ORIGINAL ARTICLE

Eyelid tumours and pseudotumours in Hong Kong: a ten-year experience

CME

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Objective To describe the clinicopathological characteristics of patients with eyelid tumours in Hong Kong.

Design Retrospective case series.

Setting A tertiary eye centre in Hong Kong.

Patients A computerised retrieval system was used to identify all patients who underwent eyelid mass excisions with histological reports, encountered in the period 2000 to 2009, in a tertiary eye centre. The demographics (age, gender), clinical features (laterality, tumour topography), and the pathological diagnosis of each patient were documented. Descriptive statistical tabulation and analyses were performed on the data.

Results In all, 198 patients were identified; all were Chinese. Their mean age was 54 years for benign lesions and 68 years for malignant ones. Women were more commonly affected. Benign tumourous lesions occurred more commonly on the upper (n=91; 54%) than lower eyelid (n=79; 47%), whereas malignant lesions more often affected the lower (n=17, 61%) than upper (n=11, 39%) eyelid. The distribution of left and right eye involvement was similar (103 vs 101, respectively). In six patients, there were bilateral benign lesion. Regarding benign masses, 45 (27%) were intradermal neavi, 38 (22%) were squamous papillomas, 25 (15%) were seborrhoeic keratosis lesions, 14 (8%) were epidermoid cysts, and 7 (4%) were compound naevi. Regarding malignant eyelid tumours, the most common was basal cell carcinomas (n=12, 43%), 5 (18%) were squamous cell carcinomas, 3 (11%) were actinic keratosis lesions, and 2 (7%) each were sebaceous gland carcinomas and melanomas.

Conclusion Benign lesions constituted the majority of these eyelid tumours. Among the malignant lesions, basal cell carcinoma was the commonest type, with lower lid involvement in majority. Sebaceous gland carcinoma is not rare, which is in contrast to Caucasian populations. The relative frequencies of the most common malignant tumours in Hong Kong differed substantially from those reported in other Asian studies.

Key words
Adenocarcinoma, Sebaceous; Carcinoma, basal cell; Carcinoma, squamous cell; Eyelid neoplasms; Orbital pseudotumor

Hong Kong Med J 2013;19:150-5

New knowledge added by this study

- This is the first comprehensive clinicopathological study of its kind in Hong Kong regarding these commonly seen but not well-understood tumours and pseudotumours.
- The study provides an important synopsis on the spectrum of these conditions which challenge ophthalmologists, with most referrals being from general practitioners.

Implications for clinical practice or policy

- Giving general practitioners and general surgeons a perspective of the spectrum of the more-challenging eyelid tumours may increase their awareness of suspicious lesions for referral.

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Introduction

An eyelid mass could be aesthetically disturbing to patients as well as diagnostically difficult for attending primary care physicians. Due to the special health care system in Hong Kong, a patient with an eyelid mass could be referred to and managed by specialists in ophthalmology, dermatology, plastic surgery, head and neck surgery, general surgery, or family medicine. It is usually the ophthalmologists, however, who get the most diagnostically challenging and surgically demanding cases; most such cases being referred

by general practitioners. Such referrals may be due to the compelling need to excise a diagnostically ambiguous mass for pathological clarification and the inherent surgical dexterity needed to manage such periocular lesions. Therefore, a clinicopathological review of the patients managed by the ophthalmic surgeons may fill the knowledge gap regarding these 'difficult cases' and provide a panoramic view of the spectrum of such tumourous eyelid entities seen in daily practice.

The literature is relatively sparse on the clinicopathology of eyelid tumourous lesions in Chinese as opposed to Caucasian populations.[1-10] A simple extrapolation of Caucasian data on eyelid tumourous lesions may not be applicable to the Chinese due to the well-known ethnic disparity in these diseases and their epidemiological characteristics. For instance, basal cell carcinoma (BCC) is the most common eyelid malignancy in both Caucasians and Chinese, but the latter show a predilection to more sebaceous gland carcinomas (SGCs).[8,9] The largest clinicopathological study in 2639 eyelid specimens has shown that 2276 (86%) were benign and 363 (14%) were malignant.[1] In this Beijing Tongren Eye Centre study, Xu et al[1] reported that the commonest benign conditions were inflammatory lesions, melanocytic naevi, papillomas, dermoids, epidermoid cysts, and epithelial cysts. By contrast, the most common malignant tumours were BCC, SGC, lymphoma, squamous cell carcinoma (SCC), and malignant melanoma. The epidemiological characteristics of eyelid lesions from other similar studies in China have not been concordant.[9] Notably, differences may even be discernible in similar studies conducted at different times in the same centre.[1,3] Interestingly, the histopathological spectrum and relative frequencies of eyelid tumourous entities showed differences between subjects of Chinese ethnicity and those of other Asian ethnicities. In the Taiwan study by Lin et al,[6] the three commonest tumours were BCC (65%), SCC (13%), and SGC (8%). In Singapore, however, the three most common lesions were BCC (84%), SGC (10%), and SCC (3%).[5] On the contrary, a Japanese study showed almost equal frequency of all three carcinomas (approximately 20-40%).[11] Such differences may be attributed to different study designs, dissimilar case referral patterns, inconsistent histopathological diagnostic criteria, and possible temporal changes in the frequency of the tumourous lesions. For example, one report claimed a significant increase in the frequency of BCC in younger cohorts.[6]

Our study was therefore designed to give local medical practitioners, especially primary care physicians, a better perspective of the characteristic epidemiological traits of the more challenging eyelid tumours and pseudotumours in Hong Kong.

香港眼瞼腫瘤及假瘤的情況：十年經驗分享

目的 描述香港眼瞼腫瘤患者的臨床病理學特徵。

設計 病例系列回顧。

安排 香港一所提供第三層醫療服務的眼科中心。

患者 利用電腦檢索系統找出所有在2000至2009年期間於上述眼科中心進行眼瞼腫塊切除手術的病人的病理學報告，並分析每名病人的人口因素（年齡及性別）、臨床特徵（左或右邊、腫瘤範圍），以及病理診斷。然後根據資料進行描述性統計製表和分析。

結果 研究期間共有198名病人，他們均為華籍。良性腫瘤病人的平均年齡54歲，惡性腫瘤病人的平均年齡68歲。女性佔多數。良性腫瘤的情況，上眼瞼（n=91；54%）比下眼瞼（n=79；47%）較多；相反，惡性腫瘤的情況，下眼瞼（n=17；61%）比上眼瞼（n=11；39%）較多。腫瘤牽涉左右兩邊的情況相若，分別為103及101例；其中6名病人左右兩邊均有良性腫瘤。良性腫瘤的種類如下：真皮痣45例（27%）、上皮乳突瘤38例（22%）、脂漏性角化症25例（15%）、表皮囊腫14例（8%）及混合型黑色素細胞痣7例（4%）。惡性腫瘤方面，最常見的是基底細胞癌（12例；43%），其次是鱗狀細胞癌5例（18%）、日光性角化灶3例（11%）、皮脂腺癌2例（7%）及黑色素瘤2例（7%）。

結論 眼瞼腫瘤中良性病灶佔大多數。惡性腫瘤中最常見的是基底細胞癌，大多牽涉下眼瞼。與白種人不同的是，華籍患者的皮脂腺癌相對地較常見。香港最常見惡性腫瘤的相對比率與其他亞洲地區存在一定差異。

Methods

This was a retrospective study conducted from 2000 to 2009 in a tertiary eye referral centre, namely the Department of Ophthalmology and Visual Sciences, Prince of Wales Hospital, Hong Kong. All the eyelid tumourous cases referred to the oculoplastic clinic and managed by surgical excision were enrolled. The charts of eligible cases were retrieved, and the demographics (age, gender), clinical features (laterality, tumour topography), and the pathological diagnoses (as reported) were logged. The data were then subjected to descriptive statistical tabulation and analysis.

Results

In the study population, there were 121 female and 77 male (total, 198) patients with pathologically confirmed eyelid tumours. In all, 170 (86%) of these eyelid were benign, and 28 (14%) were malignant or semi-malignant. Regarding benign tumours, the upper lid was more often involved (n=91, 54%) than the lower eyelid (n=79, 47%). Regarding the

malignant group, the lower eyelid was involved more (n=17, 61%) than the upper eyelid (n=11, 39%). In the benign group, the male-to-female ratio was 1:1.57; in the malignant group it was 1:1.54.

The mean patient age at diagnosis was 54 years in the benign group, and 68 years in the malignant group. The left eye was involved in 103 patients and the right eye in 101; in six of these cases there were benign warts (presenting simultaneously) in both eyes.

In the group of benign lesions (n=170; Table 1), the most common diagnoses were intradermal naevus (n=45, 26.5%), warts (n=38, 22.4%), seborrhoeic keratosis (n=25, 14.7%), epidermoid cyst (n=14, 8.2%), and compound naevus (n=7, 4.1%). In the group with malignant or semi-malignant tumours (n=28; Table 2), the most frequent lesions were BCC (n=12, 42.9%; Fig 1), SCC (n=5, 17.9%), actinic keratosis (n=3, 10.7%; Fig 2), SGC (n=2, 7.1%; Fig 3), and melanoma (n=2, 7.1%). The remaining two patients had poorly differentiated tumours (a lymphoma and a metastasis).

TABLE 1. Histological spectrum and frequencies of benign eyelid lesion at the Prince of Wales Hospital Eye Centre from 2000 to 2009 (n=170)

Histopathological type	No. (%) of cases
Intradermal naevus	45 (26.5)
Warts	38 (22.4)
Seborrhoeic keratosis	25 (14.7)
Epidermoid cyst	14 (8.2)
Compound naevus	7 (4.1)
Haemangioma	5 (2.9)
Chalazion	5 (2.9)
Fibroepithelial polyp	5 (2.9)
Xanthelasma	4 (2.4)
Pyogenic granuloma	3 (1.8)
Neuroma	3 (1.8)
Solar lentigo	2 (1.2)
Trichoepithelioma	2 (1.2)
Eccrine poroma	2 (1.2)
Syringoma	2 (1.2)
Sebaceous hyperplasia	1 (0.6)
Interface dermatitis	1 (0.6)
Angiolipoma	1 (0.6)
Calcinosis	1 (0.6)
Pilomatrixoma	1 (0.6)
Steatocystoma	1 (0.6)
Pleomorphic adenoma	1 (0.6)
Apocrine hidradenoma	1 (0.6)

TABLE 2. Histopathological spectrum and frequencies of malignant or semi-malignant eyelid tumours at the Prince of Wales Hospital Eye Centre from 2000 to 2009 (n=28)

Type of tumour	No. (%) of cases	Gender ratio	Mean age ± standard deviation (years)
Basal cell carcinoma (Fig 1)	12 (42.9)	1:1	69 ± 17
Squamous cell carcinoma	5 (17.9)	1:0.67	71 ± 6
Actinic keratosis (Fig 2)	3 (10.7)	0:1	73 ± 11
Sebaceous gland carcinoma (Fig 3)	2 (7.1)	0:1	72 ± 4
Melanoma	2 (7.1)	0:1	79 ± 15
Lymphoma	1 (3.6)	1:0	69
Others	3 (10.7)	0:1	67 ± 5

Discussion

The data extracted at our centre provided objective evidence of the point prevalence of histologically proven eyelid tumours in a Hong Kong setting. To our knowledge, it is one of the largest local case series describing the epidemiology and frequency of eyelid tumours in referred patients. Eyelid cancer is uncommon in Hong Kong. Incidence rates vary markedly in different parts of the world, being relatively high in fair-skinned populations.[2,7,12] Such

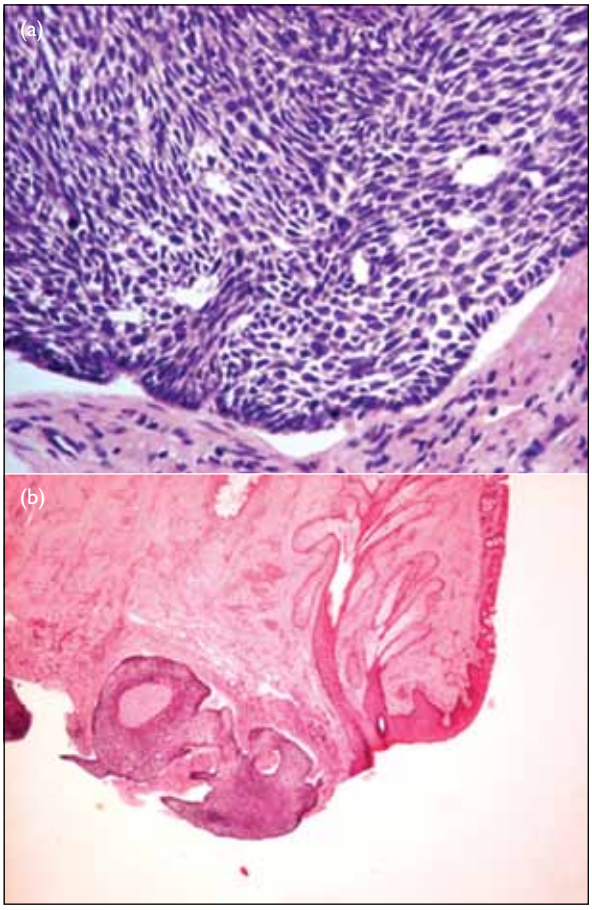

FIG 1. Histophotographs of basal cell carcinoma with features of proliferation of spindle basal cells with nuclear crowding
With pleomorphism and basaloid tumour cells (H&E): (a) × 40, (b) × 4

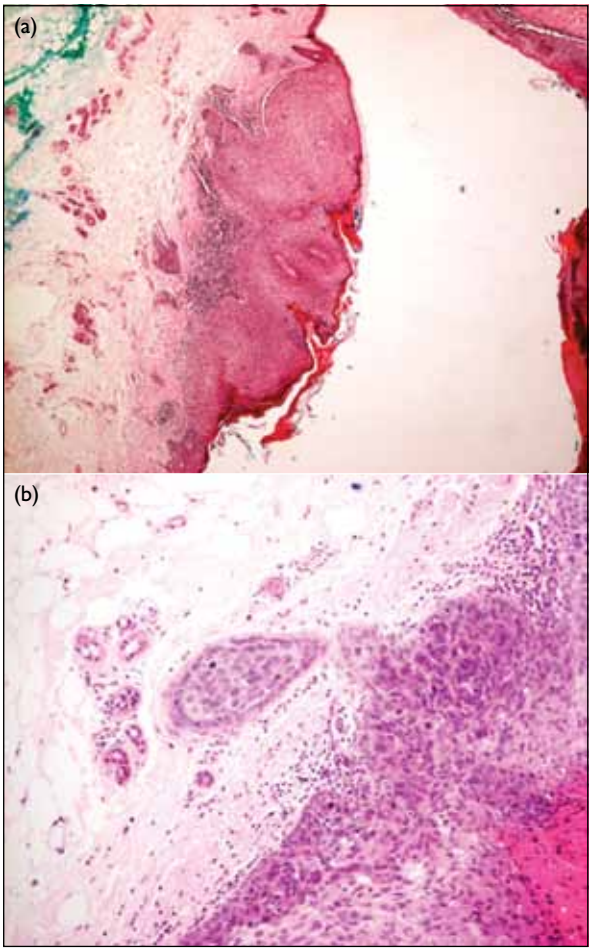

FIG 2. Histophotographs showing actinic keratosis, with features of superficial hyperkeratosis, parakeratosis and dysplastic squamous cell (H&E): (a) x 4, (b) x 20

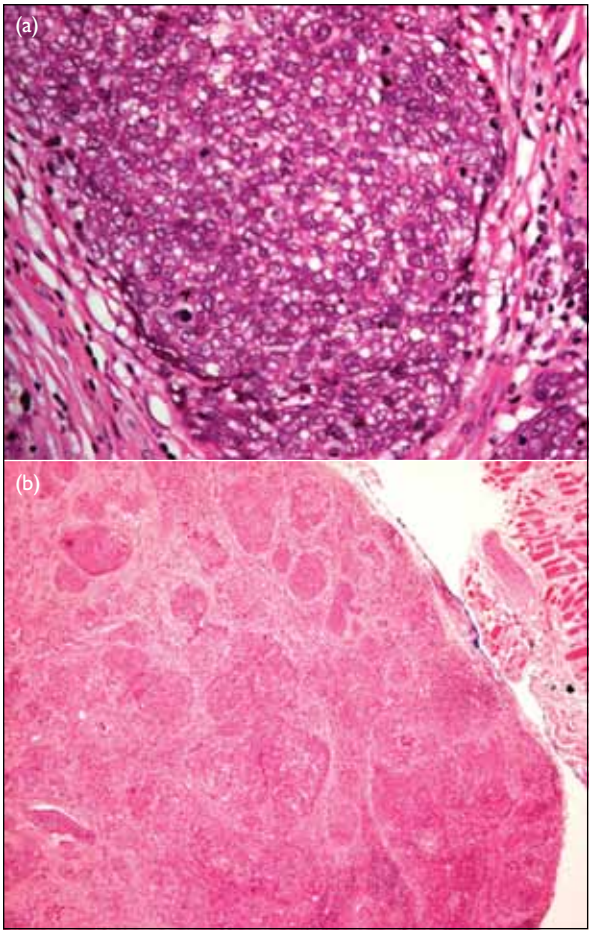

FIG 3. Histopathographs of a sebaceous gland carcinoma, a yellow tan mass with foamy multiple vacuolated cytoplasm and abundant intracytoplasmic lipid (H&E): (a) x 40, (b) x 4

regional differences in eyelid cancer rates may be due to differences in skin types, sunlight exposure, disease awareness, and surveillance practices. According to the Fitzpatrick's classification,[13] the Hong Kong population have skin types III to IV, which are less susceptible to sun-related injuries than skin types I and II (in fair-skinned Caucasians).

In the spectrum of eyelid tumours, benign lesions account for a much larger percentage. In the current study, benign lesions accounted for approximately 86% of cases, which was similar to that reported in Xu et al's study (involving 2638 patients) from Beijing.[1]

The histopathological spectrum and relative frequencies vary markedly in different countries. In the current study, the five most common malignant or semi-malignant tumours were BCC, SCC, actinic keratosis, SGC, and melanoma. We extracted data for relative frequencies for comparison from our counterparts with the same ethnicity—the Beijing group[1] and the Northern part China.[3] The relative frequencies of the five major malignant or semi-malignant tumours varied significantly in the two series (P<0.001, Chi squared test; Table 3[1-3,5,6,10,14]). Differences in the spectrum of malignant eyelid lesions mainly affect the frequencies of lymphomas and SCC. The diagnosis of lymphoma relies on laboratory tests which are difficult to be standardised, and may therefore explain the variations in the frequency in different regions. Whilst, SCCs involving eyelids are uncommon, our report may be an overestimate, as two of the cases entailed secondary eyelid involvement from adjacent maxillary SCCs and not primary eyelid lesions.

According to traditional textbook knowledge, SGC is very rare. By contrast, our study agrees with others from Asia (describing frequencies of 7.9% in Taiwan,[6] 38.6% in Beijing,[1] 10.2% in Singapore[5]), which suggests that it contributes to a recognisable proportion of all malignant eyelid tumours. Thus, SGC should always be considered in Asian patients, as to a large extent, the surgical approach and management principles differ when compared to those for other malignant tumours. Diagnosis of SGC is challenging. In one series, only 32% of cases

TABLE 3. The relative frequencies of the most common malignant tumours in different regions*

Types of malignant tumour†	Relative frequency (%)							
	Hong Kong, Liu et al (present study)	Beijing, Xu et al[1]	Northern China, Dai et al[3]	Taiwan, Lin et al[6]	Singapore, Lee et al[5]	Japan, Abe et al[17]	India, Sihota et al[10]	Minnesota, Cook and Bartley[2] ‡
BCC	43	41	37	62	84	33	30	91
SCC	18	5	8	13	3	48	28	9
SGC	7	39	31	8	10	13	33	-
MM	7	4	3	2	1	4	4	1
Others	4	9 (Lymphoma)	2 (Lymphoma)	4 (Carcinoma NOS§)	1 (Other NOS)	2 (Lymphoma)	4 (Lymphoma)	-

* Chi squared test comparing the frequencies of lesion between Hong Kong, Beijing, and Northern China shows discrepancy (P<0.001)
† BCC denotes basal cell carcinoma, SCC squamous cell carcinoma, SGC sebaceous gland carcinoma, and MM malignant melanoma
‡ In Minnesota, only 96% of cases reported with confirmed histological diagnosis[2]
§ NOS denotes not otherwise specified

were correctly diagnosed,[15] as the lesions were often mistaken for blepharoconjunctivitis, chalazion, BCC, or SCC.

As reported in many studies, BCC is still the most common cancer of the eyelid, accounting for 80 to 90% of all such cancers in the western literature.[2,7,14,16] It also ranked highest in frequency (43%) in our study and elsewhere in Asia (41% in Mainland China,[1] 33% in Japan,[17] 30% in India,[10] and as high as 84% in Singapore[5]; Table 3). The mean age at diagnosis of BCC of the eyelid in our study was 69 years, which is comparable to that in western populations.[7]

In contrast to BCC, SGC is usually rare in Caucasians, accounting for only 1 to 5.5% of all eyelid malignancies.[4] Notably, SGC of the eyelid is relatively common in Asians. The highest rate of 39% was reported in a Chinese cohort from Beijing.[1] By contrast, in a Caucasian group studied by Cook and Bartley in Minnesota,[2] there were no SGC cases. That SGCs appear to be more common in Asians could be related to genetic/racial factors.[8] The frequency with which they are encountered in referred patients appears to vary according to location, being 7% in Hong Kong versus 39% in Beijing.[1] The reason of this large discrepancy is unknown. Clearly, SGC is consistently encountered more often than reported in Caucasian studies. Evidently, SGC is more common in women than in men[15,18]; among the largest series about 73% of afflicted patients were women.[15] In our study, the two patients with SGCs were women, and female predominance has also been suggested from Singapore but no such gender predilection was reported in other Asian studies.[1,3] Patients with SGC are usually in their fifth to ninth decade[4]; the mean age of our two patients was 72 years.

The relative frequencies of SCC in various studies show a wide variation, being as high as 48% in Japan.[17] A tendency to over-diagnose this condition may be due to its resemblance to other lesions.[19] The prevalence of SCC is evidently relatively high in India.[10] In the current study, the male-to-female ratio was 1:0.67 with slight male predominance, which is consistent with the studies by Dai et al[3] and Sihota et al.[10] In our series, the mean age at diagnosis was 71 years.

Malignant melanoma accounts for majority of the skin cancer deaths, although it constitutes only 1% of all the skin cancers.[2] In our study, it accounted for 7% of all the lesions. The relatively higher proportion than in adjacent Asian areas was likely due to our small sample of malignant lesions. To improve the accuracy of predicting their prevalence and incidence in the general population, a larger sample (longer recruitment period) appears necessary.

Benign lesions are still the more common among eyelid tumourous lesions. There is a statistically significant difference between benign and malignant tumour groups in terms of age at diagnosis; in our series the mean age at diagnosis for all eyelid malignancies was 68 years, similar to that found in Singapore,[5] Taiwan,[20] and Japan.[17]

All the malignant lesions were more common in the lower than upper lid, which has also been reported previously.[16] The predominance of BCC in the lower lid was described in many studies,[2,7,16,21,22] as also observed in our study. In contrast, a greater proportion of SGCs occur in the upper lids,[4,8,23] which was also what we observed. This has been attributed to the greater number of meibomian glands in the upper lid.[4] Notably, SGCs are considered as one of the ocular adnexal tumours having the highest mortality; mortality rates ranging from 6 to 30% have been reported.[4] They are difficult to diagnose as they may masquerade as chronic blepharoconjunctivitis or chalazion.[15] Reportedly, the mean time to recurrence or metastasis after treatment is longer for BCCs than for SGCs, suggesting that the former must be followed up for longer periods.[20] Wang et al[20] compared patients with these two common eyelid tumours, and reported that SGCs had higher recurrence, metastasis, and mortality rates than BCCs.

For comparison purposes, this study presents the latest eyelid tumour data analysed to reveal prevalence/incidence trends. Clearly, a longer recruitment period involving several eye centres is necessary. Although sun exposure is widely accepted as a risk factor for developing BCC, SCC and melanoma, the mechanism of carcinogenesis in these lesions is not yet clear.

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