Benign Lymphoid Hyperplasia of the Conjunctiva in Children

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Benign lymphoid hyperplasia of the conjunctiva occurs infrequently in children, and its presentation, clinical course, and appropriate management are not well established. We describe 2 children with nasal conjunctival masses that on pathological examination demonstrated benign lymphoid hyperplasia. Local irradiation of residual tissue was deferred, and the lesions remained stable for 1 year in one case and for 3 1/2 years in the other case. No systemic involvement had occurred. Although the natural history of extranodal lymphoid hyperplasia in children is poorly documented, most cases of nodal lymphoid hyperplasia in children are at very low risk of malignant transformation. Careful observation for local and systemic disease is indicated for ocular adnexal lymphoid hyperplasia in children until a more complete understanding of its natural history is available.

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Most clinical experience with conjunctival lymphoid lesions is with adult patients, and the behavior of such tumors in children and adolescents is not well established. In this report, we describe the clinical course and histopathologic findings in 2 boys who developed benign lymphoid hyperplasia of the conjunctiva.

REPORT OF CASES

CASE 1

A 12-year-old healthy white boy was referred to us for evaluation with a 3-week history of a painless pink mass in the left nasal bulbar conjunctiva, which was initially treated with topical corticosteroids without response. Examination of the left eye revealed a salmon-pink mass with a smooth surface in the nasal bulbar conjunctiva with involvement of the adjacent semilunar fold (Figure 1, A). A left nontender postauricular node was also noted.

An excisional biopsy of the conjunctival mass was performed. Light microscopic examination (Figure 1, B) revealed a diffuse infiltrate of mature lymphocytes involving the conjunctival substantia propria with multiple deep and superficial lymphoid follicles with germinal centers. Plasma cell infiltrate was also seen in the superficial substantia propria. The endothelial cells lining the vasculature appeared unremarkable.

Immunohistochemical stains with anti-CD-20 (a B-cell marker) (Figure 1, C) showed heavy staining of the cells in a diffuse fashion, but relative sparing of the germinal centers. Moderate anti-CD-45RO (a T-cell marker) immunoreactivity was seen in scattered cells of the germinal centers of the well-defined follicles and in scattered cells in areas of the diffuse infiltrate (Figure 1, D).

Systemic evaluation by a pediatric oncologist that included a complete physical examination, magnetic resonance imaging studies of the orbits, brain, and body, a complete blood cell count, an erythrocyte sedimentation rate, serum protein electrophoresis, and lactate dehydrogenase and uric acid level measurements, did not reveal any abnormalities.

Postoperatively, the patient received a short course of oral and topical corticosteroids that was terminated within 3 weeks. The postauricular node decreased in size a few weeks after the biopsy. One year later, only the small residual nodule within the semilunar fold that was left at the time of excision remained, and it was unchanged. No evidence of recurrence was seen.
CASE 2

A 7-year-old African American boy with an unremarkable medical history developed a painless pink conjunctival mass in the left caruncle. The mass increased in size for the first 2 months, but then remained stable for the next 2 months. On initial examination, the vision and motility of both eyes were normal. A solid, freely mobile mass was noted at the left caruncle that measured approximately 12 mm × 5 mm (Figure 2, A). In addition, a 9-mm × 6-mm almond-shaped mass deep in the inferior fornix was seen. No regional lymphadenopathy was appreciated. An excisional biopsy of the caruncula mass was performed.

Further evaluation included computed tomography of the orbits, chest, and abdomen, a bone marrow biopsy, and a systemic evaluation, including a complete blood cell count, erythrocyte sedimentation rate, serum protein electrophoresis, and lactate dehydrogenase and uric acid level measurements. No abnormalities or evidence of systemic disease were identified.

Postoperatively, the patient was treated with topical corticosteroids for 3 weeks, and oral corticosteroids that were tapered for 6 months. No reduction of the residual mass in the inferior fornix was noted. At last examination 3 years after the discontinuation of treatment, the child had normal vision and motility in both eyes. The semilunar fold of the left eye demonstrated mild hypertrophy. The mass in the inferior fornix remained unchanged (Figure 2, B).

Pathologic findings were similar to case 1. The substantia propria was markedly thickened by a polymorphic lymphocytic infiltrate. Well-defined lymphocytic follicles with germinal centers were noted within the lesion (Figure 2, C). The superficial substantia propria mainly demonstrated plasma cell infiltration that extended into the overlying epithelium. Well-defined vascular channels lined by flattened endothelial cells were seen throughout the substantia propria. Immunohistochemical testing with anti–CD-20 and anti–CD45-RO antibodies demonstrated
the polymorphic nature of the lesion.

**COMMENT**

In this article we report 2 cases of benign lymphoid hyperplasia of the conjunctiva occurring in childhood and document a benign clinical course up to 12 months in one case and 3½ years in the other. In a retrospective study of 40 patients with both benign and malignant conjunctival lymphoproliferative lesions, Siegelman and Jakobiec\(^1\) found that such lesions develop frequently in patients older than 40 years, with a median age of 55 years for patients with benign lesions. No patients between the ages of 11 and 20 years were reported to have benign lymphoid hyperplasia.\(^1\) Furthermore, unlike benign lymphoid lesions of the orbit where the incidence of systemic involvement and mortality have been studied, the incidence of malignant transformation and systemic disease in conjunctival lymphoid lesions remains unclear.\(^3-5\) Some reports have suggested a more favorable outcome for conjunctival lymphoid lesions compared with those in the orbit.\(^3,5\) In case 1, an enlarged postauricular node was observed that spontaneously decreased in size. It is unclear if the nodal enlargement actually represented the same process seen in the conjunctiva.

The extent of systemic evaluation appropriate at the time of diagnosis is uncertain, but, in addition to a careful physical examination with attention to local lymphadenopathy, it might include a complete blood cell count, serum protein electrophoresis, erythrocyte sedimentation rate, and chest and abdominal radiological imaging.\(^6\) While it is accepted that patients with ocular adnexal lymphoid lesions should undergo repeated ocular and systemic evaluations to identify extraocular disease, the frequency and extent of such systemic evaluation are also debated. In a review of a series of patients with lymphoid proliferation of the orbit, conjunctiva, and eyelids, Knowles et al\(^1\) have reported that approximately 10% of patients of unspecified age followed up for 36 months or longer who presented with clinical stage I disease developed extraocular lymphoma between age 38 and 53 months. Therefore, the authors have recommended repeated systemic evaluation every 6 months for 5 years. However, with the notable exception of reactive lymphoid hyperplasia associated with chronic Epstein-Barr virus infection, reactive lymphoid hyperplasia in childhood is not expected to produce a lymphoma. Therefore, no consensus exists regarding guidelines specific to benign, localized conjunctival lesions in children that might be expected to have an extremely low probability of malignant transformation and extraocular extension.

Both patients in this report had residual conjunctival tumor after re-

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**Figure 2.** Case 2. A, The left eye prior to surgical resection. Note the pink nasal conjunctival mass that involves the plica semilunaris and extends over much of the nasal bulbar conjunctiva. B, The left eye 3½ years after surgical excision. Note the mild scarring of the plica semilunaris and the elongated mass in the inferior fornix. C, Microphotograph of the conjunctival biopsy specimen showing the diffuse lymphocytic infiltrate with follicle formation in the substantia propria (hematoxylin-eosin, original magnification ×40).
section and the management of such lesions is not well defined in the literature. It is uncertain how aggressively low-grade tumors should be treated and whether local irradiation is helpful to prevent later transformation to a higher-grade lymphoma. Also, substantial radiation-related vision-threatening risks exist. We therefore elected to merely observe both patients, and both have demonstrated stability to date. The poor response to topical and oral corticosteroids on the residual lesions in both cases is notable and we therefore suggest that long-term corticosteroids are probably unwarranted. However, we acknowledge that recurrence and transformation might still occur, and recommend indefinite periodic local and systemic reevaluation.

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REFERENCES