

EVALUATION OF THE EYELID AND PERIOCLAR TUMORS

Göz Kapağı ve Perioküler Tümörlerin Değerlendirilmesi

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ABSTRACT

Objective: Our aim was to determine and compare the demographic and histopathological features of eyelid and periocular tumors.

Material and Methods: The medical records of the patients who had eyelid and periocular tumor surgery were retrospectively analyzed at the ophthalmology clinic. The data included age, gender, tumor location and histopathological outcomes and comparative study was performed between the benign, malignant and premalignant tumors. Detailed site of the tumor was described as right and left or bilateral, upper and lower. Medial and lateral canthal tumors and eyebrow tumors were described as periocular tumors. SPSS computer statistical software (version Chicago) was used for statistical analysis. Chi-square test was used for the significant differences.

Results: A total of 190 patients with histopathologic confirmation were evaluated; 160 were (84.2%) eyelid lesions and 30 (15.8%) were periocular lesions. One hundred and forty (87.5%) of the eyelid lesions were benign, 17 (10.6%) of eyelid lesions were malignant and 3 (1.8%) of lesions were premalignant. Twenty (66.7%) of the periocular lesions were benign, 9 (30%) malignant and 1 (3.3%) was premalignant. Benign tumors were found to occur at younger ages compared to malignant ($p=0.03$) and premalignant lesions ($p=0.038$). One hundred and ten (68.7%) of benign tumors were seen in women and 50 (31.3%) in men. In contrast to benign tumors, malignant and premalignant tumors were more common in males ($p=0.003$). Malignant tumors were found to be significantly higher in the right eyes. There was a statistically significant difference in malignancy between periocular and eyelid tumors ($\chi^2=8.488$, $p=0.014$). Malignant tumors were found to be significantly higher in periocular lesions. Epidermal cyst (17.5%) was the most common benign tumor. Basal cell carcinoma was the most frequent malignant type (73.1%).

Conclusion: Gender of male, lower lid location and senility are the risk factors that should be concerned in eyelid and periocular tumors.

Keywords: Benign tumor, malignant tumor, eyelid, periocular region

ÖZ

Amaç: Amacımız göz kapağı ve perioküler tümörlerin demografik ve histopatolojik özelliklerini belirlemek ve karşılaştırmaktır.

Gereç ve Yöntemler: Göz hastalıkları kliniğinde göz kapağı ve perioküler tümör cerrahisi geçiren hastaların tıbbi kayıtları retrospektif olarak incelendi. Veriler yaş, cinsiyet, tümör yerleşimi ve histopatolojik sonuçları içeriyordu ve benign, malign ve premalign tümörler arasında karşılaştırmalı çalışma yapıldı. Tümörün ayrıntılı bölgesi sağ ve sol veya iki taraflı, üst ve alt olarak tanımlandı. Medial ve lateral kantal tümörler ve kaş tümörleri perioküler tümörler olarak tanımlandı. İstatistiksel analiz için SPSS bilgisayar istatistik yazılımı (versiyon Chicago) kullanıldı. Anlamlı farklılıklar için ki-kare testi kullanıldı.

Bulgular: Histopatolojik doğrulaması yapılan toplam 190 hasta değerlendirildi, 160'ı (%84.2) göz kapağı lezyonu ve 30'u (%15.8) perioküler lezyonu. Göz kapağı lezyonlarının 140'ı (%87.5) benign, 17'si (%10.6) malign ve 3'ü (%1.8) premalign idi. Perioküler lezyonların 20'si (%66.7) benign, 9'u (%30) malign ve 1'i (%3.3) premalign idi. Benign tümörlerin malign ($p=0.03$) ve premalign lezyonlara ($p=0.038$) göre daha genç yaşlarda ortaya çıktığı bulundu. Benign tümörlerin 110'u (%68.7) kadınlarda 50'si (%31.3) erkeklerde görüldü. Benign tümörlerin aksine malign ve premalign tümörler erkeklerde daha sıkı ($p=0.003$). Sağ gözde malign tümörler anlamlı derecede yüksek bulundu. Perioküler ve göz kapağı tümörleri arasında malignite açısından istatistiksel olarak anlamlı bir fark vardı ($\chi^2=8.488$, $p=0.014$). Malign tümörler perioküler lezyonlarda anlamlı olarak daha yüksek bulundu. Epidermal kist (%17.5) en sık görülen benign tümördü. Bazal hücreli karsinom en sık görülen malign tipti (%73.1).

Sonuç: Erkek cinsiyeti, alt kapak yerleşimi ve yaşlılık, göz kapağı ve perioküler tümörlerde dikkat edilmesi gereken risk faktörleridir.

Anahtar Kelimeler: Benign tümör, malign tümör, göz kapağı, perioküler bölge



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INTRODUCTION

Eyelid and periocular skin are vulnerable to trauma and minor injuries including aging and sun exposure. Therefore, the tumors rising from these regions are not rare in ophthalmology practice. Various malignant and benign tumors have been described in the literature due to the diversity of anatomical structures in this region (1). These tumors are mostly originated from dermis and epidermis however vascular and neural structures, tars, palpebral conjunctiva, hair follicles, sebaceous gland can also be the originating structures of eyelid tumors (2-4). Previous studies have emphasized that mostly benign lesions of the eyelid tumors were predominant in that region (2-4). Some of the tumors that appear clinically benign can sometimes be diagnosed as malignant or premalignant in histopathological examination (5). Tumors that are clinically misdiagnosed may lead to more extensive surgery, which may result in cosmetic and physiological problems especially in lower eyelid and medial canthal area lesions. Thus, histopathological examination of eyelid tumors is very important in making a definitive diagnosis.

We aimed to determine the clinical features of tumor types and to compare the demographic and histopathological features of both eyelid and periocular tumors.

MATERIALS AND METHODS

Study Population/ Study Conduction

Between the years October 2018 and February 2022, the medical records of the patients retrospectively collected and analyzed in tertiary hospital ophthalmology clinic of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital. Collected data included age, gender, tumor location, and histopathological outcomes. The study group was divided into three regarding the histopathology (benign, malignant, premalignant), also location was the second comparison data including

eyelid or periorbital predominance. Comparative study was performed between the tumors regarding their histopathological diagnosis. As well as the overall locations of tumors; detailed site of the tumor was described as unilateral (right/left) or bilateral, upper and lower. Canthus location (medial /lateral) and eyebrow location was described as periocular region. The name and identity of the patient was kept confidential (Figures 1-5).



Figure 1: Basal cell carcinoma located in the lateral and medial canthal regions

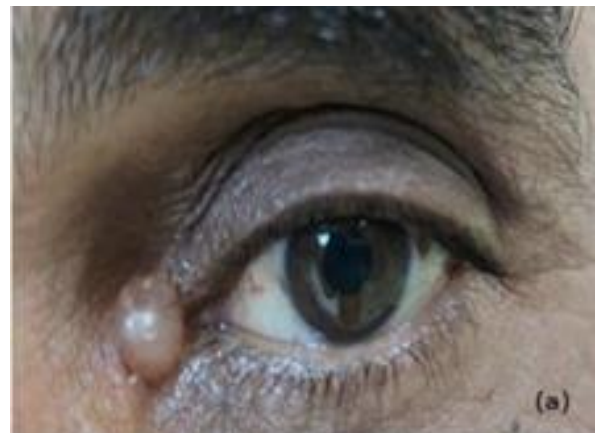


Figure 2: a; Cyst in the medial canthus, b; Epidermal cyst on the lateral canthus



Figure 3: Metastatic lymphoma appearance of the upper eyelid



Figure 4: Papilloma located in the lateral aspect of the upper eyelid



Figure 5: Xanthelasma located both in the upper and lower eyelid

Description of Anatomical Sites

1) Eyelid: Upper lid tumors and lower lid tumors with a maximum distance of 20 mm from the ciliated margin

2) Periocular region:

a) Canthal region: Tumors 10 mm away from the medial and 15 mm away from the lateral canthus

b) Eyebrow: Tumors 10 mm above the right and left eye eyebrow

Treatment Approach: All the patients were clinically evaluated about the feature of their lesions preoperatively. Irregular lesions, ulceration, bleeding, and eyelash shedding were presumed malignant while description of benign lesions was made with well-defined borders. While adequate surgical excision provided complete cure in benign and malignant tumors, some of the malignant tumors required reconstruction procedures in addition to wide surgical excisions. None of the patients were referred to further treatment with either chemotherapy or radiotherapy or combined.

Exclusion Criteria: Patients with palpebral conjunctival lesions and clinically premalignant lesions were excluded from the study, Inflammatory lesions unresponsive to medical therapy such as chalazion were also excluded. Patients who did not have pathology reports were excluded.

Ethical Consideration: Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee of Non-interventional Research, Turkey approved the protocol (date: 31/03/2022; issue number: 2022-03/63). All the patients signed the consent form before the surgical procedure. Data of the patients were treated according to the Declaration of Helsinki Guidelines.

Statistical Analysis: Statistical analyses were made using with IBM SPSS 19.0 for Windows Statistical software (SPSS, Chicago, IL). The numerical data were expressed as mean \pm standard deviation. All data were subjected to descriptive statistical analyses. The chi-square test was used for the significant differences

between the groups defined above. A *p* value of <0.05 was considered statistically as significant in all analyses.

RESULTS

During the 3.5 years of interval, a total of 190 patients with histopathologic confirmation were evaluated. Of the 190 patients, 160 (84.2%) eyelid lesions and 30 (15.8%) periocular lesions were reviewed and enrolled in the study. Eighty-seven-point five percentage of the eyelid lesions were benign, 10.6% of eyelid lesions were malignant and 1.8% of lesions were premalignant. Sixty-six-point seven percentage of the periocular lesions were benign, 30% malignant and 3.3% was premalignant. Gender, tumor site and histopathological distribution of the eyelid and periocular tumors are given in Figure 6.

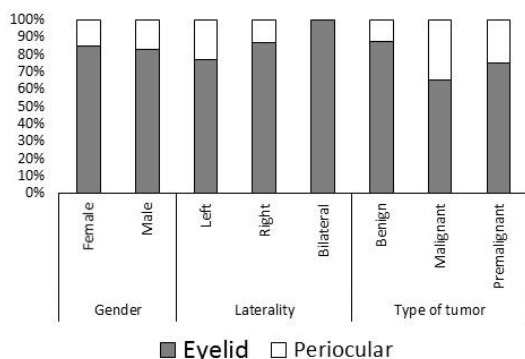


Figure 6: Gender, tumor site and histopathological distribution of the eyelid and periocular tumors

Demographic data were analyzed and the results revealed that the mean age was 50.46 ± 14.13 years in benign tumors. In patients with malignant and premalignant tumors the mean age was 60.61 ± 14.74 years and 68.25 ± 4.45 years respectively. Eta coefficient between age and malignant tumors was found to be 0.286, indicating a negligible correlation with an 8.2%

effect of age. Benign tumors were found to occur at younger ages compared to malignant ($p=0.03$) and premalignant lesions ($p=0.038$). Age distribution of patients according to the histopathological diagnosis was given in Figure 7.

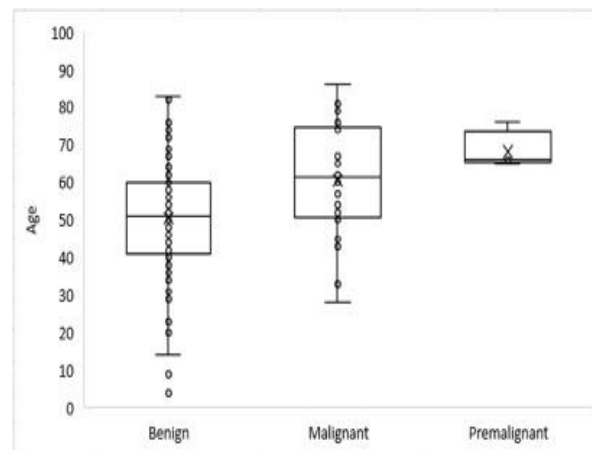


Figure 7: Age distribution of the patients according to the histopathological diagnosis

Gender of the patients those had benign tumors were found as 110 (68.7%) in female and 50 (31.3%) in male. In contrast to benign tumors malignant and premalignant tumors were more common in males ($p=0.003$).

Chi-square test showed that there was a statistically significant difference in malignant tumors between right and left eyes ($\chi(4)=10.828$, $p=0.029$). Malignant tumors were found to be significantly higher in the right eyes, while no significant difference between the eyes were observed in benign and premalignant lesions (Table 1). Chi-square test showed that there was no statistically significant difference between lower and upper eyelids in malignant, benign or premalignant lesions ($\chi(2)=2.296$, $p=0.317$) (Table 1). Chi-square test showed that there was a statistically significant difference in malignant tumors between periocular and eyelid tumors ($\chi(2)=8.488$, $p=0.014$). Malignant tumors were found to be significantly higher in periocular lesions (Table 1).

Table 1: Summary of comparisons according to demographic and clinical characteristics of benign, malignant, and premalignant tumors

	Benign	Malignant	Premalignant	P value
Age, year	50.46±14.13	60.61±14.74	68.25±4.493	0.038
Gender				
Female	110 (68.7%)	10 (38.4%)	1 (25%)	0.030
Male	50 (31.3%)	16 (61.6%)	3 (75%)	
Laterality				
Right	62 (75.6%)	18 (22%)	2 (2.4%)	0.029
Left	72 (87.8%)	8 (9.8%)	2 (2.4%)	
Eyelid				
Bilateral	26 (100%)	0	0	0.317
Lower	65 (84.4%)	11 (14.3%)	1 (1.3%)	
Upper	75 (90.4%)	6 (7.2%)	2 (2.4%)	
Location				
Eyelid	140 (87.5%)	17 (65.4%)	3 (75%)	0.014
Periocular	20 (12.5%)	9 (34.6%)	1 (25%)	

Table 2: The demographic and clinical characteristics of benign, malignant and premalignant tumors

	Number (%)	Mean Age ±SD	F/M	R/L/B	L/U	E/PO
Benign	Epidermal cyst	28 (14.7%)	47.57±15.36	18/10	10/17/1	13/11 24/4
	Xanthelasma	26 (13.7%)	47.04±8.13	21/5	1/6/19	8/18 26/0
	Squamous papilloma	25 (13.2%)	51.56±16.16	14/11	9/14/2	12/10 22/3
	Seborrheic keratosis	23 (12.1%)	59.87±10.28	18/5	12/10/1	12/7 19/4
	Intradermal nevus	20 (10.5%)	47.75±12.79	14/6	11/6/3	9/9 18/2
	Others ¹	10 (5.3%)	54.70±14.32	8/2	6/4/0	3/6 9/1
	Hydrocystoma	5 (2.6%)	50.60±12.63	4/1	4/1/0	2/2 4/1
	Verruca vulgaris	5 (2.6%)	45.20±11.32	2/3	1/4/0	3/2 5/0
	Chronic inflammation	4 (2.1%)	54.75±17.58	3/1	2/2/0	0/1 1/3
	Compound nevus	3 (1.6%)	45.33±8.22	2/1	2/1/0	0/3 3/0
	Others ²	3 (1.6%)	46.00±10.20	2/1	0/3/0	0/2 2/1
	Hemangioma	3 (1.6%)	43.33±1.89	1/2	1/2/0	1/2 3/0
	Pyogenic granuloma	3 (1.6%)	39.00±24.83	2/1	1/2/0	2/0 2/1
	Trichoepithelioma	1 (0.5%)	63.00	1/0	1/0/0	0/1 1/0
	Trichilemmoma	1 (0.5%)	69.00	0/1	1/0/0	2/3 1/0
Malignant	Basal cell carcinoma	19 (10%)	59.74±12.69	7/12	14/5/0	9/2 11/8
	Metastatic tumors ³	3 (1.6%)	67.67±15.46	0/3	1/2/0	0/3 3/0
	Sebaceous carcinoma	2 (1.1%)	73.50±12.50	2/0	1/1/0	1/1 2/0
	Malignant melanoma	1 (0.5%)	28.00	1/0	1/0/0	1/0 1/0
	Squamous cell carcinoma	1 (0.5%)	63.00	0/1	1/0/0	1/0 0/1
	Premalignant tumors ⁴	4 (2.1%)	68.25±4.49	1/3	2/2/0	1/2 3/1

SD: Standard Deviation, F: female, M: male, R: right, L: left, B: bilateral, L: lower, U: upper, E: eyelid, PO: periocular
Others¹ (Spiroadenoma, Molluscum contagiosum, inverted follicular keratosis, neurofibroma, pleomorphic adenoma, tubular adenoma, demodex folliculitis, fibroepithelial polyp), Other benign cysts² (Keratinous cyst, trichilemmal cyst, ductal cyst), metastatic tumors³ (Lymphoma), Premalignant tumors ⁴ (carcinoma in situ, actinic keratosis)

General demographic data and histopathological diagnosis of benign and malignant tumors were defined in Table 2. The first three common benign tumors were found as epidermal cyst (17.5%), xanthelasma (16.3%) and seborrheic keratosis (14.4%) respectively. On the other hand, among malignant tumors basal cell carcinoma (BCC) was the most frequently type (73.1%), metastatic tumors were the second (11.5%) and sebaceous gland carcinoma was the third with a ratio of 7.7 %. Premalignant lesions were actinic keratosis 3 (75%) and 1 carcinoma in situ with a rate of (25%).

Seventy-five percentage of malignant tumors were applied a large excision and 2 of them [1 due to BCC, 1 due to squamous cell carcinoma (SCC)] required reconstructive procedures. All of the metastatic tumors were undergone for biopsy procedures in order to make definite diagnosis for metastatic lymphoma. Surgical margin was negative in all patients operated for BCC. None of the patients with malignant tumors received chemotherapy, radiotherapy or chemoradiotherapy. None of the patients with benign tumors needed further reconstructive surgery. No recurrence was observed in the 3.5-year follow-up time in any malignant tumor and premalignant lesions did not progress to malignant tumors. No mortality was observed among benign or malignant eye tumors.

DISCUSSION

In this study, the majority of all patients served as benign tumors (84.2%) and 13.6% composed the malignant tumors, which was similar to data from Turkey (87.1% and 88.7%) (6,7), China (86.2%) (8), Switzerland (84%) (1), and Taiwan (95%) (9). In several studies, the most common benign tumor has been reported differently. Şendul et al., Deprez et al. and Gundogan et al. reported the most common benign eyelid tumor as squamous papilloma (17.7%, 26% and 21.8% respectively) (1,6,10). Huang and colleagues reported the most common benign eyelid tumors as intradermal nevus (21.1%), followed by seborrheic keratosis (12.6%) and

xanthelasma (11.2%), and epidermal cyst (8.2%) (9). Yumusak et al. reported that seborrheic keratosis was the most common benign eyelid tumor (7). The first three common benign tumors in our study were found as epidermal cyst (17.5%), xanthelasma (16.3%) and seborrheic keratosis (14.4%) respectively. Similar to our findings, Asproudis et al. published that the most common benign eyelid lesions were cysts (20%) (11). This similarity can be explained by the fact that they have the same geographic conditions to our country.

Deprez et al. defined BCC as the most common malignant eyelid tumor (86%), and the frequencies of SCC and sebaceous gland carcinoma (SGC) were (7%) and (3%), respectively (1). Huang et al. concluded the most common malignant eyelid tumors as BCC (57.8%), SGC (21.1%) and SCC (10.1%) (9). Asproudis et al. sorted the malignant eyelid tumors as 86% BCC, 7% SCC, and 7% basosquamous cell carcinomas (11). Yu et al. demonstrated the most common malignant eyelid lesions as: BCC (56.5%) SGC (34.6%), SCC (3.8%) and lymphoma/plasmacytoma (1.7%) (12). Kaliki et al. reported the most common malignant eyelid tumors as SGC (n=285, 53%), BCC (n=128, 24%), SCC (n=99, 18%), and miscellaneous tumors (n=24, 4%) (13). Eventually, when the previous studies were taken into consideration BCC was the most frequently seen malignant tumor, however the frequency of other malignancies differed from one study to another. Supporting the previous studies, BCC was also found as the most common malignancy in our study population. Cancer may affect the eye and orbit as a direct result of metastatic neoplastic infiltration, compression, or circulating antibodies involving paraneoplastic retinal degeneration (14). Unlike the previous literature, metastatic tumors such as lymphoma was observed in the second frequency after BCC in our series (10). The explanation for this result can be attributed to our hospital which is a referral center for cancer patients. Such differences in tumor types and sequence may be due to differences in skin type, genetic predispositions,

individual awareness of the disease, health policies, and surveillance.

According to gender evaluation for all study group there was a significant difference between female and male group with a result of male predominance in malignant tumors and female predominance in benign tumors. While Sendul et al. did not find any significant gender ratio difference among patients with malignant eyelid tumors, Huang et al. reported male predominance similar to us (6,9). This interesting proportion can be due to the environmental and occupational circumstances of male participants.

Similar to some studies, malignant tumors and premalignant lesions tended to occur at older ages compared to benign tumors (6,8). This result may emphasize of the impact of aging and exposure to several traumatic factors such as high levels of solar radiation on malignant tumors.

Although there was no statistically significant difference between lower and upper eyelids in malignant, benign or premalignant lesions, we noted that BCC predominantly located in lower eyelid similar to some studies (9,12,15).

In this study, we also examined periocular tumors with a different approach to eyelid tumors.

Eighty-seven-point five percentage of the excised eyelid lesions were benign, 10.6% of were malignant. Sixty-six-point seven percentage of the excised periocular lesions were benign, 30% malignant. Malignant tumors were found to be significantly higher in periocular lesions. This difference may be due to the fact that the inner canthus, outer canthus and eyebrow are more exposed to trauma and sunlight than the eyelid.

Parallel to recent studies, we observed larger excision and reconstructive procedures in malignant eyelid and periocular tumors when compared to benign tumors (8,14). Eyelid and periocular malignancies differ from the other cutaneous malignancies of the same cell type in terms of the unique anatomic considerations and the functional impact of surgical resection and

reconstruction on ocular protection and visual function. It is critical for the patient to apply early, as it is an important anatomical region, in order to prevent several complications even exenteration of the globe.

In summary, our results indicate that benign lesions are generally found in younger individuals and occur with equal frequency in the upper and lower eyelids. In contrast, malignant lesions occur predominantly in elderly, male patients and usually tend to locate in the lower eyelid. The type and size of the tumor, the distance of the tumor to the eyelid margin, to the medial and lateral canthus are of the important factors affecting the prognosis of the disease, the outcome of the surgery and the cosmetic results. Thus, the histopathological examination is a crucial issue for both treatment approach and surgical resections especially to differentiate benign, premalignant lesions and locally aggressive and destructive malignant tumors.

Conflict of Interest: The author declare that they have no conflict of interest.

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