

ORIGINAL PAPER

Eyelid tumors: histopathological and clinical study performed in County Hospital of Oradea between 2000–2007

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Abstract

The work assessment is to analyze eyelid tumors diagnosed in the last years in our hospital. We found 471 tumoral and pseudotumoral cases, in which malignant tumors predominated, with 255 cases. The most affected age range was the sixth decade and the majority of tumors were located to lower eyelid. The histopathological study allowed us to establish the lesions type and subtype. The Meibomian gland cysts, squamous papillomas and basal cell carcinomas were the most frequent related with this three of category lesions represented by pseudotumors, benign tumors and malignant tumors. Early diagnosis of these lesions can determine a favorable prognosis, especially in cases of malignant tumors.

Keywords: eyelid, pseudotumors, benign tumors, malignant tumors.

☐ Introduction

The eyelid neoplastic pathology is very polymorphic and mostly based on different types of skin cancer (basal cell carcinoma, squamous carcinoma, accessory glands carcinomas, and malignant melanoma). Many cutaneous and eyelid diseases are quite similar because of the common ontogenetic origin. Ninety percent of skin cancers arise to head and neck and 10% from them are located at eyelid level [1].

The eyelid tumors are the most frequent neoplasms in ophthalmologic practice, including a large variety of benign or malignant tumors. This lesions represents 15% of face tumors and 5–10% from all cutaneous tumors. The maximum incidence is after 60-year-old and the most tumors are situated in the lower eyelid and internal canthus [2]. Although the clinical and histopathological aspects are polymorphic, the most frequent benign tumors are the papillomas and the most common malignant eyelid tumor is basal cell carcinoma [3–7].

Tumoral eyelid lesions, especially the malignant ones, represent an interdisciplinary pathology like general medicine, dermatology, maxillofacial plastic surgery and ophthalmology. All these have the responsibility for an early diagnosis, which is the prognostic of malignant lesions key.

☐ Material and Methods

We accomplished a retrospective analysis of eyelid tumors from the in-patients of County Hospital of Oradea in the last eight years, between 2000–2007. The biological material comprised a number of 471 pseudotumors and eyelid tumors. We analyzed the both sex and age distribution of lesions, the location, clinical diagnosis and histopathological result of tumors. The retrospective cases were selected from the eyelid casuistry lesions of the Pathology Lab in the same hospital. The new cases were processed by common histopathological technique using formalin fixation, paraffin embedding and Hematoxylin–Eosin staining.

The aim of histopathological analysis was to establish the type and subtype for the benign lesions, and the depth of invasion, the status of safety surgical borders, the presence of metastasis for malignant tumors.

☐ Results

The study comprised 471 cases, in which we found 114 pseudotumors, 102 benign tumors and 225 cases of malignant tumors (Table 1).

Related to gender, 259 cases (54.9%) were male and 212 cases (45.1%) were female patients. It was a little predominance for the male patients, more pronounced in malignant tumor cases.

Table 1 – The distribution of eyelid lesions types

Lesion	Pseudotumors	Benign tumors	Malignant tumors
No. of cases	114	102	255
%	24.2	21.6	54.2

The mean age of patients group was 49.5 years with range between 11–88-year-old. The pseudotumoral lesions were more frequent in younger patients, prevailing in the fourth decade. In the fourth and fifth decade, we found the majority of benign tumors, and in the fifth and sixth decade the malignant tumors ones (Table 2).

Table 2 – The distribution of pseudotumors and eyelid tumors based on age

Decade [years]	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90
Pseudotumors	5	17	34	20	23	8	4	3
Benign tumors	2	11	32	28	12	8	9	–
Malignant tumors	–	–	35	73	76	42	29	–

The topography analysis of lesions showed the frequency of locations: 222 cases at lower eyelid, 201 cases at upper eyelid, 34 cases at internal canthus and nine cases at external canthus level (Table 3).

Table 3 – The topography of eyelid lesions

Location	Lower eyelid	Upper eyelid	Internal canthus	External canthus
Pseudotumors	31	75	6	2
Benign tumors	45	54	3	–
Malignant tumors	146	77	25	7
Total	222	206	34	9

From the 255 malignant tumor cases, which were histopathologically diagnosed, 241 cases were clinically suspected of malignant lesions, with a diagnosis accuracy of 94.5%. The histopathological study of cases allowed us to establish the lesions type and subtype.

The most analyzed eyelid pseudotumors had a clinical diagnosis of eyelid cystic tumor and we found them in almost all life decades, the majority being in the sixth decade. The most common location was on upper eyelid (75 cases), with a predominance for male patients (40/35). The histopathological analysis revealed Meibomian gland cysts in 30 cases (6.3%), Zeiss gland cysts

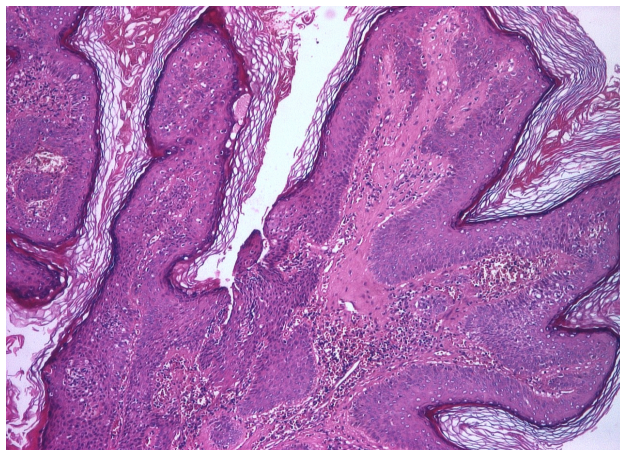
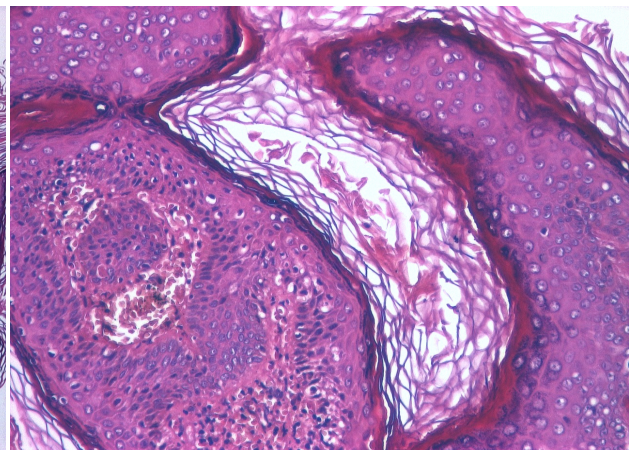
in 25 cases (5.2%), epidermal cysts in 18 cases (18.3%) and xantelasma in 41 cases (8.7%).

Histopathologically speaking, the majority of benign eyelid tumors were squamous papillomas (84 cases), followed by seborrheic keratosis, acantholytic and hyperkeratotic types (11 cases), dermic nevocellular nevus (five cases) and capillary hemangiomas (two cases) (Figures 1 and 2).

The malignant eyelid tumors were represented by basal cell carcinoma with 185 cases (39.2%), squamous carcinoma with 50 cases (10.5%), sebaceous carcinoma in five cases (1.1%) and malignant melanoma in 15 cases (3.2%).

The topography of basal cell carcinomas was on lower eyelid in 112 cases, upper eyelid in 67 cases and internal canthus in six cases. These tumors were diagnosed in patients with ages between 28–87-year-old, with the same frequency for males and females. The most common histopathological aspect was represented by solid growth pattern with different associated tumoral subtypes, like cystic or keratinization pattern, and rarely with pigmented areas or even marked stromal sclerosis like in morpheaform type. The surgery borders of resection were non-invaded in 147 cases, one of them was invaded in 18 cases, and the both were invaded in six cases (Figures 3 and 4).

Squamous cell carcinomas were diagnosed in 50 cases, having clinical diagnoses of vegetative or ulcero-vegetative malignant eyelid tumors. In six cases was not any clinical suspicion about a malignant tumor. The lesions predominate to male patients (28/22), with an incidence peak in sixth decade of life. The tumors were located in most cases at lower eyelid level with 29 cases. Histopathological aspects corresponded to well differentiated tumors in 37 cases, moderately differentiated in seven cases and poorly differentiated lesions in six cases. The depth of invasion analysis revealed microcarcinoma in three cases, frank invasive carcinoma without metastatic adenopathy in 41 cases, and invasive carcinoma with metastatic adenopathy in six cases. Invasion was absent to the surgery borders of resection in 46 cases and it was present in four cases, whereby two cases with the both invaded borders (Figures 5 and 6).

**Figure 1 – Eyelid squamous papilloma (HE stain, ob. 4×).****Figure 2 – Eyelid squamous papilloma (HE stain, ob. 10×).**

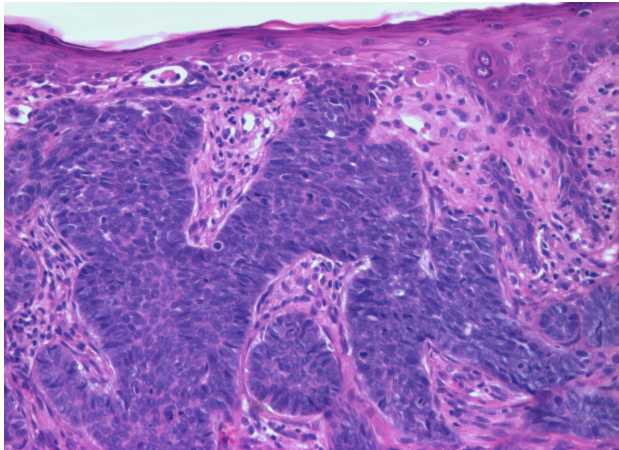


Figure 3 – Basal cell carcinoma (HE stain, ob. 10×).

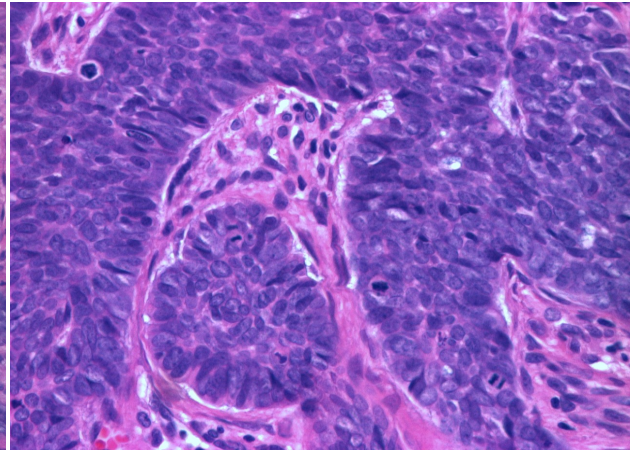


Figure 4 – Basal cell carcinoma (HE stain, ob. 20×).

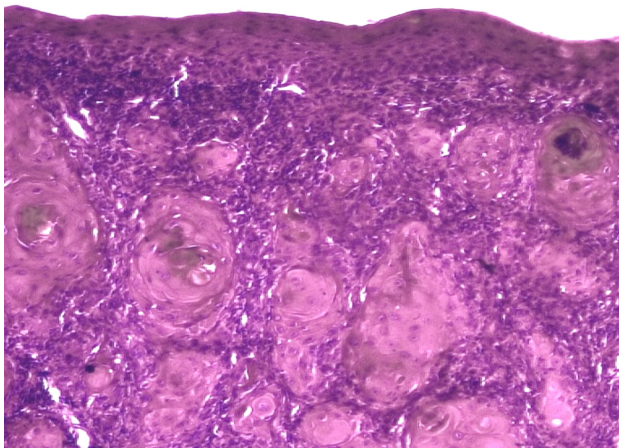


Figure 5 – Moderately differentiated squamous cell carcinoma (HE stain, ob. 4×).

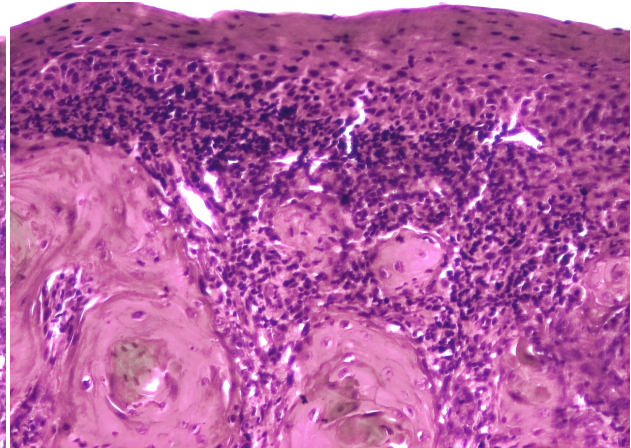


Figure 6 – Moderately differentiated squamous cell carcinoma (HE stain, ob. 10×).

Malignant eyelid melanoma were diagnosed in 15 cases, with casual predominance of male patients (8/7). The most affected age range was the sixth one and the predominant location was upper eyelid one. These tumors presented mixed cellularity (epithelioid and fusiform cells) and a medium degree of pigmentation. Based on depth of invasion we attained the cases distribution as follows: nine cases in Clark III stage and six cases in Clark IV stage. One of the surgery safety borders was invaded in two cases. No case we found with metastasis at the diagnosis moment.

We found few cases of sebaceous carcinomas (five cases), which represented 1.1% from all analyzed tumors and 1.1% from the malignant ones. The tumors were diagnosed between sixth and eighth decade, with an around equal distribution related to gender (3/2). In all cases, the location was the upper eyelid one. All tumors were histopathologically well differentiated, with typical aspect and lobular growth pattern, with the sebaceous differentiation and comedonecrosis presence in centre of neoplastic lobules (Figures 7 and 8).

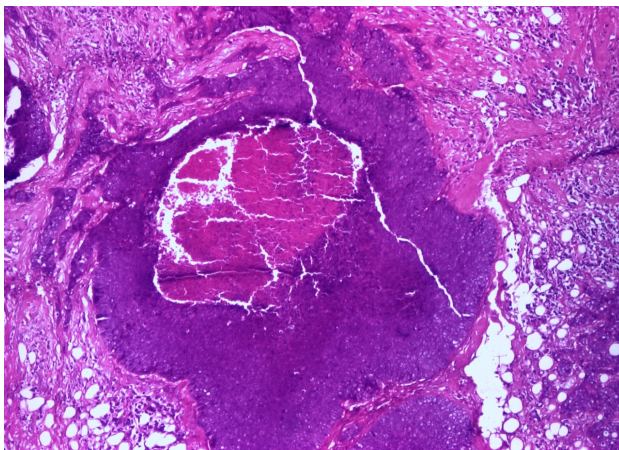


Figure 7 – Meibomius gland carcinoma with comedonecrosis (HE stain, ob. 4×).

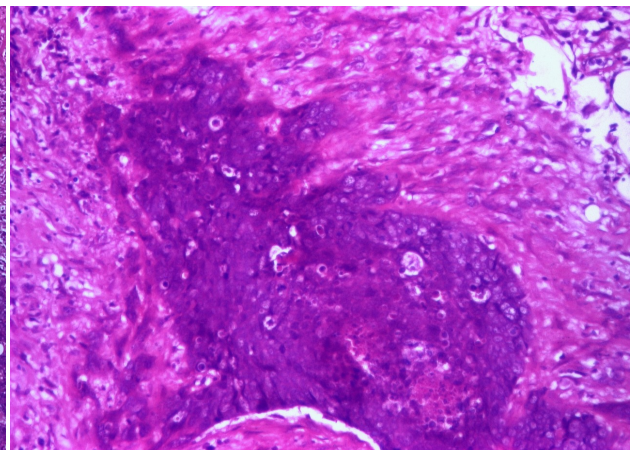


Figure 8 – Meibomius gland carcinoma with sebaceous differentiation (HE stain, ob. 10×).

Discussion

For the eyelid tumors we studied, we identified pseudotumors in 114 cases, benign tumors in 102 cases and 255 cases of malignant tumors. The benign lesions (pseudotumors, benign tumors) represented 45.8% from all cases, unlike malignant ones, which were encountered in 54.2% cases. Pornpanich K *et al.* [6] found also that the majority of eyelid lesions were benign eyelid tumors while malignant eyelid tumors contributed 10.8% of the total eyelid lesions. Another recent study indicated an absolute predominance of benign tumors from malignant ones, representing 84% from all cases [7].

The topography analysis of eyelid neoplastic lesions, showed that the most common location was lower eyelid (222 cases), followed by upper eyelid (206 cases), internal canthus (34 cases) and external canthus (nine cases). In literature data, tumors developed more commonly in the lower (37.0%) than the upper eyelid (33.9%) [8]. Tumors developed most commonly on the lower eyelid ($n=85$; 48.9%) and in the medial canthal region ($n=48$; 27.6%), but involved the right and left sides with equal frequency [9].

The neoplastic benign lesions were represented by squamous papillomas in 84 cases, seborrheic keratosis in 11 cases, dermic nevocellular nevus in five cases and capillary hemangiomas in two cases. The 255 cases of malignant lesions comprised basal cell carcinomas for 185 patients (39.2%), squamous cell carcinomas in 50 cases (10.5%), sebaceous carcinoma in five cases (1.1%) and malignant melanoma in 15 cases (3.2%).

Many trials studied the incidence of eyelid tumors with different histopathological types. A recent study with a large casuistry, including 5504 tumors, indicated that 86% were benign tumors, the most frequent being squamous cell papilloma (26%) seborrheic keratosis (21%), melanocytic nevus (20%), hidrocystoma (8%), and xanthoma/xanthelasma (6%) [7]. In the same study, malignant neoplasms were represented by basal cell carcinoma (86%), followed by squamous cell carcinoma (7%) and sebaceous carcinoma (3%).

Another retrospective study recorded in five years (2000–2004), 53 (17.8%) inflammatory conditions, 212 (71.4%) benign eyelid tumors and 32 (10.8%) malignant eyelid tumors, included 13 sebaceous gland carcinomas, 12 basal cell carcinomas, three malignant melanomas, two squamous cell carcinomas, one apocrine adenocarcinoma and one metastatic carcinoma [6].

Wang JK *et al.* [8], analyzing 127 eyelid cancers, found 79 basal cell carcinomas (62.2%), 30 sebaceous gland carcinomas (23.6%), 11 squamous cell carcinomas (8.7%), five malignant melanomas (3.9%), one Kaposi's sarcoma (0.8%), and one metastatic cancer (0.8%).

Another cohort study diagnosed malignant eyelid tumor during the 15 years (1976–1990) included 174 malignant tumors and 158 were basal cell carcinomas (90.8%), 15 were squamous cell carcinomas (8.6%), and one (0.6%) was a malignant melanoma [9].

Analyzing malignant tumors of the eyelid non-basal cell and non-squamous cell carcinoma, Margo CE *et al.* [3] found that these tumors of the eyelid other than basal cell and squamous cell carcinoma are uncommon and

usually occur in elderly white persons. In order of frequency, were melanoma, sebaceous carcinoma, and lymphoma.

Ni Z [10] studied a large casuistry with 3510 cases, realized on 40 years (1953–1992) and found the malignant tumors as follows: basal cell carcinomas (430 cases, 37.6%), Meibomian gland carcinomas (363, 31.7%), squamous cell carcinomas (216 cases, 18.9%), melanomas (56 cases, 4.9%) and malignant lymphomas (21 cases, 1.8%). During the same period, the benign tumors were: papillomas (658 cases, 27.9%), pigmented nevi (578 cases, 24.4%), cysts (427 cases, 18.1%), angiomas (222 cases, 9.4% including 10 lymphangiomas) and verrucae (212 cases, 9.0%). He reported some tumors with rarely eyelid location, like reticulum cell sarcoma, adenocystic carcinoma, malignant mesenchymoma, mucinous adenocarcinoma, Bowen's disease, basosquamous carcinoma, basosebacious carcinoma, teratoma, granular cell tumor (myoblastoma), angio-lymphoid hyperplasia with eosinophilia, osteoma.

Basal cell carcinomas were the most frequent malignant neoplasm, which were found in our study (185 cases) and represented 82.2% from all malignant eyelid tumors and 39.2% from all analyzed lesions. The maximum incidence of lesions was in fifth and sixth decade and the common location was the lower eyelid one. The most common histopathological aspect was represented by solid growth pattern with different associated tumoral subtypes (cystic, keratinisation, pigmented, morpheaform).

The worldwide frequency of basal cell carcinomas is about 80–90% from all eyelid cancerous lesions, being the most common malignant eyelid tumor [3, 9]. The mean age of patients group was 68.9 years with a large age range, between 28.7–91.3 years. In a study realized by Spraul CW [11], it was showed that these tumors were located at lower eyelid level in the most cases (63.1%), followed by medial canthus (29.8), upper eyelid (5.7%) and lateral canthus (1.4%). The most frequent histopathological type was solid pattern one, followed by mixed type with sclerosis areas (12.1%) and morpheaform type (10.6%). Authors estimate that tumors with positive surgical safety borders or with the presence of sclerosis type must be following regularly.

In our study, we observed 50 cases of squamous cell carcinomas, representing 10.7% from eyelid tumoral pathology. The maximum incidence of lesions was to male patients in sixth decade and the common location was the lower eyelid one. These tumors were well differentiated in majority of cases and only 12% from patients presented metastatic adenopathy. One of the special ways for tumor dissemination is represented by perineural one and we met invasion at that level in 18% cases.

The incidence of eyelid squamous carcinomas is the second one between malignant neoplasms with this location, representing 5–10% from all eyelid malignant tumors [12]. The tumoral incidence per 100 000 people is around 0.09–2.42% [9]. The studies realized between 1985–2002, regarding incidence of these neoplasms, indicate increase on patients with age under 50 years [13]. The most frequent location is lower eyelid

(48–68%), follows by medial canthus (24–36%), upper eyelid (22–31%) and lateral canthus (9–16%) [14, 15].

Many of eyelid squamous carcinomas are well differentiated (48%) or moderately differentiated (35%) [14, 15]. It is important to specify the perineural invasion, because this process ensure orbital and periorbital structures tumoral dissemination and also intracranial and along the branches of trigeminal nerve, extraocular motor nerve and facial nerve [16]. The rate of regional metastasis is different reported in studies, between 10–24% [12, 16, 17].

Malignant melanomas of eyelid level represent 1% from all malignant eyelid tumors and less then 1% from cutaneous melanomas. In spite of reduced incidence, these tumors represent 2/3 from all deaths induced by cutaneous cancers. Further, the frequency increase, doubling on every ten years in industrialized countries. The lesions affected mainly females, which are in seventh decade of life [18].

We diagnosed sebaceous carcinoma only in five cases, in patients with age between 48–83-year-old. All tumors had an upper eyelid location. The lesions were well differentiated, with typical sebaceous features. Sebaceous carcinoma is an aggressive malignant neoplasm with sebaceous differentiation. It represents 0.2–4.7% from all malignant neoplasms in western countries, being more common in Asia, with 30–40.6% from eyelid carcinomas [8, 9, 19, 20]. The patient age related with the time of surgery intervention is between 45–84-year-old (mean 70.6 years) and the upper eyelid location is more common then lower eyelid [19, 21]. The clinical and histopathological diagnosis is rarely and difficult because of sebaceous differentiation [22]. Some researchers emphasized that the tumoral differentiation and depth of invasion are related with the presence of metastasis and tumoral relapses [23].

Conclusions

Because of different tissues at eyelid level, a variety of tumoral types and subtypes can arise, but the most of them are carcinomas. The early diagnosis and proper treatment of these tumors may predict favorable prognosis.

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Received: March 29th, 2009

Accepted: January 30th, 2010