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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

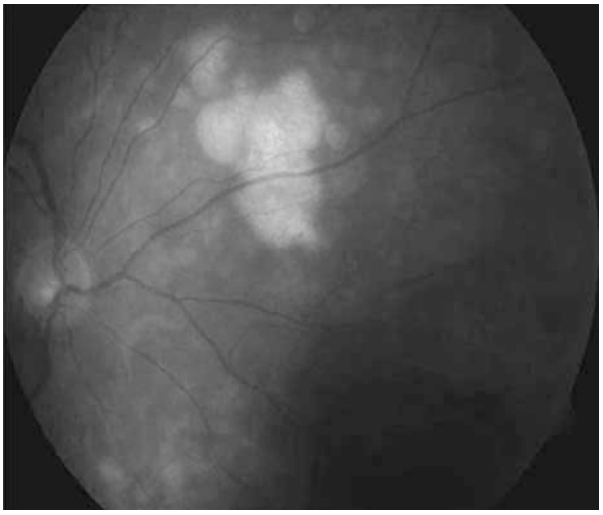

Figure 1 Black and white fundus photograph of the right eye, revealing intraretinal infiltrates in early phase of disease manifestation.

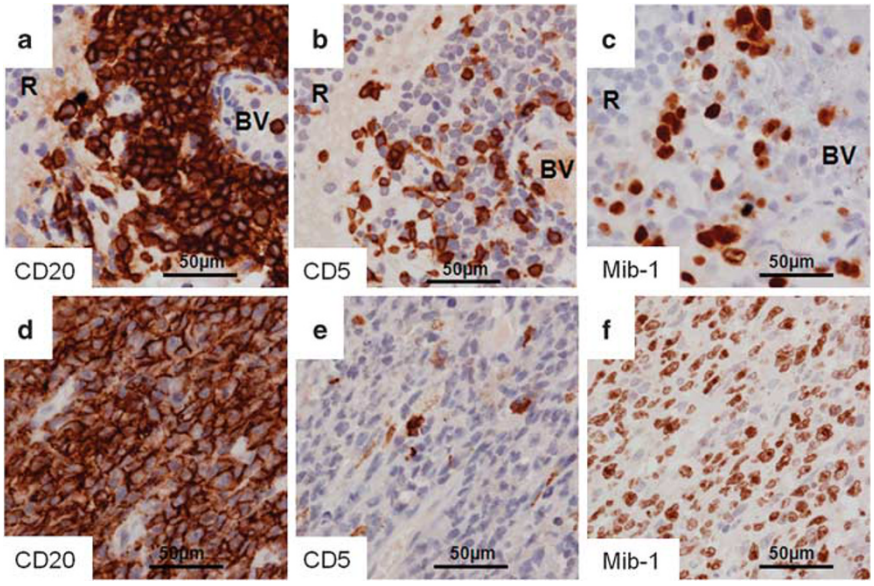

Figure 2 Immunostaining of initial choroidal biopsy from the right eye (a, b, and c) followed by immunostaining of choroid from the enucleated right eye after 6 months (d, e, and f). (a) Choroid immunostained for CD20 (brown, peroxidase technique), demonstrating extensive infiltration by medium-sized 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.

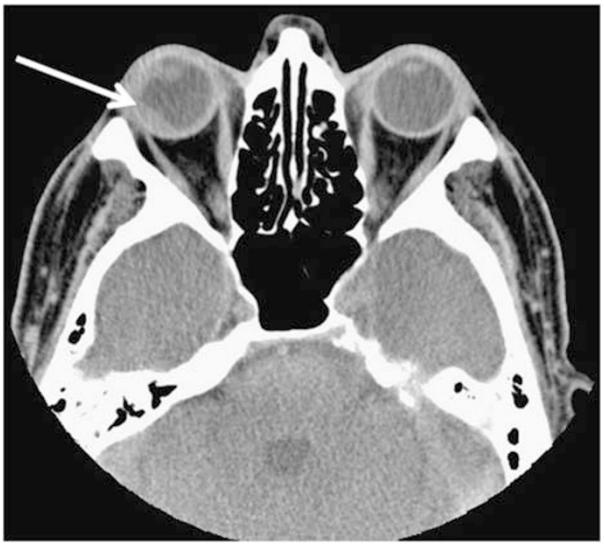

Figure 3 CT showing a chorioretinal mass (arrow) in the right orbit, predominantly affecting the lateral and posterior parts of the globe, as well as transscleral extension laterally at the time of the choroidal biopsy. No retro-global abnormality is identified.

leopard-like spots on the choroid (Figure 1). The visual acuity in the right eye declined rapidly over the next 4 months to hand movements (left-eye spared), and because MRI of the orbits was clear, biopsies of the choroid and vitreous were performed and were suggestive of lymphoma involvement by B cells (Figures 2a–c). Radiation therapy to the right orbit was discussed, but declined by the patient because of the risk of radiation-induced optic neuropathy to his left eye. Over the next 6 months, the right eye became painful with no perception of light.

A CT scan of the orbits revealed a chorioretinal mass with extrascleral extension but could not differentiate between a leukaemic deposit and a melanoma (Figure 3). The general health of the patient began to deteriorate with the spleen enlarging and his red cell count, as well as platelets, declining. The haematologists commenced chemotherapy of fludarabine–cyclophosphamide–rituximab, but this caused prolonged thrombocytopenia after two courses and no improvement in ocular symptoms, and therefore was discontinued. As there was no visual potential in the right eye (left eye remained unaffected) and because it had become painful, enucleation was performed. Histopathology revealed diffuse large B-cell lymphoma (Richter transformation) with optic nerve involvement, extraocular muscle, and orbital infiltration (Figures 2d–f). Because of the aggressive nature of the lymphoma (Figure 4) and despite further chemotherapy, the patient died 6 months after enucleation.

Comment

We know of only three reported cases of Richter syndrome that involved the eye but none with extrascleral extension.[2,3] This must be included in the differential of patients with CLL who present with ocular inflammation.

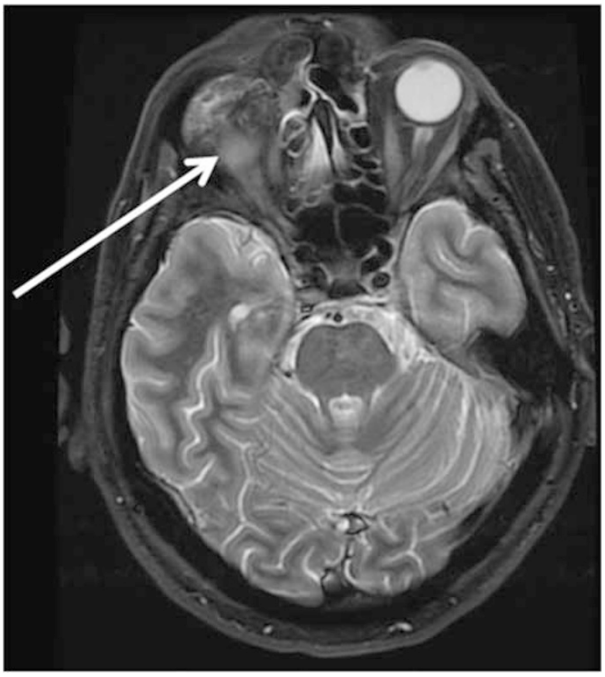

Figure 4 MRI of orbits with gadolinium, 1 month post right enucleation, showing a medpor orbital implant and enhancing soft-tissue mass surrounding the right optic nerve (arrow) in keeping with recurrent lymphoma.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Re 'Isolated eyelid edema in Melkersson–Rosenthal syndrome: a case series'

Rawlings *et al*[1] have reported on a series of five patients with isolated eyelid edema and have made the diagnosis of Melkersson–Rosenthal syndrome on the basis of granulomatous inflammation. Melkersson–Rosenthal syndrome is described as a granulomatous disease with the triad of facial palsy, facial edema, and a fissured tongue, although the complete triad is reported to be seen in only 25% of cases.[2]

We have recently reported on a series of 15 patients with chronic eyelid edema, and in 9 of these cases (60%) there was an associated diagnosis of acne rosacea.[3] Granulomatous inflammation was present in some of these patients, and this has been reported before in the presence of acne rosacea.[4] Indeed, acne rosacea and Melkersson–Rosenthal syndrome have some overlap in their clinical and pathological features and both are classified as granulomatous dermopathies. The illustrations of Cases 1 and 2 in the series of Rawlings *et al*[1] show facial features that would be consistent with acne rosacea, with rhinophymatous change and thickened glabellar skin. I suspect these two illustrated patients do indeed have acne rosacea rather than Melkersson–Rosenthal syndrome, and it would be of interest to know whether any of the other three patients in the series also showed features of rosacea.

It is likely that Melkersson–Rosenthal syndrome is over diagnosed when the other features of the syndrome are absent, and many of the reported cases of eyelid edema as the only feature of the syndrome are more likely to have acne rosacea as the underlying cause of their eyelid edema. Such phymatous change in the eyelid was certainly the commonest cause in our series, which to date is the largest published series of chronic eyelid lymphedema.

Conflict of interest

The author declares no conflict of interest.

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Sir,

Response to Dr McNab

We thank Dr McNab[1] for his comments on our report of isolated eyelid edema in Melkersson–Rosenthal Syndrome (MRS).[2] He suggests that our cases are better considered examples of acne rosacea, and cites his own study[3] and the case report of Lai *et al*[4] in support of this.

In Dr McNab's case series, histopathological examination of eyelid skin from five patients with a clinical diagnosis of acne rosacea and chronic eyelid edema showed some degree of granulomatous inflammation in three specimens.[3] The granulomas were not illustrated but were described as 'poorly formed' (case 4), 'single' (case 11) and 'surrounding dilated lymphatics' (case 15). Lai *et al*[4] also referred to the presence of 'ill-defined perivascular granulomas' but did not illustrate them. Other studies of chronic eyelid edema in rosacea did not mention dermal granulomas.[5,6] In none of our cases was rosacea felt to be the primary underlying cause, either clinically or histopathologically.

In our practice, we do not regard poorly defined granulomas as indicative of any specific diagnosis. Granulomatous rosacea is typically characterised by a tuberculoid (necrotising) or sarcoid-like response, possibly to the contents of hair follicles. In our series, the granulomas were neither tuberculoid nor sarcoid-like but were sharply defined, perivascular, and perilymphatic, often with an intralymphatic component. In addition, and illustrated in our paper, discrete granulomas were identified in orbicularis muscle and anterior orbital soft tissue, which does not appear to have been described in rosacea.

Dr McNab may be correct in saying that MRS is over diagnosed in cases of isolated eyelid edema.[1] Nevertheless, the clinico-pathological pattern that we and other authors have ascribed to monosymptomatic MRS appears quite distinct. Until our understanding of the etiology and pathogenesis of oro-facial granulomatosis, of which MRS is one part, increases, we see no justification for regarding these cases as a form of granulomatous rosacea.

Conflict of interest

The authors declare no conflict of interest.