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Bilateral ocular panadnexal mass as initial presentation of systemic blastoid variant of mantle-cell lymphoma

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ABSTRACT

A 66-year-old man developed a slowly enlarging, bilateral, painless, periorbital, and orbital swelling with ptosis, nonaxial proptosis, chemosis, exposure keratopathy, and decreased vision in both eyes. He had fever, night sweats, and weight loss (B-symptoms), along with lymphadenopathy and elevated serum lactate dehydrogenase, with no prior history of lymphoma. A transpalpebral incisional biopsy revealed a rare case of mantle-cell lymphoma of blastoid variant, stage IVB. The main immunophenotype characteristics were cyclin D1+, CD5+, CD10−, CD23−, Bcl-6−/+, and a high (up to 80%) Ki-67 proliferation index. Following an excellent response to the immune-chemotherapy treatment plan, all ocular adnexal lymphoma manifestations disappeared completely; however, 13 months after the initial presentation, there was a recurrence of the disease with rapid worsening and death. The blastoid variant of mantle cell lymphoma, a rare subtype of mantle-cell lymphoma, is a highly aggressive neoplasm, ultimately having a fatal outcome. As the initial manifestation of the disease, ocular adnexal region blastoid variant of mantle-cell lymphoma is an exceptional event, with only one previous case reported.

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1. Introduction

Lymphoproliferative lesions of the ocular adnexa represent 1%–2% of all lymphomas and approximately 8% of all extranodal lymphomas.[3,5,10–12,15] Lymphomatous involvement of the ocular adnexal region (OAR) may be as follows: (1) primary (extranodal) OAR lymphoma, (2) secondary OAR lymphoma (nodal, extranodal, or systemic; lymphoma in the OAR with known preexisting extraocular disease), and (3) OAR lymphoma as first presentation site of previously unknown or undiagnosed systemic (nodal or extranodal) disease. Lymphoma is the most common orbital malignancy and the second most common conjunctival malignancy.[3,5,10–12,15,17] Most OAR lymphomas are localized at presentation—primary extranodal—or involvement of the OAR is a presenting site of systemic lymphoma.[3,5,10–12,15,17]

Mantle-cell lymphoma (MCL) rarely affects the OAR, comprising 1%–7% of all OAR lymphomas. The most common location for OAR MCL is the orbit with or without synchronous lacrimal gland or conjunctival or eyelid involvement.[3,5,6,9–17] The blastic or blastoid cytological variant of mantle-cell lymphoma (bMCL) is a rare, but distinct, entity that is considered to be a highly aggressive and ultimately fatal subtype of B cell non-Hodgkin lymphoma, with a homogeneous population of cells displaying lymphoblastic morphology.[2,4] Here, we describe a case of biopsy and cytogenetically proven, bilateral, synchronous, slightly asymmetrical, massive, ocular pan-adnexal bMCL as an initial presentation of the disease, the second reported case of OAR bMCL in the literature.

2. Case report

2.1. *Clinical findings*

A 66-year-old man presented in October, 2013, with a 9-month history of slowly enlarging, bilateral (synchronous and relatively symmetrical, but with the right side more prominent), painless, periorbital, and orbital swelling/mass. The patient also presented with mechanical ptosis, proptosis, and downward dystopia (nonaxial proptosis) more severe on his right side, chemosis that was severe on the right side, with exudation and conjunctival keratinization, and lagophthalmos with exposure keratopathy that was also more severe in the right eye (Fig. 1A). There was almost complete loss of vision in his right eye and decreased visual acuity in his left eye. Symptoms also included a feeling of resistance, irritation, and weight loss of 15 kg.

On initial examination, he had light perception without accurate projection in the right eye and 20/60 acuity in his left eye, with no relative afferent pupillary defect. His intraocular pressures were 30 mm Hg right eye and 32 mm Hg left eye. Exposure keratopathy and chemosis, with sticky hard exudate and keratinization, were more pronounced on the right side. Eye movements were restricted. The posterior segments of both eyes were unremarkable.

A multislice computerized tomography scan (Fig. 1B) showed a bilateral, homogeneous, expansile, enhancing, well-demarcated, solid, periorbital and orbital mass of soft-tissue density, mainly in the superotemporal quadrant, with involvement of the lacrimal gland, superior and lateral rectus and superior oblique muscles, optic nerve, and lacrimal sac. There was no CNS or sinonasal involvement.

Laboratory investigations showed elevated serum lactate dehydrogenase (612 U/L, normal 220–460), low hemoglobin (115 g/L, normal 138–175), low serum calcium (2.00 mmol/L, normal 2.15–2.65), high white cell count (22.17 $\times$ 10^9/L, normal 3.4–9.7), low neutrophil count (34.9 $\times$ 10^9/L, normal 44–72), high lymphocyte count (55.6 $\times$ 10^9/L, normal 20–46), low platelet count (0.003/L, normal 0.158–0.425), low red blood cell count (4.01 $\times$ 10^9/L, normal 4.34–5.72), and low hematocrit (0.349%, normal 0.415–0.530).

The patient's past medical history was significant only for low-grade hypothyroidism without substitution therapy. He had worked for 35 years at a paint and varnish factory, and his father died of bone cancer at the age of 70 years. There was no history of Sjögren syndrome, Mikulicz syndrome, IgG4-related disease, Graves disease, systemic lupus erythematosus, bullous pemphigoid, or granulomatosis with polyangiitis. The serologies for human immunodeficiency virus and hepatitis B and C viruses were all negative. There was no prior history of lymphoma. No pathologic skin lesions were present. At presentation, enlarged cervical, axillary, and inguinal lymph glands were found. The spleen was nonpalpable. A chest X ray and abdominal and pelvic ultrasonography were within normal limits.

The clinical diagnosis was bilateral ocular adnexal lesion suspected of being a lymphoproliferative malignancy, with an International Prognostic Index 5 (high intermediate risk) and a Performance Score (Eastern Cooperative Oncology Group) >1. A transcutaneous, transpalpebral incisional surgical biopsy of the periorbital part of the tumor on both sides was performed under local anesthesia, and the specimens were sent for histopathological evaluation.

2.2. *Histopathologic and immunohistochemical findings*

After fixation in 10% buffered formalin, the 2 biopsy specimens were whitish-yellowish pieces of tissue, measuring 1.5 cm $\times$ 1.1 cm $\times$ 0.5 cm and 1.7 cm $\times$ 1.1 cm $\times$ 0.7 cm, respectively. Microscopy examination (Fig. 2A) revealed a relatively uniform, hypercellular, diffuse, and slightly nodular, malignant lymphoid proliferation of intermediate-sized cells. The cells showed angulated, cleaved, irregular or round nuclear contours, finely dispersed nuclear chromatin, small nucleoli, and a narrow rim of cytoplasm. The cells were limited to the zone surrounding the residual germinal centers that could still be recognized. There was no necrosis. Hyalinized small-sized blood vessels were also present.

Immunohistochemical staining (Fig. 2B-D) demonstrated diffuse and strong positivity for cyclin D1, CD5, CD20, CD44, CD79a, MUM-1, and Bcl-2, with scattered focal moderate positivity for Bcl-6, p53 (<20% of cells), IgM, and lambda light chain > kappa light chain, and a very high percentage of nuclear staining for Ki-67 (60%–80%). The tumor cells were negative for CD3, CD10, CD15, CD23, CD30, CD56, CD68, CD138, IgG, and TdT. Among the tumor cells were a moderate number of small T cells (CD3+) and histiocytes (CD68+). A relatively