SURVEY OF OPHTHALMOLOGY VOLUME 51 • NUMBER 1 • JANUARY–FEBRUARY 2006

ELSEVIER

CLINICAL PATHOLOGIC REVIEWS

STEFAN SEREGARD AND MILTON BONIUK, EDITORS

Primary Testicular and Intraocular Lymphomas: Two Case Reports and a Review of the Literature

Dana J. Wallace, BS,[1] Chandra R. Altemare, MD,[1] De Fen Shen, PhD,[1] Marc D. deSmet,[2] Ronald R. Buggage, MD,[1] Robert B. Nussenblatt, MD,[1] and Chi-Chao Chan, MD[1]

[1]National Eye Institute, NEI, Bethesda, Maryland, USA; and [2]Academic Center University of Amsterdam, the Netherlands

Abstract. Testicular lymphoma is a rare neoplasm of the testis that is most commonly seen in older patients. It metastasizes preferentially to extranodal sites, including the skin, central nervous system, Waldeyer ring, contralateral testis, and lung. Two case reports of patients with a history of testicular lymphoma who developed involvement of the vitreous and retina are presented. These are interesting cases as the testis, central nervous system, and eye are all immune privileged organs, which may account for occurrence of disease in these sites. Histopathologic examination of diagnostic vitrectomy specimens from both cases showed atypical lymphoid cells with immunoglobulin heavy chain (IgH) gene rearrangements, consistent with the diagnosis of intraocular B-cell lymphoma. The results of a literature review of all reports of ocular involvement with testicular lymphoma are discussed. Patients with testicular lymphoma are at risk for relapse, particularly in the central nervous system. Clinicians should be suspicious for intraocular lymphoma in patients with a history of testicular lymphoma who present with vitritis or retinal lesions. (**Surv Ophthalmol 51**:41–50, 2006. © 2006 Elsevier Inc. All rights reserved.)

Key words. immune privileged organ • immunohistochemistry • intraocular lymphoma • microdissection • PCR • retina • testicular lymphoma • vitreous

Introduction

Testicular lymphoma is a rare disease entity that accounts for only 1–9% of all testicular neoplasms and 1% of all non-Hodgkin lymphomas. Although it is the most common testicular tumor in men over the age of 60, testicular lymphoma is rarely seen in younger males (< 30 years).[31] Testicular lymphoma has a marked tendency to metastasize, particularly to extranodal sites, including the skin, central nervous system (CNS), Waldeyer ring, contralateral testis, and lung. Clinical reports of ocular involvement in testicular lymphoma are rare.[24] We report two patients with testicular lymphoma who developed ocular involvement in the vitreous and retina, clinically mimicking primary intraocular lymphoma (PIOL). Based on a review of the literature, these cases were compared with all known reports of ocular involvement with testicular lymphoma.

Case Reports

CASE 1

A 75-year-old white man with a previous history of testicular lymphoma presented with a chief com-

0039-6257/06/$–see front matter
doi:10.1016/j.survophthal.2005.11.002

plaint of decreased vision OU in March 1998. Ocular examination revealed bilateral vitritis that was greater in the right eye. Systemic evaluation included normal blood work and a bone marrow biopsy that revealed monoclonal gammopathy of undetermined significance. Imaging studies of the brain, chest, and abdomen were all negative. Cytologic examination of a diagnostic vitrectomy specimen from the right eye was negative for malignancy in May 1999. The patient had a past medical history significant for coronary artery disease status post myocardial infarctions in 1968 and 1994, congestive heart failure, chronic obstructive pulmonary disease, and Parkinson disease. In March 1985 he was diagnosed with prostate carcinoma that was successfully treated with resection and pelvic radiation therapy. He was diagnosed with right testicular lymphoma that was treated with an orchiectomy in July 1992 followed by prophylactic orchiectomy of the left testis in August 1992 and an unknown regimen of chemotherapy. His medications included simvastatin, metoprolol, cimetidine, carbidopa/levidopa, amitriptyline, aspirin, diclofenac, vitamin E, ipratropium, albuterol, beclomethasone, and nitroglycerine as needed.

Ocular examination in March 2000 revealed a visual acuity of 20/50 OD and 20/80 OS with intraocular pressures of 16.5 mm Hg OD and 14 mm Hg OS and no afferent pupillary defect. He scored 15/16 OD and 0/16 OS on the Ishihara color plates. Anterior segment examination was normal except for the presence of 2+ nuclear sclerosis OU and a fine dusting of cells on the inferior aspect of the posterior capsule OD. Posterior segment examination of the right eye revealed trace vitreous cells without haze and no apparent retinal lesions. The optic nerve cup-to-disk ratio was 0.4. Examination of the posterior segment of the left eye revealed marked vitritis with 3+ vitreous cells and 2+ haze. Mottling of the retinal pigment epithelium and subretinal infiltrates in the posterior pole were noted in the left eye although the vitritis obscured the view of the macula (Fig. 1A). The cup-to-disk ratio of the optic nerve was 0.4.

Fluorescein angiogram of the right eye revealed no cystoid macular edema. Angiography of the left eye provided a limited view. A repeat angiogram post vitrectomy in the left eye in late March 2000, however, revealed multiple blocking defects typical of those described in patients with PIOL (Fig. 1B).[6,64] Imaging studies included an MRI of the brain which revealed periventricular white matter changes consistent with small vessel ischemia, but there was no evidence of tumor. Computerized tomography of the chest, abdomen, and pelvis was unremarkable with no evidence of tumor. Examination of the cerebrospinal fluid (CSF) revealed the absence of malignant cells and no erythrocytes, although there were 25 white blood cells present, 95% of which were lymphocytes. Cytokine analysis of the CSF revealed an IL-6 level $<$ 7.8 pg/ml (normal IL-6 level $<$ 15.6 pg/ml) and an IL-10 = 15.4 pg/ml (normal IL-10 level $<$ 11.7 pg/ml) with an IL-10: IL-6 ratio of 1.97.

Histopathologic examination of the diagnostic pars plana vitrectomy specimen from the left eye revealed malignant large B lymphoid cells. Consequently, the patient returned to his referring ophthalmologist and oncologist for treatment.

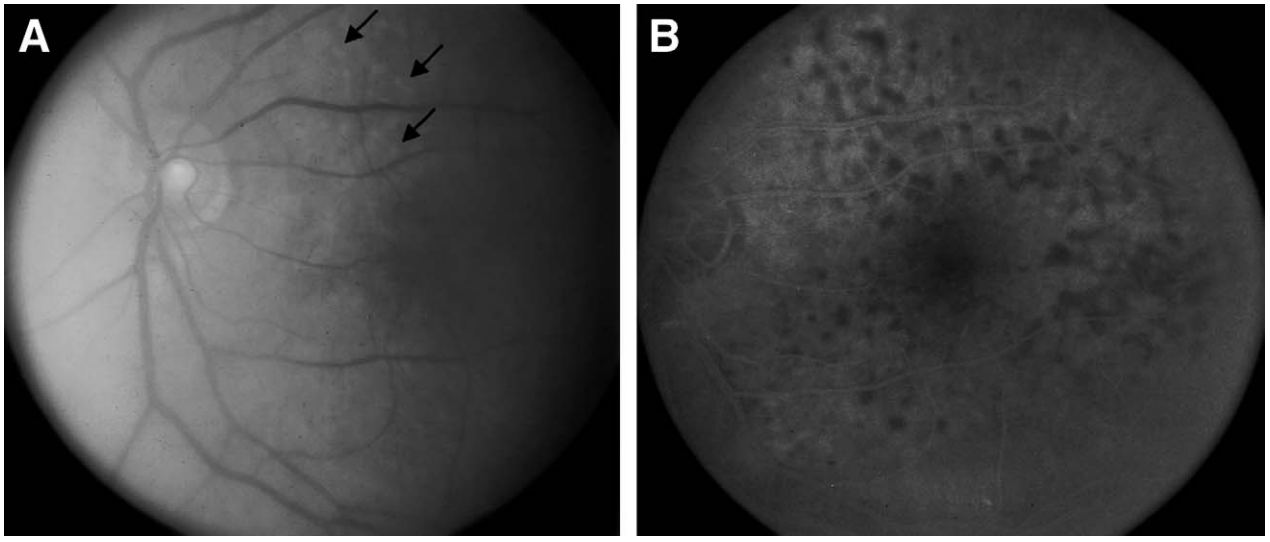

Fig. 1. *A:* Fundus photograph from case 1 showing vitreous haze and subretinal infiltrates (arrows). *B:* Fluorescein angiogram from Case 1 showing multiple small hypofluorescent lesions.