Antiendothelial Cell Antibodies (AECA) in Patients with Uveoretinitis

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Introduction

Intraocular inflammation accompanies a variety of systemic inflammatory diseases whose etiology remains unclear despite many recent advances in the study of their immunopathology. In European countries, the most frequent diseases associated with uveoretinitis are ankylosing spondylitis, sarcoidosis, inflammatory bowel disease, and multiple sclerosis. In the Middle East and the Orient, Behçet’s disease and Vogt-Koyanagi-Harada syndrome are more frequent, and HLA-B (27) associated disease less so. The main diseases associated with scleritis and keratitis are rheumatoid arthritis and Wegener’s granulomatosis, and it is unusual for these conditions to be associated with uveoretinitis. Why the eye should become so frequently involved in these multiorgan diseases is not known.

Despite prolonged investigation and follow-up, half of all patients with uveoretinitis will have no associated systemic disease. Progress in understanding idiopathic uveoretinitis is hampered by the inaccessibility of biopsy material, the low diagnostic power of clinical examination, and the difficulties of relating abnormalities found in peripheral blood to changes occurring within the eye.

The signs of ocular inflammation are uniquely available for observation by fundus biomicroscopy and angiography; it is therefore surprising how rarely clinical examination alone can provide a definitive diagnosis. These limitations have led to a confusing variety of descriptive terms in the literature on uveoretinitis. The majority of patients with vision-threatening uveoretinal inflammation require sys-

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temic immunosuppressive therapy to control retinal vascular leakage and occlusion rather than persistent inflammation in the uvea. It therefore seems appropriate to use the term retinal vasculitis, rather than the commonly used term uveitis, to describe this group of patients, as the predominant site of their disease lies in the retinal vasculature. In this review we use the term uveoretinitis as a generic term to include all forms of uveal and retinal inflammation whereas retinal vasculitis is used to describe those patients with significant inflammation of the retinal microvasculature.

The diagnosis of patients with idiopathic uveoretinitis is not helped by the lack of diagnostic tests for many of the diseases with which it is associated epidemiologically. Diseases such as multiple sclerosis, Behçet's disease, and sarcoidosis are partly defined by the presence of multiple sites of inflammation: isolated ocular involvement by the same disease process therefore remains unclassifiable until other organs become involved. As idiopathic uveoretinitis can precede the full clinical expression of diseases such as sarcoidosis, multiple sclerosis, and Behçet's disease by many years, the correct diagnostic classification of a patient may change over time.

The investigation of idiopathic uveoretinitis by examining peripheral blood is beset with problems. First, the presence of occult systemic disease can never be definitively excluded without unjustifiably invasive investigation. Second, the relationship between inflammatory changes in the blood and the various patterns of intraocular inflammation is, in the absence of biopsy material, conjectural. Third, those with the most severe uveoretinitis and therefore the most likely to exhibit abnormalities in peripheral blood are also those most likely to be maintained on long-term systemic immunosuppression, thus adding to the difficulties of interpreting the changes in peripheral blood.

Histological changes in enucleated eyes with uveoretinitis show a similar picture in a wide variety of clinical conditions. The major feature is a lymphocytic infiltration of the retina and uveal tissue. There are frequently perivenular accumulations of lymphocytes in the retinal and ciliary body circulation, and granulomas may occur in both the choroid and retina. A strict retinal vasculitis, with a primary inflammation within retinal vessels, has not been demonstrated, and, even in severely ischemic forms of retinal inflammation, vascular occlusions are likely to result from perivascular and intraluminal inflammation rather than a primary retinal vasculitis.

In this article we examine studies that have analyzed anti-endothelial cell antibodies (AECA) in patients with uveoretinitis and discuss the implications of these findings for the understanding of the pathogenesis of retinal vasculitis.