

Malignant and Benign Eyelid Lesions in San Francisco: Study of a Diverse Urban Population

Sean Paul, MD

Dat T. Vo, BS

Rona Z. Silkiss, MD, FACS

Purpose

To describe the incidence and epidemiology of primary eyelid tumors diagnosed in a diverse urban medical center in San Francisco from 2004-2007.

Design

Retrospective eyelid pathology data review.

Participants

A total of 855 primary eyelid tumors retrieved from the California Pacific Medical Center Surgical Pathology database between January 2004 and December 2007. All 855 were histopathologically verified and used for analysis.

Methods

The histopathological diagnosis of benign and malignant eyelid tumors was stratified based on age, gender, ethnicity, and tumor location.

Main Outcome Measure

Incidence of eyelid neoplasia.

Results

The mean age of patients treated for an eyelid lesion was 60.1 years. Of the eyelid lesions 24.1% were malignant and 75.9% were benign. The most common eyelid malignancy was basal cell carcinoma (71.8%), followed by squamous cell carcinoma

(9.7%), melanoma (9.2%), and sebaceous cell carcinoma (7.3%). The most common benign lesions were seborrheic keratosis (19.7%), followed by lipogranuloma (13.7%), intradermal nevus (12.2%), and hidrocystoma and fibroepithelial polyps (each with 8.6%).

Conclusions

Eyelid tumors affecting an ethnically diverse population were studied. The data demonstrate an increased number of basal cell carcinomas among male patients relative to previous studies.¹⁻⁴ This may be secondary to the increased incidence of HIV/AIDS in the San Francisco area. The data also corroborate previous reports that Asian ancestry, though increased in the San Francisco area as well relative to other populations studied, is not a risk factor for developing sebaceous carcinoma outside of Asia.⁵

Introduction

Eyelid lesions are common concerns amongst patients. Internists, family practitioners, dermatologists, and ophthalmologists are often requested to determine if a lesion is benign or malignant.

Histopathological diagnosis and clinical correlation have been studied in published case reviews. Studies overseas have also examined the incidence in specific populations.^{1-3,6,7} Benign tumors greatly outnumber malignant tumors.¹⁻⁵ Basal cell carcinoma has been shown to have the highest incidence among malignancies.⁸ Lin et al. described a significantly higher incidence of sebaceous gland cell carcinoma in Taiwan.¹

In this case series review, the authors examined the incidence and histopathology of eyelid tumors in an American urban medical center with a diverse patient population. Eyelid tumor pathology data were gathered from the California Pacific Medical Center in San Francisco, California, from 2004 to 2007. The authors had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

While previous studies regarding eyelid tumors have relied on national tumor registries in various countries and regions within the United States, this study focused solely on eyelid tumors at a specific hospital in an urban setting with a known diverse population.

Materials and Methods

California Pacific Medical Center (CPMC) provides pathology services for its four-hospital network and referring community physicians. Pathologists working at CPMC collect, process, and interpret pathology specimens. The reports are placed into an electronic database available to CPMC physicians. Items registered include the patient’s name, gender, age, location of tumor, and histopathological diagnosis.

The investigators of this study reviewed the data specific to eyelid tumors. Duplications in data entry were eliminated to aid in the accuracy of analysis. For this analysis, the authors examined eyelid tumor data between January 2004 and December 2007 from the CPMC pathology database under the search entry ‘eyelid.’

Individual state tumor registries do not specifically track eyelid tumors and malignancies. The use of the CPMC registry allowed us a unique opportunity to study the spectrum of eyelid tumors in an urban population.

This study received approval of the Institutional Review Board of California Pacific Medical Center.

Results

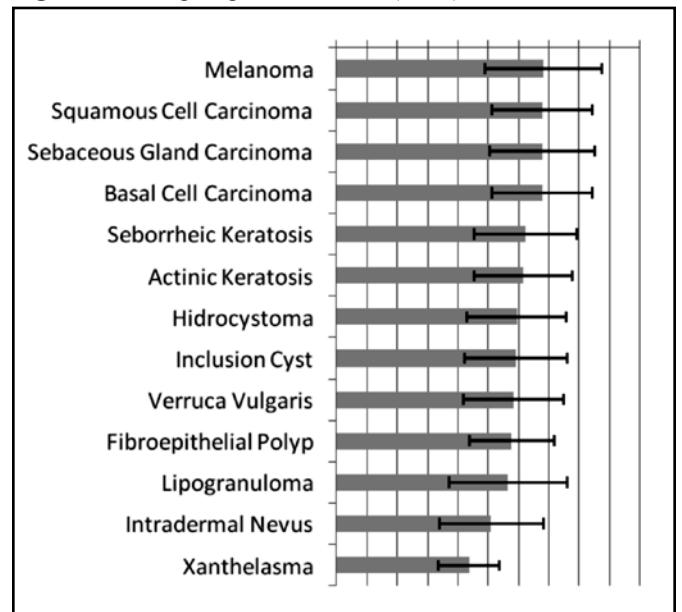
A total of 855 people with eyelid lesions diagnosed from January 2004 to December 2007 were identified from the CPMC tumor database. There were 453 females (53.0 %), 400 males (46.8 %), and 2 (0.2 %) unspecified gender. Neither the ethnicity nor HIV status of the patients was specifically identified.

Of these 855 cases, 206 were found to be malignant neoplasms and 649 were benign neoplasms (Table 1). The mean age was 60.1 years with a range of 1-96 years. Malignant tumors were diagnosed primarily in patients with an average age over 60, and most benign tumors, other than seborrheic keratosis and actinic keratosis, were diagnosed in patients under the age of 60 (Figure 1). There was no evident left-sided or right-sided preference seen amongst most tumors. However, squamous cell carcinoma and melanoma demonstrated a slight preference for the left eyelid. Seborrheic keratosis demonstrated a preference for the right eyelid.

Table 1: Eyelid Tumors at California Pacific Medical Center from 2004-2007.

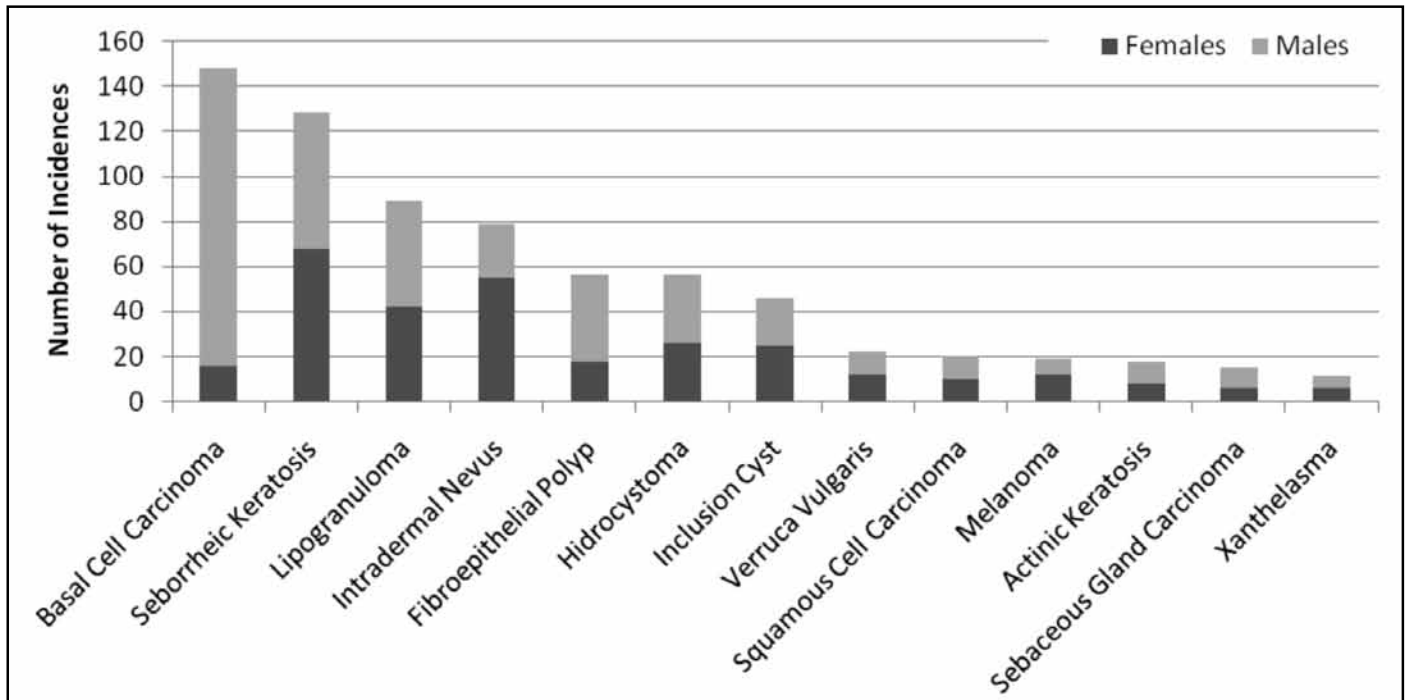
Tumor Type	Number
Malignant Lesions, n=206 (24.1%)	
Basal Cell Carcinoma	148
Squamous Cell Carcinoma	20
Melanoma	19
Sebaceous Gland Cell ca and variants	15
Other Cancers	4
Benign Lesions, n=649 (75.9%)	
Seborrheic keratosis	128
Lipogranuloma and Chalazion	89
Intradermal nevus	79
Hidrocystoma	56
Fibroepithelial polyp	56
Inclusion cysts (epidermoid)	46
Verruca Vulgaris	22
Actinic Keratosis	18
Other benign tumors	155
Total Lesions, n=855	

Figure 1: Average Ages for Tumors (n>10).



Malignant Lesions

In this study, eight different malignant lesions were reported. Basal cell carcinoma (BCC) was the most commonly diagnosed tumor (n=148) (Photo 1). BCC accounted for 71.8% of all malignant lesions and accounted for 17.3% of all lesions. While other tumors found in this study did not show evidence of gender preference, BCC occurred predominantly in men. The incidence of tumor presentation in men compared to women was 8.25:1

Figure 2: Eyelid Lesions Per Gender.

(Figure 2). These data reveal a significant increase in reported BCC among male patients compared to previous studies (Table 2).¹⁻⁴ This tumor also showed a preference for the lower eyelid in 132 of the 148 lesions.

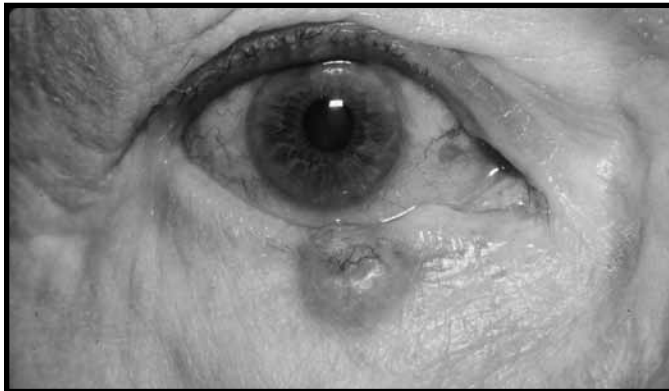
Photo 1: Basal Cell Carcinoma of the Lower Eyelid.

Photo Courtesy of Rona Z. Silkiss, M.D.

Table 2: Comparison of BCC by study.

BCC Male to Female Ratio	
Study	M:F Ratio
Taiwan (2006) ¹	1.3
Olmsted County, MN (1999) ²	1.4
Finland (2005) ³	1.1
Switzerland (2009) ⁴	25
San Francisco (Current Study)	8.25

Photo 2: Squamous Cell Carcinoma of the Lower Eyelid.

Photo Courtesy of Rona Z. Silkiss, M.D.

The second most common tumor was squamous cell carcinoma (SCC) with n=20 (Photo 2). SCC occurred in 9.7% of malignancies examined and represented 2.3% of all lesions. These tumors had a slight preference for the left eyelid, were evenly distributed between men and women, and were preferentially seen on the lower lid.

Melanoma was the third most common malignancy with an n=19 (Photo 3). They accounted for 9.2% of all malignant eyelid lesions and 2.2% of all lesions reported. The cases of melanoma seen in this study favored female patients as well as the left side and the lower eyelid.

The fourth most common malignancy was sebaceous gland carcinoma (SGC) with n=15 (Photo 4). This represented 7.3% of eyelid malignancies reported and 1.8% of all lesions. Patients with SGC did not show preference for eyelid side nor for gender, but showed a very strong preference for the upper eyelid.

Out of the 15 clinical samples, 86.7% of the tumors (n = 13) were located on the upper lid while only two, or 13.3%, were located on the lower lid. The preference for the upper lid is linked to an increased number of meibomian glands located in the upper lid (30) versus the lower lid (20).^{9, 10}

Other cancers of note in this study included malignant B cell lymphoma n=2, Merkel cell carcinoma n=1, and an adnexal malignant tumor n=1.

Photo 3: Melanoma of the Lower Eyelid.



Photo Courtesy of Rona Z. Silkiss, M.D.

Photo 4: Sebaceous Gland Carcinoma of the Upper Eyelid



Photo Courtesy of Rona Z. Silkiss, M.D.

Benign Lesions

Benign lesions accounted for 75.9% of all tumors in this study. The average age of individuals diagnosed with a benign lesion was less than 60 years. There were numerous types of benign lesions; those with over ten occurrences are described in this study.

Seborrheic keratosis was the most common benign neoplasm of the eyelid with n=128, representing 19.7% of benign lesions. These lesions were seen equally in male and female patients, demonstrated a preference for the upper lid and location on the right side. These have been reported in multiple studies as the most common benign tumor in older individuals. This was substantiated by the CPMC experience.

Photo 5: Chalazion of Bilateral Eyelids.



Photo Courtesy of Rona Z. Silkiss, M.D.

Chalazion (n=89) accounted for 13.7% of all benign lesions (Photo 5). These were evenly distributed between men and women as well as on the right and left sides. There was a slight preference for the lower eyelid in this study. Lesions in this groups included chalazions, which are lipogranulomas of the meibomian glands or glands of Zeis.

Intradermal nevus (n=79) represented 12.2% of all benign lesions (Photo 6). Lesions examined in this study were diagnosed more often in female patients and were found predominantly on the lower eyelid. There was no right- or left-sided preference.

Photo 6: Intradermal Nevus of the Lower Eyelid



Photo Courtesy of Rona Z. Silkiss, M.D.

Photo 7: Hidrocystoma of the Lower Eyelid.

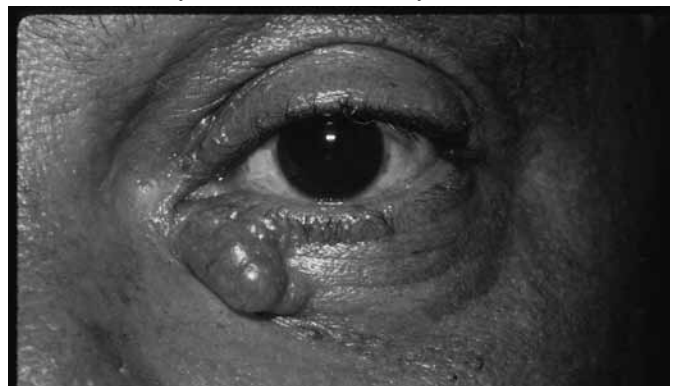


Photo Courtesy of Rona Z. Silkiss, M.D.

Hidrocystomas (n=56) represented 8.6% of benign lesions (Photo 7). Most of the lesions examined in this study were found on the lower lid. Side or gender preference was not demonstrated. These are cysts of the sweat glands including eccrine, sebaceous, and apocrine subtypes.

Fibroepithelial polyps (n=56) represented 8.6% of all benign lesions. There was a slight preference for the right eyelid, and most cases were diagnosed in males. There was an even distribution of this lesion on both the upper and lower eyelids. These are also known as acrochordons and skin tags.

Inclusion (epidermoid) cysts (n=46) demonstrated a slight preference for the right eyelid, but no gender or upper or lower eyelid preference was seen. These accounted for 7.1% of benign tumors.

Verruca vulgaris (n=22) are virus-borne lesions commonly known as warts. These accounted for 3.4% of benign lesions. Most of these cases were seen in female patients and on the left eyelid. There was an even distribution on both the upper and lower lids.

Actinic keratosis (n=18) are pre-malignant lesions that accounted for 2.8% of benign lesions (Photo 8). These lesions, unlike most of the other benign lesions, had a mean age over 60. There was a strong preference for these lesions to be seen on the lower lid, and most cases were on the right side. There was no gender preference.

Photo 8: Actinic Keratosis of the Eyelid.



Photo Courtesy of Rona Z. Silkiss, M.D.

There were 155 additional benign lesions of which there were n<10. This accounted for 23.9% of benign lesions and 18.1% of all lesions in the study. Examples of lesions included in this group are: sebaceous adenoma, benign capillary hemangioma, molluscum contagiosum, lipoma, milia, and syringoma.

Discussion

Using the data from the CPMC pathology database, the authors examined the characteristics of eyelid lesions in the diverse San Francisco community.

To our knowledge, this is the first study of the distribution of eyelid lesions in a richly diverse ethnic US population. Based

on data from the US Census Bureau in 2007, the San Francisco county population was comprised of 57.7% Whites, 31.6% Asian Americans, 14.0% Hispanic/Latinos, 6.9% Blacks, 2.7% Multi-racial, and 0.5% Native Americans.¹¹ Note that, as some census takers reported multiple races, the total is over 100%.¹⁰ This population contrasts with previous studies in which largely homogenous populations were studied (i.e., Taiwan, Minnesota, and India).^{1,12,13}

An important consideration in this study is that data were retrieved from the pathology logs of CPMC due to limitations from individual states and cities in the United States not keeping formal records of eyelid tumors. Studies referenced in this paper retrieved their data from a variety of sources including national and local cancer registries as well as hospital pathology laboratory data (Table 3). The authors still believe that this study shows an interesting overview of data from a busy, community hospital, caring for a diverse urban population that is important for ophthalmologists and other physicians.

Table 3: Eyelid Tumor Study Data Retrieval Sources.

Study	Data Retrieval
Taiwan ¹	Taiwan National Cancer Registry
Olmsted County, MN ²	Olmsted County, Minnesota Computerized retrieval system
Finland ³	Finnish Cancer Registry
Switzerland ⁴	Laboratory of Ophthalmopathology of the Hôpital Ophtalmique Jules Gonin, Lausanne, Switzerland
Singapore ⁶	Singapore Cancer Registry
Florida ⁷	Florida Cancer Data System
India ¹³	Ocular Pathology Records
NCI Sebaceous Gland Cancer ⁵	National Cancer Institute's Surveillance, Epidemiology, and End Results database

The authors report an increased incidence of basal cell carcinoma in the male population. Factors that may explain the increase of basal cell carcinoma of the eyelid of this population include: the higher incidence of HIV/AIDS (26 cases per 100,000 persons in San Francisco County versus 12.5 cases per 100,000 persons in the United States in 2007),¹⁴ sun exposure as well as increased public awareness of disease presentation, surveillance, and better diagnostic and reporting techniques.

In general, the popularity of cosmetic surgery may contribute to the increased incidence of eyelid tumor diagnosis even among men and minorities. In 2007, the American Society for Aesthetic Plastic Surgery reported that the number of both surgical and nonsurgical cosmetic procedures performed on men increased 17%. Twenty-two percent of the aesthetic procedures were performed on racial and ethnic minorities between 2006 and 2007.¹⁵

Our study confirms that the incidence of malignant eyelid lesions increases with age. While some of the lesions showed left- or right-side preferences, we were unable to provide reasons for whether a lesion presented on the left or right except for those lesions induced by sun exposure. Left-side preference when it occurs (i.e., melanoma) may be related to sun exposure specifically while driving. This phenomenon has been studied in truck drivers in Turkey where there is an effect of increased ultraviolet light exposure on one side of the face.¹⁶

In agreement with other published studies, BCC was the most common malignancy reported. In contrast to other studies demonstrating an equal male/female distribution, our data demonstrated a significant difference in the number of men diagnosed over women with basal cell carcinoma.² We believe that this may be due to the higher use of sunscreen by women, the use of occlusive makeup or sunscreen containing makeup in women, the culture of sun bathing and water sports among men and the higher number of men with HIV/AIDS in the San Francisco community.¹⁴ These data were corroborated by a report of HIV-infected patients with non-melanoma cancers in San Francisco in the early 1990s.^{17, 18} In 2007, at the Fourth International AIDS Society Conference on HIV Treatment, Pathogenesis and Prevention, a study evaluating the incidence of skin cancer in HIV patients in the United States demonstrated a rate of BCC (200 cases per 100,000 PY) that was 2.3-fold higher than that seen in the HIV-negative population. The rate of melanoma was elevated by 3.1-fold compared with the general population.¹⁴ Additionally in 2009, Crum-Cianflone et al. reported that with the advent of highly active antiretroviral therapy (HAART), the incidence rates of cutaneous non-AIDS-defining cancers, in particular basal cell carcinoma, exceeded the rates of cutaneous AIDS-defining cancers such as Kaposi sarcoma.¹⁹

Thus, we postulate that a relationship exists between the increased basal cell carcinomas among male patients seen in the San Francisco County population with a relatively higher number of HIV/AIDS patients. Interestingly, while most other studies describing basal cell carcinoma distribution showed nearly a 1:1 male to female ratio, Deprez et al. saw a significantly higher ratio of male to females with a diagnosis of basal cell carcinoma (25:1) in the Swiss population. While this sig-

nificant finding was not discussed directly in their study, Switzerland has the highest adult prevalence of HIV/AIDS cases in the adult population in Western Europe (0.6%), which could explain this finding and support our hypothesis.

Increased numbers of sebaceous gland carcinoma were seen in the Taiwanese and Indian populations.^{1, 12} This was not seen in the San Francisco population despite including a significantly higher Asian population than other parts of the United States (Table 4). These results confirmed a recent study by Dasgupta et al. that concluded that established Asian/Pacific Islander ancestry is not a risk factor for developing sebaceous carcinoma.⁵

Table 4: Asian Population Demographics in United States and Taiwan.

City	Percentage Asian Race
SF, CA	31.3
Olmstead County, MN	5
LA, CA	10.4
NYC, NY	11.8
Houston, TX	5.3
Atlanta, GA	1.9
Miami, FL	0.8
Raleigh, NC	3.8
Boston, MA	8.2
Denver, CO	3.3
Chicago, IL	4.9
St. Louis, MO	2
Dallas, TX	2.5
Ethnic Groups in Taiwan	
	Percentage
Taiwan	84
Mainland Chinese	14
Indigenous	2

Table 5: Comparison of Eyelid Studies.

Study	Years Study Conducted	Sample Size (n)	Length of Study (years)	Average Cases/Year
San Francisco (current study)	2004-2007	855	4	213.8
Taiwan ¹	1980-2000	1166	21	55.5
Olmsted County, MN ²	1976-1990	174	15	11.6
Finland ³	1953-1997	6241	44	141.8
Switzerland ⁴	1989-2007	5504	18	305.8
Singapore ⁶	1968-1995	325	27	12.0
Florida ⁷	1981-1994	206	13	15.8
India ¹³	1982-1992	313	10	31.3

Studying the San Francisco population revealed a significant increase in incidence of eyelid tumors found compared to previous studies other than Deprez, et al., who interestingly observed more cases per year in the Swiss population (Table 5).^{1-4, 6, 7,13} The current findings may be due to increased awareness of and screening for skin tumors as well as the economic ability of patients to care for these lesions. Observed as well were an increased number of men with basal cell cancer in a population with an increased number of HIV patients. The authors conclude that skin cancer screening is recommended in a known population with an increased incidence of HIV/AIDS.

We acknowledge the limitations of this study. Specifically, various pathologists reviewed the slides over the several year interval. The authors concede that this study may not represent the entire San Francisco population and that, without national and state registries, it is nearly impossible to do so. Nonetheless, this study provides an interesting overview of eyelid neoplasia in a diverse urban population which displays important changes in epidemiological characteristics in a specific United States population.

Sean Paul, MD, Department of Ophthalmology, University of Oklahoma, Dean McGee Eye Institute, Oklahoma City, Oklahoma.

Dat T. Vo, BS, Greeney Children's Cancer Research Institute, University of Texas Health Science Center at San Antonio.

Rona Z. Silkiss, MD, FACS, California Pacific Medical Center, San Francisco.

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