

# Conjunctival CD5+ MALT lymphoma and review of literatures

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## Citation

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## Abstract

We report a 35-year-old woman with multicentric CD5-positive mucosa associated lymphoid tissue (MALT) lymphoma of conjunctival region. In this case, the histologic features were typical of marginal zone/MALT lymphoma with reactive follicles, marginal zone (centrocyte-like) cells, and plasma cells. Immunohistochemically, the malignant cells expressed markers of B-cell lineage and unusually CD5 positive. Our patient treated with chemotherapy. It has thought that CD5-expression is a marker for unusual and aggressive clinical course. The occurrence of multicentric conjunctival CD5-positive MALT lymphoma in the younger age further support to the notation that CD5+ MALT-lymphomas arising in the ocular adnexa might be characterized by an unusual clinical course.

## INTRODUCTION

Ocular adnexal lymphomas present usually as a primary disease of the orbital soft tissue, conjunctiva, and eyelid. The majority of lymphomas occurring in the ocular adnexa are B-cell non-Hodgkin lymphomas [1]. These are predominantly extranodal marginal zone B-cell lymphomas (MZL), according to the Revised European American Lymphoma (REAL) classification, but they can also include mantle-cell lymphoma (MCL) [12].

Extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT lymphoma) histologically comprises small to medium-sized B cells. The neoplastic cells infiltrate the reactive follicles, showing follicular colonization, and have typical lymphoepithelial lesion [3]. The neoplastic cells express pan B-cell antigens (CD19, CD20, CD22). Typically, they are negative for CD5, CD10, and CD23 [2].

The prognosis for ocular adnexal lymphomas is closely related to the age of patients, clinical stage at presentation, localization, blood lactate dehydrogenase values, signs and symptoms of disease, response to treatment, histologic type, and immunohistochemical markers such as MIB-1 (Ki-67) and p53 [4]. Characteristically, MZL of the MALT type affects older patients and may remain localized for years, while disseminated disease involving bone marrow and peripheral blood is rare. Localized tumors may cure with local irradiation, whereas disseminated stages of the disease

are not curable and transformation into a large cell NHL may occur [2]. In recent studies, several cases of conjunctival CD5-positive MALT lymphoma have been reported [356]. In this study, we described a case of conjunctival MZL of the MALT type with an unusual clinical course, a CD5+ immunophenotype and favorable response to chemotherapy.

## CASE HISTORY

A 35-year-old Iranian woman admitted to hospital with a 7-month history of left epibulbar mass. Physical examination of the left eye revealed two pink conjunctival mass, measuring 30×15 mm, involving the palpebral conjunctiva and superior and inferior cul-de-sac. (Fig. 1A,B) The best corrected visual acuity was 20/20 in both eyes. Extraocular motility was full. The cornea, anterior chamber, iris, lens, and fundus of the left eye were normal. The right eye was completely unremarkable. The intraocular pressure was normal for the both eyes. Conventional histological examination was performed on an incisional biopsy of the conjunctival tumor. Microscopically, the tan-pink conjunctival specimen consisted of a diffuse dense lymphocytic infiltrates, which displayed an expansive growth pattern within the marginal zone, surrounding reactive follicles.

These neoplastic cells were cytologically heterogeneous, consisting of small lymphocytes, centrocytelike cells, plasmacytoid cells. The tumor cells infiltrated the conjunctival epithelium with the formation of

lymphoepithelial lesions. (Fig. <sup>2A</sup>) Another feature of this tumor was “follicular colonization,” a secondary infiltration of the germinal centers by the neoplastic marginal zone B-cells. Immunohistochemically, they were characterized by positivity for CD20. The neoplastic cells were negative for CD3. CD10 had positive reactivity only in the germinal centers. General expression of CD20 revealed the B cell nature of the tumor infiltrate, but it was interesting that CD5 expression in about 50% of tumor cells was positive. (Fig. <sup>2B</sup>) With exception of CD5 expression, the morphological findings and growth pattern of the neoplastic cells, led us to diagnosis of a malignant small cell B-cell non-Hodgkin lymphoma and sub-typed as extranodal marginal zone B-cell lymphoma of MALT type.

General physical examination of the patient showed no abnormality. There were no lymphadenopathies or hepatosplenomegaly. Staging investigations, which included full blood count, chest-ray, computer tomography scans, and magnetic resonance imaging of the thorax, abdomen, and of the head and neck, as well as bone marrow aspiration biopsy, confirmed the localized conjunctival tumor. (stage IE, according to the Ann Arbor clinical staging system) [7]. The patient predominantly treated with combined chemotherapy regimens cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with regarding the risk of relapse with radiotherapy. No recurrence of the orbital lesion or any systemic involvement was noted during the follow up period of 12 months.

**Figure 1**

Figure 1A: Superior conjunctival mass



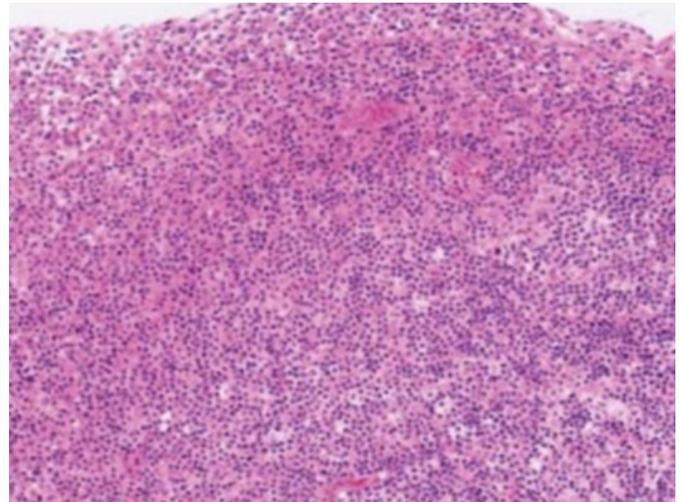
**Figure 2**

Figure 1B: Inferior conjunctival mass



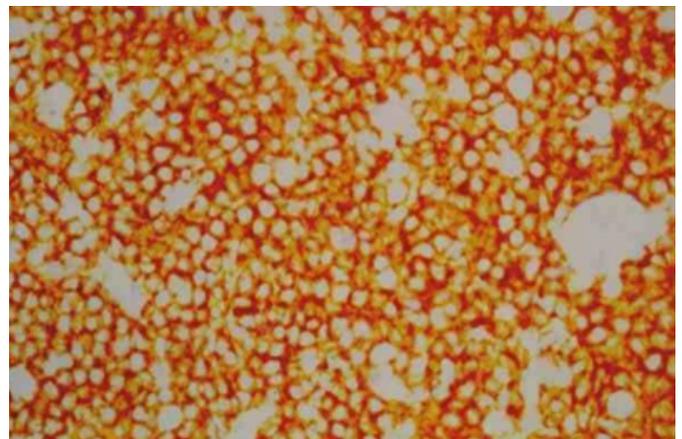
**Figure 3**

Figure 2A: Photomicrograph of conjunctival MALT lymphoma showing lymphomatous infiltrate and invasion of conjunctival epithelium producing lymphoepithelial lesions.



**Figure 4**

Figure 2B: Tumor cells stain positively for CD5



**DISCUSSION**

The immunophenotypic profiles of low-grade B cell NHL are complex and still under investigation. Especially the T cell antigen CD5 is used to subclassify this group of B cell lymphomas. The MALT lymphomas express pan-B-cell antigens but typically lack CD5 expression [2]. CD5 is a T-cell antigen that is expressed on normal B-cells and occasionally on B-cell neoplasm [8]. The T cell antigen CD5 has been reported in B cell NHL between 3% and 40% [9].

Whether CD5 expression is relevant to the prognosis of patients with MALT lymphoma is controversial [5]. In the conjunctival region, we reviewed the cases of three patients with CD5-positive MALT lymphoma (Table 1). The cases of one patients formally reported by Wenzel et al. were presented as a more aggressive disease than typical MALT lymphoma [6]. Local recurrence was noted in this case, and patient had rapid generalization to the contralateral conjunctiva, mediastinal lymph nodes and the esophagogastric. The investigators suggested that CD5 expression might be a marker of propensity for local relapse and dissemination to the other extranodal sites. In contrast the two cases of CD5-positive MALT lymphoma arising in conjunctival region that were reported by Ballesteros et al. and later by Heuring et al, the tumor was localized at presentation and no bone marrow involvement or systemic dissemination were noted [3,5]. The former patient had no follow-up data and the latter patient had a short period (18 months) of follow up after radiotherapy. Although our patient did not have systemic dissemination, but had multicentric involvement.

Conjunctival lymphoma usually presents in elderly patients but our patient presented in younger age.

In one study among the 20 relapsing patients initially treated with radiotherapy, 40% showing MALT type lymphomas. In addition, this study reported three patients with low-grade lymphoma treated with chemotherapy alone and experienced complete remission [10]. Also Lee et al reported three patients who underwent cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy, 2 of whom experienced complete remission [11].

Concerning the present patient, had multicentric tumor (left upper eyelid and lower eyelid) at presentation and CD5+, was predominantly treated with combined chemotherapy regimens with regarding the risk of relapse with radiotherapy. We speculated that early application of

systemic treatment could be beneficial in this subset of patients with MALT-type lymphoma, as reflected by short, but marked clinical improvement of patient following application of chemotherapy.

In conclusion, this case of CD5+ MZL shows that the aberrant expression of CD5 occurs in rare cases of histologically typical marginal zone B-cell lymphoma. The current case was clinically and pathologically localized at presentation. However, because of the short follow-up time and because of the small number of cases reported in the literature, more cases of MZL with CD5 expression must be evaluated to clarify the relationship of this unusual phenotype with the clinical course and further studies are needed in this extremely rare cohort of patients in order to identify optimal therapeutic approaches.

**Figure 5**

Table 1: Review of conjunctival CD 5+MALT lymphoma

Authors	Status ,therapy	Age (years)
Recent study	multicenter tumor, no recurrence, 12 months	Chemotherapy 35
Wenzel et al 6	Contralateral conjunctiva, mediastinal lymph node and esophagogastric involvement	Radiotherapy followed by chemotherapy 73
Ballesteros et al 3	Conjunctival tumor present for 15 years before diagnosis	Therapy not available 70
Heuring et al 5	no recurrence or systemic involvement, 18 months	Radiotherapy 79

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