

# Benign Reactive Lymphoid Hyperplasia of the Caruncle and Plica: Report of Five Cases

Abbas Bagheri, MD; Babak Bab-Sharif, MD; Mohammad Abrishami, MD;  
Mojgan Rezaei Kanavi, MD; Hosein Salour, MD

*Shaheed Beheshti Medical University, Tehran, Iran*

**Purpose:** To report the clinical and histopathologic features of five cases of benign reactive lymphoid hyperplasia (BRLH) of the caruncle and plica semilunaris.

**Patients and Findings:** Over a period of ten years, five patients with fish-flesh pinkish mass lesions in the caruncle and plica semilunaris were referred for evaluation. After performing systemic work-up, all lesions were treated by surgical excision. The appearance and clinical course was compatible with BRLH; histopathologic and immunohistochemical evaluations confirmed this diagnosis. The patients were followed for 2-108 months and no recurrence or complications were observed during this period.

**Conclusion:** BRLH must be considered in the differential diagnosis of pinkish mass lesions of the caruncle and plica semilunaris. Histopathologic and immunohistochemical evaluation should be performed to rule out lymphoma. Surgical excision seems to be appropriate and does not entail complications in the short-term.

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**Correspondence to:** Abbas Bagheri, MD. Associate Professor of Ophthalmology, Ophthalmic Research Center, Labbafinejad Medical Center, Boostan 9 St., Pasdaran Ave., Tehran 16666, Iran; Tel: +98 21 22585952, Fax: +98 21 22590607, e-mail: abbasbagheri@yahoo.com

## INTRODUCTION

The caruncle and plica semilunaris contain cutaneous and mucous membrane elements and a variety of benign and malignant lesions may involve these structures. Benign reactive lymphoid hyperplasia (BRLH) is a rare benign lesion of unknown etiology which may manifest as a fish flesh or gravelly mass in the sub-epithelial layer of the caruncle and plica semilunaris.<sup>1-4</sup> This lesion is composed of polyclonal infiltration of T and B lymphocytes and mature lymphoid follicles with tangible-body macrophages scattered in the center.<sup>3,5</sup>

There are limited reports of BRLH of the caruncle and plica.<sup>6</sup> In this report we describe the clinical and histopathological features, and

management of five patients with this rare lesion who were referred to Labbafinejad Medical Center, Tehran, Iran from 1997 to 2006.

## PATIENTS AND FINDINGS

Table 1 summarizes the demographic and clinical characteristics of the patients who included four male and one female subjects aged 6 to 18 years. None of them had history of ocular trauma or any other ocular or systemic disease. All lesions were unilateral and located in the caruncle in three eyes and on the plica semilunaris in two other cases. The lesion was pink and smooth with fish flesh appearance and distinct margins. Other ocular examinations were unremarkable.

All lesions were completely excised under local (four cases) or general (one case) anesthesia two to six months after occurrence. Histopathology disclosed non-keratinized squamous epithelium containing goblet cells and lymphoid infiltration consisting of mature lymphatic follicles of variable size in the stroma. Few mitoses and tangible-body macrophages were found in the center of the follicles (Fig. 1). Few small lymphocytes and scattered plasma cells and eosinophils were also seen in marginal areas (mantle zones) of the follicles. The lymphoid follicles were reactive for both B (CD 20) and T (CD3 or CD43) lymphocyte markers

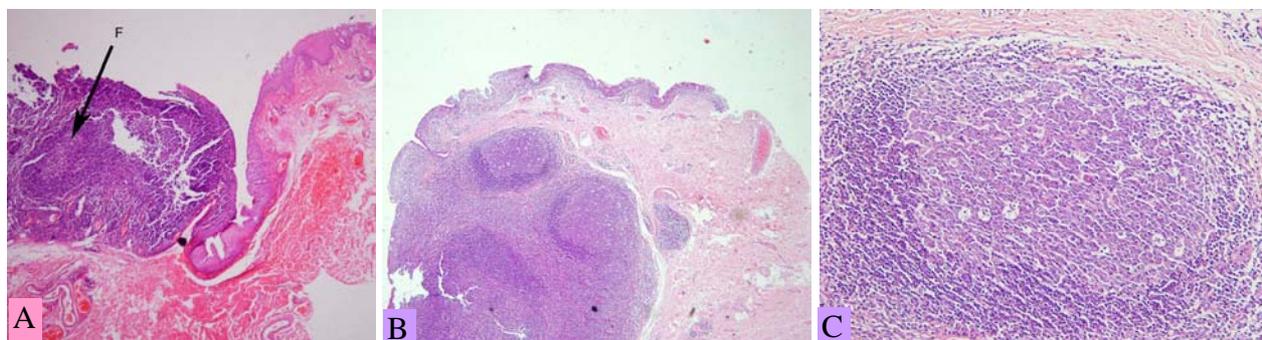
on immunohistochemical staining indicating a polyclonal lymphoid infiltration (Fig. 2). Immunohistochemical staining was also performed on specimens in cases # 4 and 5 for detection of oncoprotein b-cl2 which was non-reactive in the follicle centers of both specimens (Fig. 3) favoring follicular hyperplasia.

The surgical site healed during a few weeks in all cases. No case of recurrence occurred and none of the eyes developed postoperative limitation of ocular movement or symblepharon after two months to 9 years of follow-up. Figure 4 shows the pre- and postoperative status of the involved eyes.

**Table 1** Demographic and clinical characteristics

No.	Sex	Age (yr)	Involved eye	Location of lesion	Duration (months)	Size (cm)	F/U (months)	Immunohistochemistry
1	M	16	Right	Caruncle	3	1×1.5×1.5	108	Positive for CD20/CD43
2	F	15	Right	Caruncle	6	2.5×2.5×1	105	Positive for LCA/CD20/CD43
3	M	6	Left	Caruncle	2	1×0.5×0.2	9	Positive for CD43/CD20
4	M	18	Right	Plica	2	1×1×0.5	5	Positive for CD43/CD20, Negative for b-cl2
5	M	15	Left	Plica	2	0.5×0.85×0.65	2	Positive for CD3/CD20, Negative for b-cl2

F/U, follow-up period; M, male; F, female

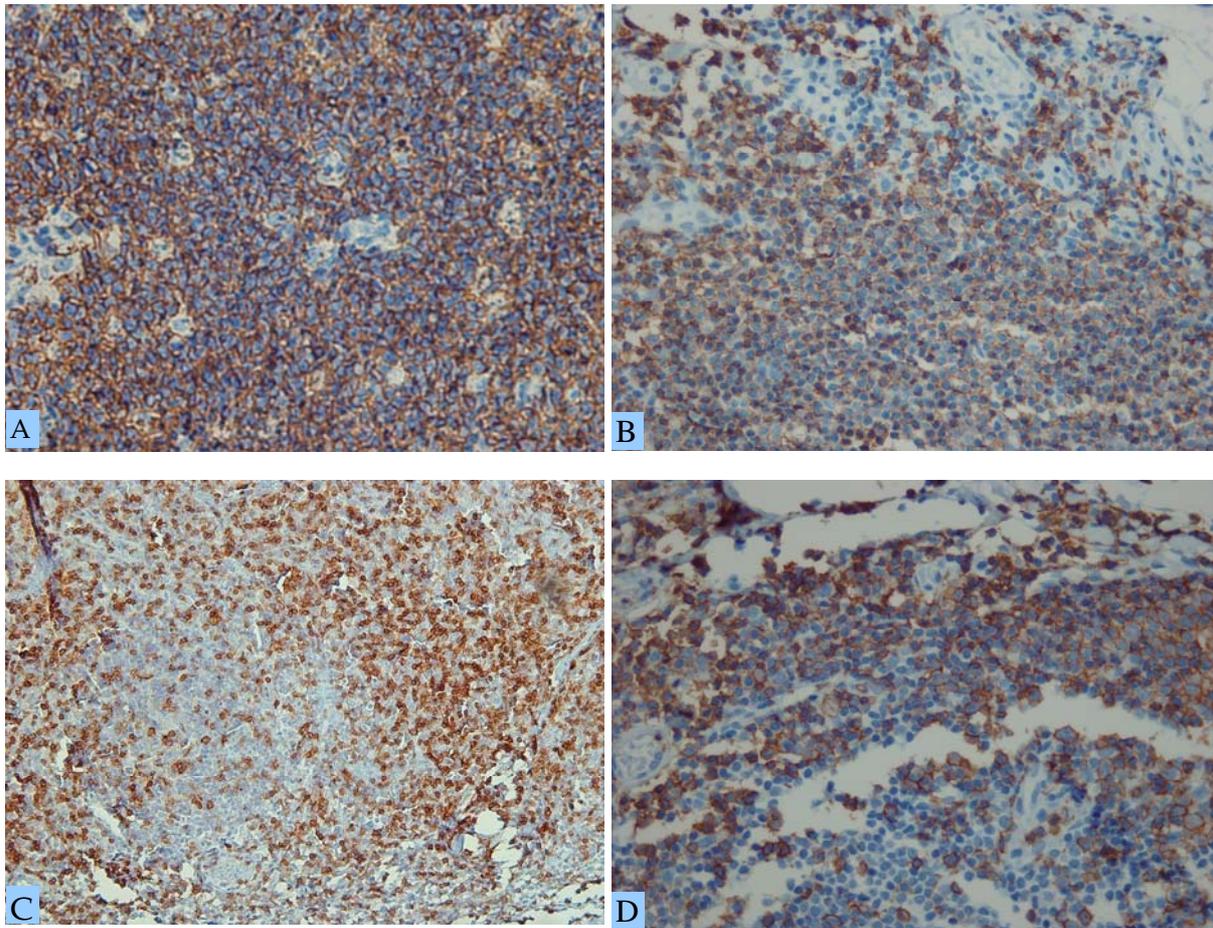


**Figure 1** Presence of mature lymphoid follicles in the subepithelial layer of the conjunctiva in cases #4 (A, arrow, 25x) and #5 (B, 10x) and lymphoid follicles with pale centers and dark margins in case #5 (C, 50x). Hematoxylin-Eosin staining.

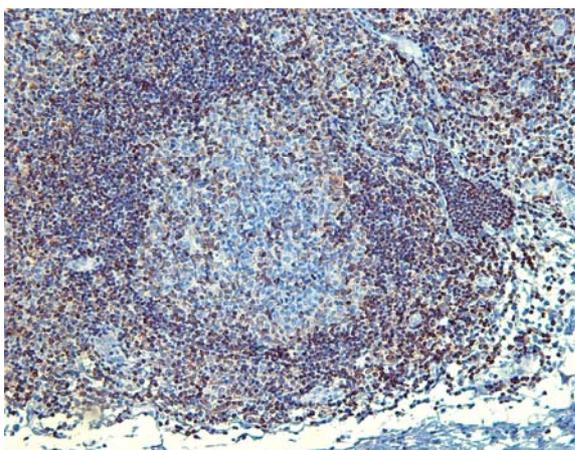
## DISCUSSION

The normal conjunctiva does not contain lymphocytes, however when these cells infiltrate the conjunctiva in large numbers, they form lymphoid follicles with germinal centers. Reactive lymphoid hyperplasia should be considered in the differential diagnosis of such conditions.<sup>7</sup> This lesion accounts for approxi-

mately 11% of lymphoproliferative lesions in ocular appendages and rarely occurs in children. Its manifestations, clinical course and management have not been clearly established.<sup>3,8</sup> Lymphoid hyperplasia of the caruncle and plica semilunaris manifest as smooth fish flesh lesions which may be misdiagnosed as lymphoma, leukemia or amyloidosis.<sup>3</sup>

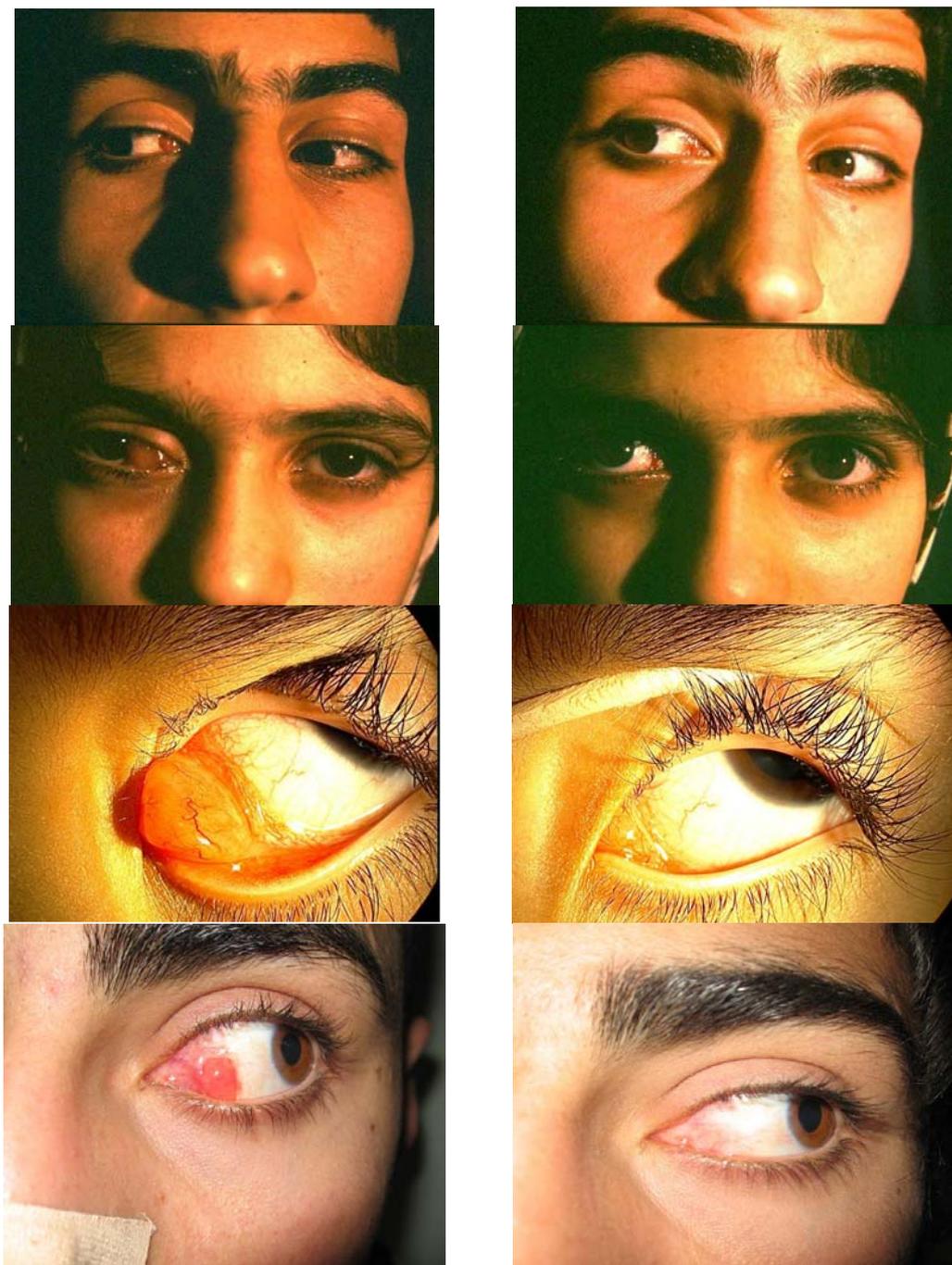


**Figure 2** Immunogenic reactivity of lymphoid infiltrations for CD20 in cases #5 (A, 100x) and #4 (B, 100x) as well as marginal cells in lymphoid follicles for CD3 in case #5 (C, 50x) and for CD43 in case #4 (D, 100x).



**Figure 3** Immunohistochemical staining for b-cl2 oncoprotein in case #5 (50x); follicle centers are non-reactive.

BRLH often manifests histologically as a polymorphic population of lymphoid cells with polyclonal infiltration of T and B lymphocytes in the absence of Dutcher cells. The presence of multiple lymphoid follicles with distinct margins of irregular shape and variable size with pale centers suggests BRLH rather than follicular lymphoma. Cellular mitosis, if any, is limited to germinal center of the follicles, where scattered tangible-body macrophages exist and give a starry sky pattern to the follicle center. These characteristics are typical of benign reactive follicles rather than neoplastic follicles. In the germinal zones of benign reactive follicles, small dark cells without mitosis represent mature lymphocytes and plasma cells.<sup>5</sup>



**Figure 4** Pre- (left) and postoperative (right) photographs of four cases.

Immunohistochemistry for b-cl2 oncoprotein seems to be of value in distinguishing follicular hyperplasia from neoplasia; neoplastic B cells are reactive for this oncoprotein whereas reactive B cells do not stain for b-cl2 oncoprotein.<sup>9</sup> Histopathological and immuno-

histochemical characteristics of the lesions in our cases were compatible with BRLH.

In a study on 57 patients with caruncle lesions at Wills Hospital, only 7% were due to chronic inflammation and these patients were 24 to 82 years of age. Interestingly, preoperative

clinical diagnoses in this group included papilloma in two cases and a nonspecific lesion and epithelial cyst each in one. Overall, none of the cases had BRLH.<sup>2</sup> It should also be noted that certain cases of reactive lymphoid hyperplasia were previously classified as inflammatory pseudotumors,<sup>3</sup> which may be the reason for the absence of the diagnosis of BRLH in the former report. Luthra et al<sup>10</sup> in a study on 112 cases of caruncle lesion reported four (3.6%) cases of BRLH based on pathological examination.

Lymphoid tumors include benign lymphoid hyperplasia, atypical lymphoid hyperplasia and malignant lymphoma. Most lymphoid tumors of ocular appendages are local and confined, however they have been associated with systemic lymphoma at presentation of the ocular lesion or during follow-up.<sup>5,6</sup> The malignant potential of BRLH may be predicted by light microscopy, immunohistochemistry and biomolecular investigation for T-cell receptor genes and immune globulins.<sup>4</sup> Due to the high risk of non-Hodgkin lymphoma in reactive lymphoid hyperplasia, systemic evaluation and regular follow-up is prudent in these patients.<sup>11</sup> None of the cases in our series had evidence of systemic lymphoma after a period of two months to more than nine years.

In conclusion benign reactive lymphoid hyperplasia must be considered in the differential diagnosis of caruncle or plica semilunaris mass lesions with fish flesh appearance. Histopathological and immunohistochemical studies should be performed to exclude systemic lymphoma or other malignant lesions. Surgical excision of the lesion seems to be harmless and curative.

#### REFERENCES

1. Warga M, Szurman P, Rohrbach JM. Tumors of the caruncle of uncertain malignancy. *Klin Monatsbl Augenheilkd* 2005;222:733-735.
2. Shields CL, Sheids JA, White D, Augsburger JJ. Types and frequency of lesions of the caruncle. *Am J Ophthalmol* 1986;102:771-778.
3. Yanoff M, Fine B.S. Conjunctiva. In: Ocular Pathology. Philadelphia: Mosby; 2002: 215-240.
4. Leisegang TJ, Deutsch TA, Grand MG. Conjunctiva. In: American Academy of Ophthalmology. Ophthalmic pathology and intraocular tumors. San Francisco: The Academy; 2003: 55-57.
5. Green WR. Orbit/Lymphoid tumors. In: Spencer WH. Ophthalmic Pathology, an atlas and textbook; 4th ed. W.B. Saunders Co; 1994, on CD Rom.
6. Dharmies F, Validire P, Meyer A, Morel X, Halhal M, Elmaleh C, et al. Inflammatory pseudotumor of the caruncle. *J Fr Ophthalmol* 2003;26:204-207.
7. Klintworth GK, Eagler RC. Diseases of the nervous system and sensory organs. In: Danjanov I, Linder J. Andersons pathology. 10th ed. Philadelphia: Mosby; 1996: 2838-2840.
8. Mc Load SD, Edward DP. Benign lymphoid hyperplasia of the conjunctiva in children. *Arch Ophthalmol* 1999;117: 832-835.
9. Wang T, Lasota J, Hanau CA, Miettinen M. Bcl-2 oncoprotein is widespread in lymphoid tissue and lymphomas but its differential expression in benign versus malignant follicles and monocytoid B-cell proliferations is of diagnostic value. *APMIS* 1995;103:655-662.
10. Luthra CL, Doxanas MT, Green WR. Lesions of the caruncle. A clinicopathologic study. *Surv Ophthalmol* 1978; 23:183.
11. Polito E, Leccisotti A. Prognosis of orbital lymphoid hyperplasia. *Graefes Arch Clin Exp Ophthalmol* 1996;234:150-154.