Original Article

Epidemiological Study and Treatment Outcome of Primary Ocular and Adnexal Malignancies in a Rural Indian Tertiary Eye Care Center

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Abstract

Purpose: Malignancies of the eye and adnexa are rare, and account for only 0.2–0.8% of all human malignancies. Although specific tumor related studies are reported in the literature, a study of all the ocular malignancies are very few, and to the best of our knowledge, none from a rural population. The purpose of this study was to examine the prevalence and treatment outcomes of primary ocular malignancies in rural India. M**aterials and Methods:** A retrospective analysis of 92 histopathologically proven primary ocular and adnexal malignancies encountered at Pravara Rural Medical College, Loni, over a period of 20 years (July 1994–June 2014) was undertaken. Patients of all age groups were included. **Results:** Squamous cell carcinoma was found to be the most common primary ocular malignancy. A bimodal peak was observed in the age distribution, one during the first decade due to retinoblastoma and the second in the fifth decade due the other malignancies. Squamous cell carcinoma was the most common malignancy with 38.04%, followed by retinoblastoma 25%. A combined approach of surgery, chemotherapy and radiotherapy was used to save life, salvage the eye and possibly maintain useful vision. Reconstruction of the orbital and periorbital region was also done wherever possible. **Conclusion:** Retinoblastoma was the most common malignancy in the first decade of life. Squamous cell carcinoma was the most common malignancy overall. The presence of HIV in cases of squamous cell carcinoma, especially among young patients, should be kept in mind. The outcome of management is better, with possible cure, if diagnosis is made early and proper surgery along with other adjuvant measures are undertaken.

Keywords: Epidemiological study, periocular malignancies, primary ocular malignancies, rural India

Introduction

Malignancies of the eye and adnexa are rare and account for only 0.2–0.8% of all human malignancies.[1] Although specific tumor related studies are reported in the literature, a study of all the ocular malignancies are very few, and to the best of our knowledge, none from a rural population. The purpose of this study was to examine the prevalence and treatment outcomes of primary ocular malignancies in rural India.

Materials and Methods

A retrospective analysis of 92 histopathologically proven primary ocular and periocular malignancies encountered at Pravara Rural Medical College, Loni, over a period of 20 years (July 1994–June 2014) was undertaken. The ethical clearance was obtained from Pravara Institute of Medical Sciences, Loni, Maharashtra, India; and there was adherence to the tenets of the Declaration of Helsinki, during the study. The data as per the pro forma was collected from the files and records.

Patients who had <1 year of follow-up were excluded. The study included only primary ocular and periocular malignancies.

Results

A total of 92 primary ocular and periocular malignancies were documented during this period. 49 (53.26%) were males and the rest 43 (46.73%) were females. The mean age of presentation was 45.68 years (±3.26). The age

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Table 1: Age distribution of patients

Age group (years)	Males (*n*)	Males of total (%)	Females (*n*)	Females of total (%)	Total (*n*)	Total (%)
0–10	9	9.78	10	10.86	19	20.65
11–20	5	5.43	2	2.17	7	7.60
21–30	5	5.43	4	4.34	9	9.78
31–40	6	6.52	2	2.17	8	8.69
41–50	6	6.52	5	5.43	11	11.95
51–60	11	11.95	8	8.69	19	20.65
61–70	3	3.26	6	6.52	9	9.78
71–80	3	3.26	4	4.34	7	7.60
Over 80	1	1.08	2	2.17	3	3.26
Total	49	53.26	43	46.73	92	100

Table 2: Distribution of ocular malignancies by type

Type of ocular malignancy	Number of cases (*n*)	Percentage of cases
Squamous cell carcinoma	35	38.04
Retinoblastoma	23	25
Basal cell carcinoma	16	17.39
Malignant melanoma	7	7.60
Meibomian gland carcinoma	5	5.43
Rhabdomyosarcoma	3	3.26
Sebaceous gland carcinoma	3	3.26
Total	92	100

distribution of these patients is described in Table 1, and the types of malignancies are described in Table 2. The mean age was 47.24 years (±3.74) in males and 43.39 years (±3.04) in females. A bimodal peak was observed in the age distribution, one during the first decade due to retinoblastoma and the second in the sixth decade due to the other malignancies. A bimodal peak was observed in the age distribution, one during the first decade due to retinoblastoma and the second in the fifth decade due the other malignancies. The majority of the study cases were formed by squamous cell carcinoma with 35 cases (38.04%), and retinoblastoma 23 cases (25%). A high percentage of patients (65.71%) with squamous cell carcinoma were HIV positive, most of them being in the 15–35 years age group. In all, 16 cases (17.39%) were diagnosed with basal cell carcinoma. The rest of the cases were formed by malignant melanoma (both extraocular and intraocular) with seven cases (7.6%), meibomian gland carcinoma with five cases (5.43%), rhabdomyosarcoma with three cases (3.26%), and sebaceous gland carcinoma with three cases (3.26%). The average life expectancy after treatment was more than 3 years, lowest being in malignant melanoma and the highest in basal cell carcinoma. The overall favorable visual outcome was achieved in 62.65% of cases.

Out of total 23 cases of retinoblastoma, 7 (30.43%) were bilateral. The average age of presentation was 2.4 years. There were 13 males and 10 females. Bilateral retinoblastoma children were treated initially with chemotherapy followed by enucleation of the worse eye. Among these bilateral retinoblastoma cases, none was found to have trilateral retinoblastoma after the computed tomography scan report. Six patients underwent the only enucleation without radiotherapy or chemotherapy as histopathology suggested no involvement of the optic nerve and there was no evidence of metastasis. However, they were kept under regular follow-up. Three patients required total exenteration of the orbit due to late presentation. Four patients received combined radiotherapy and chemotherapy after enucleation. Three patients received only radiotherapy. However, 7 (30.43%) bilateral cases received only chemotherapy before enucleation. Follow-up ranged from 2 months to as high as 12 years. Average follow-up period was only 1.2 years. Only one child had 12 years follow-up since the age of 4 years up to the age of 16 years, who was fitted with customized ocular prosthesis with the help of prosthetics department.

Among 35 cases of squamous cell carcinoma, 23 (65.71%) were of limbal origin, 7 (20%) cases were only conjunctival origin and 5 (14.28%) cases were from the lid. The average age of presentation was 24.4 years. Among these 35 cases, 23 (65.71%) were positive for HIV. Among 30 cases of squamous carcinoma of cornea and conjunctiva, 28 cases underwent excision with superficial keratectomy wherever required. Ten patients were given topical mitomycin C drop (0.04%) after excision. Three cases of corneo-conjunctival origin and two cases originating from lid required exenteration with full thickness skin graft followed by radiotherapy and chemotherapy. Two cases originating from lid were managed with reconstructive surgery of the lid followed by chemotherapy.

Among 16 diagnosed cases of basal cell carcinoma average age of presentation was 52.3 years. 14 were managed with different types of reconstructive surgery of the lid ranging from simple excision, tangent flap reconstruction, rotational full thickness pedicle flap and full thickness skin graft from the post the auricular region. Three cases required a combination of chemotherapy and radiotherapy as they showed evidence of distant metastasis during the follow-up period. Two underwent exenteration due to late presentation.

Although malignant melanoma of the eye and periocular region is very rare among Indian population, we came across a total seven cases (7.60%) during this period. 6 were of intraocular origin, and only one was conjunctival malignant melanoma. Average age at the time of presentation was 56.4 years. All the six cases of intraocular origin, were choroidal malignant melanoma as confirmed after histopathology. Two cases had extraocular spread at the time of presentation and underwent exenteration with full thickness skin graft which was retained in position with our novel method by using a dental mold. Once the skin graft was taken up, customized ocular prosthesis was made by Prosthetic Department of our dental college. Interestingly, this also evolved with time, from spectacle supported one to removable one which can adhere with the surrounding skin with perfect skin color.

Out of six cases of choroidal malignant melanoma, 5 had distant metastasis which was treated with appropriate chemotherapy. The sixth patient had no distant metastasis at the time of presentation but was lost after first follow-up. The most interesting patient from our malignant melanoma series was of conjunctival malignant melanoma which was treated with excision of the mass with partial sclerectomy followed by cadaveric scleral graft. This patient surfaced after 2 years of initial follow-up with secondaries over the submandibular region for which she refused any further surgery or chemotherapy.

Among five cases of meibomian gland carcinoma all were being treated as chalazion outside. In fact, 3 had so-called chalazion curettage once or twice. The most striking feature of all the cases was the consistency of the mass which was hard and the age of the patient. The average age of presentation was 65.8 years, highest average age among all primary ocular malignancies. All patients had a mass over the upper lid. The mode of surgery was wide excision with rotational full thickness pedicle flap from the lower lid. None had any sign of secondaries at the time of presentation or up to the last follow-up.

Among all our primary ocular malignancy cases, we had only three cases of rhabdomyosarcoma. One was a child of only 1 year age who presented like an acute orbital cellulitis and died within few days of our diagnosis before we could start any definitive treatment. Other two patients were in their thirties and responded well with radiotherapy and survived more than 3 years.

In our series, we came across only 3 such cases. Two were managed with wide excision of the upper lid with rotational pedicle flap from the lower lid without any adjuvant therapy. The third was managed with total exenteration with full thickness skin graft followed by chemotherapy and skin fitted ocular prosthesis.

The average life expectancy after treatment was 2.7 years, lowest being in malignant melanoma (4 months) and the highest in basal cell carcinoma (9 years). Overall favorable visual outcome (vision better than 6/60) was achieved in 62.65% of cases.

Discussion

Our study included 53.26% of males and 46.73% of females as compared to 45.8% of males and 54.2% of females as per a study in Nepal and closer to 53.6% and 46.4% in Singapore.[2,3] The study expressed bimodal age distribution with one peak around 15 years and another around 55 years similar to other reports.[3-6]

We found 35 cases of squamous cell carcinoma of which 23 were of limbal origin, 7 cases were only conjunctival origin and 5 cases were originating from the lid. The most common malignancy in this study was squamous cell carcinoma (38.04%), supported by other studies in Nepal and Sudan.[4] Poso *et al*. also reported it as the commonest tumor in their study with 33.5% cases.[5] Ultraviolet spectrum could be a factor for high incidence of this tumor as a large number of persons work in the open sun, especially farmers and workers are exposed to it.

The incidence of basal cell carcinoma in our study was 17.39% with an average age of presentation being 52.3 years. Reports from Sudan and Papua New Guinea revealed 6.1%, and 9.1%, respectively, with average age of 54 years.[7-9]

The incidence of sebaceous carcinoma in our study was found to be 3.26% which is comparable to study in Papua New Guinea (1.7%).[9] In a study held at Shanghai (China) it was found to be 31.7%.[10] This variation may account for the geographical factors in the study involved. Studies in Korea and India found 21.2% and 33%, respectively.[4,11] However, according to Kass and Hornblass, it accounts for 1–5.5% of all eyelid malignancies in the USA.[12]

Retinoblastoma in our series revealed 3.26%. It varies greatly from some reports of 32%, and 31.7%.[4,13] Other studies reported 20.8% and 19.8%, respectively.[8,14] Marshall observed it as the most common ocular malignancy in children.[7]

The clinical approach requires a meticulous and careful preliminary ophthalmological assessment, including an analysis of the patient and his or her family's clinical histories to identify elements useful for diagnosis and prognosis. Family history must be analyzed for neoplasms and hereditary and degenerative diseases, and in some cases, the patient's relatives must undergo examination. A systematic examination continues with a full ophthalmological evaluation. The final diagnosis is always based on the histopathological confirmation. For intraocular or orbital tumors, fine needle aspiration biopsy is necessary.

The presentation is generally late due to casual attitude of patients along with the lack of awareness, poverty and ignorance, especially in rural India. Lack of eye care services and improper management make them vulnerable to the risk of losing, not just their vision but also life. Some of

these cases need complicated surgery and long-term follow-up for a favorable outcome. Many need adjuvant radiotherapy and/or chemotherapy in addition to primary surgery. In spite of all efforts, many lives are lost due to late presentation, delayed diagnosis and consequent problems.

Treatment in ocular and orbital oncology is based on teamwork (ophthalmologist and oncologist). Currently, the approach to the ocular tumor is as conservative as possible, meaning that it attempts to destroy the neoplastic lesion while preserving the eye and the visual function. When the conservation of the eye affected by the (malignant) neoplasm endangers the life of the patient, the eye must be enucleated. Tumors of the conjunctiva, eyelids, and orbital tumors are treated conservatively: In these cases, damage to the ocular bulb must be limited as much as possible.

Systemic chemotherapy can be part of a treatment plan for ocular and orbital tumors under a multidisciplinary approach. They are used mostly in the treatment of tumors of the conjunctiva, especially in multicentric and widespread tumors. Radiotherapy is the main and most effective method for the treatment of benign and malignant eye tumors.

Timely diagnosis and management of periocular malignancies are essential because of their proximity to and potential to invade vital structures such as the orbit, sinuses, and brain. Surgical excision remains the standard of care for the majority of periorbital malignancies. Depending on tumor type, other treatment modalities may include radiation, chemotherapy, cryosurgery, topical medications, and photodynamic therapy.

The incidence of squamous cell carcinoma was much higher when compared to other studies, and the incidence of meibomian gland carcinoma was much lower.[14,15] Incidences of rest of the malignancies were comparable to previous studies. However, the strong association of squamous cell carcinoma and HIV infection is an interesting finding in our study.

This study highlights the successful management in a variety of primary ocular malignancies along with good visual and cosmetic outcome whenever possible. The outcome of management is better, with a possible cure, if the diagnosis is made early and proper surgery along with other adjuvant measures are undertaken. Further, the presence of HIV in cases of squamous cell carcinoma, especially among young patients, should be kept in mind as seen in this study.

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Conflicts of interest

There are no conflicts of interest.

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