Case Report

Taiwan J Ophthalmol 2022;12: 101-105

Access this article online

Quick Response Code:

Website:
www.e-tjo.org

DOI:
10.4103/tjo.tjo_91_20

Bilateral lacrimal glands and paranasal sinus diffuse large B-cell lymphoma following lung mucosa-associated lymphoid tissue lymphoma in one patient

Chun-Hao Huang[1], Wei-Hsun Kung[2], Cheng-Hsien Chang[2]*, Cheng-Yu Wang[3], Che-Hung Lin[4]

Abstract:

We report an atypical case of diffuse large B-cell lymphoma (DLBCL) of bilateral lacrimal glands and paranasal sinus following mucosa-associated lymphoid tissue (MALT) lymphoma of the lung. Bilateral DLBCL is rare in the literature, and only few cases of DLBCL in bilateral lacrimal gland are reported. A 71-year-old male presented with bilateral, slowly enlarging, and swelling of both eyelids. Computed tomography scan images showed bilateral symmetric, hyperdense, circumferential masses over lacrimal glands occupying most of the orbital compartment. Neither optic nerve involvement nor adjacent orbital walls erosion was noted. Bilateral excisional biopsy and pathological examination confirmed the diagnosis of DLBCL. Since DLBCL of bilateral lacrimal gland can occur in case of systemic MALT lymphoma, excision and pathological examination is mandatory, and further metastatic workup is essential.

Keywords:

Diffuse large B-cell lymphoma, lacrimal gland, lymphoma, mucosa-associated lymphoid tissue, orbital lymphoma, paranasal sinus

Departments of [1]Medical Education, [2]Ophthalmology and [3]Pathology, China Medical University Hospital, China Medical University, [4]Department of Internal Medicine, Division of Hematology and Oncology, China Medical University Hospital, Taichung City, Taiwan

***Address for correspondence:**
Dr. Cheng-Hsien Chang, Department of Ophthalmology, China Medical University Hospital, China Medical University, 2 Yuh-Der Road, Taichung City, 40447, Taiwan.
E-mail: ophchang@yahoo.com.tw

Submission: 01-09-2020
Accepted: 15-11-2020
Published: 30-04-2021

Introduction

Orbital lymphoma is the most frequent malignant tumor of the orbit and is derived from clonal expansions of lymphocytes.[1,2] The preponderance of orbital lymphoma arises from B-lymphocytes, of which mucosa-associated lymphoid tissue (MALT) lymphoma is the most frequent B-cell lymphoma.[3] MALT lymphomas usually present as a low-grade, slow-growing, indolent solid tumors without adjacent tissue destruction.[3] Compared to MALT lymphoma, diffuse large B-cell lymphoma (DLBCL) is an aggressive tumor that arises primarily or undergoes histological transformation (HT) from a preexisting low-grade B-cell lymphoma.[4] Since transformation of a MALT lymphoma is possible, excision of an orbital tumor for pathological examination in case of systemic lymphoma is mandatory.

Case Report

A 71-year-old ethnic Chinese male presented with bilateral swelling of the eyelids for 2 years. Symptoms had deteriorated in the past month, and he came to our hospital in January 2020. The eyelids were slowly enlarging without pain and tenderness. He denied fever, fatigue, weight loss, or malaise. The patient had a past medical

How to cite this article: Huang CH, Kung WH, Chang CH, Wang CY, Lin CH. Bilateral lacrimal glands and paranasal sinus diffuse large B-cell lymphoma following lung mucosa-associated lymphoid tissue lymphoma in one patient. Taiwan J Ophthalmol 2022;12:101-5.

history of MALT lymphoma Stage IE and chronic sinusitis after functional endoscopic sinus surgery.

MALT lymphoma of the lung was diagnosed by endobronchial ultrasound-guided biopsy in December 2015, presenting with a mass in the right middle lobe on computed tomography (CT) [Figure 1a]. Positron emission tomography (PET)-CT showed a localized tumor in the right middle lobe and no abnormal uptake in other regions of the body [Figure 1b]. Increasing tumor size complicated with right lower lung collapse, and pleural effusion was noted in June 2016 [Figure 1c]. External-beam radiation therapy (average dose 3000 cGy) was administered and symptoms relieved. The patient was in stable condition during the regular follow-up at the hematology outpatient department.

Ocular examination revealed bilateral large orbital mass with ptosis [Figure 2a]. Best-corrected visual acuity was 0.5 logarithm of the minimum angle of resolution (log MAR) in the right eye and 0.7 log MAR in the left eye. There was no limitation of eye movement or relative afferent pupillary defect. Both upper margin reflex distances were 1 mm. Intraocular pressure was at 24 mmHg for the right eye and 23 mmHg of the left eye with Tono-pen. External examination of the bilateral eyes showed fullness of the upper lid involving the lacrimal gland area. Bilateral firm, nontender, and masses were palpated extending from the lacrimal gland to the anterior part of the orbit. The globe was displaced downward with mild proptosis. Slit-lamp examination revealed clear cornea without anterior chamber cellular reaction, conjunctival chemosis, or hyperemia, but binocular nuclear sclerosis was noted.

CT showed bilateral diffuse involvement of the lacrimal glands, which involved both the palpebral and orbital lobes. The masses occupied most of the orbital compartment, with the larger one measuring 4.5 cm × 1.5 cm × 0.7 cm [Figure 2b and c]. The masses were well-defined, hyperdense, and homogeneous which conformed to the globe and subjacent osseous structures. There was no infiltrative bone destruction, remodeling, sclerosis, or optic nerve involvement. In addition, mucus retention, mucosa thickening, and polypoid lesions were found in the bilateral maxillary sinus, ethmoid, and frontal sinuses. Preoperative differential diagnosis included inflammatory pseudotumor and lymphoma.

Excisional biopsy of bilateral lacrimal gland masses through anterior approach orbitotomy was performed in February 2020. Two tumors located on the bilateral temporal side of the superior orbit were resected, which revealed tan and elastic masses grossly [Figure 3]. Histopathological examination showed a nodular pattern of monotonous atypical lymphocytes infiltrating the lacrimal gland, with adjacent remaining scatter follicles with germinal center formation. Increased proliferative index, confirmed by the KI67 stain, in areas of large cell transformation to aggressive large B-cell lymphoma was identified [Figure 4]. Ancillary immunohistochemical studies determined that these large atypical lymphoid cells were positive for Bcl-2, CD20, MUM-1, and admixed with some reactive CD3+ T-cells, but negative for CD3, CD5, CD10, Bcl-6, c-Myc, EBER, cyclin-D1, and CK (AE1/AE3) [Figure 4]. Pathology findings were consistent with the diagnosis of diffuse large B-cell lymphoma, which was highly suspected to be of large-cell transformation from MALT-type lymphoma. PET-CT revealed diffused numerous lesions and lymph nodes with fluorodeoxyglucose uptake malignancy [Figure 5a]. Bone marrow biopsy showed multiple aggregations of small to medium size atypical lymphoid cells with hyperchromasia and irregular nuclear membrane, and B-cell lymphoma with bone marrow involvement is considered [Figure 5b]. Nasopharyngo-fiberscope showed crust and necrotic mucosa in bilateral nasal cavities and obliterated ostiomeatal complex. Sinoscopy biopsy of the right nasopharynx, left nasal septum, and left inferior turbinate revealed the same morphology of tumor cells. Infiltration of small to large size atypical lymphoid cells with focal clear cytoplasm, prominent

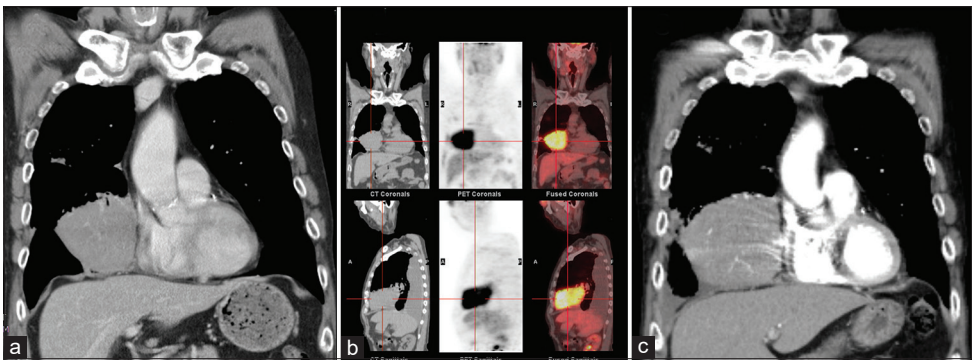

Figure 1: (a) Chest computed tomography revealing right middle lobe mass in December 2015 (b) Positron emission tomography-computed tomography showed localized tumor in the right middle lobe and no abnormal uptake in other regions of the body in December 2015. (c) Enlarged tumor complicated with right lower lung collapse and pleural effusion in June 2016

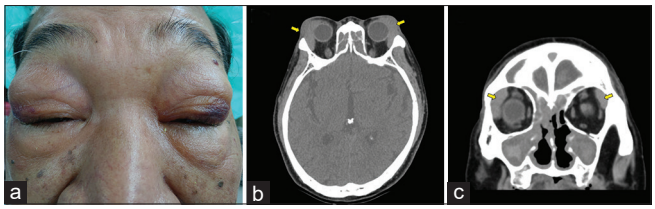

Figure 2: (a) Bilateral large orbital masses over lacrimal glands (b and c) computed tomography revealed the tumors over bilateral lacrimal glands without adjacent structure involvement (arrows)

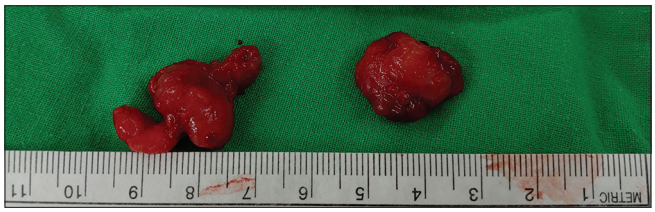

Figure 3: Two tumors located on the bilateral temporal side of the superior orbit

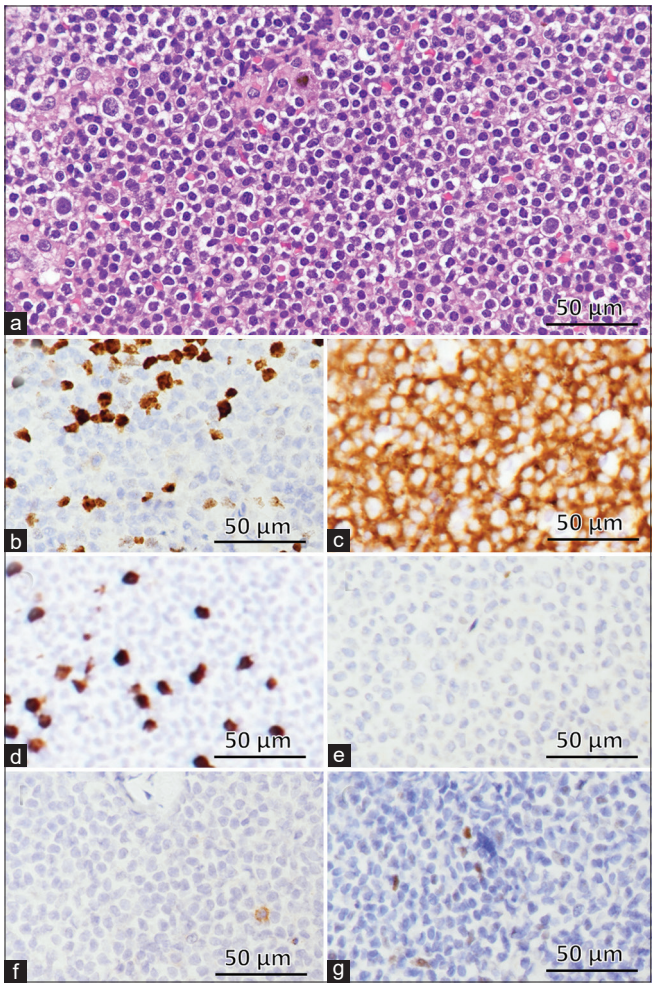

Figure 4: Histopathology and immunohistochemistry of the orbital lesions on bilateral eyes in February 2020, obtained by excisional biopsy. Diffuse infiltration with monotonous large cells in H and E stain (a), which were highly proliferative index, confirmed by the Ki67 (b). These cells were positive for CD20 (c), admixed with few CD3-positive T-cells (d). CD10, Bcl-6, and Cyclin D1 were all negative (e-g)

nucleoli, and irregular nuclear membrane was consistent with the diagnosis of DLBCL [Figure 5c]. The DLBCL was classified as Stage IV, and international prognostic index was 3. The immune chemotherapy was initiated after the staging of lymphoma. The treatment protocol was the intravenous infusion of rituximab at a dose of 375 mg/m^2 on day 1 and bendamustine at a dose of 90 mg/m^2 on day 2 every 28 days. The treatment-related adverse events were fatigue and diarrhea after immune chemotherapy. The patient finished six courses and follow-up PET-CT showed metabolic complete remission. The bone biopsy revealed a negative finding for lymphoma involvement. The patient had a good response to the treatment.

Discussion

We present a rare case of bilateral lacrimal glands and paranasal sinus DLBCL with systemic involvement following primary lung MALT lymphoma. Bilateral DLBCL is rare in the literature, and only few cases of DLBCL in bilateral lacrimal gland are reported. Bilateral gland diseases comprise inflammatory, structural, lymphoproliferative, and other uncommon diseases.[5] Inflammatory diseases occur mostly in younger patients and patients with the clinical presentation of pain and mechanical blepharoptosis. Conversely, lymphoma is more frequent in older patients without active inflammation signs.[5] Most B-cell lymphomas (90%) occur unilaterally, yet DLBCL rarely presents with bilateral involvement.[3] In our case, preoperative differential diagnosis indicated a lymphoma due to older age and a past history of MALT lymphoma. However, to our surprise, the pathological studies confirmed the diagnosis of DLBCL.

The pathway for sequential development of MALT lymphoma and DLBCL indicates the change of the malignant cells derived from the B-cell lineage, also known as HT.[6] HT is rare in the orbit, usually arises concomitantly with and at the original site of MALT lymphoma in over 8% of MALT lymphomas.[6] Primary orbital lymphoma involves only the postseptal space, including the extraocular muscles, lacrimal gland, vessels, and nerves, whereas secondary orbital lymphoma is accompanied by a history of lymphoma or concurrent systemic disease.[7] Most B-cell lymphomas occur as a primary orbital disease, while almost half of DLBCL present as a secondary lymphoma either from metastatic spread or local invasion.[3] A recent cohort study demonstrated nearly one-third of patients with orbital adnexal lymphoma had a history of lymphoma.[8] From the experience of this case, we should be aware of secondary lymphoma in the long-term follow-up, especially in patients with a past history of lymphoma. A further metastatic workup is essential.

The simultaneous presentation of orbital and paranasal sinus lymphoma is rare in patients without local invasion to or from adjacent structures. DLBCL is

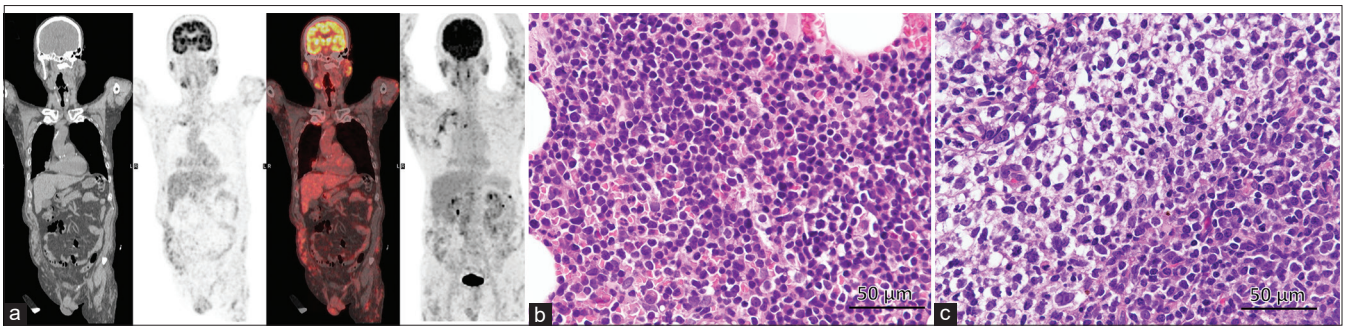

Figure 5: (a) Positron emission tomography-computed tomography revealed diffused numerous lesions and lymph nodes with fluorodeoxyglucose uptake malignancy. (b) Multiple aggregations of small to medium size atypical lymphoid cells with hyperchromasia and irregular nuclear membrane (c) Infiltration of small to large size atypical lymphoid cells with focal clear cytoplasm, prominent nucleoli, and irregular nuclear membrane

the most common paranasal sinus lymphoma, with a high percentage of local invasion to periorbital and sinuses.[3] A cohort study demonstrated around half of the paranasal sinus lymphoma has orbital involvement.[9] However, the similar histopathological morphology found in the paranasal sinus is consistent with the tumor cells in lacrimal glands, even though the imaging studies of our case showed no adjacent orbital walls erosion or optic nerve involvement.

The management of orbital lymphoma requires multidisciplinary teamwork, and tolerance of the patient should be considered. Solitary, low-grade lymphomas could have radiotherapy considered as the first-line treatment, while disseminated and high-grade lymphomas should consider chemotherapy for systemic treatment.[2] It has been shown that after the induction of combined therapy with rituximab and chemotherapy in patients with orbital DLBCL, patient outcome improves significantly.[10] In our case, the patient was more than 70 years old, and there were side effects such as fatigue after rituximab administration, thus a traditional chemotherapy regimen such as R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine/Oncovin, prednisolone) might be risky. After evaluation, we chose rituximab plus bendamustine. Bendamustine is an alkylating agent consisting of purine-like analog properties, which is authorized for the treatment of indolent non-Hodgkin's lymphoma and chronic lymphocytic leukemia. Recently, several Phase II studies indicated bendamustine plus rituximab has promising efficacy and good tolerance by patients with relapsing refractory DLBCL.[11] Consequently, if the patient is not eligible for full-dose standard R-CHOP, bendamustine plus rituximab is a good alternative.

DLBCL in the bilateral lacrimal gland is rare in literature. The simultaneous presentation of orbital and paranasal sinus lymphoma is also rare, especially if there is no adjacent structure invasion, as in our case. In the evaluation of orbital lymphoma, systemic hematological malignancy workup is vital to ensure prompt diagnosis and treatment. Treatment of orbital lymphoma needs multidisciplinary teamwork and tolerance of the patient should be considered. Bendamustine plus rituximab showed good outcomes with manageable side effects in our case, making it a good alternative for elderly patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, *et al.* The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016;127:2375-90.
2. Sjö LD. Ophthalmic lymphoma: Epidemiology and pathogenesis. Acta Ophthalmol 2009;87 Thesis 1:1-20.
3. Olsen TG, Heegaard S. Orbital lymphoma. Surv Ophthalmol 2019;64:45-66.
4. Martelli M, Ferreri AJ, Agostinelli C, Di Rocco A, Pfreundschuh M, Pileri SA. Diffuse large B-cell lymphoma. Crit Rev Oncol Hematol 2013;87:146-71.
5. Tang SX, Lim RP, Al-Dahmash S, Blaydon SM, Cho RI, Choe CH, *et al.* Bilateral lacrimal gland disease: Clinical features of 97 cases. Ophthalmology 2014;121:2040-6.
6. Maeshima AM, Taniguchi H, Toyoda K, Yamauchi N, Makita S, Fukuhara S, *et al.* Clinicopathological features of histological transformation from extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue to diffuse large B-cell lymphoma: An analysis of 467 patients. Br J Haematol 2016;174:923-31.
7. Rasmussen PK. Diffuse large B-cell lymphoma and mantle cell lymphoma of the ocular adnexal region, and lymphoma of the

lacrimal gland: An investigation of clinical and histopathological features. Acta Ophthalmol 2013;91 Thesis 5:1-27.
8. Sagiv O, Thakar SD, Manning JT, Kandl TJ, Fayad LE, Fowler N, *et al.* Prevalence of a histologic change of ocular adnexal lymphoma in patients with a history of lymphoma. Ophthalmic Plast Reconstr Surg 2019;35:243-6.
9. Wajda BN, Rabinowitz MR, Nyquist GG, Mardekian SK, Rosen MR, Rabinowitz MP, *et al.* Paranasal sinus lymphoma: Retrospective review with focus on clinical features, histopathology, prognosis, and relationship to systemic lymphoma. Head Neck 2017;39:1065-70.
10. Keating GM. Rituximab: A review of its use in chronic lymphocytic leukaemia, low-grade or follicular lymphoma and diffuse large B-cell lymphoma. Drugs 2010;70:1445-76.
11. Storti S, Spina M, Pesce EA, Salvi F, Merli M, Ruffini A, *et al*. Rituximab plus bendamustine as front-line treatment in frail elderly (>70 years) patients with diffuse large B-cell non-Hodgkin lymphoma: A Phase II multicenter study of the Fondazione Italiana Linfomi. Haematologica 2018;103:1345-50.