Clinical Features Differentiating Benign From Malignant Conjunctival Tumors in Children

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IMPACTANCE Conjunctival tumors in children are usually benign and rarely malignant.

OBJECTIVE To evaluate clinical features of conjunctival tumors in children by comparing benign tumors with their malignant counterparts.

DESIGN, SETTING, AND PARTICIPANTS This retrospective case series reviewed 806 cases of conjunctival tumor in children (aged <21 years) who were evaluated at a tertiary referral center between November 1, 1975, and July 1, 2015. This study included 262 children who were part of a published review.

MAIN OUTCOMES AND MEASURES Features of benign and malignant tumors were compared. Data were collected on patient demographics, tumor features, and specific diagnoses to determine findings related to each tumor.

RESULTS Among the 806 patients with conjunctival tumor, the top 5 diagnoses included nevus (492 [61%]), benign reactive lymphoid hyperplasia (BRLH) (38 [5%]), nodular conjunctivitis (31 [4%]), dermoid (30 [4%]), and primary acquired melanosis (27 [3%]). Overall, conjunctival tumors were benign (779 [97%]) or malignant (27 [3%]), including melanoma (18 [2.2%]) and lymphoma (9 [1.1%]). The mean age at detection was 11 years for benign tumors and 14 years for malignant tumors (P = .005), with mean difference of 3 years (95% CI, 1.2-4.6). The relative frequency of any malignancy (per all conjunctival tumors) by age bracket (0-5 years, >5-10 years, >10-15 years, and >15-<21 years) was 1%, 2%, 3%, and 7%, respectively. A comparison between nevus and melanoma found differences with melanoma in the 10 to 15 years age bracket (29% vs 61%; difference of 32% [95% CI, 10%-55%]; P = .006), mean tumor thickness (1.1 mm vs 1.5 mm; difference of 0.4 mm [95% CI, −0.29 mm to 1.12 mm]; P = .04), tumor base of 10 mm or greater (relative risk [RR] = 4.92; 95% CI, 1.73-13.97; P = .003), tumor hemorrhage (RR = 25.30; 95% CI, 11.91-53.78; P < .001), and lack of intrinsic cysts (RR = 5.06; 95% CI, 1.84-13.98; P = .002). A comparison between BRLH and lymphoma revealed lymphoma with a larger base (RR = 5.16; 95% CI, 1.19-22.19; P = .002) and diffuse location (RR = 16.50; 95% CI, 4.31-63.22; P < .001) and inferior (RR = 12.38; 95% CI, 2.88-53.16; P < .001) or superior vs nasal (RR = 8.25; 95% CI, 1.56-43.51; P = .01). The small cohort of malignant lesions precluded determining if these features were independent of one another.

CONCLUSIONS AND RELEVANCE These data, from an ocular tertiary referral center, suggest that conjunctival tumors in children are nearly always benign. The few malignant tumors included melanoma and lymphoma. Melanoma, compared with nevus, was associated with older children (aged >10-15 years) with larger tumor, hemorrhage, and lack of cyst. Lymphoma, compared with BRLH, was associated with larger size and diffuse involvement.

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Conjunctival tumors can display either benign or malignant features.1-8 The spectrum of tumors in children varies widely from the spectrum in adults.2 In a previous report of 1643 patients with conjunctival tumors from all age brackets, the most common group of tumor was melanocytic (53%); the younger patient cohort (aged <40 years) more often showed choristomatous, vascular, fibrous, xanthomatous, and myxomatous lesions, whereas the older cohort (aged >60 years) more often demonstrated premalignant or malignant squamous epithelial lesions, lipomatous, leukemic, and secondary tumors.2 Only a few reports have focused on conjunctival tumors in children, evaluating the clinical features in fairly small cohorts or using laboratory data that contain little clinical information.2,9-12 Some reports have been descriptive only, offering no statistical comparison.2,9-12 During the past 4 decades, the Ocular Oncology Service has collected clinical and histopathologic data on conjunctival tumors; recently, we published a broad overview of 5002 tumors in all age groups.13 For this study, we extracted only pediatric cases from our previous work to provide a detailed analysis of the types and frequency of conjunctival tumors in 806 cases, analyzed by 4 pediatric age brackets. We performed a statistical analysis to compare the clinical features of benign tumors with those of their malignant counterparts.

Methods

We reviewed the clinical records of all patients younger than 21 years with a conjunctival tumor who were evaluated at the Ocular Oncology Service, a tertiary referral center of Wills Eye Hospital, between November 1, 1975, and July 1, 2015. Institutional review board approval was obtained from Wills Eye Hospital. No patient informed consent was necessary because this was a retrospective study.

Of the 806 cases in our patient cohort, 262 were part of a published review12 that illustrated basic clinical features; in contrast, this study conducted a statistical analysis of the clinical features differentiating benign from malignant tumors. Basic data from this cohort were included in a major overview of all conjunctival tumors in 5002 cases13 (all age groups), but our current analysis addressed details, comparisons, and concerns limited to the pediatric age group. We collected retrospective clinical data on patients and tumors, including demographics, patient features, tumor features, and clinical and histopathologic diagnoses (when available). Patient data included patient features at initial examination, such as age, race, and sex. The ocular details included patient symptom and duration of symptom, tumor laterality, and affected eye. Tumor data included anatomic location, quadrant location, greatest tumor basal diameter and thickness, tumor color, and configuration. Details of intrinsic tumor vascularity, feeder vessels, cysts, and hemorrhage were noted.

Each tumor was classified into a general category, including choristomatous, epithelial, melanocytic, vascular, fibrous, neural, xanthomatous, myxomatous, lipomatous, lacrimal gland, lymphoid, secondary, inflammatory or infectious lesions, degenerative, and nonneoplastic masquerader. The specific tumor diagnosis and management was recorded.

Subgroup analysis was performed to determine the frequency of each type of tumor according to race, sex, age group (0-5 years, >5-10 years, >10-15 years, >15-<21 years), tumor location, and tumor quadrant (Table 1 and eTables 1-4 in the Supplement). The frequency of tumors was calculated as a percentage of all conjunctival tumors and as a percentage per each subcategory. Data were tabulated and encoded in Excel 2011 (Microsoft), and its built-in functions were used to calculate percentage and measures of central tendencies (mean and median). A comparison of the clinical features of nevus vs melanoma and benign reactive lymphoid hyperplasia (BRLH) vs lymphoma was also performed (Table 2 and Table 3). Fisher exact test and unpaired t test were used for categorical and continuous variables, respectively. Confidence intervals were calculated at 95% level of significance. Relative risk (RR) for features that were predictive of a diagnosis of melanoma relative to nevus and lymphoma relative to BRLH were also assessed.

Results

There were 806 cases of conjunctival tumors in 782 patients during this 40-year period. The mean patient age at presentation was 11 years (median, 11 years; range, 0-21 years). Patient race or ethnicity, as judged by physicians taking medical history, included white (656 [81%]), African American (71 [9%]), Asian/American Indian (53 [6%]), Hispanic American (23 [3%]), and Middle Eastern (3 [<1%]). There were 451 male patients (56%) and 355 female patients (44%). The tumor was unilateral in 758 eyes (97%) or bilateral in 24 eyes (3%). The tumor involved the right eye (423 [54%]), left eye (335 [43%]), or both eyes (24 [3%]).

The tumor category and specific diagnosis are listed in Table 1. The 5 most common categories were melanocytic (553 [69%]), choristomatous (65 [8%]), vascular (54 [7%]), lymphoid (47 [6%]), and inflammatory/infectious lesions (37 [5%]). The 5 most common specific diagnoses were nevus (492 [61%]), BRLH (38 [5%]), conjunctivitis with nodule (31 [4%]), dermoid (30 [4%]), and primary acquired melanosis (27 [3%]) (eFigures 1-4 in the Supplement).
Table 1. Conjunctival Tumors in Children Younger Than 21 Years in 806 Cases

<table>
<thead>
<tr>
<th>Category and Diagnosis</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-5 y (n = 104)</td>
</tr>
<tr>
<td>Choristomatous tumors (n = 65)</td>
<td></td>
</tr>
<tr>
<td>Dermoid (n = 30)</td>
<td>10 (33)</td>
</tr>
<tr>
<td>Dermolipoma (n = 26)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>Complex choristoma (n = 5)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Osseous choristoma (n = 3)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>Lacrimal gland choristoma (n = 1)</td>
<td>0</td>
</tr>
<tr>
<td>Benign epithelial tumors (n = 9)</td>
<td></td>
</tr>
<tr>
<td>Papilloma (n = 9)</td>
<td>2 (22)</td>
</tr>
<tr>
<td>Premalignant and malignant epithelial tumors (n = 2)</td>
<td></td>
</tr>
<tr>
<td>Conjunctival intraepithelial neoplasia mild (n = 1)</td>
<td>0</td>
</tr>
<tr>
<td>Conjunctival intraepithelial neoplasia severe (n = 1)</td>
<td>0</td>
</tr>
<tr>
<td>Melanocytic tumors (n = 553)</td>
<td></td>
</tr>
<tr>
<td>Nevis (n = 492)</td>
<td>31 (6)</td>
</tr>
<tr>
<td>Racial melanosis (n = 10)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Ocular melanocytosis (n = 6)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Primary acquired melanosis (n = 27)</td>
<td>1 (4)</td>
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<tr>
<td>Malignant melanoma (n = 18)</td>
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<tr>
<td>Vascular tumors (n = 54)</td>
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<tr>
<td>Pyogenic granuloma (n = 11)</td>
<td>3 (27)</td>
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<tr>
<td>Telangiectasia (n = 5)</td>
<td>1 (20)</td>
</tr>
<tr>
<td>Lymphangiectasia (n = 9)</td>
<td>2 (22)</td>
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<tr>
<td>Capillary hemangioma (n = 13)</td>
<td>10 (77)</td>
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<tr>
<td>Cavernous hemangioma (n = 1)</td>
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</tr>
<tr>
<td>Lymphangioma (n = 13)</td>
<td>4 (31)</td>
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<tr>
<td>Arteriovenous malformation (n = 1)</td>
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</tr>
<tr>
<td>Glomangioma (n = 1)</td>
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</tr>
<tr>
<td>Fibrous tumors (n = 4)</td>
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<tr>
<td>Fibrous histiocytoma (n = 2)</td>
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</tr>
<tr>
<td>Fibroma (n = 1)</td>
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<tr>
<td>Myofibroblastic reactive tumor (n = 1)</td>
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<tr>
<td>Neural tumors (n = 1)</td>
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<tr>
<td>Schwannoma (n = 1)</td>
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<td>Xanthomatous tumors (n = 6)</td>
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<tr>
<td>Juvenile xanthogranuloma (n = 6)</td>
<td>3 (50)</td>
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<td>Myxomatous tumors (n = 1)</td>
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<tr>
<td>Myxoma (n = 1)</td>
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</tr>
<tr>
<td>Lipomatous tumors (n = 3)</td>
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<tr>
<td>Lipoma (n = 3)</td>
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<tr>
<td>Lacrimal gland tumors (n = 1)</td>
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<tr>
<td>Dacryops (n = 1)</td>
<td>0</td>
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<tr>
<td>Lymphoid tumors (n = 47)</td>
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</tr>
<tr>
<td>Benign reactive hyperplasia (n = 38)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Lymphoma (n = 9)</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Secondary tumors (n = 2)</td>
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<tr>
<td>Dacryoadenoma (n = 1)</td>
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</tr>
<tr>
<td>Pilomatricxoma (n = 1)</td>
<td>1 (100)</td>
</tr>
</tbody>
</table>

(continued)
Table 1. Conjunctival Tumors in Children Younger Than 21 Years in 806 Cases* (continued)

<table>
<thead>
<tr>
<th>Category and Diagnosis</th>
<th>0-5 y (n = 104)</th>
<th>&gt;5-10 y (n = 221)</th>
<th>&gt;10-15 y (n = 244)</th>
<th>&gt;15-&lt;21 y (n = 237)</th>
<th>Total per Category</th>
<th>Total per All Conjunctival Tumors (N = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory/infectious lesions (n = 37)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Conjunctivitis (n = 31)</td>
<td>7 (23)</td>
<td>13 (42)</td>
<td>8 (26)</td>
<td>3 (10)</td>
<td>31 (84)</td>
<td>31 (4)</td>
</tr>
<tr>
<td>Episcleritis (n = 3)</td>
<td>0</td>
<td>0</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td>3 (8)</td>
<td>3 (&lt;1)</td>
</tr>
<tr>
<td>Scleritis (n = 3)</td>
<td>0</td>
<td>0</td>
<td>1 (33)</td>
<td>2 (67)</td>
<td>3 (8)</td>
<td>3 (&lt;1)</td>
</tr>
<tr>
<td>Degenerative lesions (n = 2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pterygium (n = 2)</td>
<td>1 (50)</td>
<td>0</td>
<td>0</td>
<td>1 (50)</td>
<td>2 (100)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Nonneoplastic masquerader (n = 19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cyst (n = 12)</td>
<td>7 (58)</td>
<td>0</td>
<td>3 (25)</td>
<td>2 (17)</td>
<td>12 (63)</td>
<td>12 (1)</td>
</tr>
<tr>
<td>Foreign body (n = 2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (100)</td>
<td>2 (11)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Hemorrhage (n = 2)</td>
<td>1 (50)</td>
<td>0</td>
<td>0</td>
<td>1 (50)</td>
<td>2 (11)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Mascaroma (n = 1)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (5)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Chemosis (n = 1)</td>
<td>0</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
<td>1 (5)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Axenfeld nerve loop (n = 1)</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (5)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Total, No. (%)</td>
<td>104 (13)</td>
<td>221 (27)</td>
<td>244 (30)</td>
<td>237 (29)</td>
<td>806 (100)</td>
<td>806 (100)</td>
</tr>
</tbody>
</table>

* Analysis is based on tumor category and diagnosis per age group.

The frequency of tumor onset by age bracket (0-5 years, >5-10 years, >10-15 years, >15-<21 years), shown in Table 1, revealed several tumors with peak detection between 0 and 5 years, such as dermoid (33%), complex choristoma (60%), racial melanosis (40%), capillary hemangioma (77%), juvenile xanthogranuloma (50%), and inclusion cyst (58%). Other tumors showed peak detection between 15 and 21 years, such as dermolipoma (35%), primary acquired melanosis (63%), melanoma (61%), pyogenic granuloma (36%), and lymphoma (56%), among others.

Of the total 806 cases in our cohort, 779 (97%) were benign and 27 (3%) were malignant (Figure 1 and Figure 2). The malignant tumors included melanoma (18 [2.2%]) and lymphoma (9 [1.1%]). The mean age at detection was 11 years for nonmalignant tumors and 14 years for malignant tumors (P = .005), for a mean difference of 3 years (95% CI, 1.2-4.6). The frequency of time on onset of any malignant tumor by age bracket was 4%, 14%, 25%, and 57%, respectively. The relative frequency of any malignancy per all conjunctival tumors by age bracket was 1%, 2%, 3%, and 7%, respectively.

The tumor category and specific diagnosis by patient race or ethnicity (white, African American, Asian/American Indian, Hispanic American, and Middle Eastern) and sex (male or female) are listed in eTable 1 in the Supplement. Of the 492 patients with conjunctival nevus, 83% were white, 6% were African American, 8% were Asian/American Indian, 3% were Hispanic American, and less than 1% was Middle Eastern. This group comprised 57% males and 43% females. Of the 18 patients with conjunctival melanoma, 89% were white and 11% were African American. This group comprised 33% males and 67% females. Of the 38 patients with conjunctival BRLH, 74% were white, 18% were African American, and 8% were Hispanic American. Of these patients, 66% were male and 34% were female. Of the 9 patients with conjunctival lymphoma, 56% were white and 44% were African American. Males made up 67% of these patients and females made up 33%. The only tumors to show a difference per race (white vs African American) were nevus (83% vs 6%; P < .001), papilloma (56% vs 44%; P = .007), lymphoma (56% vs 44%; P = .007), and racial malignancy (20% vs 50%; P < .001). The only tumors to show differences per sex (male vs female) were dermoid (30% vs 70%; P = .004) and conjunctivitis with nodule (74% vs 26%; P = .04).

An analysis of specific tumor diagnosis by location and quadrant is shown in eTable 2 in the Supplement. The most common limbal tumors (n = 328) were nevus (239 [73%]), primary acquired melanosis (17 [5%]), dermoid (13 [4%]), melanoma (10 [3%]), racial melanosis (8 [2%]), and conjunctivitis with nodule (7 [2%]). The most common fornical tumors (n = 33) were BRLH (5 [15%]), lymphoma (4 [12%]), and dermolipoma (4 [12%]). The most common caruncular tumors (n = 51) were nevus (36 [71%]), papilloma (3 [6%]), and BRLH (2 [4%]). The most common tarsal tumors (n = 17) were pyogenic granuloma (3 [18%]), conjunctivitis with nodule (3 [18%]), papilloma (2 [12%]), BRLH (2 [12%]), and cyst (2 [12%]).

The clinical features of the most common tumors are listed in eTable 3 in the Supplement. The mean tumor basal dimension per tumor (increasing order) included nevus (4.7 mm), melanoma (5.7 mm), BRLH (8.2 mm), dermoid (10.6 mm), capillary hemangioma (12.1 mm), dermolipoma (14.0 mm), and lymphangioma (14.9 mm).

Tumor management is listed in eTable 4 in the Supplement; the most common approaches were surgical excision (447 [55%]), observation (320 [40%]), and topical or systemic antibiotics or corticosteroids (35 [4%]). For nevus, the first management approaches were surgical excision (307 [62%]).
Table 2. Comparison of Features of Conjunctival Nevus vs Melanoma in Children Younger Than 21 Years in 510 Cases

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. (%)</th>
<th>P Value</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nevus (n = 492)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>12 (12) [0.3-21]</td>
<td>.003a</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>31 (6)</td>
<td>0.62b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>&gt;5-10</td>
<td>156 (32)</td>
<td>0.07b</td>
<td>1.01 (0.05-20.47)</td>
<td>.99</td>
</tr>
<tr>
<td>&gt;10-15</td>
<td>164 (33)</td>
<td>0.80b</td>
<td>2.07 (0.12-36.53)</td>
<td>.62</td>
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<tr>
<td>&gt;15-&lt;21</td>
<td>141 (29)</td>
<td>0.006b</td>
<td>4.80 (0.29-79.56)</td>
<td>.27</td>
</tr>
<tr>
<td>Race/ethnicity</td>
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<tr>
<td>White</td>
<td>410 (83)</td>
<td>.75b</td>
<td>1 [Reference]</td>
<td>.99</td>
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<tr>
<td>African American</td>
<td>29 (6)</td>
<td>.30b</td>
<td>1.72 (0.41-7.13)</td>
<td>.46</td>
</tr>
<tr>
<td>Asian/American Indian</td>
<td>38 (8)</td>
<td>.38b</td>
<td>0.33 (0.02-5.43)</td>
<td>.44</td>
</tr>
<tr>
<td>Hispanic American</td>
<td>13 (3)</td>
<td>&gt;.99b</td>
<td>0.92 (0.06-14.64)</td>
<td>.96</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2 (&lt;1)</td>
<td>&gt; .99</td>
<td>4.30 (0.33-56.59)</td>
<td>.27</td>
</tr>
<tr>
<td>Sex</td>
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<td>0.05b</td>
<td>2.59 (0.99-6.81)</td>
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</tr>
<tr>
<td>Male</td>
<td>282 (57)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>210 (43)</td>
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<tr>
<td>Anatomic location</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Limbus</td>
<td>239 (49)</td>
<td>.64b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>Extralimbal bulbar</td>
<td>189 (38)</td>
<td>&gt;.99b</td>
<td>0.89 (0.34-2.29)</td>
<td>.81</td>
</tr>
<tr>
<td>Fornix</td>
<td>2 (&lt;1)</td>
<td>&gt;.99b</td>
<td>3.97 (0.29-53.36)</td>
<td>.29</td>
</tr>
<tr>
<td>Tarsus</td>
<td>0</td>
<td>&gt;.99b</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Plica semilunaris</td>
<td>23 (5)</td>
<td>&gt;.99b</td>
<td>0.49 (0.03-8.21)</td>
<td>.62</td>
</tr>
<tr>
<td>Caruncle</td>
<td>36 (7)</td>
<td>&gt;.99b</td>
<td>0.67 (0.09-5.12)</td>
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<tr>
<td>Diffuse</td>
<td>3 (1)</td>
<td>&gt;.99b</td>
<td>2.98 (0.21-42.5)</td>
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<td>Quadrant location</td>
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<tr>
<td>Temporal</td>
<td>300 (61)</td>
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<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>Nasal</td>
<td>152 (31)</td>
<td>.32b</td>
<td>1.51 (0.57-3.98)</td>
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</tr>
<tr>
<td>Superior</td>
<td>15 (3)</td>
<td>.46b</td>
<td>2.15 (0.29-15.92)</td>
<td>.46</td>
</tr>
<tr>
<td>Inferior</td>
<td>22 (4)</td>
<td>.59b</td>
<td>1.49 (0.19-11.28)</td>
<td>.69</td>
</tr>
<tr>
<td>Diffuse</td>
<td>3 (1)</td>
<td>&gt;.99b</td>
<td>4.08 (0.28-58.74)</td>
<td>.30</td>
</tr>
<tr>
<td>Distance to limbus, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>2.3 (0.5) [0-15]</td>
<td>.16a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 mm, No. (%) [95% CI]</td>
<td>261 (53) [0-0]</td>
<td>&gt;.99b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>≥1 mm, No. (%) [95% CI]</td>
<td>231 (47) [1-15]</td>
<td>1.10 (0.44-2.75)</td>
<td>.83</td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pigmented</td>
<td>253 (51)</td>
<td>&gt;.99b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>Nonpigmented</td>
<td>239 (49)</td>
<td>1.06 (0.43-2.62)</td>
<td>.91</td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Round/oval</td>
<td>187 (38)</td>
<td>.22b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>Irregular/geometric</td>
<td>302 (61)</td>
<td>.22b</td>
<td>2.12 (0.71-6.33)</td>
<td>.18</td>
</tr>
<tr>
<td>Diffuse</td>
<td>3 (1)</td>
<td>&gt;.99b</td>
<td>5.33 (0.34-83.34)</td>
<td>.23</td>
</tr>
<tr>
<td>Largest basal diameter, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>4.7 (4) [0.4-28]</td>
<td>.16a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 mm, No. (%) [95% CI]</td>
<td>468 (95) [0.4-9]</td>
<td>1 [Reference]</td>
<td>.1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>≥10 mm, No. (%) [95% CI]</td>
<td>24 (5) [10-28]</td>
<td>.01b</td>
<td>4.92 (1.73-13.97)</td>
<td>.003</td>
</tr>
<tr>
<td>Thickness, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>1.1 (1) [0.2-5]</td>
<td>.04a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 mm, No. (%) [95% CI]</td>
<td>208 (42) [0-0.5]</td>
<td>.81b</td>
<td>1 [Reference]</td>
<td>.99</td>
</tr>
<tr>
<td>≥1 mm, No. (%) [95% CI]</td>
<td>284 (58) [1-5]</td>
<td>1.14 (0.45-2.91)</td>
<td>.76</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
and observation (185 [38%]). For melanoma, the approach was surgical excision in all cases (18 [100%]). For BRLH, management included surgical excision (21 [55%]), topical or systemic antibiotics or corticosteroids (12 [32%]), and observation (5 [13%]). For lymphoma, the approaches were surgical excision (4 [44%]), external beam radiotherapy (4 [44%]), and topical or systemic antibiotics or corticosteroids (1 [11%]).

A comparison of features between benign tumors and their malignant counterparts is listed in Table 2 and Table 3. Regarding nevus vs melanoma (Table 2), compared with nevus, melanoma had an older age of onset between 15 and 21 years (29% vs 61%, respectively; difference of 32% [95% CI, 10%-55%]; $P = .006$), had a greater mean thickness (1.1 mm vs 1.5 mm; difference of 0.4 mm [95% CI, −0.29 mm to 1.12 mm]; $P = .04$), had a tumor base of 10 mm of greater (5% vs 22%; RR = 4.92; 95% CI, 1.73-13.97), had tumor hemorrhage (<1% vs 17%; RR = 25.30; 95% CI, 11.91-53.78), and occurred less often with cysts (67% vs 28%; RR = 5.06; 95% CI, 1.84-13.98). Of the 18 melanomas, a tumor base greater than 10 mm was found in 4 cases, hemorrhage in 3 cases, and cysts in 5 cases.

A comparison of features of BRLH vs lymphoma (Table 3) showed a similar mean age at detection (12 years vs 12 years), race distribution (74% white vs 56% white), and sex distribution (66% males vs 67% males). The differences revealed lymphoma more often had diffuse involvement (0% vs 22%; RR = 16.50; 95% CI, 4.31-63.22), a location in an inferior quadrant (3% vs 33%; RR = 12.38; 95% CI, 2.88-53.16), a superior quadrant (5% vs 22%; RR = 8.25; 95% CI, 1.56-43.51), and a mean basal diameter greater than 10 mm (32% vs 78%; RR = 5.16; 95% CI, 1.1-22.19).

### Discussion

There have been few clinical series on conjunctival tumors in children and no previous series to perform a statistical analysis of comparative clinical features. In 1975, Elsas and Green reported from a laboratory on 302 cases and identified choristomatous (33%), melanocytic (29%), nonneoplastic simulating conditions (23%), papilloma (7%), and other rare lesions (6%). In 1987, Cunha et al again from a laboratory, evaluated 282 conjunctival tumors in children and found choristomatous (22%), melanocytic (23%), nonneoplastic simulating conditions (30%), papilloma (10%), and other lesions (14%). Later in 2007, Shields and Shields provided a clinical analysis of conjunctival tumors in 1643 patients with 262 children, including choristomatous (10%), melanocytic (67%), nonneoplastic simulating conditions (10%), papilloma (2%), and other lesions (13%). Here, we present data specifically on conjunctival tumors in children correlated with demographic and clinical features with diagnosis. In addition, for the first time in the literature, to our knowledge, we provide a statistical analysis of features differentiating benign tumors from their malignant counterparts.

Based on demographics, most conjunctival tumors were found in white children more than in African American or Asian children (Table 2 in the Supplement). White children demonstrated greater incidence of nevus, papilloma, and lymphoma compared with African American children. Compared with white children, African American children showed greater frequency of racial melanosis. We noted greater frequency of dermoid in females and conjunctivitis with nodule in males.

Based on malignant potential, we found a relatively low incidence at only 3%. The conjunctival malignancies included melanoma (2.2%) and lymphoma (1.1%). A comparison of age at detection revealed that malignant tumors (vs nonmalignant tumors) occurred in older children (mean age, 14 years vs 11 years; $P = .005$), who are generally between 15 and 21 years (Table 1). Analysis of relative frequency of malignancy (per all conjunctival tumors) was 1% to 3% for younger children and teenagers (0-15 years) and 7% for older teenagers (>15-<21 years). When conjunctival nevus vs melanoma in children was assessed, the mean age at detection (12 years vs 15 years; $P = .003$) was younger with nevus, and most melanoma occurred in the oldest age bracket of 15 years to 21 years (29% vs 61%; $P = .006$). Thus, onset of a melanocytic conjunctival lesion in children is most likely a nevus (vs melanoma) if they are 10 years or younger (99% vs 1%) or between 10 and 15 years (97% vs 3%), but if they are between 15 and 21 years (93% vs 7%), the risk for melanoma substantially increases.

Conjunctival melanoma in children can simulate conjunctival nevus (Table 2). A comparison of features of nevus and melanoma found differences with melanoma in older...
Table 3. Comparison of Features of Conjunctival Benign Reactive Lymphoid Hyperplasia vs Lymphoma in Children Younger Than 21 Years in 47 Cases

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. (%)</th>
<th>P Value</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>12 (13)</td>
<td>0.3-19</td>
<td>.92*</td>
<td></td>
</tr>
<tr>
<td>0-5 (%)</td>
<td>1 (3)</td>
<td>1 (11)</td>
<td>.35*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>&gt;5-10 (%)</td>
<td>9 (24)</td>
<td>2 (22)</td>
<td>&gt;.99*</td>
<td>0.36 (0.06-2.36)</td>
</tr>
<tr>
<td>&gt;10-15 (%)</td>
<td>19 (50)</td>
<td>1 (11)</td>
<td>.06*</td>
<td>0.10 (0.01-1.06)</td>
</tr>
<tr>
<td>&gt;15-&lt;21 (%)</td>
<td>9 (24)</td>
<td>5 (56)</td>
<td>.10*</td>
<td>0.71 (0.15-3.38)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>28 (74)</td>
<td>5 (56)</td>
<td>.42*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>African American</td>
<td>7 (18)</td>
<td>4 (44)</td>
<td>.18*</td>
<td>2.40 (0.78-7.38)</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>0</td>
<td>&gt;.99*</td>
<td>NA NA</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3 (8)</td>
<td>0</td>
<td>&gt;.99*</td>
<td>0.77 (0.05-11.54)</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>0</td>
<td>0</td>
<td>&gt;.99*</td>
<td>NA NA</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25 (66)</td>
<td>6 (67)</td>
<td>&gt;.99*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Female</td>
<td>13 (34)</td>
<td>3 (33)</td>
<td>1.03 (0.29-3.59)</td>
<td>.96</td>
</tr>
<tr>
<td><strong>Anatomic location</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bulbar, extralimbal</td>
<td>15 (39)</td>
<td>2 (22)</td>
<td>.46*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Limbal</td>
<td>4 (11)</td>
<td>0</td>
<td>.57*</td>
<td>0.72 (0.04-12.70)</td>
</tr>
<tr>
<td>Fornix</td>
<td>5 (13)</td>
<td>4 (44)</td>
<td>.05*</td>
<td>3.78 (0.85-16.81)</td>
</tr>
<tr>
<td>Tarsus</td>
<td>2 (5)</td>
<td>0</td>
<td>&gt;.99*</td>
<td>1.20 (0.07-19.33)</td>
</tr>
<tr>
<td>Plica semilunaris</td>
<td>10 (26)</td>
<td>0</td>
<td>.17*</td>
<td>0.32 (0.02-6.21)</td>
</tr>
<tr>
<td>Caruncle</td>
<td>2 (5)</td>
<td>1 (11)</td>
<td>.48*</td>
<td>2.83 (0.36-22.29)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>0</td>
<td>2 (22)</td>
<td>.03*</td>
<td>8.50 (2.31-31.25)</td>
</tr>
<tr>
<td><strong>Quadrant location</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Temporal</td>
<td>4 (11)</td>
<td>0</td>
<td>.57*</td>
<td>1.36 (0.08-24.41)</td>
</tr>
<tr>
<td>Nasal</td>
<td>31 (82)</td>
<td>2 (22)</td>
<td>.001*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Superior</td>
<td>2 (5)</td>
<td>2 (22)</td>
<td>.16*</td>
<td>8.25 (1.56-43.51)</td>
</tr>
<tr>
<td>Inferior</td>
<td>1 (3)</td>
<td>3 (33)</td>
<td>.02*</td>
<td>12.38 (2.88-53.16)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>0</td>
<td>2 (22)</td>
<td>.03*</td>
<td>16.50 (4.31-63.22)</td>
</tr>
<tr>
<td><strong>Distance to limbus, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>5.6 (6.0) [0-12]</td>
<td>5.6 (4.0) [0.5-10]</td>
<td>.99*</td>
<td></td>
</tr>
<tr>
<td>&lt;1 mm, No. (%) [95% CI]</td>
<td>4 (11)</td>
<td>1 (11)</td>
<td>.99*</td>
<td>1.05 (0.16-6.75)</td>
</tr>
<tr>
<td>≥1 mm, No. (%) [95% CI]</td>
<td>34 (89)</td>
<td>8 (89)</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td><strong>Color</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pigmented</td>
<td>0</td>
<td>0</td>
<td>&gt;.99*</td>
<td>NA NA</td>
</tr>
<tr>
<td>Nonpigmented</td>
<td>38 (100)</td>
<td>9 (100)</td>
<td>NA NA</td>
<td></td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Round/oval</td>
<td>21 (55)</td>
<td>3 (33)</td>
<td>.29*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Irregular/geometric</td>
<td>17 (45)</td>
<td>6 (67)</td>
<td>2.09 (0.59-7.38)</td>
<td>.25</td>
</tr>
<tr>
<td><strong>Largest basal diameter, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>8.2 (6.0) [2-30]</td>
<td>17.3 (14.0) [2-36]</td>
<td>.002*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>&lt;10 mm, No. (%) [95% CI]</td>
<td>26 (68)</td>
<td>2 (22)</td>
<td>.02*</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>≥10 mm, No. (%) [95% CI]</td>
<td>12 (32)</td>
<td>7 (78)</td>
<td>5.16 (1.19-22.19)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Thickness, mm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (median) [range]</td>
<td>2.3 (2.0) [0.5-6]</td>
<td>1.4 (2.0) [0.5-2.0]</td>
<td>.05*</td>
<td></td>
</tr>
<tr>
<td>&lt;1 mm, No. (%) [95% CI]</td>
<td>3 (8)</td>
<td>2 (22)</td>
<td>.24*</td>
<td>2.40 (0.67-8.54)</td>
</tr>
<tr>
<td>≥1 mm, No. (%) [95% CI]</td>
<td>35 (92)</td>
<td>7 (78)</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
</tbody>
</table>

(continued)
children (>15–<21 years) (29% vs 61%; difference of 32% [95% CI, 10%–55%]; \( P = .006 \)), with a greater mean tumor thickness (1.1 mm vs 1.5 mm; difference of 0.4 mm [95% CI, −0.29 mm to 1.12 mm]; \( P = .04 \)), a tumor base of 10 mm or greater (RR = 4.92), a lack of intrinsic cysts (RR = 5.06), and tumor hemorrhage (RR = 25.30). However, the small cohort precluded determining if these features were independent of each other. Of the 18 melanomas, a tumor base greater than 10 mm was found in 4 cases, hemorrhage in 3 cases, and cysts in 5 cases.

Similar to conjunctival melanoma in children, cutaneous and uveal melanoma in children is uncommon and shows higher incidence in the oldest age bracket of children.14-16 Acquired cutaneous nevi first appear at about age 1 year and increase in number during the second and third decades of life, whereas cutaneous melanoma in children is usually detected in the older age bracket of 15 to 21 years.14,15,19 Cutaneous melanoma is the single most common cutaneous cancer in children and adolescents younger than 20 years.19 It has increased at an annual rate of 2.7% in young white women in the United States.20 A large analysis of 1230 cases of pediatric cutaneous melanoma found that the risks were greatest for females 15 to 19 years and those with low climatic UV-B exposure.19

With regard to choroidal nevus and melanoma, both are rare in children.16-18,21 In a study of 3422 eyes with choroidal nevus, the lesion was found in children (2%), mid-adults (23%), and older adults (75%).16 Similarly, choroidal melanoma is rare in children (1%) and is more often found in mid-adults (53%) and older adults (45%).17 However, of those children with choroidal melanoma, detection is usually in the second decade of

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**Table 3. Comparison of Features of Conjunctival Benign Reactive Lymphoid Hyperplasia vs Lymphoma in Children Younger Than 21 Years in 47 Cases (continued)**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign Reactive Lymphoid Hyperplasia (n = 38)</th>
<th>Lymphoma (n = 9)</th>
<th>( P ) Value</th>
<th>Relative Risk (95% CI)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional features*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cysts</td>
<td>4 (11)</td>
<td>0</td>
<td>.57*</td>
<td>0.46 (0.03–6.82)</td>
<td>.58</td>
</tr>
<tr>
<td>Feeder vessels</td>
<td>12 (32)</td>
<td>1 (11)</td>
<td>.41*</td>
<td>0.33 (0.05–2.36)</td>
<td>.27</td>
</tr>
<tr>
<td>Intrinsic vessels</td>
<td>21 (55)</td>
<td>2 (22)</td>
<td>.14*</td>
<td>0.29 (0.07–1.29)</td>
<td>.11</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0</td>
<td>0</td>
<td>&gt;.99*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.  
* t Test.  
\( ^* \) Fisher exact test.  
\( ^\text{c} \) No vs yes presence of features for relative risk calculation.
life (mean age, 12 years). The European Ophthalmic Oncology Group found the cumulative frequency of posterior uveal melanoma in children increased by 0.8% per year between 5 and 10 years and increased to 8.8% per year at 17 years and beyond.

Regarding race, conjunctival melanoma was found in whites (89%) and African Americans (9%). Hu et al reviewed the population-based incidence of conjunctival melanoma and found that the white to African American incidence of conjunctival melanoma for all ages was 2.6:1, which is different from the ratio for uveal melanoma of 18:1 but is similar to other mucosal melanoma at 2.3:1.

Conjunctival lymphoma represented another malignancy in children. A comparison (BRLH vs lymphoma) revealed lymphoma with a larger mean basal dimension (8.2 vs 17.3; \( P = .002 \)) and location as diffuse vs bulbar (RR = 8.5), superior vs nasal (RR = 8.25), inferior vs nasal (RR = 12.38), and diffuse vs nasal (RR = 16.50) (Table 3). Thus, a classic lymphoid tumor in the nasal bulbar region of the eye was more likely to represent BRLH, whereas a tumor in the superior, inferior, or both locations could represent lymphoma. Understand, however, that classification of lymphoid proliferations has evolved during the past 40 years and that conditions previously labeled as BRLH could ultimately represent low-grade lymphoma on the basis of flow cytometry and gene rearrangement studies that were not previously available.

Limitations
There are limitations to this database as the data were collected over 40 years in a retrospective fashion. In addition, all diagnoses were made by ocular oncologists on the basis of clinical features, but not all were confirmed histopathologically because many benign conditions are managed with observation. Furthermore, the number of patients with malignant tumors was small, so the power for comparison with the far more common benign conditions may not detect all clinical differences.

Conclusions
 Conjunctival tumors in children are typically benign and most often represent nevus, BRLH, primary acquired melanosis, dermoid, and dermolipoma. Other pediatric conjunctival tumors have been described in the literature. Malignant conjunctival tumors in children are rare and include melanoma and lymphoma. A comparison of features (nevus vs melanoma) found differences, with melanoma occurring in the older age bracket (>15–<21 years; RR = 4.80); having greater mean tumor thickness (1.1 mm vs 1.5 mm; difference of 0.4 mm [95% CI, −0.29 to 1.12 mm]; \( P = .04 \)), a tumor base of 10 mm or greater (RR = 4.92), and tumor hemorrhage (RR = 25.3); and lacking intrinsic cysts (RR = 5.06).
responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: C. L. Shields.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: C. L. Shields, Sioufi, Alset, Say.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: C. L. Shields, Sioufi, Alset, Say.

Administrative, technical, or material support: C. L. Shields, Sioufi, Alset, Say.

Study supervision: C. L. Shields, Sioufi, Alset, Say.

Conflict of Interest Disclosures: All authors have completed and submitted the ICJME Form for Disclosure of Potential Conflicts of Interest and none were reported.

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REFERENCES


