Clinical-pathological characteristics of patients treated for cancers of the eyelid skin and periocular areas

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Abstract

Background. Malignant cancers of the eyelid skin and the periocular area comprise 5–10% of facial skin malignant cancers. Basal cell carcinomas (BCCs) dominate, comprising approx. 80–90% of cancers of this area of the face. Considerably less often, in 9–14% of cases, squamous cell carcinomas (SCCs) are observed.

Objectives. The aim of this study is to provide an epidemiological-clinical assessment of patients treated over the period 2006–2015 for primary malignant cancers of the eyelid skin considering histological diagnosis and clinical staging.

Material and methods. This study was based on an analysis of the medical records of 262 patients. Demographic data, age, sex, size and location of lesions, histological types, and clinical staging were assessed.

Results. In the analyzed group of 262 patients, most were over the age of 60 years. Primary cancers were most frequently located in the area of the medial canthus of the eye and in the lower eyelid skin. They were mainly lesions of 6–10 mm and 16–20 mm with histologically diagnosed basal cell carcinoma of nodular and cystic types.

Conclusions. The most represented group was that of patients aged 60–70 years with primary cancers located in the medial canthus of the eye (47.3%) and in the lower eyelid. Basal cell carcinoma was diagnosed, mainly nodular and cystic types.

Key words: skin, malignant tumor, eyelid, epidemiological studies

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(<5 mm) of the benign lump type in cases where histopathological examination of the material suggested the presence of basal cell carcinoma. Over time, an increase in the number of patients with eyelid skin cancer was observed. The statistical analysis of the material did not confirm a statistically significant relationship between the increase in the number of patients treated in particular 10-year age brackets and their sex. The difference between the number of patients in subsequent age brackets and the previous age bracket was statistically insignificant. Patients were referred for surgical treatment mostly by dermatologists, ophthalmologists, oncologists, general practitioners, and maxillofacial surgeons.

Patients admitted to the Clinic did not report any complaints, including pain, in most cases. The reason for being referred for treatment were mostly non-healing skin ulcerations and periocular tissue wounds, visual impairment caused by a growing tumor mass obscuring the field of vision, bleeding, and, rarely, aesthetic reasons.

In the case of 124 patients, who constituted 47.3% of patients, primary cancers were located in the area of the medial canthus of the eye, while in the case of 83 patients (31.7%) they concerned the lower eyelid. In 26 patients (9.9%), it was the upper eyelid, while in 29 patients (11.1%), lesions were located in the area of the lateral canthus of the eye.

The statistical analysis of the data shows that the occurrence of cancers in the area of the medial canthus of the eye was considerably more frequent than in the remaining areas, which was statistically confirmed ($p < 0.05$).

The sizes of lesions in several cases varied between less than 5 mm, found in 22 patients (8.4%), to more than 20 mm. Cancers ranging in size between 6 and 10 mm were treated most often (in 113 patients; 43.1%). Lesions between 11 and 15 mm were present in 40 patients (15.3%), whereas those between 16 and 20 mm occurred in 67 cases (25.5%). Lesions larger than 20 mm which spread into the surrounding tissues were found in 7 patients (2.8%). The statistical analysis

shows that the differences in the frequency of eyelid primary cancers between 6 and 10 mm in size were statistically significant ($p < 0.05$) in comparison with the remaining eyelid and periocular area cancerous lesion sizes.

On the basis of clinical examination and histopathological verification, BCCs were observed most frequently, namely, in 213 patients (81.4%), while SCCs were found in 38 patients (14.5%). In 8 cases, i.e., 3.0%, eyelid adenocarcinomas were present, whereas 3 patients (1.1%) were diagnosed with eyelid skin malignant melanomas. The occurrence of BCC cancer was 4 times higher than the remaining types of malignant periocular area skin cancers.

An assessment of the patients with regard to the relationship between the type of malignant cancer and its location was conducted. Basal cell carcinomas were most frequently located in the medial canthus of the eye (in 102 patients; 47.9%), while in 68 cases (31.9%), it was found in the lower eyelid. The outbreak of BCCs in the upper eyelid affected 23 patients (10.8%), while 20 patients (9.4%) had it in the lateral canthus of the eye. Squamous cell carcinomas were also most often located in the medial canthus of the eye (in 17 patients; 44.7%), while in 11 patients (28.9%), it was located in the lower eyelid. Table 3 presents data regarding the relationship between the type of malignant cancer and its location with respect to the histopathological diagnosis, which shows that both BCCs and SCCs were mostly located in the medial canthus of the eye and concerned the lower eyelid.

The statistical analysis of the data regarding location shows that there are no statistically significant differences between the type of malignant cancer confirmed by histopathological examination and its location in periocular tissues ($p = 0.6134$).

Over the period 2006–2015, a total of 213 patients were treated at the clinic for different types and forms of eyelid and periocular area BCC. Data regarding the particular forms of BCC is presented in Table 4.

Table 3. Location and histopathological type of malignant cancer

Location	SCCs	BCCs	Adenocarcinoma	Melanoma malignum	Total
Lower eyelid; n (%)	11 (28.9)	68 (31.9)	2 (25.0)	2 (66.7)	83 (31.7)
Upper eyelid; n (%)	2 (5.3)	23 (10.8)	1 (12.5)	0	26 (9.9)
Medial canthus; n (%)	17 (44.7)	102 (47.9)	4 (50)	1 (33.1)	124 (47.3)
Lateral canthus; n (%)	8 (21.1)	20 (9.4)	1 (12.5)	0	29 (11.1)
Total; n (%)	38 (100)	213 (100)	8 (100)	3 (100)	262 (100)
p-value	$\chi^2(9) = 7.23$; $p = 0.6134$				

SCCs – squamous cell carcinomas; BCCs – basal cell carcinomas.

Table 4. Occurrence of particular BCC forms in the group of treated patients

Number	Morphological types of BCCs				
	nodular	ulcerative	cystic	cicatricial	pigmented
213	90 (42.2%)	21 (9.8%)	81 (38.0%)	13 (6.1%)	8 (3.9%)

BCCs – basal cell carcinomas.

Table 5. Type of BCCs depending on location

Location	Morphological types of BCCs				
	nodular n (%)	ulcerative n (%)	cystic n (%)	cicatricial n (%)	pigmented n (%)
Lower eyelid	23 (33.8)	18 (26.5)	18 (26.5)	7 (10.3)	2 (2.9)
Upper eyelid	11 (47.8)	3 (13.0)	7 (30.4)	2 (8.7)	0
Medial canthus	51 (50)	0	46 (45.1)	3 (2.9)	2 (2.0)
Lateral canthus	5 (25.0)	0	10 (50.0)	1 (5.0)	4 (20.0)
Total	90 (42.3)	21 (9.9)	81 (38.0)	13 (6.1)	8 (3.8)
p-value	$\chi^2(12) = 60.13; p = 0.0000$				

BCCs – basal cell carcinomas.

Most often, in a total of 90 patients (42.2%), the nodular form of BCC was diagnosed, while there were 81 cases (38.0%) with the cystic form of BCC. The pigmented form of BCC found in 3.9% of patients was the least frequently represented. The primary cancers of BCC in an ulcerative form were present in 21 patients (9.8%), while 13 patients (6.1%) suffered from the cicatricial type of BCC. The frequency of occurrence of the nodular and cystic forms in the analyzed material was similar. There were no statistically significant differences between the occurrence of these 2 forms ($p = 0.2880$). The nodular and cystic forms occurred statistically more frequently than the remaining variants of BCC. With respect to the further ulcerative form, in terms of occurrence, the difference was statistically significant for both the nodular type ($p = 0.0027$) and the cystic type ($p = 0.0069$). The statistical analysis shows that the nodular and cystic forms of BCC occurred considerably more frequently in the periocular area than did the remaining variants of BCC.

A detailed assessment of the particular morphological forms of BCC shows that the lower eyelid was the location of mainly nodular and cystic lesions which, together with the cicatricial forms, accounted for more than 80% of cases. The lesions located in the upper eyelid were the most common nodular variations (in 47.8% of cases). In the medial canthus of the eye area, the nodular form also occurred most frequently (in 51 patients), while the cystic form was diagnosed in 46 patients (45.1%). The cicatricial and the pigmented forms were mostly located in the lateral canthus area of the eye. The material presented indicates that the differences in the occurrence of the types and forms of BCC cancer were significantly related to their location ($p = 0.0000$). The abovementioned data is presented in Table 5.

Over the period 2006–2015, 38 patients with SCCs of the periocular area skin were treated. The degree of histo-

pathological differentiation according to the Broder's scale regarding the percentage of mature, differentiated cells and atypical cells is shown in Table 6. Most frequently, in 19 patients, forms of well-differentiated cancer cells (G1) were observed; 13 patients (34.9%) were diagnosed with cancer of type G2 (moderately differentiated) and 6 patients (15.8%) had a poorly differentiated type of cancer (G3). There were no anaplastic SCCs (type G4) in the discussed material.

The statistical analysis demonstrates that differences in the occurrence of particular stages of histologically mature SCCs located in the periocular area were not statistically significant ($p > 0.05$).

On the basis of the simplified TNM classification (feature T), developed by the Union of International Cancer Control (UICC), the clinical staging of eyelid skin cancer was assessed.² In the analyzed group, the most frequent were outbreaks of cancer in stage $T_2M_0N_0$ (43.1%). Tumors in stage $T_3M_0N_0$ were operated on in 40.8% of patients. Stage $T_1M_0N_0$ was treated in 35 patients (13.3%). The analysis confirmed that the differences in the occurrence of eyelid skin cancers in clinical stages ranging from T_1 and T_2 , T_1 and T_3 , T_1 and T_4 , T_2 and T_4 , T_3 and T_4 were statistically significant. A detailed overview of the clinical staging of eyelid cancers is included in Table 7.

It seemed of interest whether there is a relationship between the clinical staging of malignant skin cancers (TNM) and their location in the periocular area. In the analyzed group of patients, the malignant cancers located in the medial canthus area of the eye were the most frequently operated on (in the cases of 124 patients [47.3%]). They were mostly in the T_3 and T_4 clinical stages. In this location, there were also 3 patients in the T_4 stage who required a wide-margin excision of tissues surrounding the cancer. Detailed data regarding the relationship between

Table 6. Broder's eyelid SCC differentiation stages

Number	Differentiation stages of SCCs		
	G ₁	G ₂	G ₃
38 (100.0%)	19 (50.0%)	13 (34.2%)	6 (15.8%)
p-value	$p_{G_1-G_2} > 0.05; p_{G_1-G_3} > 0.05; p_{G_2-G_3} > 0.05$		

SCCs – squamous cell carcinomas.

Table 7. Clinical staging of eyelid cancers according to the TNM classification

Number	T ₁ N ₀ M ₀	T ₂ M ₀ N ₀	T ₃ M ₀ N ₀	T ₄ M ₀ N ₀
262 (100%)	35 (13.3%)	113 (43.1%)	107 (40.8%)	7 (2.8%)
p-value	$p_{T_1-T_2} < 0.05; p_{T_1-T_3} < 0.05; p_{T_1-T_4} < 0.05; p_{T_2-T_4} < 0.05; p_{T_3-T_4} < 0.05; p_{T_2-T_3} > 0.05$			

Table 8. Clinical stage depending on primary outbreak location

Location	Clinical stage according to feature T				
	T ₁	T ₂	T ₃	T ₄	total
Medial canthus; n (%)	10 (28.6)	52 (46.1)	59 (55.3)	3 (42.8)	124 (47.3)
Lateral canthus; n (%)	0	17 (15.1)	11 (10.2)	1 (14.3)	29 (11.1)
Lower eyelid; n (%)	9 (25.7)	35 (31.0)	37 (34.5)	2 (28.6)	83 (31.7)
Upper eyelid; n (%)	16 (45.7)	9 (7.8)	0	1 (14.3)	26 (9.9)
Total; n (%)	35 (100.0)	113 (100.0)	107 (100.0)	7 (100.0)	262 (100.0)
p-value	(p > 0.05)				

the clinical staging and the location of the cancers is shown in Table 8.

The differences in the occurrence of the particular clinical stages of cancers and their location were not statistically significant ($p > 0.05$).

Discussion

In the analyzed group of patients operated on at the Department of Maxillofacial Surgery of the Frederic Chopin Clinical Regional Hospital in Rzeszów, the dominant group were patients aged over 60 years, which is in accordance with the epidemiological data published by other authors and regarding not only primary cancers, but also the recurrence of facial skin malignant cancers.^{13,14}

The most frequently histologically diagnosed eyelid skin cancer in the examined group was BCC, which occurred in 81.4% of patients. A similar frequency of occurrence was noted by Spiteri and McCormick, as well as Allali et al.^{1,15} Among the excised BCCs, the most often diagnosed form were the nodular and cystic variations, which were found in 38.0% of patients. This was confirmed by statistical analysis. Similar results were obtained by Ben Simon et al.^{8,14}

The nodular and cystic types of BCC occurred considerably more often in the medial canthus area of the eye in comparison to the remaining periocular areas. The location was the medial canthus of the eye in the examined group in 47.3% of the overall number of periocular area tumors operated on. The results of these examinations are compliant with the observations published by Ilijn et al.^{6,10,13}

An analysis of our own material shows that the largest group were the cancers with diameters ranging from 10 to 20 mm and classified as T₂ or T₃ according to the UICC classification. This may result from the characteristics of the patients who qualified for surgical treatment at the Department. They were patients aged over 60 years, mostly afflicted with ailments and diseases of other systems. Minor lesions are mostly operated on at dermatological, laryngological and general surgery clinics. Histopathological verification of the excised eyelid tumors allowed for a diagnosis of SCC in 38 patients (14.5%) with dominant, well-differentiated G₁ cancer constituting 50%

of histological diagnoses. There was no statistically significant correlation between the clinical stage of the SCC and the location of the tumor. The results obtained from these observations correspond with the publication published by Nemet's and Donaldson's teams.^{9,10} On the basis of the retrospectively studied characteristics of the treated patients, the following conclusions are presented.

Conclusions

Between 2006 and 2015, 262 patients were treated for periocular area skin cancers at the Department of Maxillofacial Surgery of the Frederic Chopin Clinical Regional Hospital in Rzeszów. They represent 12.7% of all patients hospitalized due to head and neck skin cancers at that time.

The most represented group (45.3%) was that of patients aged between 60 and 70 years.

Primary cancers were mostly located in the medial canthus of the eye (47.3%) and in the lower eyelid (31.7%).

In 81.4% of treated patients, BCCs of mainly nodular and cystic types were diagnosed, while 14.5% of patients had SCCs.

The majority of the treated patients were diagnosed with cancer outbreaks in the T₃ (16–20 mm) and T₂ (6–10 mm) clinical stages.

References

1. Spiteri N, McCormick A. Periocular basal cell carcinoma. *OiP*. 2013;14: 97–106.
2. Wang CJ, Zhang HN, Wu H, et al. Clinicopathologic features and prognostic factors of malignant eyelid tumors. *Int J Ophthalmol*. 2013;6(4):442–447.
3. Coroi MC, Roșca E, Mușiu G, Coroi T, Bonta M. Eyelid tumors: Histopathological and clinical study performed in County Hospital of Oradea between 2000–2007. *Rom J Morphol Embryol*. 2010;51(1):111–115.
4. Cook BE, Bartley GB. Treatment options and future prospects for the management of eyelid malignancies. *Ophthalmology*. 2001;108(11): 2089–2098.
5. Cook BE Jr, Bartley GB. Epidemiologic characteristics and clinical course of patients with malignant eyelid tumors in an incidence cohort in Olmsted County, Minnesota. *Ophthalmology*. 1999;106(4): 746–750.
6. Esmali B, Wang B, Deavers M, et al. Prognostic factors for survival in malignant melanoma of the eyelid skin. *Ophthalmic Plast Reconstr Surg*. 2000;16(4):250–257.
7. Hamada S, Kersey T, Thaller VT. Eyelid basal cell carcinoma: Non-Mohs excision, repair and outcome. *Br J Ophthalmol*. 2005;89(8):992–994.

8. Kale SM, Patil SB, Khare N, et al. Clinicopathological analysis of eyelid malignancies: A review of 85 cases. *Indian J Plast Surg.* 2012;45(1): 22–28.
9. Nemet AY, Deckel Y, Martin PA, et al. Management of periocular basal and squamous cell carcinoma: A series of 485 cases. *Am J Ophthalmol.* 2006;142(2):293–297.
10. Donaldson MJ, Sullivan TJ, Whitehead KJ, Williamson RM. Squamous cell carcinoma of the eyelids. *Br J Ophthalmol.* 2002;86(10):1161–1165.
11. Vaziri M, Buffam FV, Martinka M, Oryschak A, Dhaliwal H, White VA. Clinicopathologic features and behavior of cutaneous eyelid melanoma. *Ophthalmology.* 2002; 109(5):901–908.
12. Burns SJ, Foss AJ, Butler TK. Outcome of periocular sebaceous gland carcinoma. *Ophthalmic Plast Reconstr Surg.* 2005;21(5):353–355.
13. Iljin A, Zieliński T, Antoszewski B, Sporny S. Clinicopathological analysis of recurrent basal cell carcinoma of the eyelid. *Postepy Dermatol Alergol.* 2016;33(1):42–46.
14. Ben Simon GJ, Lukovetsky S, Lavinsky F, Rosen N, Rosner M. Histological and clinical features of primary and recurrent periocular basal cell carcinoma. *ISRN Ophthalmology.* 2012:354829.
15. Allali J, D'Hermies FD, Renard G. Basal cell carcinomas of the eyelids. *Ophthalmologica.* 2005;219(2):57–71.