RESEARCH PAPER

Ocular and Periocular Tumors in Asian Indian Children and Adolescents

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Objective: To describe eye tumors in Indian children (age ≤ 21 years) presenting to a multi-tier ophthalmology hospital network in India. **Methods:** Hospital-record review. **Results:** During the 3-year study period (November, 2015-October, 2018), 2911 children were diagnosed with 3003 eye tumors. The three most common benign tumors included conjunctival nevus (445, 22%), orbital dermoid cyst (206, 10%), and periocular infantile capillary hemangioma (181, 9%). The three most common malignant tumors included retinoblastoma (835, 88%), xeroderma pigmentosa related ocular surface squamous neoplasia (38, 4%), and rhabdomyosarcoma (17, 2%). Based on the age group, retinoblastoma (*n*=834, 28%) was the most common tumor in all groups, except adolescence where conjunctival nevus (*n*=194, 21%) was the most common. **Conclusion:** Overall, retinoblastoma is the most common tumor in children encountered in a referral based comprehensive ocular oncology practice in India.

Keywords: *Cancer, Conjunctival nevus, Eye, Retinoblastoma*.

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The incidence of cancer in children and adolescents is comparatively low [1,2], and the most common malignancies in children include leukemia, lymphoma, and central nervous system tumors [3].

Retinoblastoma has been reported in a population-based registry study to be the fourth most common cancer in children aged 0 to 14 years, constituting 6% cases, but it was rare in older children and adolescents (<1%) [3]. There is no big data analysis focusing on ocular tumors in children and adolescents. In this study, we describe the profile of benign and malignant ocular tumors in Indian children and adolescents.

METHODS

This was a retrospective hospital-based study of children diagnosed with eye tumors presenting between November, 2015 and October, 2018 to four referral centers spread across four states in India. For this study, a patient was considered as a child when the age was 21 years or lower [4]. They were further classified as neonate (birth to 27 days), infant (28 days to 12 months), toddler (1 to 2 years), childhood (3 to 11 years), and adolescence (12 to 21 years) [4]. Consent for electronic data privacy was obtained from the patient (if age at presentation was >18 years) or parents/guardians (if age of the patient was ≤18 years) at the time of registration. No identifiable information of the patient was used for analytical purposes. Each patient underwent a comprehensive ophthalmic examination, and data were entered into a browser-based in-house developed electronic medical records system (eyeSmart EMR). The study was approved by the Institutional Ethics Committee of the institute.

The data of all children diagnosed with eye tumors during the study period was retrieved from the EMR database. The patients with a confirmed clinical and/or histopathological diagnosis were included in this study. All patients who underwent surgical intervention had a confirmed histopathological diagnosis. Those with uncertain diagnosis or inadequate data were excluded. The data on patient demographics, ocular diagnosis, tumor status, and anatomical category were used for analysis.

Statistical analyses: Descriptive statistics was used to elucidata demographic and diagnostic data using Microsoft Excel 2013 (Microsoft Corporation, Redmond, USA).

RESULTS

Of the 728,077 new patients presenting to the four centers of the network during the period under study, 118,648 (16%) patients were at or below the age of 21 years. Of these, 3506 (2.9%) were diagnosed with eye tumors. Of

these, 595 patients who did not have a confirmed diagnosis of eye tumor were excluded from the study, and 2,911 (2.4%) patients (51% males) with a definitive diagnosis of benign or malignant tumor, either by clinical examination or confirmed by histopathology were included in the study.

The median age (range) at diagnosis was 7 years (2 days to 21 years). The age-wise distribution of patients with eye tumors included neonates (*n*=18, 0.6%), infants (*n*=242, 8.3%), toddlers (*n*=511, 17.5%), childhood (*n*=1259, 43.2%), and adolescents (*n*=655, 22.5%). Majority of patients (24%) were in the age group of 6 to 11 years.

There were 3,003 tumors (69% benign) in 2,911 patients, which were segregated into nine anatomical categories. The most common anatomical part involved was the conjunctiva with 949 (31.6%) cases and the least was lacrimal sac with 1 case ***(Table* I)**.

The three most common tumors included retinoblastoma (835, 28%), conjunctival nevus (445, 15%), and orbital dermoid cyst (206, 7%). Amongst the benign tumors, the three most common were conjunctival nevus (445, 22%), orbital dermoid cyst (206, 10%), and periocular infantile capillary hemangioma (181, 9%). Amongst the malignant tumors, the three most common were retinoblastoma (835, 88%), Xeroderma pigmentosa-related ocular surface squamous neoplasia (OSSN) (38, 4%), and rhabdomyosarcoma (17, 2%). The most common tumor in the eyelid was infantile capillary hemangioma (*n*=181, 6%); in caruncle inclusion cyst (*n*=9, <1%); in conjunctiva, conjunctival nevus (*n*=445, 15%); in iris trauma-related iris stromal cyst (*n*=15, <1%); in ciliary body, medulloepithelioma (*n*=5, <1%), in retina, retinoblastoma (*n*=835, 28%); in choroid, toxocara granuloma (*n*=15, <1%), in orbit, dermoid cyst (*n*=206, 7%); and in lacrimal sac, granuloma (*n*=1, <1%).

The most common tumor in younger children (0-2 years, 800 tumors) and older children (3 to 11 years, 1277 tumors) was retinoblastoma (50% and 31%, respectively), In adolescents (12-21 years, 926 tumors), conjunctival nevus (194, 21%) was the most common. Distribution according to the age is presented in ***Table* II**.

Table I Anatomical Distribution of Ocular and Peribocular Tumors and Tumor Status According to Age Group

Feature	*Benign (n=2058)*	*Malignant (n=945)*	*All cases (N=3003)*
Tumor location			
Conjunctiva	907 (96)	42 (4)	949 (32)
Retina	68 (7)	842 (93)	911 (30)
Orbit	483 (90)	54 (10)	536 (18)
Eyelid	469 (99)	5 (1)	474 (16)
Choroid	51 (98)	1 (2)	52 (2)
Iris	49 (98)	1 (2)	50 (2)
Caruncle	23 (100)	0	23 (<0.8)
Ciliary body	7 (100)	0	7 (<0.2)
Lacrimal sac	1 (100)	0	1 (<0.2)
Age category			
Neonate	15 (0.7)	5 (0.4)	20 (0.7)
Infant	160 (8)	94 (9.9)	254 (8)
Toddler	218 (11)	308 ( )	526 (18)
Childhood	835 (41)	442 ( )	542 (43)
Adolescence	830 (40)	96 ( )	926 (30)

All values in n (%).

Histopathological confirmation of diagnosis was available in 792 (26%) tumors, while the remaining 2211 (74%) tumors were diagnosed clinically. Accurate clinico-pathological correlation was noted in 747 (94%) tumors, while discordance between clinical and histopathological diagnosis was noted in 45 (6%) tumors. Of the cases with a discordant clinical and histopathological diagnosis, three tumors had a clinical diagnosis of benign tumor, while histopathology revealed a malignant tumor; 9 (1.1%) tumors had a clinical diagnosis of malignant tumor, while histopathology revealed a benign tumor; and 26 (3.3%) tumors had a different diagnosis in the same category of benign tumors; and 7 (0.9%) tumors had a different diagnosis in the same category of malignant tumors.

Table II Ocular and Periocular Tumor Distribution According to Age in Indian Children and Adolescents

Age group	*Commonest tumor (n=3003)*	*No. (%)*	*Commonest benign tumor (n=2058)*	*No. (%)*	*Commonest malignant tumor (n=945)*	*No. (%)*
Neonate	Retinoblastoma	4 (20)	Dermolipoma	2 (12)	Retinoblastoma	4 (80)
Infant	Retinoblastoma	95 (37)	Infantile capillary hemangioma	94 (59)	Retinoblastoma	95 (99)
Toddler	Retinoblastoma	302 (57)	Infantile capillary hemangioma	48 (22)	Retinoblastoma	302 (98)
Childhood	Retinoblastoma	394 (31)	Conjunctival nevus	240 (29)	Retinoblastoma	394 (89)
Adolescence	Conjunctival nevus	194 (21)	Conjunctival nevus	194 (24)	Retinoblastoma	39 (40)

WHAT THIS STUDY ADDS?

- Retinoblastoma was the most common ocular tumor encountered in a referral-based ocular oncology set-up.
- The most common tumor in each age group differs, with retinoblastoma being common in children and conjunctival nevus in adolescents.

DISCUSSION

Both benign and malignant ocular tumors can occur during childhood and adolescence [5-11]. We found conjunctival nevus to be most common benign tumor in children and retinoblastoma as the most common malignant tumor. Retinoblastoma was also the most common tumor in children encountered in this referral-based hospital setting.

The limitations of our study include the retrospective nature of the study and possible referral bias since it is a hospital-based study. However, the strength of the study includes larger number of patients and accurate diagnosis by a trained ocular/ophthalmic oncologist, resulting in a good clinico-pathological correlation in 94% tumors, whenever histopathological diagnosis was available.

Reddy, *et al*. [5] reviewed 75 ocular tumors in children aged 3 months to 12 years and found 52% to be benign; retinoblastoma (44%) was the most common tumor, constituting 92% of all malignant ocular tumors in children. In their study, non-specific conjunctival granuloma was the most common benign tumor constituting 33% of all benign tumors in children [5].

In a review of 806 children with conjunctival tumors, 97% were benign and 3% were malignant with the most common benign conjunctival tumor being nevus (61%) [12]. Conjunctiva was the most common tissue involved by a tumor in our study also, with nevus being the most common. OSSN was the second most common malignant tumor in our patients. All children and adolescents with OSSN had associated xeroderma pigmentosum. It is well established that patients with xeroderma pigmentosum develop ocular and periocular tumors at younger age compared to the general population [13].

In conclusion, benign tumors are more common in children and adolescents except in cases with retinal tissue involvement. Eventhough benign tumors may not be life-threatening, immediate intervention is warranted in cases which are vision-threatening. Pediatricians, who are the first point of contact in most of these cases, play an important role in diagnosis of pediatric ocular tumors and appropriate referral.

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