Conjunctival lesions are rarely seen in mantle cell lymphoma. Here, we report a patient who developed bilateral conjunctival lesions in the course of chronic lymphocytic leukemia as an initial diagnosis, resulting in the final diagnosis of mantle cell lymphoma by conjunctival biopsy. A 66-year-old man developed conjunctival salmon-pink lesions on both sides in the 1.5-year course of chronic lymphocytic leukemia. He also had irregularly shaped masses with low tissue density in the orbital apex on both sides. Bilateral conjunctival biopsy showed subepithelial infiltration with lymphoid cells, positive for CD20, CD5, and cyclin D1, but negative for CD3, CD10, and CD23. Immunohistochemical restaining of the previous bone marrow biopsy specimen demonstrated lymphoid cells positive for cyclin D1, confirming the diagnosis of mantle cell lymphoma with leukemic presentation. As the case presenting stage IV lymphoma with systemic lymphadenopathy, he underwent 3 courses of combination chemotherapy with fludarabine and cyclophosphamide, and then 6 courses of bendamustine with rituximab, leading to complete remission for the following 3 years. In conclusion, mantle cell lymphoma should be included in the differential diagnosis of conjunctival salmon-pink lesions.

Keywords: mantle cell lymphoma, conjunctiva, conjunctival biopsy, leukemia, salmon-pink lesion

INTRODUCTION

Lymphoma involves ocular adnexa, which consists mainly of lacrimal glands and sacs, extraocular muscles, eyelids, and conjunctiva. Ocular adnexal lymphoma predominantly presents as an orbital mass. Mantle cell lymphoma is generally a well-recognized pathological type in the list of ocular adnexal lymphomas. However, conjunctival involvement with lymphoma in general, and more specifically with mantle cell lymphoma, is relatively rare.

Conjunctival salmon-pink lesions are a hallmark of conjunctival infiltration with lymphoid cells. The primary lymphoma, occurring in the conjunctiva, is predominantly extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT), called MALT lymphoma. The other rare types of lymphoma involving the conjunctiva that have been reported so far are T-cell lymphoma, Burkitt lymphoma, mantle cell lymphoma, and blastic plasmacytoid dendritic cell neoplasm. The conjunctival lesions could also be caused by benign lymphoid hyperplasia and leukemic infiltration.

In this study, we report a patient who developed bilateral conjunctival lesions in the course of chronic lymphocytic leukemia as an initial diagnosis. Conjunctival biopsy demonstrated mantle cell lymphoma, which was also supported by immunohistochemical restaining of the previous bone marrow biopsy specimen.

CASE REPORT

A 66-year-old man noticed blurred vision in both eyes associated with bilateral buccal pain 10 days previously, bilateral lower lid swelling 7 days previously, and bilateral lower lid induration 3 days previously. Upon referral from a hematologist in October 2010, he showed reddish lesions in the lower conjunctival fornix on both sides (Fig. 1). The best-corrected visual acuity was 0.5 in the right eye and 0.7 in the left eye. The intraocular pressure in both eyes was 20 mmHg. He had clear media and normal fundi in both eyes. Computed tomographic scan disclosed ill-defined lesions with low tissue density at the orbital apex along the optic nerve in bilateral orbit (Fig. 1).
He was identified as having leukocytosis by a health check in March 2009, and was diagnosed at another hospital with chronic lymphocytic leukemia, based on fluorescence-activated cell sorting of the peripheral blood and immunohistochemistry of a bone marrow biopsy in April 2009. The abnormal bone marrow cells were positive for CD5, CD20, and CD23. About half a year later, in September 2009, he developed appendicitis, and the surgically excised specimen showed the infiltration of lymphocytes that were positive for CD5, CD20, and CD23.

Biopsy of conjunctival lesions on both sides in October 2010 showed subepithelial infiltration with small to medium-sized lymphoid cells that were positive for CD20, CD5, and cyclin D1, but negative for CD3, CD10, and CD23 on immunohistochemical staining, leading to the diagnosis of mantle cell lymphoma (Fig. 2). Immunohistochemical restaining of the previous bone marrow biopsy specimen demonstrated lymphoid cells positive for cyclin D1 (Fig. 3), confirming the diagnosis of mantle cell lymphoma with leukemic presentation.

Systemic lymphadenopathy was disclosed by computed tomography, which reaffirmed the stage IV mantle cell lymphoma. The patient underwent 3 courses of combination chemotherapy with fludarabine and cyclophosphamide from October 2010 to January 2011, leading to resolution of the orbital masses. As the lymphoma cells still remained in the blood, coupled with pleural effusion, he underwent 6 courses of bendamustine, combined with rituximab, as salvage chemotherapy for the progressive disease, resulting in complete remission in August 2011. He was followed for the following 3 years without any treatment.

DISCUSSION

A key for the diagnosis of mantle cell lymphoma is the nuclear overexpression of cyclin D1. In the present patient, conjunctival and orbital infiltration was initially considered as leukemic infiltration since the patient had been diagnosed with chronic lymphocytic leukemia based on bone marrow biopsy and fluorescence-activated cell sorter analysis. The bone marrow specimen was not stained for cyclin D1 immunohistochemically on that occasion. After mantle cell lymphoma was diagnosed by conjunctival biopsy, immunohistochemical restaining of the bone marrow biopsy specimen confirmed cyclin D1 overexpression in infiltrating lymphoid cells.

To the best of our knowledge, there have been three case reports describing conjunctival mantle cell lymphoma. These 3 patients showed unilateral conjunctival lesions: two patients with no systemic manifestations and one patient with hepatosplenomegaly and bone marrow involvement. In contrast, the present patient showed bilateral conjunctival lesions by mantle cell lymphoma. Mantle cell lymphoma is well known, although noted rarely, for leukemic presentation, which might have led to the bilateral conjunctival and orbital involvement in the present patient.

Fig. 1. A 66-year-old man. Hepatosplenomegaly in January 2010 (1A), bilateral orbital apex lesions in June 2010 (1B) and in October 2010 (1C) on computed tomographic scans. Right (1D) and left (1E) conjunctival lower fornix lesions in October 2010. Note more apparent orbital apex lesions in October (1C) than in June (1B).
Fig. 2. Right conjunctival biopsy in a 66-year-old man in October 2010. Subepithelial infiltration with small to medium-sized lymphoid cells (H&E stain), which are positive for CD5, CD20, bcl2, and cyclin D1, but negative for CD23. A small number of cells are positive for Ki67. Original magnification, × 40 in all panels, except for × 20 in the top left H&E panel. Bar = 50 µm in all panels, except for the top left HE panel where bar = 100 µm.
It should be noted that abnormal lymphoid cells in the initial bone marrow specimen and the following appendectomy specimen were positive for CD23, while lymphoid cells in the conjunctival biopsy specimen were negative for it. It is, in general, difficult to differentiate CD23-positive leukemic mantle cell lymphoma from chronic lymphocytic leukemia, as diagnosed upon the initial presentation of the present patient. Furthermore, lymphoma cells in the conjunctiva did not express CD23, which was detected by conjunctival biopsy, one year after the appendectomy specimen showed positive expression of CD23. The CD23 expression by lymphoma cells in mantle cell lymphoma would vary from tissue to tissue and also vary along the time course of the disease.

In conclusion, mantle cell lymphoma should be considered in the list of differential diagnoses for conjunctival salmon-pink lesions. Conjunctival biopsy is recommended to confirm the preceding diagnosis or establish a new diagnosis.

CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

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Conjunctival mantle cell lymphoma