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Pathological outcomes of eyelid tumors

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Abstract

Aim: To evaluate and compare the pathological outcomes, demographic and clinical features of benign and malignant tumors of the eyelid.

Materials and Methods: The records of patients who were operated on for eyelid tumors in the oculoplastic surgery unit of our clinic were retrospectively reviewed. The age and sex of the patient, the location and laterality of the tumor, the histopathological diagnosis of the lesion, and whether it was benign or malignant were recorded.

Results: A total of 251 patients who were operated on for eyelid tumors and underwent histopathological examination were included in the study. Histopathological results showed benign eyelid tumors in 230 patients (91.6%) and malignant eyelid tumors in 21 patients (8.4%). The age of the patients in the malignant eyelid tumors group was significantly higher than in the benign eyelid tumors group ($p<0.001$). The localization rate on the right side was significantly higher in malignant eyelid tumors compared to benign eyelid tumors ($p=0.003$). The lower eyelid localization rate was significantly higher in malignant eyelid tumors than benign eyelid tumors ($p<0.001$).

Conclusion: Although the majority of eyelid tumors are benign, the pathological results of the patients are extremely important so that malignant masses that appear benign are not overlooked. It should be kept in mind that these tumors have a high probability of malignancy, especially in advanced age and lower eyelid locations, and may lead to serious morbidity if treated late.

Introduction

The periocular region is at higher risk for skin cancers than other regions due to direct exposure to ultraviolet (UV) radiation. More than 80% of non-melanoma skin cancers occur in the head and neck region. 4.6-5.4% of these cancers are seen, especially in the eyelids [1]. Delayed excision and reconstruction of periocular tumors are difficult due to the limited skin tissue in this area. In addition, treatment of these tumors is important for the patient's visual function and cosmetic acceptability. In our study, the records of patients who underwent surgery for a mass in the eyelid were evaluated retrospectively, and their histopathological results were reported.

Materials and Methods

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved by the local medical ethics committee (Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee, numbered: 2022-347). Signed informed consent was obtained from all participants (including the children's parents or guardians) for the research and publication of the images. Records of patients who underwent surgery for eyelid tumors in the oculoplastic surgery unit of Başakşehir Çam and Sakura City Hospital between July 2019 and March 2023 were retrospectively examined. The sample group consisted of 251 patients determined by power analysis (5% margin of error, 85% power, and 92% effect size). The patients' age, sex, localization and laterality of the tumors, histopathological diagnosis of the lesion, and whether it was benign or malignant were recorded. Patients who underwent periocular mass excision without a histopathological diagnosis, palpebral conjunctival lesions, and/or tumors located outside the periocular area were excluded from the study. Excision and primary suturation of the tumor area was the main surgical approach in patients with macroscopically small and benign eyelid tumors. In patients with large and malignant clinical findings, eyelid reconstruction was planned according to the results of

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an incisional biopsy, and wide surgical resection was performed.

Statistical analysis

SPSS software (IBM SPSS Statistics for Windows, Version 28.0; Armonk, NY, IBM Corp.) was used for statistical analyses. Mean, standard deviation, median, minimum, maximum value, frequency, and percentage were used for descriptive statistics. The data were analyzed using the Kolmogorov-Smirnov test to assess the normality of the sample distribution. Mann-Whitney U test was used to compare quantitative data between groups. Chi-Square test was used to compare qualitative data between groups. The statistical significance threshold was established at $p<0.05$.

Results

A total of 251 patients with a mean age of 45.6 ± 19.3 years (min-max: 3-94 years) who underwent surgery due to eyelid tumors were included in our study. The pathological results were benign in 230 patients (91.6 %) and malignant in 21 patients (8.4 %). Of the patients, 157 (62.5 %) were female, and 94 (37.5 %) were male (Table 1). Whereas the median follow-up period for benign eyelid tumors was 2 months (mean: 2±1.71, min-max: 1-3 months), the median follow-up period for malignant eyelid tumors was 22 months (mean: 21.71±5.29, min-max: 12-35 months). Patients with malignant periocular region tumors had a greater mean age than those with benign eyelid tumors (66.6 ± 16.6, 43.7 ± 18.4, respectively) ($p<0.001$).

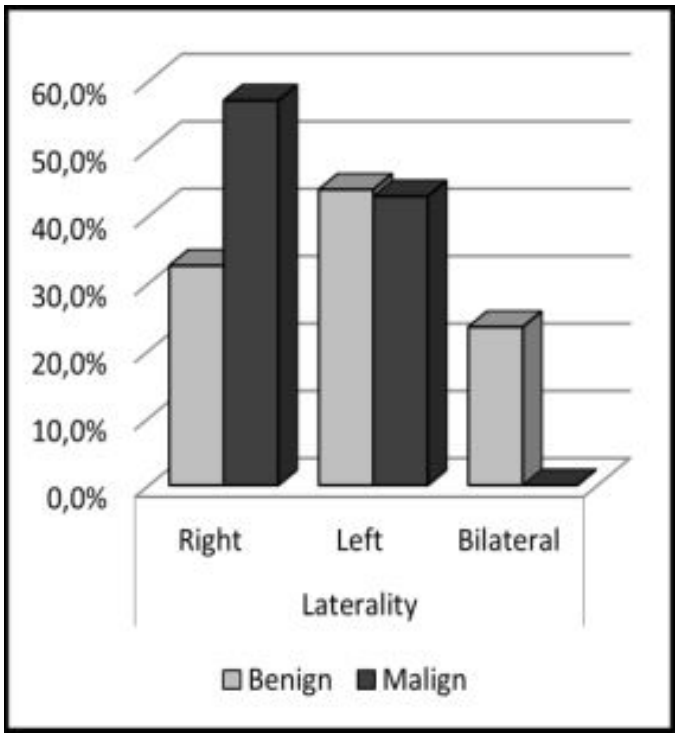

Figure 1. Lateralization of benign and malignant eyelid tumors. Malignant eyelid tumors tended to be more common on the right side compared with benign tumors ($p = 0.003$).

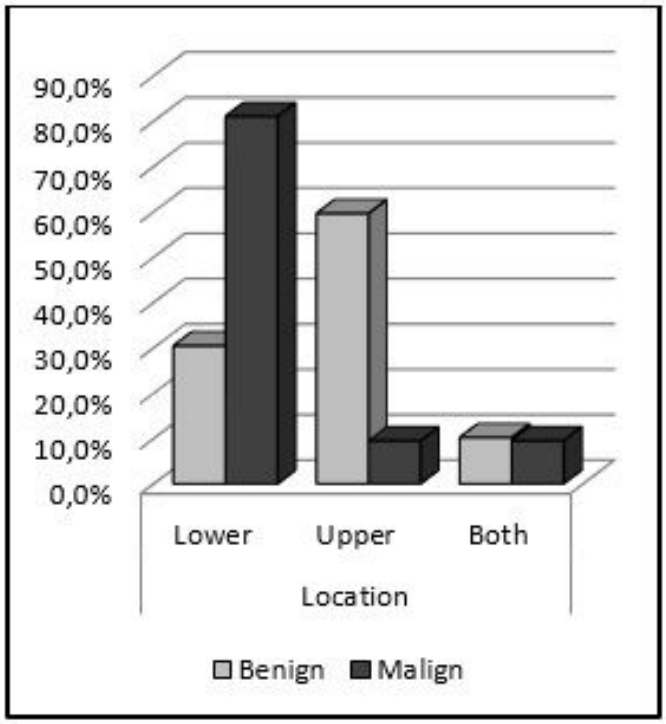

Figure 2. Localization of benign and malignant eyelid tumors. The rate of localization of the lower eyelids in malignant tumors was significantly higher than in the benign group ($p<0.001$).

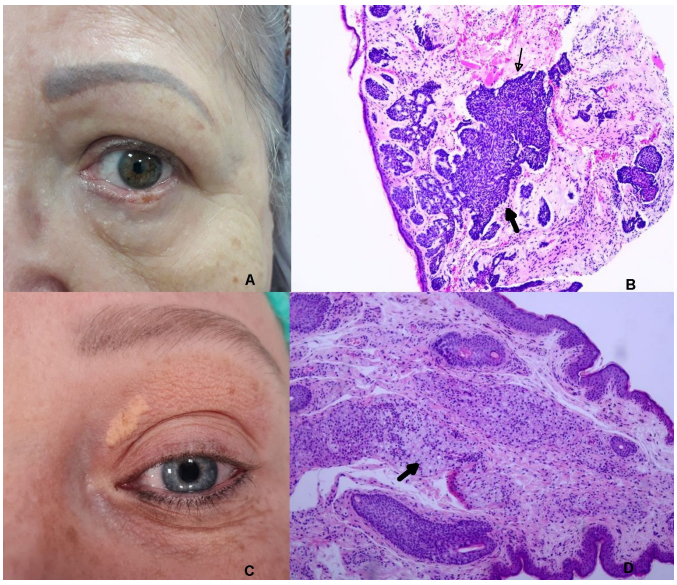

Figure 3. (A) Macroscopic view of basal cell carcinoma (B) Basal cell carcinoma: basaloid lobular with peripheral palisade (thin arrow); cleft around lobular and mucinous stroma (thick arrow); H&E, 10x (C) Macroscopic view of xanthelasma (D) Xanthelasma: large, pale, fat-laden macrophages in the dermis (thick arrow), H&E, 10x.

Malignant eyelid tumors tended to be more common on the right side than benign tumors (57.1%, 32.6 %, respectively) ($p=0.003$) (Figure 1). Malignant eyelid tumors were found to be significantly higher in males than females

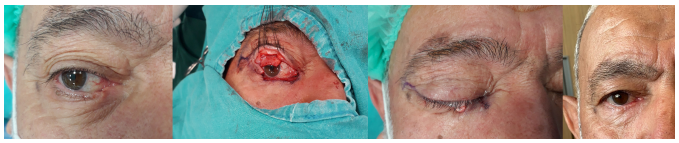

Figure 4. Preoperative, intraoperative, and postoperative 1st week and 1st year follow-up images of the patient who underwent reconstruction with a tarso conjunctival flap and a skin advancement flap due to basal cell carcinoma.

Table 1. Demographic and clinical features of eyelid tumors.

Variables	(n=251)	(%)
Gender		
Female	157	62.5
Male	94	37.5
Laterality		
Right	87	34.7
Left	110	43.8
Bilateral	54	21.5
Location		
Lower	87	34.7
Upper	139	55.4
Both	23	9.2
MC	1	0.4
LC	1	0.4
Tumor		
Benign	230	91.6
Malign	21	8.4
Treatment		
Benign tumor, excision	230	100
Malign tumor, Primary suture repair	4	19
Hughes tarsoconjunctival flap repair	5	23.8
Glabellar flap repair	3	14.3
Tenzel flap repair	8	38.1
Radiotherapy	1	4.8
Recurrence		
Yes	0	0.0
No	251	100

Both: (upper eyelid and lower eyelid of the same eye), MC: Medial canthus, LC: Lateral canthus.

($p<0.001$). The rate of localization of the lower eyelids in malignant tumors was significantly higher than in the benign group (81% and, 30.4%, respectively) ($p<0.001$) (Figure 2). The recurrence rate after treatment did not differ significantly between the benign and malignant groups ($p>0.05$) (Table 2). Basal cell carcinoma (BCC) was reported histopathologically in 3 patients who underwent excision without biopsy because they were thought to be benign. Secondary wide excision was performed in only one of these patients because of a positive surgical margin.

The most frequently reported eyelid tumors were xanthelasma 56 (24.3%), intradermal nevus 48 (20.9%), fibroepithelial polyp 19 (8.3%), and epidermal cyst 16 (6.9%). Periocular malignant tumors were basal cell carcinoma in 18 (85.7%), squamous cell carcinoma in 2 (9.5%), and sebaceous gland carcinoma (SGC) in 1 (4.8%) (Table 3). Figure 3 shows the macroscopic and pathological specimens of two patients with basal cell carcinoma and xanthelasma who were followed up at our clinic. None of the patients with benign tumors required reconstructive surgery. Total excision and primary suture were sufficient in 4 (19%) patients with malignant tumors. A Tenzel flap was applied for full-thickness eyelid defects after excision in 8 (38.1%) patients. In 5 patients (23.8%), the Hughes tarsoconjunctival flap was applied to the posterior lamella and the skin advancement flap to the anterior lamella for total excision and defect reconstruction (Table 1) (Figure 4). Radiotherapy was started in one patient with the diagnosis of basal cell carcinoma due to orbital spread. None of the patients underwent exenteration.

Discussion

Due to the skin and glandular structures of the eyelids, the eyelid is a region where many benign and malignant tumors are common compared to other parts of the body. Since some masses in this region are macroscopically similar in the early period of their development, a definitive diagnosis must be made pathologically, and treatment and follow-up should be determined accordingly. Eyelid reconstruction is more difficult than that of other parts of the body because of their limited surface area and proximity to the ocular surface. Thus, to avoid difficult reconstruction, tumors in this region should be diagnosed and treated as early as possible. Various factors such as race, geography, and genetics influence the incidence of periocular tumors. Previous studies have reported 84–95% of eyelid tumors are benign [2-5]. In our study, similar to the literature, benign tumors were found in 91.6% of the pathological results of eyelid tumors. Studies have reported that the most common benign eyelid tumors are squamous papilloma and intradermal nevus [3-5]. In our study, unlike the literature, the most common benign eyelid tumor was xanthelasma (24.3%), followed by intradermal nevus (20.9%). Although xanthelasma was the most common benign tumor in our study, this could be because other researchers did not request a pathological diagnosis since xanthelasma is easily recognized macroscopically. It may also be caused by race, environmental, and nutritional conditions that play a role in the formation of xanthelasma. Huang et al. [5] reported that benign eyelid tumors were more common in the upper lid than in the lower lid and did not differ in terms of laterality. In our study, similar to previous studies, we observed that upper eyelid involvement was more common in benign eyelid tumors. Rates regarding the laterality of eyelid tumors vary [4-6]. In our study, benign tumors were seen more frequently in the left eye than in the right eye. Based on the current data, we believe that laterality does not have any effect on tumor characteristics. In our study, as in other studies, benign eyelid tumors did not show a sex difference.

Table 2. Statistical comparison of demographic and clinical features and recurrence between benign and malignant tumors.

	Benign tumors of eyelid		Malign tumors of eyelid		p
	(n=230)	(%)	(n=21)	(%)	
Gender					
Female	152	66.1	5	23.8	**<0.001 X^2**
Male	78	33.9	16	76.2	
Laterality					
Right	75	32.6	12	57.1	
Left	101	43.9	9	42.9	**0.003 X^2**
Bilateral	54	23.5	0	0.0	
Location					
Lower	70	30.4	17	81.0	
Upper	137	59.6	2	9.5	
Both	23	9.2			**<0.001 X^2**
MC			1	4.7	
LC			1	4.7	
Recurrence					
Yes	0	0.0	0	0.0	1.000 X^2
No	230	100	21	100	

X^2 Chi-square test. P<0.05 is statistically significant, Both: (upper eyelid and lower eyelid of the same eye), MC: Medial canthus, LC: Lateral canthus.

Table 3. Demographic data, pathological types, and clinical features of benign and malignant eyelid tumors.

	n=251	%	Gender (M/F)	Laterality (R/L/BL)	Location (U/L/B)
Benign tumors of eyelid					
Xanthelasma	56	24.3	5/51	5/3/48	42/5/9
Intradermal nevus	48	20.9	8/40	26/22/0	30/17/1
Fibroepithelial polyp	19	8.3	10/9	6/12/1	12/5/2
Verruca vulgaris	11	4.8	6/5	5/6/0	6/4/1
Hydrocystoma	12	5.2	5/7	4/5/3	2/6/4
Seborrheic keratosis	8	3.5	4/4	1/6/1	2/5/1
Dermoid cyst	10	4.4	5/5	6/4/0	10/0/0
Epidermal cyst	16	6.9	8/8	4/12/0	10/4/2
Keratinous cyst	5	2.1	2/3	1/3/1	3/1/1
Squamous papilloma	15	6.5	6/9	6/9/0	3/11/1
Hemangioma	8	3.5	4/4	2/6/0	4/4/0
Others[1]	22	9.6	15/7	9/13/0	13/8/1
Malign tumors of eyelid					
BCC,Solid type	4	19	2/2	4/0/0	0/4/0
BCC,Nodular type	8	38.1	8/0	2/6/0	1/7/0
BCC,Infiltrative type	6	28.6	3/3	4/2/0	1/4/1
Squamous cell carcinoma	2	9.5	2/0	1/1/0	0/1/1
Sebaceous gland carcinoma	1	4.8	1/0	1/0/0	0/1/0

[1]Poroma, chalazion, nörofibroma, tricoepitelioma, polimatrixoma, aktinic keratosis, licenoid keratosis, inverted foliculer keratosis, epidermal nevüs, fibrous histiocytoma, moll cyst, infundibuler follicul cyst, calsinosis kutis Basal cell carcinoma (BCC), Male (M), Female (F), Laterality: Right (R), Left (L), Bilateral (BL), Location: Upper (U), Lower (L), Both ((B) (Upper eyelid, Lower eyelid, Medial canthus, Lateral canthus).

Although malignant tumors are less common than benign tumors, they cause large defects in the eyelids, which have a smaller area than the body, due to their aggressive nature. The prevalence of malignant eyelid tumors is subject to geographical variation, and genetic and racial predispositions may also play a role [7]. Huang et al. [5] reported 5% of the eyelid tumors in their study to be malignant, while Sendul et al. [4] reported 12.9% to be malignant. In

our study, we found histopathologically malignant tumors at a rate of 8.4%. Similar to other studies, we concluded that malignant periocular region tumors are more likely to develop in older patients [2-4]. The most common malignant eyelid tumor is BCC, with studies reporting the incidence of BCC among all malignant eyelid tumors to be between 56.5% and 86% [4-6, 8]. In our study, BCC (85.7%) was the most common malignant eyelid tumor. Malignant eyelid tumors were significantly more likely to be located in the lower eyelid than benign eyelid tumors (81.0% and 30.4%, respectively).

Although SCC and SGC are less common than BCC, they are often more biologically aggressive and potentially fatal tumors. SGC is rare in Caucasians and accounts for 1–5.5% of all eyelid malignancies [9-11]. In our patients, sebaceous gland carcinoma (4.8%) was the third most common malignant eyelid tumor. Wang et al. [7] reported SGC with a rate of 23.6% in their study, which included 127 malignant eyelid tumors. Previous studies have reported the prevalence of eyelid SGC to be between 1.5% and 32.6% [10, 12, 13]. This wide distribution suggests that genetic and racial predispositions play a significant role in the development of SGC [10]. It has been reported in the literature that the incidence of SGC is higher in women and in upper eyelid localizations [7, 14-18]. Gundogan et al. found no cases of SGC in their study and reported SCC in only one out of 22 malignant eyelid tumors [19]. In our study, SCC was the second most common malignant eyelid tumor with a prevalence of 9.5%.

Total excision and reconstruction were performed after incisional biopsy in all patients in our study who had extensive involvement and required reconstruction of the defect. Additional eyelid reconstruction was required after excision in 16 (76.2%) patients with malignant eyelid tumors. With a sample of 125 malignant lesions, Tesluk [20] reported that clinicians' accuracy in predicting malignancy was 92.8%. In our study, BCC was pathologically reported in three (1.2%) patients whose tumors were evaluated as benign and who underwent excision without biopsy. A secondary wide resection was performed because only one of these patients had a positive surgical margin. Pieh et al. [21] reported a recurrence rate of 5.36% in BCC after primary surgery. Medial canthus localized sclerosing type BCC was reported to be the most common recurrence. In high-risk cases, they recommended adjuvant therapy, such as radiotherapy. Only one of our patients with malignant eyelid tumor had lower lid nodular-type BCC close to the medial canthus. The patient underwent reconstruction with wide excision and glabellar flap. We did not observe any recurrence of malignant eyelid tumors during our 2-year follow-up. In our study, radiotherapy was administered to a patient with BCC because of orbital invasion who did not accept surgery. Wang et al. [7] reported a 5-year recurrence rate of 5.2% for BCC and 26% for SGC. They also recommended longer follow-up because recurrences in BCC may occur later in life. Our retrospective study examining patients with a 5-year treatment and follow-up period may explain why we found no tumor recurrence. We believe that a longer follow-up period would produce a more reliable estimate of recurrence. Another important limitation of our study is that, since it was a single-center study, the number of patients was lower than in multicenter studies.

Conclusion

In our study, demographic characteristics and histopathological analysis of eyelid masses in patients diagnosed at our hospital over a 5-year period were reported. The histopathological diagnostic distribution of eyelid masses varies according to geography, as it is affected by environmental factors, such as race, age, sex, and exposure to sunlight. However, as our study supports, in many studies, malignant eyelid tumors are seen at older ages and in the lower eyelid compared to benign eyelid tumors. Because of the limited surface area of the eyelids and difficulties in reconstruction, all eyelid tumors should be identified histopathologically at an early stage. It should be noted that early diagnosis and appropriate treatment of malignant eyelid tumors can reduce the risk of cosmetic deformity and morbidity caused by these tumors.

Ethical approval

Ethical approval was received for this study from Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (numbered: 2022-347).

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