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Case report

Bilateral lacrimal gland lymphoma: Case report and literature review ☆,☆☆

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ABSTRACT

Ocular adnexal lymphoma accounts for approximately 1%-2% of non-Hodgkin lymphomas and 8% of extranodal lymphomas. Lacrimal gland lymphoma, especially bilateral lacrimal gland lymphoma, is rare, and imaging is often utilized to differentiate lacrimal lymphoma from other types of masses that involve the lacrimal gland and the fossa. We describe a 74-year-old male patient presenting with bilateral eye proptosis, lachrymose without pain, and no changes in eyesight. Brain-orbit magnetic resonance imaging revealed bilateral lacrimal fossa masses with regular contours, moderate enhancement, and restriction on diffusion imaging, consistent with a lymphoma diagnosis, which was confirmed by histopathological results. Positron emission tomography-computed tomography was used to determine lymphoma grading. MRI, especially diffusion imaging, can be useful for guiding clinicians in the diagnosis and differentiation of lacrimal gland lymphoma from other lesions.

Introduction

Several etiologies can affect the lacrimal gland, such as inflammatory lesions, lymphoproliferative lesions, and salivary gland–type tumors [1]. Lacrimal gland lymphoma is commonly characterized as a mucosa-associated lymphoid tissue (MALT) type that tends to affect older patients between the ages of 50 and 70 years with a female preponderance. Bilateral involvement is reported in 10%-15% of lacrimal gland lymphoma cases [2–4]. Patients typically present with painless lacrimal gland masses. The combi-

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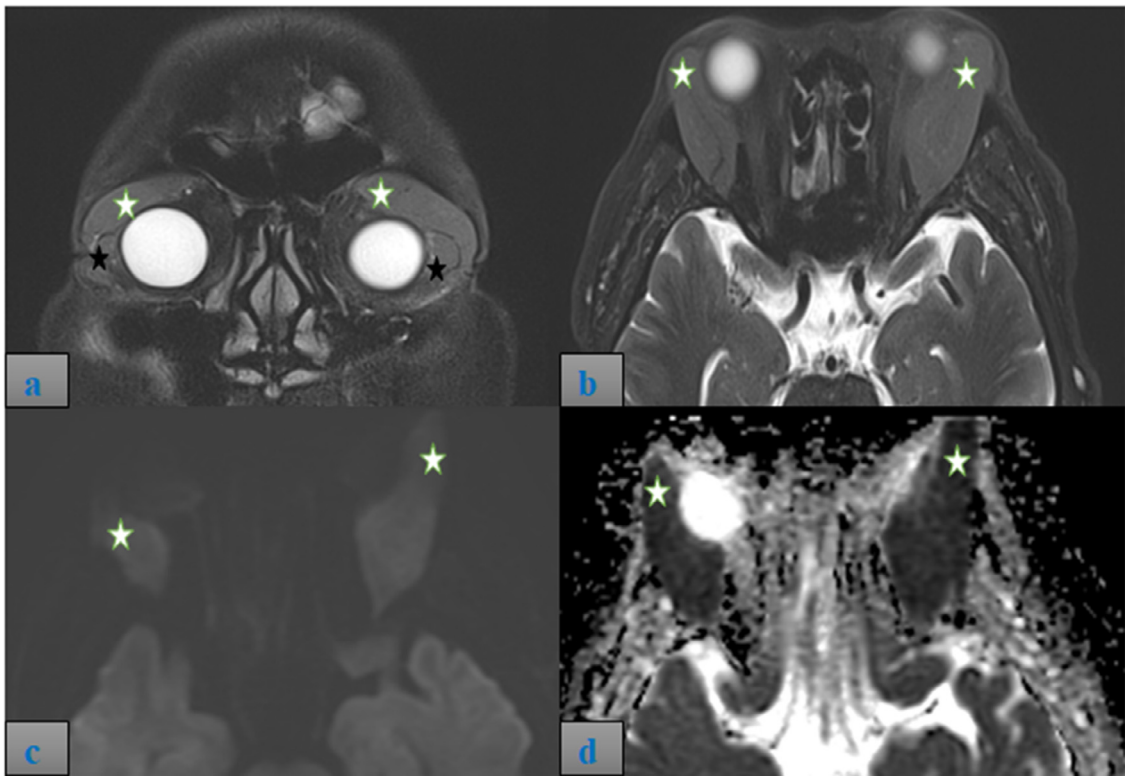

Fig. 1 – MRI images: (A) Coronal fat-saturated T2WI (T2FS) showing bilateral lacrimal gland masses involving both orbital lobes (white stars) and palpebral lobes (black stars). (B) Axial T2FS revealing that the masses are isointense to muscle and gray matter (white stars). (C) Axial diffusion-weighted imaging (DWI) showing slight hyperintensity relative to gray matter (white stars). (D) Axial apparent diffusion coefficient (ADC) map showing remarkably hypointensity relative to gray matter (white stars). MRI: magnetic resonance imaging.

nation of clinical presentation and imaging features can be used to differentiate among various lacrimal gland lesions, including laterality, the portion of gland involvement, enhancement patterns, and bony involvement [1]. Currently available treatment modalities for lacrimal gland lymphoma patients include surgical resection, radiotherapy, single-agent or combination chemotherapy, monoclonal anti-CD20 antibody, and interferon immunotherapy [5]. The prognosis for lacrimal gland lymphoma is relatively good, and overall survival can differ significantly among lymphoma subtypes [6].

Case presentation

A 74-year-old man with unremarkable medical history was admitted to our hospital with bilateral eye proptosis and reporting a feeling of pressure in the eyes without pain. The symptom duration lasted approximately 2 years, and at that time of the onset, the patient underwent brain magnetic resonance imaging (MRI) at a different hospital with a normal result. Over several recent months, the patient described worsening symptoms. In addition to feeling pressure, the patient experienced eye redness and lachrymosity. The patient denied any changes in vision, fever, night sweats, or weight loss. Examination revealed bilateral eye proptosis, restricted extra-ocular movements, and normal eyesight. The preliminary diagnosis was lacrimal gland inflammation; however, tumors in the posterior ocular segment needed to be excluded. Therefore, brain and orbit MRI with gadolinium injection was performed. On brain and orbit MRI, 2 masses were detected at the bilateral superolateral corners of the orbits, which were compatible with the lacrimal glands. The masses were well-defined, with regular contours, appeared hypointense on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI), appeared hyperintense on fluid-attenuated inversion recovery (FLAIR), appeared restricted with hyperintensity on diffusion-weighted imaging (DWI), and appeared hypointense on the apparent diffusion coefficient (ADC) map, with moderate enhancement (Fig. 1). These lesions, which appeared more prominently on the left side, resulted in bilateral exophthalmos, compressing the lateral and superior rectus muscles and the levator muscles, without optic nerve or orbital bone involvement. The diagnosis on imaging favored lacrimal gland lymphoma; however, pseudotumor inflammation, sarcoidosis, and Sjögren's syndrome were also considered and required exclusion. Positron emission tomography-computed tomography (PET-CT) imaging showed increased fluorodeoxyglucose (FDG) uptake by the masses, with a maximum standard uptake value (SUV_{max}) of 17.3, and one lymph node on the left IB showed increased FDG uptake, with an SUV_{max} value of 8.6 (Fig. 2). Orbital mass biopsy revealed a small B-cell lymphoma of lacrimal gland origin, favoring a di-

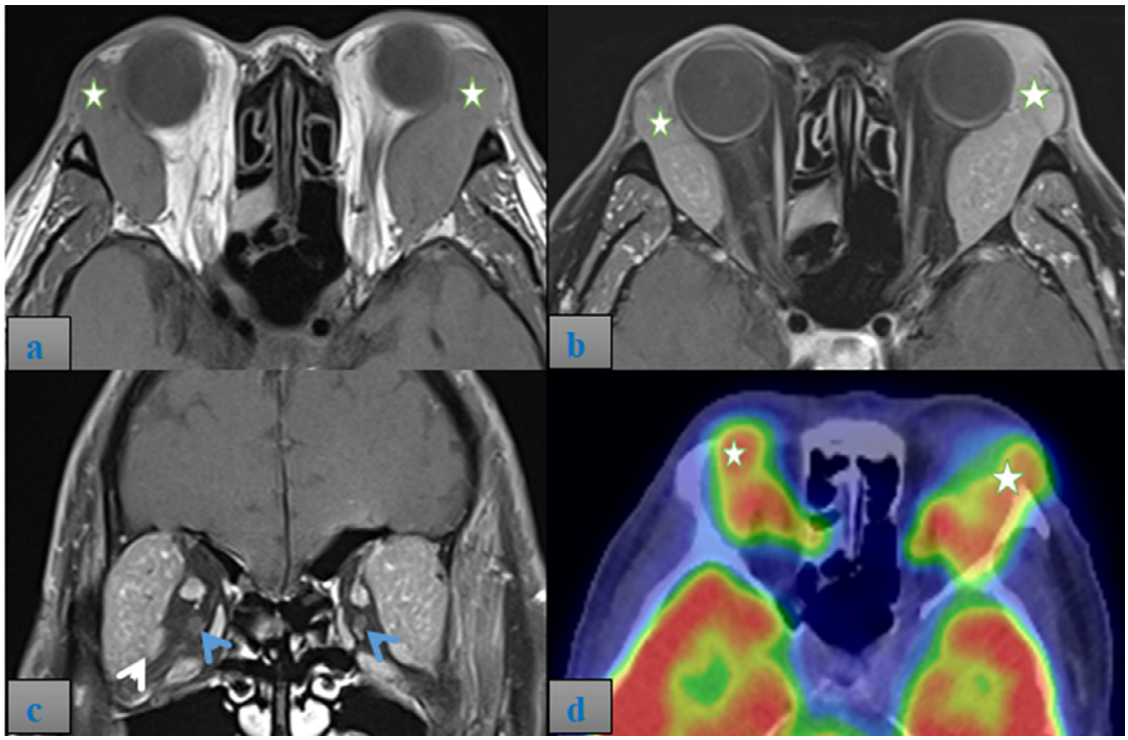

Fig. 2 – MRI images: (A) Axial T1-weighted imaging (T1WI) showing isointensity relative to muscle and gray matter (white stars). (B) Axial fat-saturated T1-weighted images (T1FS) with gadolinium administration, revealing moderate homogeneous enhancement (white stars). (C) Coronal T1FS with gadolinium administration, showing compression of the lateral rectus muscles (white arrowhead) and the displacement of the optic nerves, without infiltration or invasion (blue arrowhead). (D) Axial positron emission tomography-computed tomography image showing increased FDG uptake, similar to that observed in the cerebral cortex (white stars).

agnosis of extranodal marginal zone MALT lymphoma with CD20 positivity (Fig. 3). No abdomen, chest, or bone marrow involvement was observed, compatible with Grade II lymphoma according to the Ann Arbor classification. After diagnosis at our hospital, the patient returned to his hometown in Korea for further consultation and treatment. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Discussion

The lacrimal gland is an eccrine secretory gland for tear production that is situated in the superolateral aspect of the orbit and consists of 2 lobes: the orbital lobe and the palpebral lobe. The orbital lobe is larger and is the most common origin of lacrimal gland epithelial neoplasms, whereas the lymphoproliferative and inflammatory processes tend to involve both lobes of the gland. The normal thickness of the lacrimal gland is approximately 4-5 mm, and the glands are usually symmetric; therefore, asymmetry is a pivotal indicator of abnormality [1, 7].

Lymphoid tumors involving the lacrimal gland include benign lymphoid hyperplasia, atypical lymphoid hyperplasia, and lymphoma [4]. Lacrimal gland lymphoma is B-cell non-Hodgkin lymphoma, and MALT lymphoma is the most frequent histology subtype [4, 7]. In an international multicenter retrospective study examining lacrimal gland lymphoma, Vest et al. [6] showed that the majority of lacrimal gland lymphomas were of B-cell origin. The relationship between *Helicobacter pylori* and gastric MALT lymphoma is well-established; however, the pathogenic relationship between *H. pylori* and lacrimal MALT lymphoma remains unknown. Some theories suggest a link between *Chlamydia* infection and lymphoma in the lacrimal gland [3, 7, 8].

Lacrimal gland lymphoma most commonly occurs among older adults, with a female predominance. The clinical presentations include a palpable mass, eye proptosis, eyeball displacement, or restricted eye movements. Lacrimal gland lymphoma rarely involves the optic nerve, allowing the preservation of eyesight. Unlike sarcoidosis and Sjögren's syndrome, dry eye is unusual in lacrimal gland lymphoma [6, 9]. Rasmussen et al. [9] reported that signs of a palpable mass and eye proptosis were observed in 85% and 56% of lacrimal gland lymphoma patients, respectively, whereas dry eye and decreased visual accuracy were observed in only 2 patients each (7%). In the study by Vest et al. [6], patients with dry eye and decreased visual accuracy represented only 6% and 10% of lacrimal gland lymphoma patients, respectively. Our patient had eye propto-

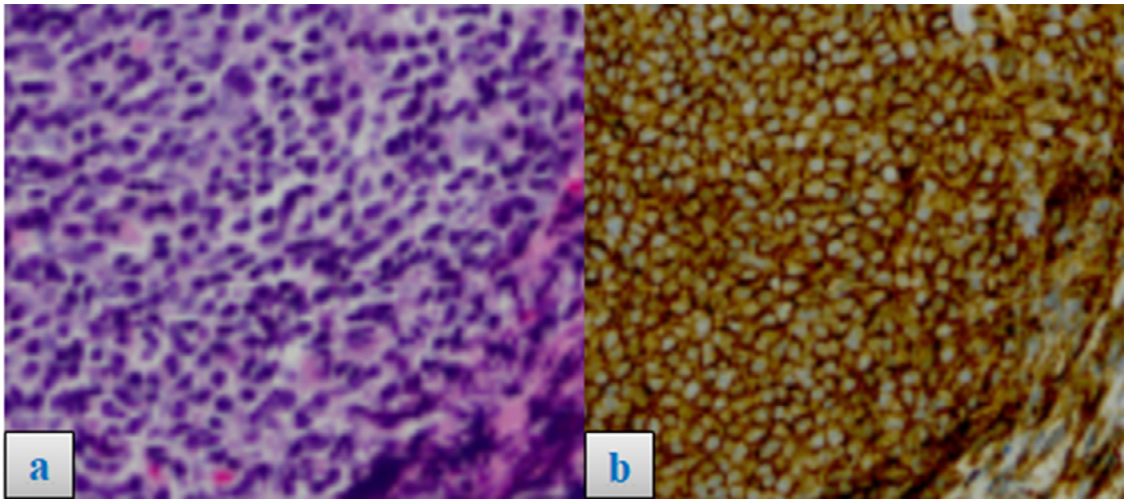

Fig. 3 – Photomicrograph (original magnification, ×400): (A) hematoxylin-eosin staining shows the diffuse effacement of the lacrimal gland parenchyma by small, irregular lymphocytes with round nuclei. (B) CD20 staining shows a diffuse, strong positive signal in neoplastic cells.

sis, swelling without pain, and no evidence of dry eye or decreased visual accuracy.

Advances in CT and MRI techniques have improved their usefulness as tools for morphological diagnosis and differential diagnosis [2]. On CT imaging, lymphoma appears isodense relative to muscular density and shows mild enhancement after contrast administration. Typically, lacrimal gland lymphomas tend to displace adjacent structures rather than infiltrating the orbit without causing bone destruction [1, 7]. On MRI, lacrimal gland lymphoma appears homogeneous and isointense relative to the muscle on T1WI, isointense-to-slightly hyperintense relative to the brain cortex on T2WI, and moderate enhancement occurs after gadolinium administration. Similar to intracranial lymphoma, lacrimal gland lymphoma shows restriction on DWI due to its densely cellular nature. The various histological lymphoma subtypes present with similar manifestations and can be difficult to differentiate based on imaging criteria alone [1]. In our case presentation, restriction on DWI was a beneficial indication for the final diagnosis. Causes for consideration in the differential diagnosis for bilateral lacrimal gland enlargement include lymphoid hyperplasia, sarcoidosis, Sjögren's syndrome, and orbital inflammatory pseudotumor [7]. Based on imaging alone, distinguishing among the various causes of bilateral lacrimal gland enlargement can be difficult; therefore, clinical history, clinical signs and symptoms, epidemiological factors, and histopathology serve as supportive tools for the accurate diagnosis, treatment, and prognosis in cases of lacrimal gland lymphoma [7].

The treatment regimens necessary for diffuse large B-cell lymphoma, follicular lymphoma, and small lymphocytic lymphoma are more aggressive than that for MALT lymphoma. The principal treatment strategy for lacrimal gland lymphoma is radiotherapy, with a potential benefit achieved from adjuvant chemotherapy, whereas surgery is typically avoided to preserve eye function. Rituximab, a murine/human monoclonal antibody that binds specifically to the CD20 antigen expressed by most pre-B and mature B lymphocytes, is the most commonly used agent in chemotherapy [10]. MALT lymphomas involving the lacrimal gland tend to progress slowly, and the response to treatment is relatively good; however, long-term follow-up remains necessary to fully understand the nature and spectrum of these disease types, particularly in cases of unusual histological subtypes [10, 11].

The patient in our case presented with an initial misdiagnosis and long-term treatment for lacrimal gland inflammation. The imaging features indicated the potential diagnosis of lacrimal gland lymphoma; however, the assessment of clinical symptoms and histopathology remained necessary to differentiate this case from other potential lesions, such as benign lymphoid hyperplasia, atypical lymphoid hyperplasia, and pseudotumor inflammation, to develop an appropriate treatment strategy.

Conclusion

Bilateral lacrimal gland lymphoma is a relatively rare presentation that most commonly occurs among older adults. Lacrimal gland lymphoma is a B-cell non-Hodgkin lymphoma with a frequent MALT lymphoma histology subtype. MRI, particularly DWI, can be useful for guiding clinicians in the diagnosis. Imaging can be combined with supportive tools, including clinical history, clinical signs and symptoms, epidemiological factors, and histopathology, to improve the differentiation between lacrimal gland lymphoma and other lesions, which can determine the optimal treatment strategy, prognosis, and follow-up.

Patient consent

Informed consent for patient information to be published in this article was obtained.

Statement of ethics

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contributions

Luu-Thi BN, Ngo-Van D, and Nguyen MD contributed equally to this article as co-first authors. All authors read and approved the final manuscript.

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