Many of the white dot syndromes are considered to have a granulomatous pathogenesis. The histopathologic characteristics of this case of multifocal choroiditis seen within 15 months of apparent clinical onset show that the white dot lesions were nongranulomatous perivascular choroidal infiltrates, consisting mainly of B lymphocytes. Early choroidal neovascularization was also seen.

The understanding of inflammatory disorders of the retina and choroid is limited by the relative lack of tissue for study at any stage, but particularly in the early stages of the disease. This case is unique in our experience as the pathology specimens became available as the result of sudden death 12 weeks following the diagnosis of multifocal choroiditis. The young man had had annual eye examinations as part of routine occupational health screening; thus, given the normal findings on previous examinations, the disease can only have been clinically manifest for less than 15 months before the abnormal examination results. We report on the clinical and early pathologic findings of a case of multifocal choroiditis.

**REPORT OF A CASE**

During a routine annual medical examination on July 24, 1995, a 29-year-old man was noted to have a bilateral abnormal fundal appearance. He reported no visual symptoms or other medical complaints. Findings from previous ophthalmic examinations were recorded as normal. On examination, his unaided visual acuity was 6/6 with either eye. Anterior segments were normal as were the intraocular pressures. Fundal examination revealed bilateral discrete white chorioretinal lesions with minimal pigment hypertrophy radiating nasally from the disc and then becoming circumferential. The discs showed some chorioretinal atrophy at the margins with pigment clumping. Both maculae appeared normal. A few inflammatory cells were noted in the right vitreous and there was one very small area of clinically active chorioretinal inflammation in the retinal periphery adjacent to the inferotemporal vascular arcade. Results of color vision testing and automated visual field analysis were normal. On August 14, a fluorescein angiogram showed early hypofluorescence at mid to late staining, but no leakage.

The examining ophthalmologist (S.H.) made a preliminary diagnosis of birdshot chorioretinopathy, which was later revised to punctate inner choroidopathy. HLA typing showed the patient to be HLA-A3, -A28, -B51 (5), -Bw4, -Bw6, and -B35 positive. Results of serologic testing for syphilis were negative. Values for serum angiotensin-converting enzyme were within normal limits.

**HISTOPATHOLOGIC FINDINGS**

Twelve weeks following the diagnosis the patient died in an accident. The eyes were removed and sent for histopathologic examination. There were no other relevant postmortem findings. Macroscopically the eyes were intact, but soft, which is consistent with early postmortem changes. Since lesions were said to be present in the right eye in the horizontal axis, this was cut normally by removal of upper and lower calottes. The anterior chamber was
removed from the other eye by corneal section through the pars plana. The retina was detached and was then removed, allowing the white choroidal opacities to be dissected as single blocks (Figure 2, A). These were embedded for paraffin section histologic study and electron microscopy.

Hematoxylin-cosin–stained sections showed limbal elastosis with no other abnormalities of the anterior eye structures. The choroid showed perivascular chronic inflammatory infiltrates consisting mainly of lymphocytes (Figure 2, B). There were also some lymphocytes around the inner retinal blood vessels, but no local retinal infiltration. Over the most intensely inflamed choroidal vessels, areas of early-stage neovascular membrane formation and hyperplasia of retinal pigment epithelium were seen. Bruch membrane remained intact. Transmission electron microscopy showed venules with large endothelial cells with the occasional lymphocyte migrating between them.

Immunohistochemistry using an avidin-biotin method with diamobenzidine, counterstained with Mayer hematoxylin (Figure 2, C through F) showed most of the lymphocytes present were B lymphocytes (CD20+), but mixed with a substantial number of T lymphocytes (CD3+). There was no peripheral distribution of T cells as might be found in granulomatous inflammation and few macrophages were present. Findings from HLA-DR staining were essentially negative, with weak positivity of occasional macrophagelike cells within the infiltrate. Staining for von Willebrand factor confirmed neovascularization within the regions of the largest accumulations of lymphocytes. Immunostaining confirmed the presence of T lymphocytes around small inner retinal blood vessels.

**COMMENT**

Clinically, this case falls within the clinical entity of multifocal choroiditis. The nasal distribution of lesions, peripapillary scarring, and few vitreous cells associated with an active lesion have been described in this syndrome, though they have also been described in punctate inner choriodopathy. The clinical diagnosis is hampered by the limited time in which to follow the clinical course. Perhaps in time the patient may have become symptomatic with further active lesions, fulminant vitritis, or a choroidal neovascular membrane. Whether this case truly represents multifocal choroiditis, punctate inner choriodopathy, or even presumed ocular histoplasmosis syndrome may be argued. The pathologic features, however, clearly show a multifocal choroiditis. It has been argued that the fundal white dots are a clinical presentation of a common abnormality followed by a variable immune mediated response causing a spectrum from multiple evanescent white dot syndrome to birdshot choroidopathy. The common abnormality of the white dot was proposed to be a microgranuloma. This is not evident in our case.

The choroidal infiltrates did not resemble the clearly granulomatous uveitic syndromes of sarcoidosis, sympathetic ophthalma, Harada disease, or birdshot choroidopathy. The preponderance of B cells has been reported in the primate model of chronic experimental histoplasmic choroiditis and subretinal fibrosis and uveitis syndrome, though the latter is associated with glial proliferation, which had not occurred in this case. The former model of inflammation appears similar to the abnormality we found, notably that the infiltrate could persist despite clinical quiescence. Reactivation was found with antigenic challenge, whereas, upon the CD4+ T-cell population was amplified. Clinical recurrence is common in multifocal choriditis, with 86% reported in one series. The abnormalities in this case demonstrate that the possibility is present. This specimen showed the early stage of choroidal neovascularization. This has been noted clinically in 32% of eyes.

This unique opportunity to report the pathologic characteristics of multifocal choriditis, seen within 15 months of apparent clinical onset, has shown that it is a nongranulomatous choroiditis. The persistent infiltrate with the preponderance of B cells indicates subclinical activity and the possibility for clinical recurrence and choroidal neovascularization.

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