Overview of recurrence in ocular tumors in a developing country scenario

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Abstract

Purpose: Recurrence of tumor has devastating morbidity and mortality. Present study was conducted to evaluate recurrence in ocular tumor in oculoplastic cases operated at our centre.

Methods: Prospective longitudinal observational study was conducted from December 2012 to October 2014. Patients of ocular tumors managed by surgical intervention were selected for the study. Biopsies were sent for histopathological examination. Cases were followed to look for recurrences.

Results: 68 patients required surgery for tumors. Sixteen patients were lost during follow up. Out of 39 benign cases only 4 cases (10%) had recurrence. In malignant group 5 cases (38%) had recurrence out of total 13 cases. Refusal to chemotherapy after debulking surgery led to recurrence in two cases.

Conclusion: Patient counseling regarding benefits of follow up is emphasized for early detection and management of recurrences.

Keywords: Cryotherapy, Counseling, Developing country, Ocular tumors, Recurrence.

Introduction

Dealing ocular malignancy is a challenge and even more stressful is encountering the recurrences. There are various reasons for recurrences like profile of tumor, modality of treatment and patient compliance. Treatment of ocular adnexal tumors includes conventional surgery, various histologically controlled surgical techniques, radiotherapy and electrodesiccation.[(1)] Many new treatment modalities like photodynamic therapy (PDT)[(2)] topical imiquimod[(3)] and interferon α2b[(4)] also provide a good option.

As per literature surgery remains the main treatment modality for ocular tumor.[(5)] In order to minimize the risk of incomplete excision, a wide margin excision is required, which is fairly arbitrary and varies with tumor type.[(6-8)] Margin control can also be achieved by the use of frozen section. But there are inherent inaccuracies in frozen-section techniques, and it is not unusual for frozen sections to be clear with involved margins on paraffin-fixed specimens. Routine paraffin-fixed specimens take several days to be processed, but the specimens can be processed. Moh's micrographic surgery (MMS) is widely regarded as the gold standard for tumor excision.[(9-13)] However, published relapse rates vary widely between different studies reaching from below 1% to over 4% after several years.[(14,15)] Cost and time pose restriction to MMS in selected cases.

Radiotherapy achieves comparable cure rates to surgery for small malignant tumors.[(16,17)] However there is no histological evidence of tumor clearance. The recurrence rates after radiotherapy are higher than for surgery, especially for large tumors and sclerosing subtypes.[(18-20)] When recurrence occurs it is usually difficult to diagnose, is fairly extensive and more difficult to manage.[(21)] 5-Fluorouracil (5-FU) is an antimetabolite, approved for topical treatment of BCC.[(22)] As a result of high rates of adverse effects, dependence on patient compliance and relatively lower clearance rates compared with other treatment modalities, its use is limited to treating small tumors in low-risk locations, in patients who cannot undergo treatment with better-established therapies.[(23)] In recent years there has been much interest in use of imiquimod to treat lentigo maligna, BCC subtypes, and SCC[(24-29)] but the clearance rates are inferior to surgery.[(24)] PDT relies on oxygen singlet free radicals, derived from a photochemical reaction between a photoactive molecule (photosensitizer) and light, to produce target cell injury and death.[(22,24)] BCC treatment is the most common oncologic application of PDT.[(24)] Although modest short-term cure rates have been reported[(30,31)] long-term recurrence rates are higher[(32)] and the efficacy of PDT in the long term is yet to be established.[(24)] Thus none of the above modality is gold standard for treating tumors. Cost of treatment and patient profile are important factors for consideration in treating tumors.

Taking into consideration the patient profile and low infrastructure availability, cryotherapy of the tumor bed and margins is an upcoming recommendation at many developing centers.[(33)] It provides a low cost option to micrographic surgery.[(12)] It preserves much healthy eyelid structures. Epithelium and endothelium can grow fast into the treatment area, the functional and cosmetic results are excellent. Lacrimal pathways remain patent.[(34)] Neither entropium nor ectropium develop. The treatment area can be extended without creating problems of defect coverage. Reconstructive surgery is unnecessary. The risks of dislocation of tumor cell nests or hidden growth beneath grafts are avoided. Anticoagulant therapy needs no interruption. There are no prob-

lems of wound healing should a second cryosurgical or surgical intervention be needed in the same area.[12] The tumor is frozen to −30°C to induce cryodestruction, with either a cryoprobe or liquid nitrogen spray, using a double freeze–thaw technique and protecting the globe.[5] The lacrimal apparatus is relatively resistant to cryotherapy, which can be used to treat lesions in close proximity to the punctum or canaliculus.[21]

Present study was conducted to evaluate recurrence in ocular tumor in oculoplastic cases operated at our centre.

Material and Methods

- **Ethics:** Ethical approval for the study (notice no. 52(A)/ND/2013) was provided by the institutional Ethics Committee on 24 June 2013. The study was conducted as per guidelines of the Declaration of Helsinki. Written informed consent was obtained from the study participants and patient identity has not been disclosed in any form.
- **Study design:** A longitudinal, prospective observational study was conducted from December 2012 to October 2014.
- **Selection of patients:** The patients attending outpatient department (OPD) of Ophthalmology for various oculoplastic complaints were selected for the study.
- **Inclusion Criteria:** Patients presenting with growths / masses / tumor of orbit, eye appendages (lid/lacrimal gland and apparatus), conjunctiva, cornea/ limbus, medial/lateral canthi and caruncle were included.
- **Exclusion Criteria:** All cases of tumors of uveal tissue, posterior chamber, retina, optic nerve or secondaries from other tumors in the body were not included. Also patients of tumor not willing to undergo surgery or participate as study case were excluded.
- **Methodology:** Comprehensive history was recorded and physical examination was performed. Preoperative investigations were done such as complete blood count, random blood sugar, bleeding time, clotting time, HIV & HBsAg status and Xray/ CT scan/ MRI head & orbit as per requirement.

All patients were subjected to surgical management. Excisional biopsies of resect able tumors and incisional biopsies from advance malignant tumours (which were rendered inoperable due to their size or depth) were sent for histopathological examination. Patients were followed up monthly to look for recurrences.

Results

Out of 676 cases operated for various oculoplastic complaints, 68 patients required surgery for tumors. Sixteen patients were lost during follow up.

Most common site of involvement of tumor was upper eyelid (28.8%) followed by periorbital area (21.2%) and lower eyelid (19.2%). Upper and lower eyelid together constituted about 48% of total cases. Remaining tumors were found in conjunctiva (13.5%), cornea /limbus (5.8%), medial canthus (5.8%), lacrimal sac area (3.8%) and lateral canthus (1.9%) (Table 1).

Table 1: Distribution of site of involvement

Site	Number	%
Periorbital area	11	21.2%
Upper eyelid	15	28.8%
Lower eyelid	10	19.2%
Conjunctiva	7	13.5%
Cornea / Limbus	3	5.8%
Medial canthus	3	5.8%
Lateral canthus	1	1.9%
Lacrimal sac area	2	3.8%
Total	52	100%

Thirty nine cases (75%) were benign while the remaining 13 cases (25%) were malignant.

Naevus and dermoid (6 cases each, 15.4%) were the commonest benign lesion followed by sebaceous cyst (5 cases, 12.8%) (Table 2). Most common malignant tumors were squamous cell carcinoma and sebaceous cell carcinoma (4 cases each, 30.7%). Other malignant tumors were basal cell carcinoma, adenocarcinoma, orbital melanoma, malignant spindle cell, fibrous cell tumor, refractory neuroblastoma each representing 7.7% (1 case each) (Table 3).

Table 2: Histopathological profile among benign tumor

Histopathological Profile	Number	%
Naevus	6	15.4%
Dermoid	6	15.4%
Sebaceous cyst	5	12.8%
Cavernous hemangioma	4	10.3%
Squamous papilloma	4	10.3%
Abscess	3	7.7%
Capillary hemangioma	2	5.2%
Dermolipoma	2	5.2%
Epithelial inclusion cyst	2	5.2%
Fibroepithelial cyst	1	2.6%
Plexiformneurofiroma	1	2.6%
Lacrimal cyst	1	2.6%
Cutaneous lymphoid	1	2.6%
Total	39	100%

Table 3: Histopathological profile among malignant tumor

Histopathological Profile	Number	%
Squamous cell carcinoma	4	30.7%
Sebaceous cell carcinoma	4	30.7%
Basal cell carcinoma	1	7.7%
Adeno carcinoma	1	7.7%
Orbital melanoma	1	7.7%
Malignant spindle cell fibrous cell tumor	1	7.7%
Refractory neuroblastoma	1	7.7%
Total	13	100%

Out of 39 benign cases only 4 cases (10%) had recurrence. In malignant group 5 cases (38%) had recurrence out of total 13 cases (Table 4). Maximum recurrence in benign group was seen during 3rd month of follow up. Maximum recurrence in malignant group was seen in 1st month (Table 5).

Table 4: Rate of recurrences on follow up

	Number of Recurrence	Total Cases	%
Benign	4	39	10.3%
Malignant	5	13	38.5%
Total	9	52	17.3%

Table 5: Overview of time duration of recurrence of tumor

Time duration	Benign		Malignant	
	No.	%	No.	%
Day 1	0	0%	0	0%
Day 7	0	0%	0	0%
1 month	0	0%	3	60%
3 month	2	50%	1	20%
6 month	1	25%	0	0%
1 year	1	25%	1	20%
1.5 year	0	0%	0	0%
Total	4	100%	5	100%

Discussion

676 oculoplastic cases (squint, lid abnormalities, lacrimal passage blockage etc.) were operated during the study interval. Out of these 68 patients (10.06%) required surgery for ocular tumors. Unfortunately 16 patients were lost to follow up. Thus a good motivation and counseling is required to reduce the morbidity and mortality in case of tumors. It should be explained to patient that merely getting operated does not get them rid off the tumor. They should be told about the recurrence chances and symptom to recognize them. Also emphasis on regular follow up with the operating surgeon is essential as recurrence does not necessarily manifest with a definite pattern of sign and symptom as explained during counseling.

As expected, recurrences are much higher in malignant group as compared to benign group. Thus cases which turn out to be malignant on histopathological examination should be dealt with extra caution. A record of contact information should be kept with the staff and follow up should be meticulously noted down.

Five (38.5%) out of 13 malignant cases had recurrence. Out of these 60% recurred at 1 month, 20% each at 3 month & 1 year follow up (Table 5). Two patients (one each of refractory neuroblastoma and squamous cell carcinoma) refused chemotherapy after debulking surgery which led to recurrence. Thus patient counseling is an essential part of management of malignancies. Other probability of high rate of recurrence could also be due to incomplete removal of tumor mass despite best efforts to obtain clear margins. This category included tumor like squamous cell carcinoma, basal cell carcinoma, and sebaceous cell carcinoma (one case each). Examination of the excision margin assesses the adequacy of tumor clearance is of utmost importance. In order to minimize the risk of incomplete excision, conventional surgery for periocular skin cancer usually involves a wide margin, which is fairly arbitrary, and varies with tumor type.[6,7] Margin control can also be achieved by the use of frozen section, MMS.

As discussed earlier, cryotherapy of the tumor bed and margins provides a low cost option.[12] There are many applications of cryosurgery in the field of ophthalmology. After popularization of cryoretinopexy and cryoextraction, cryotherapy with different cryogens was used to treat a variety of benign and malignant eye diseases.[35] Cryosurgery is an effective treatment modality for eyelid basal cell carcinomas. It results in good cosmetic and functional outcomes at a low cost. It is a effective means of treating tumors, achieving cure rates in excess of 90% with 5-year recurrence rates of 0–5% for small BCCs in several larger series.[12,35] Fraunfelder and colleagues described cryosurgical treatment of ocular and periocular squamous cell carcinomas in humans.[36,37] It is useful for treating patients who are unfit for surgery or have multiple lesions requiring treatment, for example, basal cell naevus syndrome.

There are no side effects of Cryotherapy unlike PDT or imiquimod hich needs supervision. It produces a profound tissue reaction resulting in swelling, erythema, blistering, and exudation of the periocular skin, which usually resolves within a fortnight.[5] Many other advantages have been mentioned earlier.

Thus, considering literature support, cryotherapy is a good option to reduce the recurrence rate of tumor especially in developing countries where facility of micrographic surgery or even frozen section is limited due to lack of resources. Cryotherapy of the tumor bed and margins is recommended for malignant tumors to reduce morbidity and mortality.

In the end we again emphasize the need of proper counseling of patients considering the drop out cases

and high recurrence rate of malignant tumors due to incomplete treatment.

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