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Brief Report

Waldenstrom macroglobulinemia involving the superior rectus muscle

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ABSTRACT

Purpose: We present the first reported case of Waldenstrom macroglobulinemia in the right superior rectus causing diplopia.

Observations: A 72-year-old man with a 6-month history of untreated asymptomatic Waldenstrom macroglobulinemia presented with 2 years of diagonal binocular diplopia that was previously thought to be due to ocular myasthenia gravis. Examination showed mild right proptosis and right hypotropia, and MRI revealed a focal lesion of the right superior rectus muscle. Orbital biopsy was performed, and histopathology showed lymphoplasmacytic infiltration among the skeletal muscle fibers of the rectus muscle. Immunostaining confirmed a B-cell preponderance, along with more extensive staining for IgM than IgG, and in situ hybridization confirmed lambda restriction. These findings corresponded with those of his previous bone marrow biopsy, confirming Waldenstrom macroglobulinemia as the etiology for the extraocular muscle mass.

Conclusions and Importance: Lymphoma of an extraocular muscle is a rare manifestation of orbital lymphoma, and the tumors are usually mucosa-associated lymphoid tissue (MALT) lymphomas (i.e. extranodal marginal zone lymphomas). There are 4 previous reports of lymphoplasmacytic lymphoma of an extraocular muscle; however this is the first reported case of such a lesion in a patient with concurrent Waldenstrom macroglobulinemia at the time of diagnosis.

1. Introduction

Waldenstrom macroglobulinemia is a lymphoplasmacytic B-cell lymphoma with elevated monoclonal immunoglobulin M (IgM) protein levels and lymphoplasmacytic infiltration of the bone marrow. Patients typically present with fatigue due to anemia, though 25% of patients are asymptomatic. Common sites of involvement include the spleen, liver, and lymph nodes.[1] There have been 4 cases reported of lymphoplasmacytic lymphoma localizing to an extraocular muscle; however these patients were not noted to have Waldenstrom macroglobulinemia on systemic work-up.[2–4] This is the first reported case of extraocular muscle involvement in a case of concurrent Waldenstrom macroglobulinemia.

2. Case report

A 72-year-old man with history of asymptomatic Waldenstrom macroglobulinemia diagnosed 6 months prior and a distant history of follicular thyroid cancer status post right lobectomy and radioactive iodine therapy (over 30 years prior) presented with 2 years of intermittent binocular diagonal diplopia previously thought to be due to ocular myasthenia gravis. Diplopia was not typically present when he first woke up and was worse in the evening. Previous work-up showed negative acetylcholine receptor and anti-MUSK antibodies. Ophthalmic examination showed mild right proptosis, a 12 prism-diopter right hypotropia, and a small-angle esotropia in primary gaze (Fig. 1).

MRI of the orbits (Fig. 2) revealed a focal mass of the superior rectus muscle with irregular contours. Given his history of thyroid cancer, thymogen scan was ordered, which showed no evidence of thyroid tissue.

Orbital biopsy of the superior rectus muscle lesion was performed, and histopathology (Fig. 3) exhibited pockets of generally mature-appearing lymphocytes and plasma cells infiltrating in between the skeletal muscle fibers (parts A-C). Dutcher bodies were identified within some of the lymphocyte nuclei (part B). Immunostaining confirmed a B-cell preponderance (parts D and E), along with more extensive staining for IgM (part F) than IgG (not shown). Kappa and lambda in situ hybridization (parts G and H) confirmed lambda restriction, with a lambda: kappa ratio of at least 2.5 to 1. The patient's bone marrow biopsy from 6 months prior had similarly exhibited a low-grade B-cell lymphoproliferative process with lambda restriction on flow cytometry, and serum protein electrophoresis had demonstrated a monoclonal

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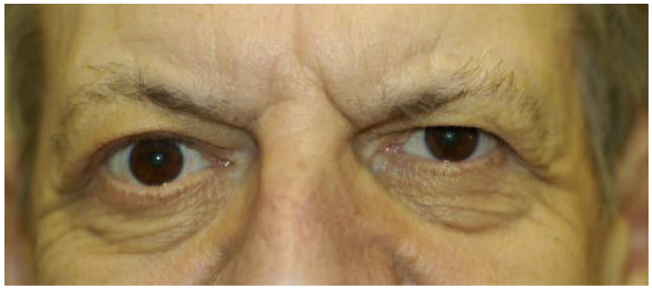

Fig. 1. External photograph showing right eye proptosis and hypotropia.

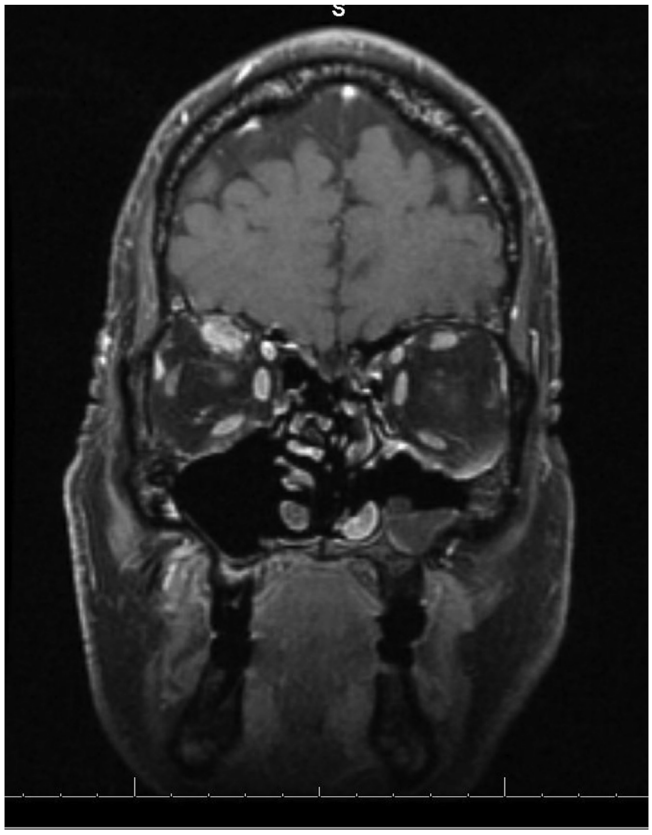

Fig. 2. Magnetic resonance imaging of the orbit (3 mm), coronal view, T1 fat saturated, post gadolinium, demonstrating enlarged, homogenously enhancing right superior rectus muscle with irregular border.

spike of IgM paraprotein; hence the superior rectus muscle lesion could be attributed with confidence to Waldenstrom macroglobulinemia.

3. Discussion

Orbital lymphoma comprises only 1% of all non-Hodgkin lymphoma, but it is the most common malignant orbital tumor in adults.[5] The majority of these masses are mucosa associated lymphoid tissue (MALT) lymphomas, i.e. extranodal marginal zone lymphomas (57%) and follicular lymphoma (19%), with diffuse large B-cell, small lymphocytic, mantle cell, and lymphoplasmacytic lymphomas appearing less often.[6] An isolated mass of an extraocular muscle is a rare presentation of orbital lymphoma, reported in an estimated 0.17% of orbital lymphomas, and can be misdiagnosed as thyroid eye disease or idiopathic orbital inflammatory syndrome.[2,4,7,8] Even more rare is a lymphoplasmacytic lymphoma of an extraocular muscle, as seen in our patient with Waldenstrom macroglobulinemia.

There is no standard therapy for Waldenstrom macroglobulinemia. Symptomatic patients are typically treated with rituximab, usually in combination with cyclophosphamide, bortezomib, or bendamustine with or without dexamethasone.[9] The most common symptom is fatigue due to anemia, though patients also present with peripheral neuropathy, hyperviscosity syndrome, night sweats, organomegaly, amyloidosis, and immune complex vasculitis. As the treatments are noncurative, there is no benefit to treating asymptomatic patients.[10] Though our patient presented with symptomatic diplopia, this resolved following debulking of the tumor during orbital biopsy. While his oncologist felt that observation was a reasonable option, he did recommend treatment with rituximab given the rectus muscle mass and an extremely elevated level of IgM. The patient declined treatment and to the best of our knowledge has had no recurrence of symptoms.

Patient consent

Consent to publish the case report was obtained. This report does not contain any personal information that could lead to the identification of the patient. Retrospective review of this case was done in accordance with the Declaration of Helsinki and the University of California Davis Health Institutional Review Board exempts single case reports from review.

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Conflicts of interest

The authors have no financial disclosures. (Please see uploaded PDF file for signatures.)

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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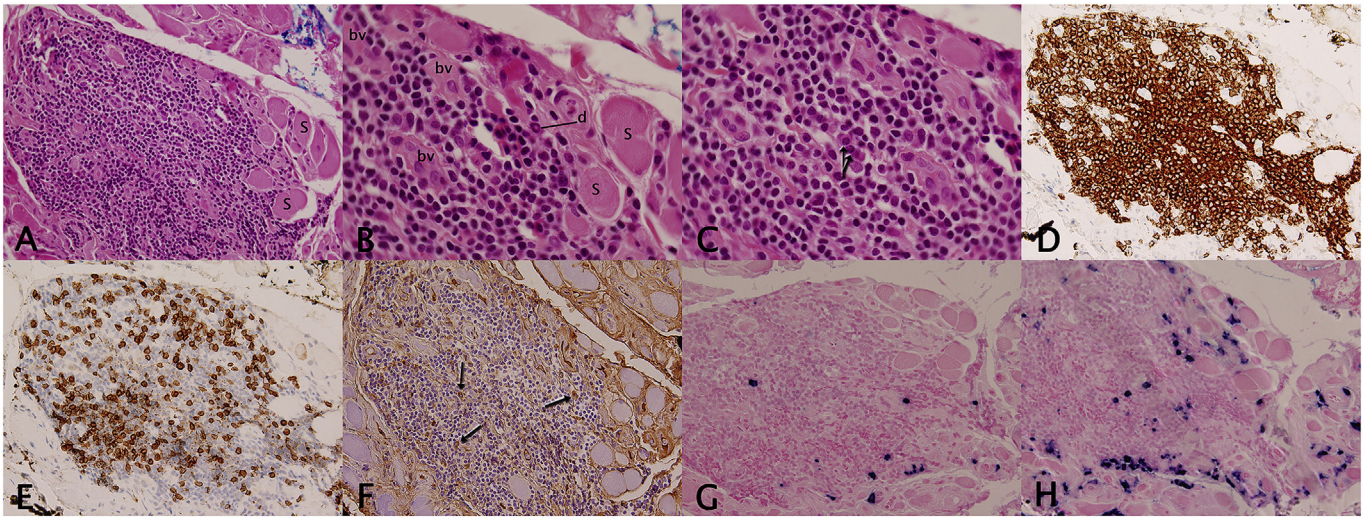

Fig. 3. Histopathology of extraocular muscle biopsy. A) A lymphoplasmacytic infiltrate is seen among the skeletal muscle fibers (s) (H&E stain, original magnification, ×400). B) At higher magnification, it is evident that the majority of the cellular infiltrate consists of mature-appearing lymphocytes. However, Dutcher bodies (d) are appreciated within some of the lymphocyte nuclei. Several blood vessels (bv) are also present in the field (H&E stain, original magnification, ×1000). C) Some plasma cells (arrows) are also seen at higher magnification (H&E stain, original magnification, ×1000). D and E) Immunostaining for the B-cell marker CD20 (D) and for the T-cell marker CD3 (E) reveal an obvious B-cell preponderance (original magnification, ×400). F) Immunostaining for IgM reveals scattered positive cells, e.g., cells designated by arrows (original magnification, ×400). G and H) In situ hybridization for kappa (G) and lambda (H) light chains reveals an obvious lambda preponderance. The lambda: kappa ratio was estimated at about 2.5 to 1 for the entire specimen, but is even greater (at more than 5 to 1) in the field shown here (original magnification, ×400).

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