Sir,

Current concepts and future directions in the pathogenesis and management of non infectious uveitis

We read with interest the excellent overview by Lee *et al*[1] on 'Current concepts and future directions in the pathogenesis and treatment of non-infectious intraocular inflammation'. The authors have remarked about the 'swing of intraocular inflammation from infective to inflammatory over last century'. However, with current novel diagnostic tools more non infectious intraocular inflammatory diseases have been recognized and treated as infective uveitis.[2] According to Russell Read, infectious uveitis accounted for 13 to 21 percent of the total uveitis cases seen at tertiary referral centers.[3] Infectious uveitis can become latent, smoldering, and mimic autoimmune uveitis. Although autoimmune uveitis responds to corticosteroids or immunosuppressives, such treatment worsens infectious uveitis.[2] The authors have also highlighted the fact there is enough compelling data to suggest trigger of innate immunity by hidden concomitant infection.[1] From that perspective, infectious causes should always be considered in all patients with uveitis. The differential diagnosis includes herpes, syphilis, toxoplasmosis, tuberculosis, bartonellosis, Lyme disease, and others.[2] Air travel, immigration, and globalization of business have overturned traditional pattern of geographic distribution of infectious diseases, and therefore one should work locally but think globally.[2] Lee *et al*[1] have remarked on dysregulation of immunity within the eye as a guiding principle for current management strategy.[1] On the contrary, with more infective entity being recognized, the focus should be more on recognizing and targetting the infective stimulus. Unfortunately, most infectious causes are only possible to detect by using very specific detection methods. Furthermore, it is often necessary to study a sample from with-in the eye to get a proper diagnosis.[2] As mentioned by the authors in the current series, anterior chamber tap can be performed to carry out PCR for infective agents but still in developing countries it is not readily available and most of the diagnosis is clinical. When non-infectious uveitis is in the differential, empiric corticosteroids must sometimes be used, at great risk, if clinical examination, ancillary testing, and any available intraocular diagnostic tests have failed to confirm a diagnosis.[4] Failing to give infectious etiologies a place on the diagnostic 'radar screen' and failure to consider infective etiology before starting immunosuppressive or biologic agents can have serious consequences to the patient.

Conflict of interest

The author declares no conflict of interest.

References

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Sir,

Response to Dr Agrawal

We thank Dr Agrawal[1] for his correspondence, which helpfully highlights the important role of infectious pathogens in the aetiology, diagnosis, and treatment of uveitis. Although the title of our review explicitly limits its scope to non-infectious intraocular inflammation, we endorse his emphasis on the importance of excluding treatable infectious uveitides before embarking on treatment with immunosuppressive agents. However, while acknowledging wide global variation in the burden of infectious diseases, historical surveys endorse our assertion that in Western populations the balance has firmly swung in favour of autoimmunity and autoinflammation—in Guyton and Woods[2] (USA), 1941 series, over 60% of uveitis cases were due to tuberculosis or syphilis, whereas half a century later, Rothova *et al*[3] (Netherlands) reported that these infections accounted for less than 3% of their cohort.

It is also important to reiterate the potential crossover between infectious and autoimmune/autoinflammatory diseases, as outlined in our overview of immunopathology; in particular the role of molecular mimicry and the key contribution concomitant infection has in giving innate immune permission to the antigen-specific adaptive immune responses we observe in the eye. We also increasingly have access to molecular biological technologies, which enable us to exclude direct intraocular infection from aqueous or vitreous biopsies, and in the absence of a proven pathogen we strongly advocate appropriate immunosuppression to maintain vision.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Ocular lymphoma with extrascleral extension as primary manifestation of Richter syndrome

Richter syndrome occurs in 3–10% of patients with chronic lymphocytic leukaemia (CLL) and represents a transformation of CLL into diffuse large B-cell lymphoma.[1]

We report what we believe to be the first case of Richter-syndrome transformation, presenting as a choroidal lesion with extrascleral extension in a patient with CLL.

Case report

A 62-year-old Caucasian male with CLL presented with sudden painless visual deterioration in the right eye; initial examination only revealed the posterior segment to be affected, with extensive vitreous cells and

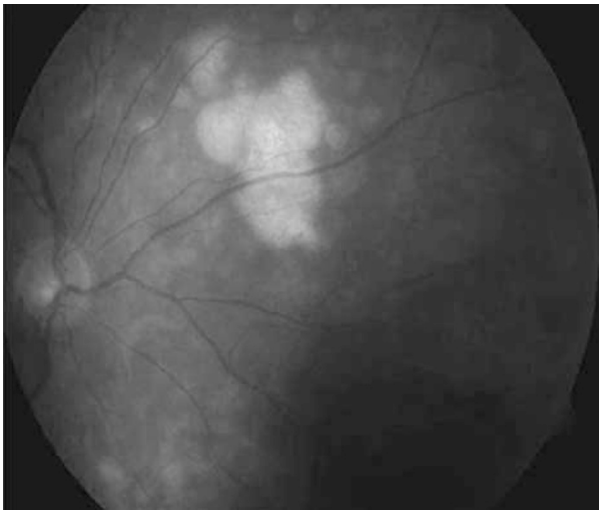

Figure 1 Black and white fundus photograph of the right eye, revealing intraretinal infiltrates in early phase of disease manifestation.

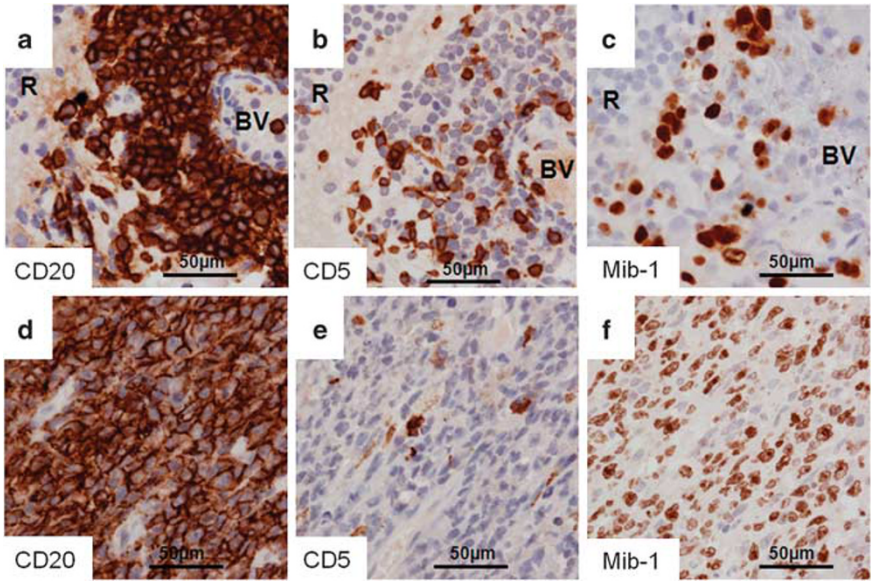

Figure 2 Immunostaining of initial choroidal biopsy from the right eye (a, b, and c) followed by immunostaining of choroid from the enucleated right eye after 6 months (d, e, and f). (a) Choroid immunostained for CD20 (brown, peroxidase technique), demonstrating extensive infiltration by medium-sized B lymphocytes. BV, blood vessel; R, retina. (b) Choroid immunostained for CD5, demonstrating very variable expression of CD5 by the B lymphocytes, although a bone-marrow trephine in 2004 confirmed a diagnosis of the B-cell lymphoma/leukaemia, CLL with cells that were uniformly CD20+ CD79a+ CD5+ and cyclin D1-negative. (c) Choroid immunostained for the proliferation marker, Mib-1, giving a very variable proliferation index that appeared to be up to 50% in places. However, overall it did not definitely exceed 30%, the World Health Organization-defined minimum for diffuse large B-cell lymphoma.[4] Because of the small size of the biopsy, it was difficult to give a definitive diagnosis of CLL or to determine whether transformation to diffuse large B-cell lymphoma might have occurred. (d) Area of extensive lymphoid infiltration in choroid from enucleated right eye immunostained for CD20, demonstrating extensive infiltration by large pleomorphic B lymphocytes. (e) Enucleation specimen immunostained for CD5, showing very little CD5 expression, as sometimes occurs during high-grade (Richter) transformation of CLL to diffuse large B-cell lymphoma.[4] (f) Enucleation specimen immunostained for the proliferation marker Mib-1, demonstrating a proliferation index of 90%, confirming the diagnosis of diffuse large B-cell lymphoma.