

Clinicopathological Analysis of 39 Patients with Corneal Tumors

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Abstract

Purpose: Corneal tumors are rarely seen in clinical practice. There is a paucity of data on the incidence of various corneal tumors, their clinical and pathological features and surgical management, especially on large patient samples.

Methods: The medical records of 39 patients with corneal tumors referred to Zhongshan Ophthalmic Center, Sun Yat-sen University, China from January 1, 1996 to December 31, 2002 were reviewed retrospectively.

Results: Of the 39 cases with corneal tumors, 31 were males and 8 were females. The right eye was affected in 24 cases and the left one in 15 cases. The mean age at diagnosis was 45.7 years, ranged from 3 to 88 years. Squamous cell carcinoma was the most common tumor in the cornea (18 cases, 46.15%), followed by pigmented naevus (12 cases, 30.77%), papillary epithelioma (3 cases, 7.69%), melanoma (1 case, 2.56%), oncosis hyperplasia (1 case, 2.56%), inverting papilloma (1 case, 2.56%), primary acquired melanosis (1 case, 2.56%), amyloid degeneration (1 case, 2.56%), inflammatory pseudotumor (1 case, 2.56%). They arose most commonly in the limbal region. All tumors were unilaterally involved. Squamous cell carcinoma of the cornea usually appears as a whitish, rough, irregular lesion or a telangiectatic, gelatinous epibulbar mass. Nevus in the cornea generally becomes clinically apparent in the first or second decade of life and the lesion may enlarge or more deeply pigmented afterwards. The corneal tumors were completely excised microsurgically in 22 cases. Six cases were treated with surgical resection combined with amniotic membrane graft. Three cases with surgical excision plus transfer of conjunctival flap. Two cases with surgical excision plus lamellar keratoplasty. Two cases with surgical excision plus cryosurgery. Two cases with orbital exenteration. One case with enucleation. One case with incision biopsy and observation.

Conclusion: Squamous cell carcinoma and nevus, the most common corneal tumors, accounted for 76.92% of all cases.

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The therapeutic outcomes depended upon early pathologic diagnosis and early surgical management. (*Eye Science* 2011; 26:148-153)

Keywords: tumor; cornea; squamous cell carcinoma; nevus; surgery

Corneal tumors are rarely seen in clinical practice. Tumors that arise in the cornea not only cause disfigure and vision impairment of the patients, but also may lead to death. Previous literatures about corneal tumors were mainly case or short series reports¹⁻¹². There was a paucity of data on the incidence of various corneal tumors, their clinical and pathological features and surgical management, especially using large patient samples. In this report we provided observations of 39 consecutive patients with corneal tumors seen in Zhongshan Ophthalmic Center, Sun Yat-sen University in China, for a 7-year period. We recorded the clinical features, pathological findings, surgical procedures and follow-up results.

Materials and methods

The medical records of all patients with the diagnosis of corneal tumors in Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China, between January 1, 1996 and December 31, 2002, were reviewed retrospectively. All patients were Chinese. The diagnosis of the corneal tumor was confirmed by pathological examination. The cases with corneal dermoid, a relatively common corneal "tumor", were excluded from our series. The following general data were collected: patients' age, gender, race, medical and family history. Specific ophthalmological data including symptoms (e.g., blurred vision, pain, tearing, red eye, lumps),

the involved eye, laterality (unilateral, bilateral), the best corrected visual acuity, intraocular pressure, anterior segment and fundus, eye movement, tumor location (central cornea, peripheral cornea, limbus, conjunctiva, orbit), the morphology and the color of the tumor were recorded, respectively. When the tumor extended to the orbit, we measured extent of exophthalmos with exophthalmometer, as well as the computed tomography (CT) scans, magnetic resonance imaging (MRI) or ultrasonography of the involved orbit. All patients were examined with chest X-ray film and blood routine analysis. All surgical specimens of the patients with corneal tumors were histopathologically examined.

Results

The incidence of various corneal tumors

A total of 39 patients with corneal tumors were admitted to our hospital during this 7-year period. All patients were unilaterally involved. The right eye was affected in 24 cases and the left one in 15 cases. Thirty one patients were male and eight were female, aged ranging from 3 to 88 years (mean 45.7 years). The corneal masses in 20 patients were benign, 19 were malignant. The general tumor categories were listed in Table 1. The patients with squamous cell carcinoma aged from 32 to 88 years (mean 59.0 years). The patients with nevus aged ranging from 3 to 52 years (mean 23.2 years). The patients with papilloma aged from 5 to 55 years (mean 38.3 years). The mean duration of the benign corneal tumor was 7.4 years (from 2 months to 50 years) at the time of presentation, and the mean duration of the malignant corneal tumor was 3.2 years (from 1 month to 20 years).

Table 1 General category of corneal tumors in 39 patients

Category of tumors	Number of patients (%)
Squamous cell carcinoma	18 (46.15%)
Malignant melanoma	1 (2.56%)
Nevus	12 (30.77%)
Squamous papilloma	3 (7.69%)
Oncosis hyperplasia	1 (2.56%)
Inverting papilloma	1 (2.56%)
Primary acquired melanosis	1 (2.56%)
Amyloid degeneration	1 (2.56%)
Inflammatory pseudotumor	1 (2.56%)

Anatomic location of various kinds of corneal tumors

The corneal tumors in most patients originated from the limbus and secondary involved the peripheral cornea. Only a few tumors arose from the cornea itself nor were located on the central cornea (Table 2) (Figures 1–4).

Table 2 Anatomic location of various corneal tumors

	Limbus and peripheral	Central
Benign tumors	17	3
Malignant tumors	16	3

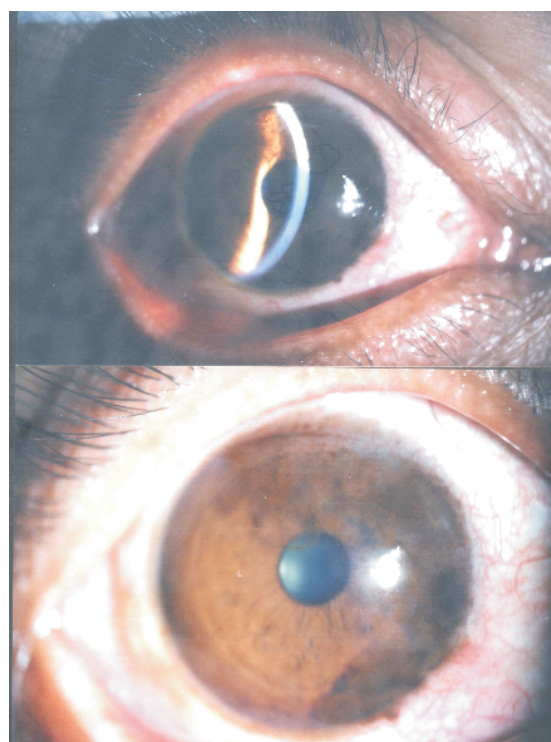


Figure 1 The slit-lamp photo of a patient with corneal nevus, showing the characteristic irregular patchy pigmentation that lied within the corneal epithelial layer.

The visual acuity of patients with various corneal tumors

As one of the most important optical media, the cornea that presented a tumor was likely to present impaired vision, listed in Table 3. The visual acuity data was not available in 3 infants with corneal nevus or 1 patient with malignant melanoma.

Symptoms and signs of various corneal tumors

General symptoms and signs are indicated in



Figure 2 The typical clinical photo of squamous cell carcinoma of cornea.



Figure 3 Another patient with corneal squamous cell carcinoma, showing a pink, irregular, telangiectatic, corneal mass.

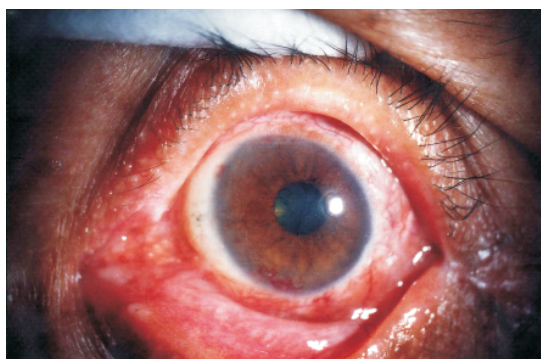


Figure 4 The same patient with corneal squamous cell carcinoma showed clear cornea with the visual acuity of 40/200 one week after lamellar keratoplasty.

Table 4. Corneal lumps were the most common symptom in patients with corneal tumors (97.44% , 38/39). Squamous cell carcinoma of the cornea usually appeared as a whitish, rough, irregular lesion or

Table 3 The best corrected visual acuity of various corneal tumors

	Corrected visual acuity	Number of Patients (%)
Benign tumors	≤20/70	3(17.65%)
	20/60~20/25	9(52.94%)
	≥20/20	5(29.41%)
Malignant tumors	≤20/70	9(50.00%)
	20/60~20/25	6(33.33%)
	≥20/20	3(16.67%)

a telangiectatic, gelatinous epibulbar mass. The second most common symptom and sign was decreased visual acuity (77.14% , 27/35). Other symptoms included foreign body sensation (28.21% , 11/39), hyperemia(23.08% , 9/39), pain (12.82% , 5/39), photophobia(5.13% , 2/39) and tenderness (2.56% , 1/39).

Table 4 Symptoms and signs of various corneal tumors

Symptoms or signs	Number of patients (%)
Corneal lump	38(97.44%)
Decreased vision acuity	27(77.14%)
Foreign body sensation	11(28.21%)
Hyperemia	9(23.08%)
Pain	5(12.82%)
Photophobia	2(5.13%)
Tenderness	1(2.56%)

Surgical management of various corneal tumors

Excision biopsy was performed in most cases with corneal tumors in this study. The malignant corneal tumors were excised 2 mm beyond the tumor margin. When the conjunctival defect was too large to be sutured directly, then an amniotic membrane graft or conjunctival flap transplantation was adopted. Additionally, lamellar keratoplasty was employed to treat corneal defects in 2 patients (Table 5).

Follow-up data

The follow-up ranged from 2 to 9 years (mean 4.11 years). Of the 39 cases, 26 patients were followed up, 12 patients were lost and 1 patient died of cardiovascular diseases (listed as a censored case). Of the 26 cases who were followed, 14 patients had malignant tumors and 12 cases among them showed no recurrence and 2 squamous cell carcinoma cases revealed tumor relapse, who showed no recurrence

Table 5 Surgical approaches of various corneal tumors

Category of tumors	Surgical approaches	Number of patients (%)
Malignant tumors	Excision biopsy	10(52.63%)
	Excision biopsy plus amniotic membrane graft	3(15.79%)
	Excision biopsy plus conjunctival flap transplant	2(10.53%)
	Excision biopsy plus lamellar keratoplasty	1(5.26%)
	Enucleation	1(5.26%)
	Exenteration	2(10.53%)
Benign tumors	Excision biopsy	12(60%)
	Excision biopsy plus amniotic membrane graft	3(15%)
	Excision biopsy plus cryotherapy	2(10%)
	Excision biopsy plus lamellar keratoplasty	1(5%)
	Excision biopsy plus conjunctival flap transplant	1(5%)
	Incision biopsy and observation	1(5%)

after reoperation. Among 12 patients with benign tumor who were followed, 11 demonstrated no recurrence, and 1 case with primary acquired melanosis revealed tumor relapse. Re-excision of the acquired melanosis was applied in this patient and he completely recovered after the second operation during the 5 years follow-up.

Discussion

Corneal tumors are mainly categorized into congenital and acquired lesions¹³. Corneal tumors are rarely seen in clinical setting. Most corneal tumors originate from the limbus. The corneal epithelial stem cells reside in the basal layer of corneal limbus and have superior proliferative capacity as compared with central corneal epithelial cells¹⁴. Corneal neoplasm constantly appears at the limbus in the interpalpreal fissure, for replacement of Bowman's layer by other tissues at this place often observed due to various causative agents such as ultraviolet light. In current retrospective investigation, all 39 patients were unilaterally affected, and 33 among them originated from the limbus. The number of cases with malignant tumors was approximately equal to that of benign ones (malignant: benign=19:20). Males were more significantly involved than females (31/8). Shields et al reported that the most frequent non-melanocytic neoplastic lesion was squamous cell carcinoma¹⁵. Of 39 patients, squamous cell carcinoma was most commonly observed, accounting for 46.15% (18/39). Among them, 4 patients were affected by intraepithelial neoplasia, which more fre-

quently attacked males than females, particularly for those patients aged above 40 years old (mean 59 years). Nevus, the most frequent benign tumor, accounted for 30.77% (12/39) of all cases, aged ranging from 3 to 52 years (mean 23.2 years). The second most common benign corneal tumor was squamous papilloma (7.69% (3/39)), and the patients aged from 5 to 55 years old (mean 38.3 years).

No obvious symptoms have been observed in the early stage of corneal tumors. Foreign body sensation, tearing or itch occurred in small part of patients. With tumor progression and enlargement, the masses were usually found by patients themselves. The mean course of malignant tumors was shorter than that of benign ones. Of our case series, the mean course of 19 patients with malignant tumors was 3.2 years, while the mean course of 20 patients with benign tumors was 7.4 years. The squamous cell carcinoma of the cornea was more differentiated than the counterparts of other systemic organs. The malignant cells could localize in epithelium for quite a long time without invading the corneal stroma. This phenomenon may correlate to the condensation texture of corneal lamina. Squamous cell carcinoma of cornea had typical clinical features. It usually appeared as a whitish, rough, irregular lesion or a telangiectatic, gelatinous epibulbar mass. As tumor progressed, it could penetrate the corneal lamina into the stroma or even intraocular tissues. However, distant metastasis from corneal tumors was seldom observed. Of our 39 cases, 2 patients with squamous cell carcinoma had intraocular tumor infiltration. Pa-

pilloma is a benign tumor, documented to be associated with human papillomavirus (subtypes 6, 11, 16, and 18) infection. It appears as a cauliflower-like or papilliform of tissue arranged in a pedunculated configuration. Of 3 cases with squamous papilloma, all appeared as pink papilliform. Nevus usually has a long time course with no or slight pigmentation before puberty. It is a thin or flat elevated lesion at first. Afterwards, it may be enlarged and deeply pigmented. Of our 12 cases with nevus, 8 patients complained of enlarging masses, which were typically located in the interpalpebral bulbar conjunctiva near the limbus and remained relatively stable throughout life with < 1% risk of evolving into malignant melanoma¹⁵. The visual acuity in 18 patients with malignant corneal tumor was remarkably reduced. Nine cases of them were < 20/70 (50%), including a case with no light perception. Of the patients with benign tumors, only 3 of 17 patients had the visual acuity of < 20/70 (17.65%).

Excisional surgery is commonly employed in corneal tumors. If the lesion is not large enough, then excisional surgery can have good therapeutic outcome. However, for primary malignant tumors of the cornea such as squamous cell carcinoma and melanoma, it is often necessary to remove more tissues 2.0 mm outside the margin of corneal mass to achieve tumor-free margins and to decrease the chance for tumor recurrence. A gentle technique without touching the tumor (no touch technique) is advised. The surgery ought to be performed using microscopic technique and the operative field should be kept dry so that cells adhere to the resected tissue. It is unwise to wet the field with balanced salt solution before the tumor is completely removed. In cases where excessive cornea is sacrificed, a lamellar keratoplasty may be employed for reconstruction. The same for conjunctiva, amniotic membrane graft or transfer of conjunctival flap may be employed. However, it is not necessary to have corneal lamellar keratoplasty in most patients with corneal tumor due to only epithelial involvement. In our cases, only 2 patients were required to have partial lamellar keratoplasty. When the tumor invaded the sclera, we should remove a thin lamella of sclera to achieve tumor-free margins. Unlike conjunctive tumor, it is

not necessary to treat the corneal tumor margin with cryotherapy. The tumor bed of the cornea is best treated with absolute alcohol wash on cotton tip applicator. Enucleation must be performed if intraocular invasion happened. In cases with tumors having invaded the orbit, subtotal or total exenteration is advised. If tumors had greater aggressiveness or greater tendency of distant metastasis in the early stage, chemotherapy or radiotherapy is needed post-operatively. Shields et al suggested that combined therapeutic approaches, consisting of extensive tumor removal, cryotherapy, and topical mitomycin C, can be effective in the management of diffuse conjunctival and corneal melanoma arising from primary acquired melanosis⁹. For the tumors that shows high relapse rate, such as squamous papilloma, Sudesh et al reported that excision with adjunctive cryotherapy of neoplasms appears to result in a lower recurrence rate¹⁶. And complete cryotherapy of mass down its stalk to its base is performed. Moreover, topical chemotherapy, like mitomycin C or interferon can be effective to decrease relapse rate³. In short, the management of patients with corneal tumor is not an easy job. Clinician often was in a dilemma as to make a choice between conservative treatment plan and enlarged treatment plan. Whether benign or malignant tumors, once conjunctiva, sclera or intraocular extension is made, excision field must be enlarged, surgery is more difficult, rehabilitation time extended, and threaten for visual function is more great. So, despite the category of tumors, cautiously management is needed. The therapeutic plans including excisional biopsy and histopathologic examination must be performed as early as possible.

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