INTRODUCTION

Approximately, 5% of skin tumors occur in the eyelids.1 Periocular skin and eyelids are common sites of neoplastic lesions of the head and neck. Eyelid tumors are rarely lethal, but late diagnosis of the tumors requires more invasive surgery and consequently will have adverse esthetic effects.2 Aside from esthetic point of view, cutaneous periocular tumors can block vision or alter the normal shape of the eyelids. Malignant tumors such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC), sebaceous gland carcinoma (SGC), and malignant melanoma can affect the eyelids leading to morbidity or even mortality. Several studies have investigated the incidence, risk factors, and clinical manifestations of eyelid tumors.1,2 The incidence of eyelid skin tumors is mostly a result of environmental factors including sunlight and ultra violet exposure and genetic factors including skin pigmentation. Therefore, the prevalence of these types of tumors shows a geographical variation. The knowledge of incidence rate of various types of eyelid tumors and their clinical manifestation can be tremendously helpful in ophthalmology clinics. However, epidemiological studies on eyelid skin masses in Tehran are rare. The present retrospective study investigated the epidemiology of eyelid tumors in a tertiary referral center for ophthalmic disorders.
MATERIALS AND METHODS

This retrospective case series was based on the review of the hospital records of the patients who had undergone biopsy of their lid lesions from the year 2000 to 2010 in the oculoplastic section of Labbafinejad Medical Center, Tehran. Snellen chart was used for measurement of visual acuity and slit lamp and indirect ophthalmoscope were used for examination of the anterior and posterior segments of the eye respectively. The lesions were examined in ambient room lighting and in some cases, photographed. All benign and malignant tumors (including recurrence) were managed by surgical excision of the lesion. In cases that were suspected to be malignant or recurrent tumors, management included surgical excision of the lesion large enough to obtain tumor-free margins, confirmed by histologic examination. Furthermore in these cases, an oncology consultation was requested in order to rule out regional lymph nodes involvement and/or distant metastasis. The data sheet filled out for each patient included age, gender, occupation, the affected eye, the length of time between the onset of the disease and referral, the symptoms at each visit, visual acuity, the location and size of the lesion, the physical appearance, limitation of ocular motility, funduscopic findings, history of trauma, history of tumors in other parts of the body, type of surgical procedure and the technique for repairing the eyelid, treatment outcomes, the follow-up examinations, the recurrence of the tumor and the characteristics of the recurrent tumor. Data were analyzed with SPSS 16.0 software (SPSS Inc., IBM Corp., New York, NY, USA). \( P < 0.05 \) was statistically significant.

RESULTS

A total of 182 patient charts were reviewed comprised of 82 cases of benign tumors and 100 cases of malignant tumors. The mean age of patients with benign tumors was 46.4 ± 20.7 years. Among patients with benign tumors, 50 cases were female and other 32 were male. The most common site of involvement was the upper lid (47 cases) followed by the lower lid (24 cases), medial canthus (5 cases), lateral canthus (2 cases), and combination of these sites (4 cases). The most prevalent type of the benign eyelid masses were melanocytic nevi (35%) followed by papillomas (19.5%) and dermoid, epidermoid or inclusion cysts (11%). Some common types of benign lid tumors have been depicted in Figure 1. The detailed histological classification of the benign masses is summarized in Table 1.

In this study, 100 cases of malignant eyelid tumors were diagnosed, which consisted of 83 cases of BCC, eight cases of SCC, six cases of SGC, two cases of malignant melanoma and one case of lymphoma. Figure 2 shows some common types of malignant tumors. The mean age of patients with malignant tumors was 63.9 ± 12.5 years. Among patients with malignant eyelid tumors, 64 patients were male and 36 patients were female. Each patient had one single malignant tumor. The distribution of the malignant tumors was almost equal for the left and the right eyelids (52 cases in the left eyelid). Demographic features and location of the involvement according to the types of the malignancies are shown in Tables 2 and 3. The incidence of malignant eyelid tumors in consecutive age groups is shown in Figure 3. BCC and SCC were more frequent in patients older than 70 (31.3% and 57.1% respectively). The patients with malignant melanoma and SGC were younger than patients with BCC and SCC. All cases of malignant melanoma were in their seventh decade of their life and 50% of the SGC cases were in their sixth decade of their life. The single case of lymphoma was 71 years old.

Table 3 summarized the site of eyelid tumors in detail. Lower lid was the most common site of involvement in malignant tumors. The mean length of time between the onset of the disease and referral of the patient for benign and malignant tumors was 89.3 ± 24.0 and 18.9 ± 12.0 months respectively. Among the malignant tumors, this time was 24 months for BCC, 11.7 months for SCC, 10.2 months for SGC, 9 months for malignant melanoma and 2 months for lymphoma. The average follow-up of patients with benign and malignant tumors was 78 months with a range of 1-110 months.

Seventeen patients (10 females and 7 males) had tumor recurrence of which 16 cases were BCC and one case was SCC. Nine cases of the recurrent BCC tumors were in the lower eyelid, three cases were in the medial canthus, two cases in the upper eyelid, one case in the lower eyelid and medial canthus and one case in the lateral canthus. The single case of recurrent SCC occurred in the medial canthus. The mean follow-up for patients with recurrent tumors following the first surgery was 66 ± 14 months (range: 22-94 months).

We did not observe any significant correlation between the site of BCC and the risk of recurrence \( (P = 0.2) \). However, as shown in Figure 4, the probability of recurrence increased 1.6 times by increasing the size of tumor \( (95\% \text{ CI}: 0.9-2.6) \), but a statistically non-significant correlation existed between the size of primary BCC and the risk of recurrence \( (P = 0.07) \).

The recurrence risk was higher in older patients and 75.6% of recurrences were among patients older than 70 (Pearson test, \( r = 0.36 \) and \( P = 0.03 \)). The length of time between the onset of the primary lesion and referral was 24.1 ± 7.5 months in patients with recurrent tumor and 24 ± 8.3 months for patients with non-recurrent tumor \( (P = 0.4) \). There was no significant correlation between gender and the risk of recurrence \( (P = 0.8) \).

The single case of SCC recurrence was in the lower eyelid and medial canthus of a 72-year-old male that happened 1 year after the surgical removal of the tumor. We did not observe any cases of lymph node enlargement or distant metastasis in our series.
DISCUSSION

Eyelid masses are one of the most common pathology examined by ophthalmologists. Between 2000 and 2010, 182 patients were referred to our clinic for eyelid masses of which 82 (45.05%) cases were benign tumors. Even though, benign tumors are the most frequent type of eyelid tumors in the general population, we observed a higher rate of malignant cases in our series. Most patients are referred to our clinic due to suspicions lesions that may be malignant or when a major surgical reconstruction is
necessary. Hence, this likely explains the over-presentation of malignant cases in our study.

In this series, the most common benign tumors were nevi (35%), squamous papillomas (19.5%) and dermoid or epidermoid cysts (11%). Different studies have reported various frequencies of benign tumors some of which are similar to our series. For example, 3 separate studies from China, Southern Taiwan and South Korea the most frequent benign tumors were, in descending order, nevus, papilloma, and cyst. The most prevalent benign masses in the studies by Kersten et al. and Ni were papilloma. In the study by Hsu and Lin the most frequent type of benign tumors in patients was dermoid cysts. In a survey from Saudi Arabia, the most common benign mass was hidrocystoma followed by chalazion. Some of these disparities are interesting due to demographic differences. For instance, in Hsu and Lin’s study that reported dermoid cysts as the most frequent tumor, only pediatric and adolescent patients below 17 years were investigated. Certain geographic and climate conditions can also influence the frequency of different types of eyelid masses, for example, the higher incidence of hidrocystoma in a Saudi study is attributed, by the author, to the warm climate and excessive activity of sudoriferous glands in the inhabitants of this region.

In our study, the mean age of patients with benign eyelid tumors was 47 years and they were more prevalent among females with greater involvement of the upper eyelid (57%). In the study of over 5,500 cases of eyelid skin tumors in a Swiss cohort, 84% were benign tumors, the most common being squamous papilloma followed by seborrheic keratosis. The mean age in these two common types of benign tumors were 56 years and 69 years, respectively. The gender distribution in most cases of benign epidermal masses was equal. There was greater involvement of the upper eyelid in some pathologic lesions including papilloma, inverted follicular keratosis and dermoid cysts. Keratoacanthoma, solar keratosis and Bowen’s disease were more common in the lower eyelid and in several cases both eyelids were equally involved. In a similar study from Thailand, 51% of benign tumors originated from the upper eyelid. Similarly, a study from Southern Taiwan reported 46% of benign cases were located in the upper eyelid. In contrast, a Chinese study, reported the lower eyelid was involved slightly more frequently than upper eyelid.

The three most common malignant tumors in our study were BCC (83%), SCC (8%), and SGC (6%). Studies from other countries have reported difference types and frequencies of malignant eyelid tumors, some of these reports have been concised in Table 4.

In most of the studies from other countries, BCC is the most frequent malignant tumor of the eyelid. Of note, the frequency of SGC is higher in Asian countries. However, in most Western countries, more than 85% of the cases are BCC. Genetic factors, ethnicity, geographical region, latitude, and people protecting themselves from sunlight can influence the prevalence of different types of eyelid tumors.

In the present study, the mean age of patients with malignant tumors was above 60. This finding is in agreement with most of the aforementioned studies as well as the study by Vitaliano and Urbach who consider age an important risk factor in non-melanoma skin tumors. In our series, two patients under 40 and 13 patients under 50 had BCC. Similar incidences of BCC have been reported in other studies in younger patients. Genetic abnormalities and rare syndromes such as basal cell nevus syndrome and xeroderma pigmentosum are possible among these younger patients with malignant eyelid tumors.

In general, 20% of BCC occur in the periorcular area of which half of the cases present in the lower eyelid, one-third in the medial canthus, 15% in the upper eyelid and 5% in the lateral canthus. Similarly, in the present study, most (61.4%) cases of BCC were in the lower eyelid. However, the incidence of BCC was lower in medial canthus compared to most of the other studies. In our study, the incidence of BCC in the medial canthus and lateral canthus was similar.

In this study, the longest period between the onset of disease symptoms and referral was that of BCC (24 months) and the shortest time was related to lymphoma. In general, BCC progress very slowly and is asymptomatic in the early phase. These tumors can appear as a pearly nodule accompanied by a central depression.

### Table 2: The demographic features of patients with malignant eyelid tumors

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>BCC</th>
<th>SCC</th>
<th>SGC</th>
<th>Malignant melanoma</th>
<th>Lymphoma</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean±SD)</td>
<td>63±12</td>
<td>73±9</td>
<td>62.3±13</td>
<td>67±4.2</td>
<td>71±0</td>
<td>0.342*</td>
</tr>
<tr>
<td>Median (range)</td>
<td>63 (25-100)</td>
<td>71.5 (59-89)</td>
<td>57 (50-82)</td>
<td>67 (64 and 70)</td>
<td>0</td>
<td>&gt;.999+</td>
</tr>
<tr>
<td>Male (%)</td>
<td>65.1</td>
<td>47.2</td>
<td>50</td>
<td>50</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Duration between onset to refer (months) Mean±SD</td>
<td>24±39.8</td>
<td>11.7±6.4</td>
<td>10.2±4</td>
<td>9.0</td>
<td>2.0±0</td>
<td>0.962*</td>
</tr>
<tr>
<td>Median (range)</td>
<td>12 (1-300)</td>
<td>12 (3-24)</td>
<td>12 (3-12)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on Kruskal-Wallis test, +Based on Chi-square test. SD: Standard deviation, P<0.05 is statistically significant, BCC: Basal cell carcinoma, SCC: Squamous cell carcinoma, SGC: Sebaceous gland carcinoma.
with fine telangiectasia and minimal ulceration. BCC lesions can manifest with typical appearance such as nodular, pigmented, ulcerous, and morphea-form. The most common type is the nodular BCC. Similar to our study, Takamura and Yamashita reported that BCC had the longest time between the onset of the disease and referral (40 months) followed by SGC (11 months), SCC (10 months) and finally lymphoma (1 month). Commonly, BCC patients are aware of the presence of a lesion for an extended period of time before visiting a physician and diagnosis. According to one study, 15 such patients were aware of a lesion at least 5 years prior to diagnosis. Therefore, due to the slow progression of BCC, a prompt biopsy of any eyelid lesion is highly recommended.

In the present study, with a mean of 6.5 years follow-up of patients, there were 16 recurrent cases of BCC and one case of recurrent SCC. The risk factors for recurrence of tumors in previous studies include the size of the primary tumor (recurrence is more than 40% in tumors larger than 2 cm and is less than 10% in tumors smaller than 2 cm), the type and the shape of the lesion and the site of the tumor in the medial canthus. The treatment strategy can also influence the recurrence rate. In our study, with four cases of tumors in the medial canthus, three recurred (75%). The recurrence rate for the tumors in the lower eyelid was 14% in our study. In addition, recurrence was related to the size of the primary tumor. In agreement with the findings of other studies, we observed that the risk of recurrence increases with increasing size of the primary tumor.

In a comprehensive review published in 1989, all the studies related to BCC were analyzed. According to the finding of this review, less than one third of the recurrent cases occur in the 1st year after surgery. Nearly, 50% of the recurrent cases occur within the 2nd year and two-thirds occur within the first 3 years postoperatively. Another finding was that the recurrence rate in a 10-year follow-up is twice the rate of 2-year follow-up and 18% of recurrence occurs between the 5th year and the 10th year. Thus, these results provide evidence for the importance of the long-term follow-up of the patients specially the patients with risk factors for recurrence. In addition, diagnosis of recurrence is tremendously important within the first few years after surgery, as the risk of recurrence is higher during this time.

Our research is the first epidemiological study of eyelid skin masses in Tehran. Due to the difference of available statistical data depending on the country and geographical region, our data provides novel information regarding demographic and histological features of eyelid tumors in our region. These epidemiological studies are extremely beneficial for the practicing ophthalmologists and the training residents and also for public health-care planning. In addition, our study highlights the importance of future research in this field and the benefits of standardized data collection techniques.

### REFERENCES


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