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LACRIMAL SAC DIFFUSE LARGE B-CELL LYMPHOMA PRESENTING AS SUDDEN-ONSET BINOCULAR DIPLOPIA

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ABSTRACT

Introduction: Diffuse large B-cell lymphoma (DLBCL) is a prevalent subtype of non-Hodgkin lymphoma (NHL) affecting predominantly elderly individuals.

Case description: A 68-year-old man with a history of hypertension, hyperlipidaemia and a small pituitary gland tumour presented with sudden-onset binocular diplopia and right-eye blurry vision. A magnetic resonance imaging (MRI) of the brain revealed enhancing soft tissue in the right superolateral orbit inseparable from the lacrimal gland, extending medially to the right superior rectus muscle and soft tissue. Further scanning showed widespread metastasis to the bilateral retroperitoneal lymph nodes, adrenal gland, spine and lymph nodes in the neck. A biopsy of the lacrimal gland confirmed DLBCL.

Conclusion: Primary lacrimal gland DLBCL is a rare and delayed diagnosis that often stems from the resemblance of its clinical manifestations to more benign conditions such as dacryocystitis, dacryostenosis or mucocele. Timely recognition and accurate diagnosis are essential for initiating appropriate treatment and improving patient outcomes.

KEYWORDS

Diffuse large B-cell lymphoma, ocular adnexal lymphoma, diplopia

LEARNING POINTS

- Lacrimal sac lymphomas represent diagnostic challenges due to their rarity, non-specific symptoms and frequent misdiagnoses as benign pathologies, hence it is crucial to include this in the differential diagnosis.
- Timely recognition and accurate diagnosis are important in improving outcomes for lacrimal sac lymphomas.

INTRODUCTION

In the United States, the annual incidence of non-Hodgkin lymphoma (NHL) is reported to be 7 cases per 100,000 individuals, with diffuse large B-cell lymphoma (DLBCL) comprising approximately 30–40% of all NHL cases across diverse geographic regions. DLBCL exhibits a predilection for the elderly population, particularly those in the 6th to 7th decade of life, with a notable male predominance. The gastrointestinal tract is identified as the most prevalent primary site for DLBCL[1].

Clinical manifestations of DLBCL commonly include B-symptoms such as weight loss, fever and night sweats,

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along with organ-specific symptoms corresponding to the involvement of specific anatomical regions, such as abdominal pain in gastrointestinal tract cases or headaches in central nervous system presentations. Due to the non-specific nature of these symptoms, DLBCL is often diagnosed at advanced stages, with approximately 50% of patients presenting at stage III or IV. Subsequent classification as concordant or discordant is determined through bone marrow biopsy, with concordant involvement predicting less favourable overall survival[2].

Ocular adnexal lymphomas, encompassing lymphomas affecting the orbits, eyelids, conjunctiva, lacrimal gland and lacrimal sac, constitute 2% of all extranodal lymphomas and stand as the most prevalent malignant tumours within the orbit. Notably, lacrimal gland DLBCL, despite DLBCL's general male predominance, exhibits a female predominance. This rarity contributes to frequent misdiagnoses as benign or inflammatory pathologies, given its infrequent occurrence and atypical presentation. Here, we present a case involving a 68-year-old man with lacrimal gland diffuse large B-cell lymphoma, who presented with sudden-onset binocular diplopia[3].

CASE DESCRIPTION

A 68-year-old man presented to the emergency department (ED) via an Ophthalmology referral for sudden, same-day onset of binocular diplopia on distance vision associated with 10 days of right-eye blurry vision and cranial third-nerve palsy. He had a past medical history of hypertension, hyperlipidaemia, a small pituitary gland tumour (0.8 cm discovered one year before admission) and a recent sinus polypectomy.

In the ED the patient arrived hypertensive, with otherwise stable vitals. His general appearance revealed a well-developed, not ill-appearing elderly male, with an unremarkable physical examination aside from cranial third-nerve palsy evidenced due to supraduction limitation of the right eye and V deviation. He was taken for a computed tomography (CT) scan of the head, a CT angiography (CTA) scan of the head, and neck and magnetic resonance imaging (MRI) scan of the orbits and brain to rule out stroke vs aneurysm vs intracranial process. The CTA of the head and neck showed no significant stenosis, aneurysms, vascular malformation or large vessel occlusion. The CT scan of the head revealed no evidence of acute intracranial haemorrhage, midline shift or mass effect. The MRI scan of the brain showed enhancing soft tissue in the right superolateral orbit inseparable from the lacrimal gland and extending medially to the right superior rectus muscle. There was soft tissue abutting and possibly eroding the posterior dorsal sella with possible invasion of posterior left cavernous sinus concerning for lymphoma vs. idiopathic orbital pseudo tumour *(Fig. 1)*.

Due to past history significant for a small pituitary gland tumour that was diagnosed one year before presentation and did not require surgery at the time, an MRI of the pituitary gland was ordered. This showed a soft tissue mass involving the sella, upper cloves and posterior dorsum sellae with extension into posterior left cavernous sinus, concerning for pituitary adenoma, meningioma or metastatic disease.

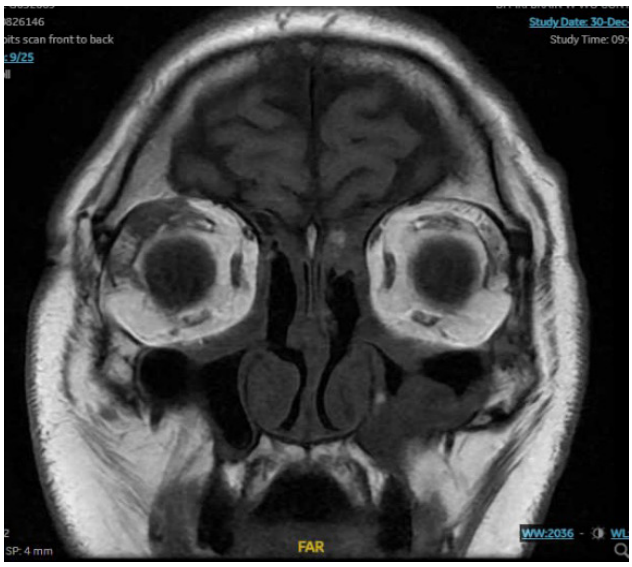

Figure 1. MRI orbits showing enhancing soft tissue in right superolateral orbit inseparable from the lacrimal gland and extending medially to the right superior rectus muscle.

Laboratory	Patient results	Normal range
8 AM cortisol	5.5 mcg/dl	6.7–22.6 mcg/dl
ACTH	18.5 pg/ml	7.2–63.3 pg/ml
TSH	3.65 uIU/ml	0.4–4.20 uIU/ml
Free T4	0.73 ng/dl mcg?	0.8–1.5 ng/dl
LH	2.44 mIU/ml	1.2–8.6 mIU/ml
Testosterone	66 ng/dl	77–357 ng/dl
Prolactin	15.4 ng/ml	1.60–18.80 ng/ml
IGF-1	180 ng/ml	59–230 ng/ml
LDH	318 U/l	140–280 U/l

Table 1. Laboratory results.

Endocrinology was consulted for the parasellar mass and stated it was unlikely to be of pituitary origin given small size of the adenoma the previous year and the rapid, vast extension of the mass. The results of the pituitary function examinations obtained are shown in *Table 1*. Neurology was consulted where a notable left cranial nerve 6 palsy and right cranial nerve 4 palsy was evidenced, and a lumbar puncture was done, which showed increased white blood cell (WBC) in the cerebrospinal fluid (see *Table 2*). A lacrimal gland biopsy was done by Ophthalmology which revealed a DLBCL with nodular proliferation of large B cells of the right lacrimal gland.

On further imaging for stage lymphoma, computed tomography arterial portography showed a bulky bilateral

	CSF
Nucleated cells	100 cells
Differential	70% lymphocyte predominance
RBC	6010
Glucose	75 mg/dl

Table 2. Cerebrospinal fluid (CSF) study.

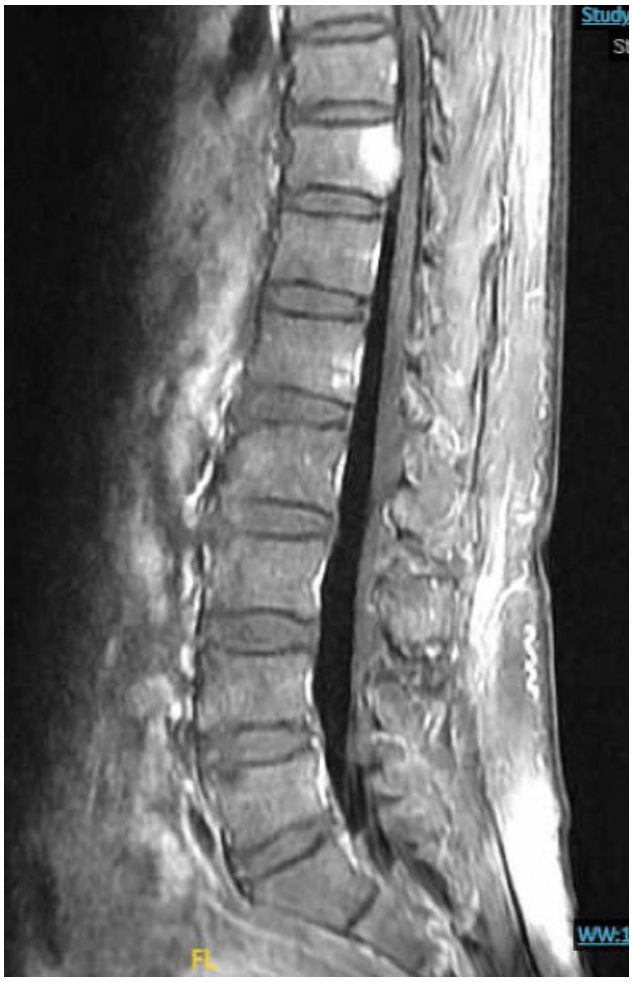

Figure 2. MRI spine showing hyperintensity signals in T1, T11, L1 concerning for metastases.

retroperitoneal lymphadenopathy measuring 2.6 cm and a 1.7 cm right adrenal lesion. Further metastases were found in the spine (T1, T11, L1) and lymphadenopathy in the right internal jugular chain and right submandibular triangle *(Fig. 2)*. The patient was then started on methotrexate and rituximab, and cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP).

DISCUSSION

Extranodal involvement is a frequently observed phenomenon in DLBCL, with predominant affliction sites typically encompassing the gastrointestinal tract, and the head and neck region. However, lacrimal sac tumours present a distinctive rarity within the spectrum of DLBCL, exhibiting uncommon clinical presentations[3]. Notably, lacrimal sac lymphomas manifest predominantly in the elderly, with an average age of onset of around 71 years. Furthermore, a discernible gender predilection is evident, with a higher incidence observed among women. This specific demographic pattern characterises lacrimal sac lymphomas as an atypical subset within the broader spectrum of DLBCL. The clinical presentation of lacrimal sac large B-cell lymphoma is often characterised by non-specific symptoms, posing a considerable diagnostic challenge. Initial misdiagnoses commonly involve confusion with conditions such as dacryocystitis or dacryostenosis, while alternative misidentifications such as mucocele have also been reported[4]. A prompt diagnosis is achieved in less than 15% of cases due to the elusive nature of the presenting symptoms. The diagnostic approach for lacrimal sac large B-cell lymphoma involves a comprehensive strategy, beginning with a biopsy incorporating flow cytometry, molecular studies and immunophenotyping. Subsequent categorisation and staging of the tumour are accomplished through the utilisation of advanced imaging modalities such as CT and MRI, as demonstrated in the assessment of our presented patient.

Meunier et al.'s study conducted a comprehensive analysis, revealing that factors such as age over 59 years, elevated lactate dehydrogenase (LDH) levels, stage IV disease, high-grade histological subgroup, and the presence of B-symptoms and bone marrow metastasis exerted a negative influence on overall survival within the general population[5]. In our reported case, the patient exhibited several adverse prognostic indicators, including an age over 59 years, elevated LDH levels at 318 and a diagnosis of stage IV disease. Notably, our patient had the absence of B-symptoms at the time of presentation. Furthermore, it is pertinent to acknowledge that most lacrimal sac lymphomas belong to the B-cell type, which typically responds favourably to radiotherapy and chemotherapy. Consequently, the prognosis for such cases is generally optimistic, emphasising the importance of subtype-specific considerations in predicting outcomes and guiding therapeutic decisions.

In the management of primary lacrimal sac lymphoma, chemotherapy and/or radiotherapy constitute the primary therapeutic modalities. CHOP regimens, comprising cyclophosphamide, doxorubicin, vincristine, and prednisone – with adjunct immunotherapy such as rituximab targeting the CD20 antigen – are commonly used, particularly in cases of DLBCLs. However, in the presented case, the therapeutic approach was augmented with the inclusion of methotrexate alongside the R-CHOP regimen. This modification was prompted by the identification of a pituitary gland tumour, raising concerns about the potential development of secondary central nervous system lymphoma. This tailored therapeutic strategy underscores the necessity of individualised treatment plans based on specific clinical presentations and associated findings. It has been found that patients diagnosed with systemic DLBCL have a worse

prognosis than those diagnosed with ocular adnexal diffuse large B-cell lymphoma[1].

In conclusion, primary lacrimal sac large B-cell lymphomas represent a rare and diagnostically challenging entity characterised by atypical presentations. The delayed diagnosis often stems from the resemblance of its clinical manifestations to more benign conditions such as dacryocystitis, dacryostenosis or mucocele. Given the rarity of this lymphoma and the potential for misdiagnosis, it is imperative for clinicians to maintain a high index of suspicion and include this malignancy in the differential diagnosis when evaluating patients with related ocular or periocular conditions. Timely recognition and accurate diagnosis are pivotal for instituting prompt therapeutic interventions and improving patient outcomes.

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