The case of an 82-year-old man who developed intraocular extension from mycosis fungoides, a cutaneous T-cell lymphoma, is presented. The patient died soon after intraocular involvement occurred. Immunohistochemistry of a skin biopsy, taken early in the course of the disease, disclosed a predominance of T cells with a helper/inducer phenotype (CD4+). However, an intraocular infiltrate obtained 7 years later contained mostly T cells with a suppressor/cytotoxic phenotype (CD8+). The occurrence of ocular invasion, the change in immunophenotype, and the predominant proliferation of CD8+ lymphocytes may have been related to the poor outcome in this patient.

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Mycosis fungoides is a malignant T-cell lymphoma characterized by infiltration of the skin by neoplastic T cells.1 Middle-aged individuals, predominantly males, are most frequently affected. In its early stages, the disease is manifest by erythematous, eczematous, flat skin patches, often involving the trunk, buttocks, and proximal thighs. These lesions often simulate, even at the histological level, other more common dermatological conditions, such as psoriasis or eczema, leading to delayed diagnosis and treatment.1-4 As the disease advances, skin lesions tend to increase in thickness, giving rise to plaques and tumors. In end stages, systemic involvement may ensue, with lymph nodes, liver, bone marrow, and lungs the most commonly affected sites.1

Microscopically, mycosis fungoides is characterized by the presence of infiltrates containing atypical lymphocytes in the superficial dermis and epidermis (Darier-Pautrier microabscesses).1 Abnormal lymphocytes with a “cerebriform” nucleus, known as Lutzner cells, are often present. In most cases, proliferating lymphocytes are T cells with a predominant helper/inducer phenotype (CD3+, CD4+, and CD8−).5 However, in some instances, T-suppressor/cytotoxic (CD3+, CD4−, and CD8+) or aberrant T-cell phenotypes have been described.6 It appears that these latter phenotypes may be associated with a more aggressive clinical course.6-8 Furthermore, a change in the immunophenotype over time has been observed in some patients, and such change also seems to be associated with more aggressive clinical behavior.6 Large-cell transformation may also occur, resulting in a morphologic structure and phenotype that are identical to those of anaplastic large-cell lymphoma.

Patients with mycosis fungoides can develop ocular involvement.2-4,9 Eyelid abnormalities appear to be the most frequent finding.2,4 Conjunctival, caruncular, and orbital tumors; corneal epithelial defects; and interstitial and ulcerative keratitis also have been observed.2,9 Intraocular extension of mycosis fungoides is rare.2-4,10 Few case reports in the literature have described the clinical and histopathological features of intraocular mycosis fungoides. In these cases, no detailed immunophenotypic characterization of the neoplastic T cells was available.

The purpose of this report is to present the clinical, histopathological, and immunohistochemical findings in a patient with mycosis fungoides and vitreous invasion. The vitreous infiltrate in this patient showed a distinct immunophenotype that was different from that observed in the skin.

In November 1992, a 75-year-old man presented with widespread eczematous patches of the skin, which were successfully treated with topical corticosteroids. In subse-
quent months, the disease became unresponsive to topical treatment, and in August 1994, a skin biopsy confirmed the diagnosis of mycosis fungoides. Malignant T cells infiltrating the epidermis and upper dermis were found. The infiltrate consisted predominantly of CD3+ and CD4+ cells, with a CD4/CD8 ratio of approximately 5:1 (an inflammatory infiltrate generally shows a 2-3:1 ratio). A few cells (<10%) expressing the B-cell marker CD79A were also present. The natural killer cell markers CD56 and CD57 were absent. Treatment with psoralen and UV light (PUVA) and radiotherapy was started, with an excellent response. During the following years, episodes of reactivation occurred but were controlled, in each instance, with chemotherapy and/or radiotherapy.

In May 1999, the patient complained of decreased vision in his left eye. Visual acuity was 20/30 OD and 20/200 OS. Slitlamp examination disclosed no abnormalities. On fundus examination, the right eye was normal (Figure 1A). Dense vitreous opacities and diffuse-dot retinal hemorrhages were seen in the left eye (Figure 1B). Intraocular extension of mycosis fungoides was suspected, and diagnostic pars plana vitrectomy was undertaken. Although affected subcutaneous nodules were found, no other evidence of systemic involvement was noted. Computed tomography of the central nervous system disclosed no abnormalities, with peripheral blood films showing lymphopenia. Bone marrow trephine was not performed.

The vitreous biopsy was fixed in 10% neutral buffered formalin, centrifuged into a cell block suspended in agar, and embedded in paraffin. Histopathological evaluation of the sample disclosed neoplastic lymphocytic cells with “cerebriform” nuclei (Figure 2A and B), consistent with the diagnosis of intravitreal involvement of T-cell lymphoma secondary to mycosis fungoides. Immunohistochemistry revealed CD3+ neoplastic cells but, in contrast to the original skin tumor, showed a CD4/CD8 ratio of 1:4 (Figure 3A and B, and Figure 4A and B). Moreover, many of the intravitreal neoplastic cells appeared to co-express CD3 and CD79A, since approximately 40% of the neoplastic cells also expressed CD79A. As in the earlier biopsy sample, CD56 and CD57 were negative. External beam radiotherapy was scheduled in an attempt to control the disease in the left eye, but the patient died soon thereafter. No autopsy was performed, with the cause of death presumed lymphoma.

COMMENT

As in previous cases of intraocular involvement,3,4,10 our patient developed ophthalmic manifestations several years after the diagnosis of mycosis fungoides and before any visible sign of systemic disease. Dense vitreous opacities were present on clinical examination, and infiltration of the vitreous with Lutzner cells was identified in the vitreous sample. Since the eyes were not available postmortem, it remains unknown whether the retinal hemorrhages detected clinically were related to in-

Figure 1. Fundus photograph. A, Right eye shows no abnormalities. B, Left eye shows haziness due to diffuse vitreous opacities.

Figure 2. Section of agar vitreous cell block showing neoplastic lymphocytes. A, Anisonucleosis is seen (hematoxylin-eosin, original magnification ×400). B, Many lymphocytes had “cerebriform” nuclei (hematoxylin-eosin, original magnification ×700).
Retinal invasion by neoplastic cells. In earlier cases, Leitch, Keltner, and Erny and their colleagues showed that atypical lymphocytes can infiltrate the vitreous, inner retina, optic nerve, choroid, and the space between the retinal pigment epithelium and Bruch’s membrane.

A predominance of a T-helper/inducer phenotype was found in our patient in a skin biopsy taken at the time of diagnosis of mycosis fungoides. In contrast, the intraocular infiltrate obtained 7 years later contained mostly T cells with a suppressor/cytotoxic phenotype, presumably representing a high-grade transformation. Moreover, many cells in the vitreous infiltrate appeared to co-express CD79A, whereas the earlier cutaneous infiltrate had lacked such cells. Cells with both CD3 and CD79A positivity may represent an aberrant phenotype. In this regard, it has been shown previously that aberrant phenotypes are found in more advanced stages of the disease.

Due to a scant vitreous sample, we were unable to test our patient for other markers, such as CD7 and CD2, that apparently are linked to a rapid progression of the disease. However, it is possible that the change in immunophenotype and the predominant proliferation of CD8 lymphocytes contributed to the poor outcome in this patient. Indeed, CD8 positivity and immunophenotypic shift in skin biopsies appears to be associated with a more aggressive disease.

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REFERENCES