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CASE REPORT

Orbital MALT Lymphoma in a Patient with Graves' Ophthalmopathy: A Unique Observation

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A 57-year-old woman with a six-year history of Graves' Disease with ophthalmopathy developed unilateral periorbital swelling. CT scan suggested a lacrimal mass. Biopsy revealed MALT lymphoma. Evaluation for other sites of lymphoma revealed no other evidence of disease. She was treated with radiation therapy only with complete disappearance of disease. This is the first known case of MALT lymphoma arising in Graves' ophthalmopathy.

Keywords Graves' disease; MALT lymphoma; Graves' ophthalmopathy

INTRODUCTION

Primary lymphomas of the thyroid occur most commonly in patients with prior long-standing autoimmune (Hashimoto's) thyroiditis. A background of chronic lymphocytic infiltration in these cases precedes the emergence of a malignant clone. The lymphomas that develop in this context are often MALT (mucosa-associated lymphoid tissue) lymphomas[1] and may resemble the reactive infiltration from which they presumably evolved. Graves' disease is part of the spectrum of autoimmune thyroiditis, and Graves' ophthalmopathy involves lymphocytic infiltration of orbital tissue, including extraocular muscles and orbital fat. With treatment of the hyperthyroidism associated with Graves' the ophthalmopathy can improve, regress, or get worse. There has not been a known case, however, of the lymphocytic infiltration of Graves' ophthalmopathy evolving into lymphoma. A review of the literature revealed two cases of orbital lymphoma associated with hyperthyroidism,[2,3] but neither had the characteristic MALT histology. This is the first known case of primary orbital MALT lymphoma developing in a patient with Graves' ophthalmopathy.

CASE REPORT

A 50-year-old woman presented with classic Graves' disease: a diffuse toxic goiter, exophthalmos, and periorbital edema. She was treated initially with beta blockers, propylthiouracil, and, after being rendered euthyroid clinically and biochemically, 17 mCi of radioiodine. Her goiter shrank and her exophthalmos regressed but her peri-orbital edema never completely resolved.

Four years later she began developing unilateral swelling of the left eye (Figure 1). Over the next two years, this progressed to the point where she sought repeat consultation from her ophthalmologist (R.W.N.). A computerized-tomography (CT) scan showed infiltration of her lacrimal gland with

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FIG. 1. Appearance of eyes before treatment.

a mass (Figure 2). Biopsy revealed Marginal Zone ("MALT") non-Hodgkin's lymphoma (Figure 3A). Immunohistochemistry showed that CD-20 was positive (Figure 3B); CD-5, 23, and 43 were negative. Slides and tissue blocks were reviewed by an outside consultant (Amy Chadburn, M.D., New York-Presbyterian Hospital, Weill Cornell Medical Center) who also found the tumor to be BCL-2 positive and concurred with the diagnosis.

Further evaluation was undertaken. History revealed no constitutional symptoms; physical examination was otherwise negative with regard to lymphoma. CT scans of the chest, abdomen, and pelvis were negative; bone marrow biopsy was normal. She was seen by Radiation Oncology (J.R.) and a complex treatment plan was developed to encompass all known disease, but spare as much of the vital structures of the eye as possible (Figure 4). She was treated with external-beam radiation utilizing a 20 MeV electron beam via a custom cerrobend cutout with a final dose of 3,600 rads in 20 fractions to the tumor volume. Calculated dose to the lens was 350 rads. Percent depth ionization measurements were performed to assess adequacy of tumor volume dose. She has had prompt and total regression of the mass on physical examination. Follow-up CT scan showed total regression of the infiltrative process.

DISCUSSION

This is the first reported case to our knowledge of Graves' ophthalmopathy evolving or transforming into a MALT lymphoma. A previous case of orbital lymphoma associated with hyperthyroidism was that of a patient with preexisting Graves' disease who developed nodular histiocytic lymphoma.[2] That case, however, manifested generalized lymphoma and, thus, could not be considered to have a primary lymphoma of the orbit. Another case[3] involved a patient with a toxic solitary thyroid nodule who had bilateral orbital lymphoma. That patient did not have Graves' disease, nor was there any evidence of thyroid ophthalmopathy prior to the development of the lymphoma. Furthermore, immunohistochemistry was not performed as part of the evaluation of either case. The relation of MALT to the subsequent development of lymphoma is a subject of contemporary interest.[4,5] The interrelationship of autoimmune diseases such as systemic lupus erythematosus and Sjögren's syndrome and the development of B-cell lymphoma also has been well documented in the recent past.[6] This case is apparently the first reported of the development of MALT lymphoma in the periorbital region of a patient with Graves' ophthalmopathy, and, thus, is the first illustration of lymphoma in periorbital tissue associated with autoimmune thyroid disease. It, thus, extends the definition of the interrelationship of MALT to the development of lymphoma and the relation of autoimmune disease to the development of subsequent B-cell neoplasms.

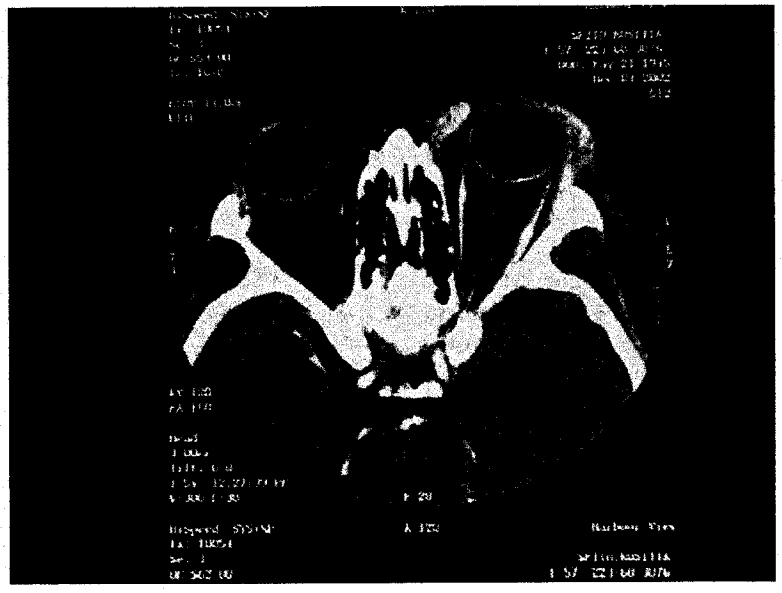

FIG. 2. CT scan showing periorbital swelling on left.

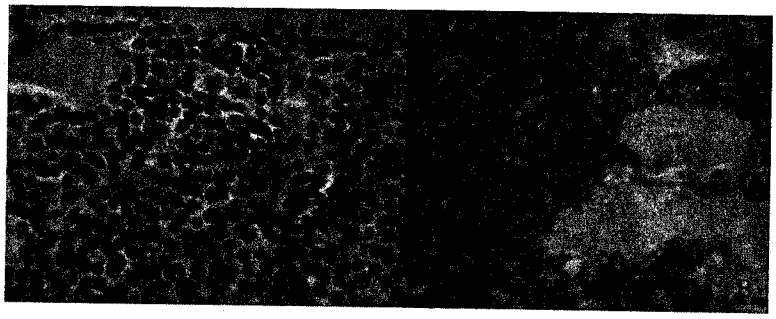

FIG. 3. MALT lymphoma (A), Positive immunohistochemistry for CD-20 (B).

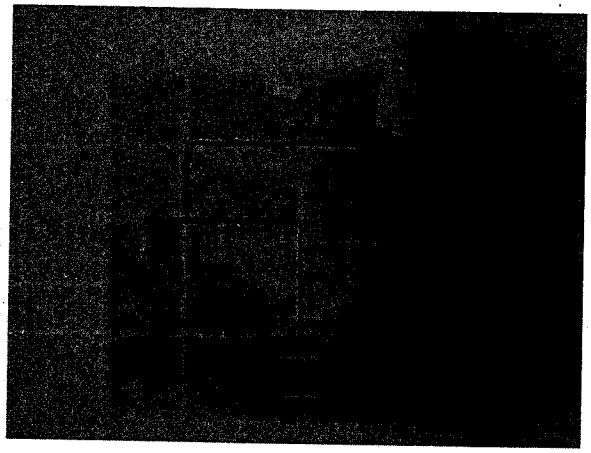

FIG. 4. Radiation Treatment Planning.

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