temic tuberculosis is common in India, ocular tuberculosis is rare. A long-standing, undiagnosed, and untreated unilateral limbal lesion may lead to secondary tarsal inflammation as seen here, raising the suspicion of an allergic origin. An intralocular depot corticosteroid could lead to tarsal necrosis, as demonstrated in these 2 cases.

In both cases, the presence of epithelioid granulomas with central caseation necrosis, Langhan giant cells, and the demonstration of acid-fast bacilli by Ziehl-Neelsen stain confirmed the diagnosis of tuberculous conjunctivitis. This was corroborated by nested polymerase chain reaction, using primers specific for the DNA of M tuberculosis.

Papillary conjunctivitis is a nonspecific sign associated with acute or chronic inflammation. In these 2 cases, the associated papillary conjunctivitis could be an additional sign of conjunctival tuberculosis or a reactive process resulting from chronic irritation and friction caused by the long-standing mass in the upper bulbar conjunctiva. We speculate that the treating ophthalmologists mistook the papillae for the giant papillae seen in vernal keratoconjunctivitis, and administered the supratarsal depot corticosteroid. This probably resulted in a flare-up of the underlying undiagnosed conjunctival tuberculosis, resulting in tarsal necrosis. While a biopsy of the tarsus was not performed in the first case, owing to extensive necrosis, caseating granulomas with acid-fast bacilli were demonstrated in the second case. The lack of response to anti-inflammatory medication, tarsal necrosis, and demonstration of acid-fast bacilli in the second case pointed to primary involvement of the tarsal conjunctiva in the disease process rather than a secondary nonspecific inflammation. These 2 cases highlight the fact that the tarsal necrosis could mimic a secondary nonspecific inflammation suggestive of an allergic cause, leading to an alternate mode of management that may have adverse effects. Following systemic evaluation for tuberculosis and human immunodeficiency virus by an internist, both patients were prescribed antitubercular drugs per the recommended regimen. Amniotic membrane transplantation aided in ocular surface reconstruction.

The causes of granulomatous inflammations of the conjunctiva include sarcoidosis, tuberculosis, Parinaud ocular glandular syndrome, syphilis, leprosy, coccidiodomycosis, tularemia, parasitcs, and foreign bodies. In patients with chronic unilateral conjunctivitis refractory to routine therapy, a diagnosis of neoplasia and floppy eyelid syndrome needs to be considered. Thorough clinical evaluation and histologic features of the excised tissue (granulomatous lesion, presence or absence of necrosis, associated inflammatory cell response) and identification of the possible infectious agents by special stains and molecular methods help differentiate these lesions.

Conjunctival scrapings and biopsy specimens may have a low sensitivity for the detection of acid-fast organisms, requiring approximately 1000 to 10000 organisms per milliliter of sample for morphologic detection and 100 to 1000 viable organisms per milliliter for a positive culture. This could explain the absence of organisms in the initial conjunctival and corneal scrapings. Polymerase chain reaction, based on the principle of DNA amplification, is highly sensitive and can detect as few as 10 microorganisms. This is a useful modality when special stains do not reveal organisms in the presence of caseating granulomas.

In summary, patients with chronic unilateral conjunctivitis need a detailed evaluation, including a conjunctival biopsy, and if possible, molecular diagnostic techniques for rapid diagnosis and institution of appropriate treatment. A high index of suspicion for tuberculosis is warranted before administering intralesional depot corticosteroid injections, as this may result in a flare-up of the underlying infection and lead to tarsal necrosis.

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References


Epstein-Barr Virus-Associated Leiomyosarcoma of the Iris in a Child Infected With Human Immunodeficiency Virus

Children with human immunodeficiency virus (HIV) infection have a higher risk of developing a malignant neoplasm, the most common of which is non-Hodgkin lymphoma, followed by leiomyosarcoma. Most leiomyosarcomas in children with HIV infection have been found in various anatomical locations, including the gastrointestinal tract, liver, spleen, and lung. The association between leiomyosarcoma and Epstein-Barr virus (EBV) infection in HIV-infected patients is known.
Reports from 1964 and 1972 described smooth muscle tumors in the iris. Foss et al, using immunohistochemical analysis, have reclassified previous reported cases as melanocytic lesions. As a result, stricter pathologic criteria for diagnosing intraocular neoplasms of smooth muscle were established in 1994. Since then, there has been only one well-documented example of iris leiomyoma reported. We report an HIV-infected girl with an iris neoplasm, histologically and immunohistochemically proven to be leiomyosarcoma.

**Report of a Case.** A 4-year-old Thai girl with vertically acquired HIV infection was born at our hospital in 1996. She was asymptomatic until age 2 years, when she developed dermatitis, dilated cardiomyopathy, hepatosplenomegaly, lymphadenopathy, and parotitis. The CD4 count was 1%. At 3 years of age, treatment with zidovudine and dideoxycytidine was started, but the adherence to antiretroviral agents was poor. Her subsequent course was complicated by pneumonia, leading to several hospital admissions.

At the age of 4 years 10 months, she experienced pain in her right eye. Ophthalmologic examination revealed a whitish mass located on the lower half of the iris, 4 mm in diameter. There was vascular dilatation on the anterior stromal surface. The lower part of the anterior chamber was shallow, with peripheral anterior synchiae. There were no signs of inflammation seen in the anterior chamber. The lens was normal. Computed tomography (CT) did not demonstrate any other intraocular lesions, but CT of the brain showed a 3-cm cystic mass in the parenchyma of the left frontal lobe. Aspiration of the cyst revealed numerous red cells, some mononuclear cells, and no malignant cells.

Inferior sector iridectomy was carried out, and the iris mass was surgically removed by an inferior limbal incision. The entire tissue was fixed in 10% formalin, routinely processed, and embedded in paraffin wax. In addition to routine staining, immunohistochemical analysis was performed with antibodies against the following proteins: S100, HMB45, muscle-specific actin, smooth-muscle actin, desmin, and EBV latent membrane protein. In situ hybridization for EBV was also performed, using EBV-encoded RNA oligonucleotide probe. Both the immunohistochemical analysis and in situ hybridization were done in the presence of adequate controls.

Microscopically (Figures 1 and 2), the lesion consisted of plump spindle-shaped tumor cells forming interlacing fascicles. The neoplastic nuclei were hyperchromatic, and some of them possessed distinct small nucleoli. There are scattered mitotic figures, approximately 5/10 per high-power field. Tumor cells strongly expressed muscle-specific actin and smooth-muscle actin, supporting the smooth muscle origin of the lesion. Desmin, S100 protein, and HMB45 were nonreactive. The above findings are characteristics of leiomyosarcoma. Evidence of EBV infection was revealed by in situ hybridization but not by immunohistochemical analysis.

At the age of 5 years 3 months, she was admitted to the hospital with persistent and severe abdominal pain. Duodenal tissue biopsy showed acid fast bacilli in the mucosa, and Mycobacterium gordonae were isolated. She died at the age of 5 years 6 months.

**Comment.** Leiomyosarcoma has been well-documented to be associated with HIV infection, and usually occurs in the visceral organs. The tumor rarely arises in the uveal tract. A literature search, using the keywords “iris,” “uvea,” “uveal tract,” and “leiomyosarcoma” from major electronic databases (MEDLINE, EMBASE, BIOSIS, and CINAHL), did not reveal any previous cases of histologically and immunohistochemically proven iris leiomyosarcoma.

Before the advent of immunohistochemical analysis, intraocular leiomyomas and their malignant counterparts, leiomyosarcomas, have been a frequent subject of debate. Spindle cell melanoma is the main differential diagnosis. Immunohistochemical study is therefore particularly important. Foss et al proposed that immunohistochemical and/or electron microscopic investigation are crucial in establishing the correct diagnosis of ocular smooth muscle tumors. In our case, the positive staining for smooth muscle markers (smooth-muscle actin and muscle-specific actin) and the absence of immunolabeling for melanoma markers (S100 protein and HMB45) strongly support the diagnosis of smooth muscle tumor and rule out the possibility of melanocytic lesion. Although histologic criteria for the distinction of benign and malignant smooth muscle neoplasms outside the uterus are not well established, the high mitotic in-
dex favors the diagnosis of leiomyosarcoma.

The presence of the cystic lesion in the left frontal lobe raises questions concerning the possible relationship between the cyst and the iris tumor and whether both represent leiomyosarcoma. If this was the case, it would be difficult to determine the primary site of the tumor. However, most reported HIV-associated intracranial leiomyosarcomas are dura-based, solid (noncystic) masses. We consider both of these lesions to be unrelated. Unfortunately, no tissue was obtained from the cyst for definite histologic evaluation.

Regarding the histogenesis, smooth muscle tumors of the iris are thought to originate from its sphincter or dilator muscle, but the concept that neoplasms can affect the iris is dubious. Our case has confirmed that a cellular progenitor of smooth muscle tumors does exist in this location. The association between EBV and smooth muscle tumors in HIV-infected subjects has been well documented, as evident in our patient. In addition to the reduction in tumor surveillance cells and the inability to remove EBV in immunocompromised subjects, it has been shown that EBV receptors are unregulated and thus may enhance viral entrance into and transformation of the human cells. The discrepancy between EBV-encoded RNA in situ hybridization and immunohistochemical characteristics of EBV latent membrane protein is the same as for previously reported EBV-associated smooth muscle tumors. Failure to detect EBV latent membrane protein may be due to the absence or subthreshold level of the antigen in this tumor cell type.

This case is the first immunohistochemically verified leiomyosarcoma of the iris that has occurred in an HIV-infected child, to our knowledge. Although the association between the tumor and EBV in immunosuppressive patients has been previously determined, this report reiterates that HIV infection facilitates the development of this tumor, even in an unusual location such as the iris.

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Adenocarcinoma of the Retinal Pigment Epithelium

Malignant neoplasms of the retinal pigment epithelium (RPE) are rare. Only a few well-documented cases have been described in the last decades.1-8 Some of these tumors developed in association with choroidal neovascular membranes,7 ocular phthisis,1,4 or congenital hypertrophy of the RPE.8 In this report we describe an additional case arising from a chorioretinal scar 17 years after the development of a subfoveal neovascular membrane.

Report of a Case. A 37-year-old man was referred to our clinic in 1980 for a progressive loss of vision in his right eye during the preceding months. His visual acuity was counting fingers OD and 20/20 OS. Funduscopy showed a subfoveal hemorrhagic lesion in the right eye, several atrophic chorioretinal scars nasal to the optic disc, and peripapillary atrophy (Figure 1A). Fluorescein angiography revealed a subfoveal neovascular membrane (Figure 1B). We assumed that a histoplasmosis-like lesion (pseudo-presumed ocular histoplasmosis syndrome) had caused the observed changes. No specific therapy was recommended. The left eye was normal.

Seventeen years later, in 1997, the patient (then 54 years old) developed a slowly progressive additional loss of his central visual field in the right eye. The visual acuity was reduced to hand motions OD, and funduscropy showed a prominent, nonpigmented subretinal mass in the macular region overlying the optic disc (Figure 2A). The surrounding retina was detached. Subretinal strands and yellowish exudates were visible. Simultaneous fluorescein and indocyanine green angiography revealed a vascularized tumor with parts of the blood supply coming from the retinal vasculature (Figure 2B and 2C). Ultrasound A- and B-scan echography revealed a solid, dome-shaped (no collar-button configuration) tumor with a prominence of 3.4 mm and 30% to 70% reflectivity.

A thorough medical examination was performed including computed tomography of the cranium, thorax, abdomen, and pelvis; bronchoscopy; panendoscopy; sonography of the abdomen; and endosonography. The results of all examinations were normal.

Clinically, an amelanotic choroidal melanoma was suspected, and enucleation was performed. Five years after enucleation, the patient is doing well with no signs of malignancy.

Macroscopically, the sectioned globe showed a dome-shaped, gray-yellow subretinal mass occupying the region anterior to the optic disc. The tumor was 8 × 5 mm at the base and 3 mm thick. It was surrounded by yellowish subretinal exudates and a shallow retinal detachment.

Histologically (Figure 3A-D), the tumor was composed mainly of nonpigmented cuboidal epithelial cells arranged in a glandulotubular pattern. Other parts exhibited a solid or trabecular growth. A few cells...