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EOPS member name: Nuno Jorge Lamas, MD/PhD

Anatomic Pathology Service
Genetics and Pathology Department
Unidade Local de Saúde de Santo António (ULSSA)
Largo Professor Abel Salazar, 4099-001 Porto, Portugal
Tel.: +351933112197
E-mail: nunojlamas.anapat@chporto.min-saude.pt

School of Medicine
Life and Health Sciences Research Institute (ICVS)
University of Minho
Campus of Gualtar, 4710-057 Braga, Portugal
E-mail: nunojlamas@med.uminho.pt

Material distributed: 1 histology H&E glass slide.

EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA (EMZL) OF THE LACRIMAL GLAND

CLINICAL HISTORY

Here, we present the case of a 72 year-old female patient with a previous history of alcoholic chronic liver disease, arterial hypertension and atrial flutter, all under medical treatment and stable. She also underwent successful cataract surgery on her left eye in 2021. In early 2024, at the Ophthalmology consultation, the patient complained of visual difficulty and a feeling of right orbital dystopia. A firm mass on the superior right orbital rim was detected, adherent to deep planes and causing inferior dystopia. The lesion had been slowly evolving for nearly two years.

The ensuing MRI study performed showed a right orbital 28 x 27 x 21 mm expansive intraorbital lesion centered in the superolateral quadrant of the right orbit, apparently limited to the extraconic compartment and indistinguishable from the lacrimal gland. The lesion had an isosignal in T1 and a slight T2 hypersignal compared to the muscles. There were some internal "septations" and vascular structures running inside the lesion, which probably represented branches of the lacrimal artery. Besides, the lesion was associated with bone thinning of the lateral wall of the orbit and caused medial and anterior deviation of the eyeball, and infero-medial deviation of the superior and lateral rectus muscles. The neuroradiology team suggested it was a slow-growing expansive lesion, favouring a pleomorphic adenoma of the lacrimal gland or a solitary fibrous tumor of the orbit.

The patient underwent surgery in our hospital and we received the surgical specimen. A representative section of the lesion is provided.

MACROSCOPY

A nodular formation weighing 7 g and measuring 35 x 30 x 15 mm was received in the Pathology laboratory. It had a smooth and bosselated outer surface, partly violaceous, partly brownish and partly yellowish. The cut surface was elastic whitish and brownish. The entire product was submitted for histopathological analysis.

MICROSCOPY

The histological analysis showed a fragment compatible with origin in the lacrimal gland, with preservation of only rare ductal structures, showing intense atypical lymphoid infiltrate, with a vaguely nodular growth pattern. The atypical lymphoid cells were medium-sized, with mostly round nuclear contours, coarse to slightly vesicular chromatin and small nucleoli, sometimes multiple. Occasional mitotic figures were observed. There were no signs of necrosis.

COMPLEMENTARY STUDIES

The immunohistochemistry study showed:

CD20 / CD79a / BCL2 / IgM – universal immunoreactivity in the cells described.
CD3 / CD5 / CD43 – immunoreactivity in background T lymphocytes.
CD21 / CD23 – highlighted the presence of expanded and disrupted follicular dendritic networks.
CD10 / BCL6 / MUM1 / Ciclina D1 / LEF1 – absence of immunoreactivity in the cells described.
IgD – lightly highlighted a few scattered B cells without a well-formed mantle.
CISH Kappa/Lambda – highlighted occasional polytypic plasma cells.
CISH EBER – negative.
Proliferative index (% Ki-67) – below 5%.

Clonality testing was requested and perfomed in two different labs, but a conclusive result could not be reached due to suboptimal quality of the genetic material.

CONCLUSION

The morphological aspects and the immunohistochemistry study are compatible with involvement of the lacrimal gland by a CD5-negative B-cell non-Hodgkin's lymphoma, favouring extranodal marginal zone B-cell lymphoma (EMZL).

DISCUSSION

Extranodal marginal zone lymphoma (EMZL), commonly referred to as mucosa-associated lymphoid tissue (MALT) lymphoma, is a rare, indolent subtype of non-Hodgkin lymphoma that typically arises in mucosal sites such as the gastrointestinal tract, salivary glands, lungs, and ocular adnexa. EMZL can arise primarily in ocular adnexal structures, or, less often, as secondary involvement by EMZL arising in other sites. Ocular adnexa EMZL often affects patients in their 50s or 60s, with a tendency for a slight predominance in females. EMZL primary involvement of the lacrimal gland is particularly uncommon, however, it represents nearly 70% of lacrimal gland lymphoma cases. In the lacrimal gland, EMZL usually presents as a painless, slowly enlarging orbital mass. Symptoms often include proptosis, eyelid swelling, or diplopia, as demonstrated in this case. Systemic symptoms are unusual. Because of its nonspecific clinical presentation, the diagnosis is frequently delayed or mistaken for other conditions, such as inflammatory pseudotumour, lacrimal gland pleomorphic adenoma or solitary fibrous tumour of the orbit.

Imaging modalities such as MRI or CT scan normally show a well-defined, homogeneously enhancing mass in the lacrimal gland area. Despite their utility in detecting orbital lesions, imaging findings are not specific enough to distinguish EMZL from other lacrimal gland neoplasms. Thus, histopathological examination remains the gold standard for the diagnosis and treatment planning. Immunohistochemistry analysis confirms the B-cell origin by showing positive staining for CD20 and CD79a. Bcl-2 is normally positive and markers such as CD5, CD10, and cyclin D1 are typically negative. In the current case, both morphological features and immunophenotyping were compatible with EMZL. Molecular studies can also reveal lymphoma-associated translocations linked with NF-kB activation. The most common is t(14;18)(q32;q21) / IGH::MALT1, which occurs in approximately one-quarter of ocular adnexal EMZL, while the others are rare.

Treatment depends on the stage and extent of disease. Localized disease (Ann Arbor stage IE) is commonly treated with external beam radiotherapy (EBRT), which provides high local control with minimal ocular side effects. In more advanced or disseminated disease, systemic therapy is mandatory, including chemotherapy and/or immunotherapy (for example, using rituximab). Given its slow progression, EMZL normally allows for conservative, organ-preserving treatment strategies.

The prognosis for lacrimal gland EMZL is generally favourable, with 5-year survival rates exceeding 90%. Yet, long-term follow-up is vital to monitor for recurrence or potential transformation into a more aggressive lymphoma. Predictors of a worse prognosis include older age, secondary disease, disease relapse, and a higher TNM stage.

Our patient was treated with two cycles of localized low-dose radiotherapy, showing excellent response. Fourteen months post-surgery, our patient remains free of local recurrence based on the recent imaging studies. Eye movement and vision are preserved, with no orbital pain. The only lingering symptom is mild dryness of the right eye, managed with lubricating drops. The patient continues under routine surveillance. The case presented here underscores the importance of considering EMZL in the differential diagnosis of lacrimal gland masses and emphasizes the vital need for a multidisciplinary approach.

ACKNOWLEDGMENTS

The present cased was studied together with Dr. Francisca Emanuel Costa, the leading hematopathologist in our Service, whom I would like to thank for her wise and precious help. The case was also sent for second observation by Professor Elaine S. Jaffe (National Cancer Institute, Bethesda, USA), who corroborated our diagnosis. I would also like to thank Professor Jaffe for her willingness to review this case and for her enriching expert comments.

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