Primary uveal B immunoblastic lymphoma in a patient with AIDS

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Abstract
A case of primary intraocular malignant lymphoma without cerebral involvement is reported in a 30-year-old man with acquired immunodeficiency syndrome. The study of the enucleation specimen showed a B immunoblastic lymphoma with a CD30 positive anaplastic large cell component. There was no involvement of the adnexal structures of the orbit. The patient subsequently completed non-surgical staging showing no extension of the tumour. The clinical course was rapidly fatal with dissemination to the pericardium and pleura.

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Among extranodal localisations of malignant lymphomas arising in acquired immunodeficiency syndrome (AIDS) patients, the eye is very rarely affected as a primary site. Most cases involve primitive cerebral or systemic malignant lymphomas, initially associated with an orbital localisation or secondary extension to the orbit. We describe the first localisation of a primitive and strictly intraocular lymphoma in an AIDS patient.

Case history
The patient, a 30-year-old Caucasian man, was an intravenous drug abuser and known to be seropositive for the human immunodeficiency virus (HIV) since April 1988. Treatment with azidothymidine was initiated in January 1989. One year later a tuberculosis was diagnosed by the study of an axillary lymph node. In April 1990 uveitis of the right eye developed followed by painful blindness. A computed tomography scan of the orbit showed an enhancing mass in the posterior and anterior chambers of the eye, displacing the lens posteriorly and invading the cornea (Fig 1). A haemorrhagic effusion was observed in the vitreous chamber. Enucleation was performed. Microscopic examination showed the intraocular tumour to be an immunoblastic malignant lymphoma. Computed tomographies of the brain, thorax, and abdomen were negative. Bone marrow aspirate and biopsy were normal. Cerebrospinal fluid examination revealed no cells suggestive of lymphoma. The chest x ray showed a fluid effusion in the pleura and pericardium. Numerous malignant immunoblasts were found in both effusion fluids. In spite of an evacuating puncture the patient died of acute respiratory distress. Autopsy was not permitted.

Methods
The eye was fixed in Bouin’s solution, embedded in paraffin, and stained with haematoxylin and cosin, Gordon Sweet's silver impregnation, and periodic acid Schiff. For immunohistochemical study, paraffin sections were analysed, using the ABC peroxidase method (Vectastain ABC Kit) with the following monoclonal antibodies: CD45, CD45 RO (UCHL 1), CD30 (Ber H2), anti-EMA, CD20 (L26), L26 (Dakopatts), CD15 (Immunotech), CD43 (MT1), MB2 (Biolyon), anti-A, G, M, immunoglobulin heavy chains, and kappa, lambda, light chains (Becton Dickinson).

Results
The eye measured 3 cm (anteriorposterior diameter) by 2.7 cm (transverse diameter). The anterior segment was deformed and occupied by a white, crumbly, and poorly limited mass measuring 1 cm, destroying the iris and displacing the lens posteriorly. A haemorrhagic effusion was present in the vitreous chamber. On histological study the tumour appeared to consist of a proliferation of large lymphomatous cells. Giemsa staining showed these cells to have a large basophilic cytoplasm and round pale nucleus with one or two large central nucleoli (Fig 2). Some had an eccentric nucleus. A number of the large cells had a moderately basophilic cytoplasm with an irregular nucleus, and were sometimes binucleated (Fig 2). Small lymphocytes with a peripheral cytoplasm and small chromatin were admixed with the large lymphomatous cells. The tumour infiltrated the anterior
and posterior chambers, the cornea, the ciliary muscle, and processes. Large necrotic areas were seen in the tumour infiltrate. The immunohistochemical study showed that all the tumour cells strongly expressed CD45 on the cell membrane (Fig 3). Ninety percent of the tumour cells showed intracytoplasmic staining and juxta-nuclear reinforcement with the MB2 antibody. Thirty percent of the tumour cell population corresponding to the large cells with irregular nuclei were positive for the anti-CD30 antibody. All the tumour cells expressed the EMA. Small lymphocytes with thick chromatin were marked with the anti-CD45 RO antibody corresponding to reactive T-lymphocytes. The study with anti-CD15 antibody, anti-CD20 (L26), and the antibodies against heavy and light immunoglobulin chains was negative. The morphological and immunohistochemical appearance of this tumour led us to diagnose high grade B malignant lymphoma of the immunoblastic type, with plasmocytic differentiation associated with a small CD30 positive anaplastic large cell population.

Discussion

Among extranodal localisations of malignant lymphomas in AIDS, ocular tumours are exceptional and have not been reported at all in many series involving numerous patients. Only a few cases of orbital lymphomas in AIDS patients have been reported in the literature. The first case of orbital lymphoma in AIDS, a Burkitt’s lymphoma, was published by Fujikawa et al in 1983. In 1984, Brooks et al described another case of Burkitt’s lymphoma arising in the orbit without any intraocular involvement. The initial evaluation of extension showed systemic diffusion with localisations in the bone marrow and testicles but without diffusion to the central nervous system. In a series of 88 extranodal lymphomas occurring in HIV positive homosexual men, Ziegler et al noted two localisations in the orbit. In 1986, Di Carlo et al reported a non-documented case of lymphoma of the orbit in an autopsy study of 30 AIDS patients who died of malignant lymphoma. In another study, extranodal involvement by non-Hodgkin’s lymphoma was identified in 77 patients and one case of conjunctival lymphoma was cited. In an autopsy series of 25 AIDS patients, Jabs et al also reported an ocular localisation of a malignant lymphoma. De Girolami et al noted one case of large cell B lymphoma arising in the eye with cerebral localisation. The histological type of some of these lymphomas was not described.

In our case the initial localisation was intraocular, restricted to the uveal tract. The evaluation of extension did not demonstrate any systemic or cerebral localisation. The discovery of numerous immunoblastic cells with plasmocytic differentiation in the pleura and pericardial effusion accounted for secondary systemic dissemination.

In non-AIDS patients intraocular lymphomas are rarely localised in the uveal tract and most often involve the vitreous chamber, the retina, and the optic nerve. In a review of 28 cases of intraocular lymphomas involving an HIV seronegative population, lymphomas of the uveal tract could invade the brain. But most frequently they showed systemic dissemination without involvement of the central nervous system. In Trudeau’s series, comprising 87 cases, initial and isolated ocular localisation represented 60% of cases. In more than 80% of these cases the evolution of the disease consisted of multisvisceral dissemination.

As in other localisations of lymphomas in AIDS, our case is a high grade malignant lymphoma with B phenotype. Moreover, a group of anaplastic large cells expressing CD30 antigen and EMA was associated with the immunoblastic proliferation cells. Such anaplastic large cell component has been described in association with large cell lymphomas of both B or T-cell type.

In summary, malignant lymphomas initially arising in the eye are exceptional in AIDS patients. In all the cases reported in the literature localisation in the eye is associated with a systemic dissemination or a simultaneous or secondary localisation. We report the first primitive and initially strictly intraocular lymphoma in AIDS.
As in Brooks' observation this ocular localisation can resemble an ocular infection, for example persistent uveitis or choroiditis,\(^6\) which is frequently seen in AIDS.\(^7\) In our case the initial diagnosis was tuberculous uveitis in a patient already treated for lymph node tuberculosis. Primitive intraocular lymphoma should therefore always be suspected in AIDS patients with symptoms of chronic uveitis or choroiditis, since the early recognition of this disorder is essential for appropriate treatment.