can be seen in the patients [1-3,8,10-14]. Orbital painless mass and

swelling were the most common ophthalmologic signs in our patients.

The differential diagnosis of orbital lymphoma includes the following: pseudotumor, orbital metastases, diffuse lymphangioma, lacrimal adenoma, and cavernous hemangioma [11-14]. Some clinical conditions may guide the suspicion of lymphoma. The clinical presentation is nonspecific and depends on the location of the lymphoma. Patients typically demonstrate pink or red salmon patches of swollen conjunctiva. Orbital presentation is most commonly observed as a painless palpable mass. Eyelid swelling and enlarged gland prolapse may occur in lymphoma. These findings should make physicians suspect lymphoma [9-14].

Limitations

There are several limitations in this single-institution retrospective analysis of orbital and ocular adnexal lymphoma. Our small sample size may have affected the statistics. The other inherent limitation is the retrospective nature of the study and associated selection biases. Despite inherent limitations, there is a lack of studies about orbital and ocular adnexal lymphoma in the literature. This study is important because it is the first to report from the south of Turkey in the literature about orbital and ocular adnexal lymphoma.

Conclusion

Lymphomas are common among orbital tumors and clinical findings change depending on the place in orbit. When patients present with ophthalmologic findings such as painless orbital mass, chemosis, or epiphora, ophthalmologists should be careful to include lymphoma in their differential diagnosis

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