CORRESPONDENCE

Fundal white dots: observations from a murine model of congenital ocular toxoplasmosis

EDITOR—In the BJO Ben Ezra and Forrester have reviewed extensively current knowledge concerning the phenomenon of multiple evanescent white dot syndrome (MEWDS), a specific clinical entity which is characterised by the presence of evanescent or permanent, small, discrete subretinal lesions, which occur in the absence of vitreous inflammation.¹

Multiple pale lesions² ³ (Fig 1) can be observed in the outer retinas of a small proportion of mice with experimentally induced congenital ocular toxoplasmosis.⁴ These focal lesions, which closely resemble MEWDS in humans, were clearly seen in the peripheral retina using indirect microscopy, and imparted an orange hue to the underlying choroid. The lesions were observed in the eyes of approximately 16% of congenitally infected mice and occurred either unilaterally or bilaterally. They were only observed from 3 weeks postpartum.

Histopathological examination of these refractive disturbances³ ⁵ within the otherwise transparent murine retina revealed that they consisted of focal elevations of the photoreceptor layer (Fig 2). Clusters of inflammatory cells in the form of lymphocytes and macrophages were a consistent feature and were located between the photoreceptor and pigment epithelial layers of the disorganised retina. Immunocytochemical labelling consistently failed to reveal Toxoplasma antigen within or in apposition to these lesions.⁶

Three dimensional reconstructions (Fig 3) of these lesions using serial sections of resin embedded tissue and standard SAS GRAPH routines, revealed that they were consistently dome-shaped, and did not result from artefactual folds in the tissue consequent upon processing or cutting of the retina.

It is our contention that the focal cellular infiltrates are liable to impair the intrinsic processing mechanisms for removal of photoreceptor elements with the result that focal elevations of the photoreceptors appear in the retina; these are then perceived clinically, under direct illumination, as small discrete elevations of the evanescent in some eyes in which progression to atrophy of the photoreceptor layer had taken place in association with retinal vasculitis. This led us to hypothesise that there may be an autoimmune component associated with the pathogenesis of the ocular toxoplasmosis in the mouse model.⁷

Ben Ezra and Forrester suggest that extravasated foci of leucocytes will render the white dot lesions pale relative to the surrounding unaffected tissue when the fundus is illuminated with white light. Based on our own observations with the mouse model of ocular toxoplasmosis, we would concur with this notion. We contend, however, that an additional contributor to the clinically observed white dot syndrome may be architectural modification to the overlying deep retina into dome-shaped configurations. This would result in refractive anomalies as well as reflectance of some of the incident light impinging on the retina. Such optical effects would also impart to the lesions a paler coloration relative to the surrounding non-affectd areas.

Reply

EDITOR.—Hay and Dutton refer to 'multiple pale lesions' in the model of congenital ocular toxoplasmosis in mice and believe that they are similar to the 'white dots' observed in humans in the various conditions we reviewed. We believe that they are confusing atrophic retinal patches and/or diffractive aberrations in the mouse model of congenital ocular toxoplasmosis with the evanescent (choroidal - retinal pigment epithelium) white dots we have described in our paper. We, therefore, would not concur with their assumption that the patches they observe are comparable with the white dots observed in humans.

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Natural outcomes of stage 1, 2, 3, and 4 idiopathic macular holes

EDITOR.—In order to evaluate the results of surgical intervention in the treatment of macular holes it is essential that we understand the natural history and visual progress of all four stages of macular holes. The paper by Hikichi et al in the BJO¹ was heralded in the accompanying editorial as providing just such an insight into the natural history of idiopathic macular holes. However, I would like to highlight some striking similarities between their data on stage 2 macular holes presented in this study and those reported by the same authors in an article entitled 'The natural history of stage 2 macular holes', published in the American Journal of Ophthalmology² (Table 1).

The authors may suggest that publication of similar data is justified as this study is the first to document the natural history of all four stages of macular holes in a single article. However, the data on stage 3 and 4 holes do little more than echo the authors' findings in


Table 1

<table>
<thead>
<tr>
<th>Data</th>
<th>AJO May 1995</th>
<th>BJO June 1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of study</td>
<td>1982-94</td>
<td>1989-94</td>
</tr>
<tr>
<td>Patient numbers</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td>MH T in size $&gt;$20%</td>
<td>41 (85%)</td>
<td>21 (84%)</td>
</tr>
<tr>
<td>MH no change in size</td>
<td>7 (15%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Vitreous opacities $&gt;$2 lines</td>
<td>54 (17%)</td>
<td>17 (68%)</td>
</tr>
<tr>
<td>Posterior vitreous separation</td>
<td>14 (29%)</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>MH = macular hole.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Data</th>
<th>AJO 1993</th>
<th>BJO June 1996</th>
</tr>
</thead>
<tbody>
<tr>
<td>Period of study</td>
<td>1979-92</td>
<td>1989-94</td>
</tr>
<tr>
<td>Stage 3 MH</td>
<td>85</td>
<td>58</td>
</tr>
<tr>
<td>Patient numbers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MH T in size $&gt;$20%</td>
<td>44 (55%)</td>
<td>32 (55%)</td>
</tr>
<tr>
<td>Stage 4 MH</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>Patient numbers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MH T in size $&gt;$20%</td>
<td>4 (14%)</td>
<td>5 (16%)</td>
</tr>
</tbody>
</table>

their 1993 American Journal of Ophthalmology article entitled "Effect of the vitreous on the prognosis of full thickness idiopathic macular holes" (Table 2). If the data on stage 2 holes in these studies have been derived from the same cohort of patients I would suggest to the authors that this duplication may detract from the scientific merit of the individual articles.

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NOTICES

Royal Society of Medicine, Section of Ophthalmology

The following meetings (beginning at 5 pm) are open to RSM members and their guests only.

TOXOPLASMOSIS, 8 February 1996

Epidemiology of toxoplasmosis; Representing people affected by toxoplasmosis; The diagnosis of ocular toxoplasmosis; Clinical aspects of toxoplasmosis.

LANG LECTURE, 14 March 1996

New perspective; corneal grafting Professor David Easty.

NEW HORIZONS IN THERAPEUTICS, 9 May 1996

The identification of human tumour antigens: a strategy for developing tumour vaccines; New developments in the management of CMV retinitis; The development of ophthalmic drugs; The challenge of gene therapy in the context of eye diseases.

Further details: Alyson Taylor, Sectional Officer, Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE. (Tel: 0171 290 2985; fax: 0171 290 2989.)

REGISTRARS' MEETING, 13 June 1996, 2 pm

For registrars to present research work and case reports. Papers to be considered for publication. Abstracts should be submitted (max. 300 words) for the attention of P Murray, The Royal Society of Medicine, 1 Wimpole Street, London W1M 8AE.

Closing date for entries is 12 April 1996.

Intraocular Implant Society, India

The Intraocular Implant Society, India (formerly the Indian Intraocular Implant Society) will hold the VI International Congress of Intraocular Implant Society, India at Chandigarh, India on 1-2 February 1996. Further details: Dr Amod Gupta, Organising Secretary, Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh – 160 012, India.

Office of Continuing Medical Education

The 18th Annual Wilmer Institute's Current Concepts in Ophthalmology will be held on 11-16 February 1996 at the Hyatt Regency Regency Beach Hotel, Dorado, Puerto Rico.

The 13th Annual Wilmer Institute's Current Concepts in Ophthalmology will be held on 10-15 March 1996 at the Manor Vail Lodge, Vail, Colorado, USA. Further details: Conference Coordinator, Office of Continuing Medical Education, Johns Hopkins Medical Institutions, Turner 20, 720 Rutland Avenue, Baltimore, MD 21205-2195, USA. (Tel: (410) 955-2959; Fax: (410) 955-0807.)

Xlth Symposium of the International Society for Genetic Eye Disease and VIIth Symposium of the Retinoblastoma Society

The Xlth Symposium of the International Society for Genetic Eye Disease and VIIth Symposium of the Retinoblastoma Society will be held on 10-14 March 1996 at the West Point Convention Centre, Hobart, Tasmania, Australia. Further details: ISGED Secretary, PO Box 309, Rosny Park, Tas 7018, Australia. (Fax: +61 02 34 44 64.)

Paediatric Week – Alder Hey Education Centre

A national study day on screening for visual defects in children – present evidence and future prospects, will be held at the Royal Liverpool Children's NHS Trust Alder Hey on Wednesday 13 March 1996. Further details: Education Centre, Royal Liverpool Children's NHS Trust Alder Hey, Eaton Road, Liverpool L12 2AP. (Tel: 0151 252 5218; Fax: 0151 252 5103.)

XI Tübingen Detachment Course: Retinal and Vitreous Surgery

The XI Tübingen Detachment course on retinal and vitreous surgery will be held on 11-12 April 1996 at Kupferbau, Gmelinstrasse 8, 72076 Tübingen, Germany. Further details: Office Professor Dr I Kreissig, Univ-Augenklinik, Schleichstrasse 12, 72076 Tübingen, Germany. (Tel: 07071 294758; Fax: 07071 293746.)