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Case Report

Spontaneous Regression of Bilateral Conjunctival Extranodal Marginal Zone B-cell Lymphoma of Mucosa-Associated Lymphoid Tissue

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We report the case of a patient who showed spontaneous regression of bilateral conjunctival extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). A 72-year-old man underwent excisional biopsy for salmon-pink lesions involving the whole circumference of the conjunctiva in the right eye and the lower fornix in the left eye. Histopathology and immunohistochemistry showed MALT lymphoma with immunoglobulin kappa monotype shared by the lesions in both eyes. Because the patient had recurrent pulmonary tuberculosis, radiation initially planned for the large residual lesion in the right eye was postponed. Over two years, including 6 mon with anti-tuberculous treatment, the large lesion in the right eye showed spontaneous regression. The spontaneous regression of conjunctival MALT lymphoma observed in this patient suggests that following excisional biopsy for histopathological diagnosis, observation is a treatment option. 〔*J Clin Exp Hematopathol 47(2) : 79-81, 2007*〕

Keywords: conjunctiva, MALT lymphoma, extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue

INTRODUCTION

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), is the predominant histopathological type of malignant lymphoma arising in the conjunctiva. In a previous study, we showed that conjunctival MALT lymphoma would regress spontaneously after excisional biopsy for histopathological diagnosis and that observation might be a treatment option for tumors of this type.[1] The question of whether conjunctival lymphomas do regress spontaneously, or the residual lesions left behind after excisional biopsy are simply minimal, remains controversial. In this study, we reported a patient who showed significant spontaneous regression of the residual lesion after excisional biopsy of MALT lymphoma.

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CASE REPORT

A 72-year-old man presented with redness of both eyes for a week in May 2004. The best-corrected visual acuity was 1.2 in both eyes. Thickened salmon-pink lesion extended from the lower fornix to bulbar conjunctiva and to the upper fornix involving the whole circumference in the right eye, while the lesion was restricted to the lower fornix in the left eye (Fig. 1). The anterior segments and fundi of both eyes were normal. Magnetic resonance imaging showed no lesions in the bilateral orbit, and gallium scan revealed no abnormally high uptake sites. A plain chest X-ray film demonstrated fascicular shadows in bilateral lung fields with thickened pleura of the right lung apex and the dull cardiopulmonary angle in the left lung, suggestive of prior tuberculosis. Blood tests including complete blood cell counts and blood biochemistry were normal. Conjunctival sac culture detected *Corynebacterium* species and methicillin-sensitive *Staphylococcus aureus* in both eyes.

In June 2004, he underwent excisional biopsy in both eyes, and used ofloxacin eye drop 4 times daily as preventive antibiotics, and 0.1% betamethasone eye drop 4 times daily as an anti-inflammatory agent, for a month postoperatively. After the biopsy, computed tomography scan of the chest showed nodular and fascicular shadows of the bilateral lung fields with pleural thickening and calcification. The patient had past history of tuberculosis in childhood. Consequently, radiation initially planned for the residual conjunctival lesion

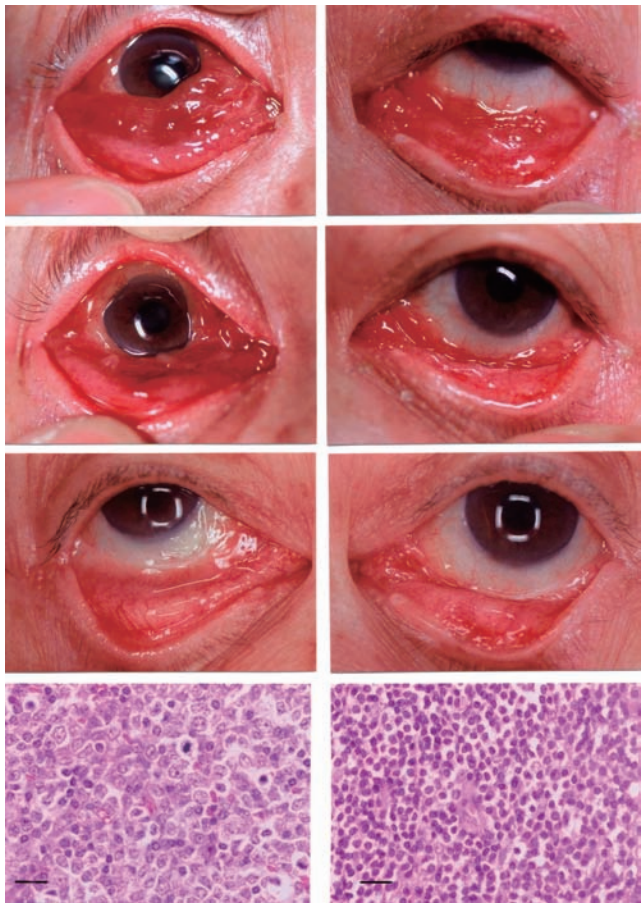

Fig. 1. Conjunctival salmon-pink lesions in both eyes of a 72-year-old man. Right eye : left row. Left eye : right row. Lesions before excisional biopsy (***top***), 10 days after the biopsy (***middle***), and 2 years after the biopsy (***bottom***). Salmon-pink lesions involve the whole circumference of the conjunctiva of the right eye ; only the lower parts of the lesions have been excised at biopsy. Note that the residual lesion has regressed spontaneously in 2 years. Lowermost column shows histopathology of the biopsy specimens, compatible with extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. The lesion in the right eye has a greater number of large cells than the one in the left eye. Hematoxylin-eosin stain. *Bar* = 20 μm.

in the right eye was postponed. After the diagnosis of recurrent pulmonary tuberculosis, the patient underwent a standard three-drug regimen (isoniazid, rifampicin, and ethambutol) for tuberculosis for 6 mon from November 2004 to April 2005. The residual conjunctival lesions in both eyes regressed gradually and disappeared in two years (Fig. 1). Repeat gallium scan showed no evidence of lesions systemically.

METHODS

The excised conjunctival tissues of both eyes were immediately brought to the pathology laboratory, fixed with formaldehyde and embedded in paraffin. Paraffin sections were cut and deparaffinized with xylene and graded alcohol series. The sections were stained with hematoxylin-eosin and also by immunohistochemistry. In brief, the sections were incubated with 3% hydrogen peroxide for 5 min to inactivate endogenous peroxidase, and blocked with 10% normal goat serum for 10 min. The sections were then incubated with primary antibodies overnight at 4℃, washed with 0.05% Tween 20- containing phosphate buffered saline three times, incubated with the second antibodies at room temperature for 30- 60 min, and washed. The color was developed with diaminobenzidine, and the nuclei were counterstained with hematoxylin.

RESULTS (Pathological Findings)

Histopathological examinations of the excised conjunctival tissues in both eyes revealed medium-sized lymphoid cells in vague nodular patterns (Fig. 1). A fraction of lymphoid cells showed differentiation to plasma cells and had Dutcher bodies. Immunohistochemical staining disclosed lymphoid cells positive for CD79a, but negative for CD3, CD5, CD10, or CD20. The lymphoid cells in the conjunctival lesions of both eyes shared an immunoglobulin kappa monotype.

DISCUSSION

In the right eye of this patient, lymphoma lesions extended at the whole circumference of the conjunctiva, and only the lower fornix lesions were excised for histopathological diagnosis. Radiation was planned for the remaining lesions of lymphoma in the right eye but was postponed due to recurrent pulmonary tuberculosis. During half a year of treatment for tuberculosis, the lymphoma lesions in the right eye showed gradual spontaneous regression, leading to the decision to choose observation as a treatment option. The lesion disappeared completely in two years after excisional biopsy.

Spontaneous regression has been recognized in low-grade malignant lymphomas.[2] In the stomach, regression of MALT lymphoma is relatively common and is sometimes associated with eradication of *Helicobacter pylori* infection.[3] *Helicobacter pylori*-recognizing T cells might control the proliferation of lymphoma cells. In the ophthalmological field, orbital/conjunctival large-cell lymphoma has been reported to regress spontaneously,[4] whereas the regression of orbital/conjunctival MALT lymphoma has been related to treatment with antibiotics.[5] Furthermore, a recent report described the detection of *Chlamydia pneumoniae* DNA by polymerase chain reaction in bilateral orbital MALT lymphoma,[6] suggesting the role of antibiotics in the regression of lymphomas.

In the patient we report here, spontaneous regression of MALT lymphoma occurred concurrently with half-a-year

treatment for pulmonary tuberculosis, suggesting that antituberculous agents might suppress chronic inflammation or eradicate other factors that facilitate lymphoma growth, thereby effecting the spontaneous regression. A second possibility is that the use of ofloxacin as a preventive antibiotic for one mon after excisional biopsy might play a role in the induction of spontaneous regression.[6]

The spontaneous regression of conjunctival MALT lymphoma observed in this patient further supports that observation is a treatment option after excisional biopsy for histopathological diagnosis. Radiation still remains as a treatment option for residual lesions, but in light of these lesions' tendency to spontaneously regress, the role of radiation should be reevaluated.

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