LETTERS TO THE EDITOR

Congenital toxoplasma chorioretinitis transmitted by preconceptionally immune women

Editor,—During pregnancy primary toxoplasmic infection of the mother is a well known cause of congenital chorioretinitis due to fetal contamination by *Toxoplasma gondii*. It is generally thought that women infected before conception have no risk of transmitting the disease to the fetus unless they are severely immunocompromised.1 We report two children with severe ocular lesions due to congenital toxoplasmosis transmitted by preconceptionally immune mothers.

**CASE 1**

A 1 year old girl was referred because of a convergent squint as a consequence of bilateral large macular scars. She had been born to an immunocompetent mother. Three months before conception, the systematic French prenatal serological screening of the mother showed a recent toxoplasmic infection diagnosed by a high titre of specific immunoglobulin M (IgM) (IgM 5200, Biotrol Merck (normal <200), IgG 40 IU/ml) (Table 1). She was treated with spiramycin 3 MIU per day for a month. At the time of referral, the mother’s titre of IgM had significantly decreased (IgM 200) and showed a slightly higher rate of IgG (140 IU/ml). Her daughter’s serological status showed a high titre of specific IgG (624 IU/ml), the presence of specific IgA (6/12 index ISAGA; immunosorbent agglutination assay, Biomerieux, index 0–12) and specific IgM (11/12 index ELISA) confirming a fetal infection. Intracerebral calcifications, suggestive of congenital toxoplasmosis, were found on the computed tomogram (Fig 1). The child was otherwise healthy and was not treated.

**CASE 2**

A 1 month old boy was referred because of a congenital cataract in the right eye and a macular atrophic lesion surrounded by an active whitish ring. He was the third child of an immunocompetent woman, a native of Saint-Domingue (Haïti).1 She had long standing toxoplasmic immunity, confirmed by the absence of specific IgM and stable IgG rates at the fourth and the 10th weeks of her pregnancy (ELISA, IgG 49 and 54 IU/ml respectively) providing proof of an anterior toxoplasmic infection (Table 1). The serology of the neonate showed evidence of active *T gondii* infection with a high IgG titre (ELISA >1200 IU/ml), a positive specific IgM (10/12 index ISAGA) as well as a positive specific IgA (6/12 specific ISAGA). The serological study of the mother, after the birth, showed a dramatically increased level of IgG (ELISA IgG > 1200 IU/ml) with specific IgA (12/12 index ISAGA); however, no specific IgM was detected. The child was operated on for his cataract and was treated orally with pyrimethamine and sulphadiazine.

**COMMENT**

Congenital chorioretinitis may be a challenging clinical situation for which fetal infections must be considered, in particular, congenital toxoplasmosis.

Because of the concept that the offspring of an immune woman is protected, the diagnosis of infection by *T gondii* may be overlooked in rare cases especially when there are only ocular manifestations. In our two cases, the mothers were considered to be immune to *T gondii*; nevertheless, they transmitted the disease to their children who presented with sight threatening manifestations and no systemic symptoms. The mothers were not immunocompromised, thus excluding toxoplasmosis reactivation due to immunodeficiency.2 Different pathophysiological mechanisms may be suggested and may be illustrated by our two cases.

Regarding our first patient, it has been reported recently that, exceptionally, congenital toxoplasmosis may be a consequence of primary maternal toxoplasmic infection preceding conception.3–5 Despite medical treatment, the parasitaemia may remain active even months after the onset of the disease and could be responsible for fetal contamination. An emerging immune response as well as the mother’s treatment, reducing the parasitaemia of the child, may explain the attenuated clinical manifestation leading to ocular manifestations without other clinical systemic involvement and without miscarriage.

The development of toxoplasmosis in the second case may be explained by reinfection of the mother.6 The mother’s positive specific IgA suggested that there was reinfection of the mother by the parasite, as these immunoglobulins are produced during the acute phase of the acute infection.7 Different virulence have been described, and reinfection by a particularly virulent strain could explain the inability of the mother’s immune system to protect the fetus.8 The absence of IgM in the mother after the birth of the child is striking and the origin remains unclear although a similar serological status has already been described in a case of spontaneous abortion due to presumed reinfection of a preconceptionally immune mother.9 The possibility of the rupture of endometrial toxoplasmic cysts, contaminating the fetus during pregnancy or at birth, can be raised according to Langer10 but this theory has been considered with reservation by other authors.11 Nevertheless, because of the IgA level in the mother of our second patient, we assume that there is reinfection and not reactivation.

Consecutive toxoplasmic infection in siblings may occur. Indeed, siblings with ocular toxoplasmosis have been reported12 and pose the question of congenital or acquired origin of these iterative intrafamilial toxoplasmic infections. In none of these papers has the congenital origin of the infection been proved calling into question congenital reinfection of these siblings.

Figure 1 Intracerebral calcifications (arrows) suggestive of congenital toxoplasmosis found on the computed tomogram.

We thank Mr Carlos Pavesio (London), consultant ophthalmic surgeon, for interesting comments concerning our two cases and Mr Phillip Harris (Edinburgh) for his help.

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Table 1 Main serological findings in the two cases

| Table 1 Main serological findings in the two cases |
|-----------------|------------------|------------------|
| **Child** | **Mother before conception** | **Mother after birth** |
| IgM | IgG | IgA | IgM | IgG | IgA | IgM | IgG | IgA |
| Case 1 | + | + | + | ++ | + | NA | + | + |
| Case 2 | + | + | + | −− | − | + | −− | ++ |

Level of specific antibodies against *Toxoplasma gondii* (+ to ++ present, − not present, or (NA) not available.

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Shinny and ocular trauma in north west Scotland

EDITOR,—Sports related eye injuries account for up to 42% of ocular trauma requiring hospitalisation1 and 10% of ruptured globes.2 The commonest cause of sports related ocular trauma seen in this department is shinny.

Shinny is a traditional game with a devoted following and a playing area which stretches from Argyll and Bute in the south to Inverness in the east to Skye in the west. It is derived from hurling and is thought to have been introduced by St Bridget who travelled to Scotland with St Columba to promote Christianity in the highlands.

The game itself is not unlike hockey with two opposing teams who attempt to score more goals than the opposition using a curved stick or ‘caman’. Two notable differences exist between the two games; however. There is no restriction on the height above which the caman may be raised or above which the ball may travel.

We report two cases of ocular trauma which are representative of the cases commonly seen in this department during the shinny season.

CASE 1

A 30 year old man was admitted after being struck on the face with a shinny stick. Visual acuity was perception of light only. A 10 mm horizontal upper lid laceration was noted with a 200 degree superior iridodialysis. The eye was exsanguinated inferiorly with zonular dehiscence above. Intraocular pressure was 15 mm Hg with no orbital fracture.

After initial primary repair of the lid the patient was treated with topical steroids and antibiotics. The eyesettled with visual acuity of counting fingers. One month after the original injury an acute rise in intraocular pressure to 54 mm Hg was lowered medically by systemic corticosteroids. The 76 year old had had successful cataract surgery 1 week previously and was treated for rheumatoid arthritis for several years; however, neither had been on systemic immunosuppressive therapy.

In the absence of any abnormality in the anterior chamber or periphery, there was no sign of another perforation. In both patients' corneas, electron microscopy documented many electron dense amorphous deposits which included collagen fibrils (Fig 2; inset). These amorphous deposits were intimately associated with normal diameter collagen though, on examination with fluorescein and rose bengal confirm this (as assessed by detailed slit lamp examination with fluorescein and rose bengal staining, and by the Schirmer test). The 38 year old and 5 years (76 year old) after surgery, with no sign of another perforation.

At the time of surgery, corneal tissue directly adjacent to the paracentral perforation, as well as tissue in the peripheral cornea, was obtained for histopathological study. In line with the lack of clinically detectable inflammation (Fig 1), light microscopic examination of both cases revealed only a few inflammatory cells surrounding the perforation and none in more peripheral areas (data not shown). In both patients' corneas, electron microscopy documented many electron dense deposits in the extracellular stromal matrix (Fig 2). These amorphous deposits were intimately associated with collagen, and might represent degraded and/or aggregating collagen fibrils resulting from the melting process. Also detected were numerous atypical, thin fibrils (Fig 2; inset). These were fairly widely interspersed with normal diameter collagen though, on occasion, they appeared in groups. Interestingly, these abnormal electron microscopic features were observed not only in stroma right at the edge of the perforation, but in more peripheral regions of the cornea as well.

COMMENT

The general clinical presentations of both these individuals, especially the lack of inflammation, are similar to previous reports of perforated paracentral corneas. Often, infiltrating macrophages and T cells that are associated with HLA class II antigens are located around corneal ulcers, and various
cytokines and proteins secreted from these cells are thought to trigger a corneal perforation. However, this pathogenesis is unlikely in our cases because little or no inflammatory cell infiltration was detected.

As in all connective tissues, collagen imports to stroma by far the majority of its tensile strength. It follows that ultrastructural collagen alterations might cause our patients' corneas to become somewhat fragile, predisposing them to non-inflammatory corneal perforations. With this in mind, it is noteworthy that the alterations of the corneal extracellular matrix we report here closely resemble those seen in ruptured hand tendons of rheumatoid arthritis.

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Figure 2 Corneal stroma surrounding the perforated area (76 year old woman). Electron dense material (arrow), possibly aggregated collagen, is located throughout the extracellular matrix. Also (inset), many atypical, thin fibres (arrowheads) are interspersed with collagen. Bar=200 nm (main figure) and 100 nm (inset).

Table 1 Kinetics of anti-toxoplasmic IgG, IgM and IgA antibodies (months) from the first serological tests at the time of onset of cervical adenopathies

<table>
<thead>
<tr>
<th>Methods</th>
<th>IgG-Ab (MEIA)</th>
<th>IgG-Ab* (U/HSDA/ml)</th>
<th>IgM-Ab (MEIA)</th>
<th>IgM-Ab (ICT-M)*</th>
<th>IgA-Ab (ICT-A)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut off</td>
<td>3</td>
<td>10</td>
<td>ND</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>T 0 (onset of cervical adenopathies)</td>
<td>71</td>
<td>ND</td>
<td>9.9</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>T 0.5</td>
<td>855</td>
<td>ND</td>
<td>8.3</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>T 2</td>
<td>4030</td>
<td>ND</td>
<td>3.6</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>T 4</td>
<td>4200</td>
<td>ND</td>
<td>1.5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>T 8 (pregnancy contraindicated)</td>
<td>1820</td>
<td>6400</td>
<td>1.4</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>T 12</td>
<td>880</td>
<td>1200</td>
<td>1.0</td>
<td>10.5</td>
<td>10</td>
</tr>
<tr>
<td>T 15 (onset of chorioretinitis)</td>
<td>680</td>
<td>6400</td>
<td>1.1</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>

*Detection of IgG antibodies by high sensitivity direct agglutination (HSDA).
†Detection of IgM and IgA antibodies by immunocapture test with revelation by a tachyzoite suspension (ICT-M, ICT-A).


Overt chorioretinitis after patient acquired toxoplasmosis in an immunocompetent subject

EDITOR,—Acquired *Toxoplasma gondii* infection is usually asymptomatic and uncomplicated unless it occurs in severely immunodepressed patients or in particular epidemiological settings.1 2 We report a case of toxoplasmic chorioretinitis (CR) occurring 15 months after patent primary infection with cervical adenopathies in an immunocompetent woman.

CASE REPORT

VK, a 31 year old woman, presented with blurred vision in the left eye, which had started a few days previously. Visual acuity on this side was preserved at 16/20. Split lamp examination showed a negative Tyndall in the anterior chamber. Ocular pressure was 10 mm Hg. Retinal examination with the three mirror method revealed a fresh and strictly peripheral chorioretinal lesion at 10 o’clock, suggestive of toxoplasmosis, with no evidence of previous scarring. Peripapillar haemorrhage and a moderate vitreal reaction were also noted. The right eye was strictly normal. Two small cervical adenopathies could be felt.

Fifteen months previously this nulliparous woman had developed cervical adenopathies, with serum anti-toxoplasmic antibody kinetics typical of very recent seroconversion (Table 1).3 Specific IgA antibodies persisted 8 months after seroconversion and the woman, who wished to become pregnant, was referred to the Reims Toxoplasmosis Group to assess the risk of maternofetal transmission.4 5

Eight days after onset of the visual disorders the anterior chamber was sampled by puncture. Aqueous humour and peripheral blood were tested for toxoplasmic DNA by polymerase chain reaction (PCR) and/or blood culturing *T gondii* research, and for specific IgG, IgM, and IgA antibodies by immunocapture tests; the Witmer–Desmonts coefficient (C) was calculated.6 7 Serological tests for viral and other parasitic infections were also done, and her immune status was thoroughly investigated (Table 2). Anti-toxoplasma chemotherapy was started immediately, with a combination of pyrimethamine–sulphadiazine and calcium folinate for 1 month. The visual disorders improved and the chorioretinal lesion healed rapidly.

COMMENT

This case is unusual in that a chorioretinal toxoplasomic lesion occurred 15 months after seroconversion in a healthy adult.

The precise date of infection was deduced from clinical arguments and the results of biological tests. The first battery of serological tests, at the onset of cervical adenopathies (T0), was carried out because the patient was intending to have children. Eight months later the persistence of specific IgA antibodies pointed to active toxoplasmosis. As we had previously observed cases of congenital transmission after preconceptional seroconversion with adenopathies, the patient was advised not to become pregnant yet.8 9 This position was borne out by the onset of chorioretinitis some months later. The ocular involvement was confirmed by sampling the anterior chamber (positive Witmer–Desmonts coefficient, and focal synthesis of specific IgA) less than 8 days after the onset of visual disorders.

Ocular lesions were long considered to be a sometimes very late complication of congenital toxoplasmosis, except in case of immunodepression (human immunodeficiency virus, organ transplantation, etc).10 11 Our patient’s immune status was strictly normal; she was...
not on immunosuppressive drugs and had no intercurrent infections. The persistence of two small cervical adenopathies and specific IgA antibodies 15 months after the primary infection illustrates the long duration of the active phase of infection in this case complicated by secondary chorioretinitis. With a well-defined interval before onset, this case of chorioretinal involvement (isolated, unilateral, and without pre-existing lesions) differs from other reported cases in which the date of seroconversion was less precise and the chorioretinitis was often associated with neurological manifestations. This case of secondary toxoplasmonic chorioretinitis in an immunocompetent woman suggests that all patients with persistent adenopathies and serological markers of active *T. gondii* infection should have regular ocular monitoring.

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Table 2 Results of the different tests performed on serum and aqueous humour

<table>
<thead>
<tr>
<th>Blood/serum</th>
<th>Aqueous humour</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpesvirus, CMV, EBV, Lyme, <em>Larva migrans</em></td>
<td>Negative</td>
<td>No viral or other parasitic infection</td>
</tr>
<tr>
<td>HIV</td>
<td>Negative</td>
<td>HIV seronegative</td>
</tr>
<tr>
<td>Immunological examination and lymphocyte subpopulations</td>
<td>Normal</td>
<td>No immune deficiency</td>
</tr>
<tr>
<td><em>T. gondii</em> DNA</td>
<td>Positive with one probe</td>
<td>Doubtful result on aqueous humour</td>
</tr>
<tr>
<td>Total IgG g/l</td>
<td>12.8</td>
<td>Witmer-Desmonts coefficient: 4.6 (suggesting local IgG-Ab synthesis)</td>
</tr>
<tr>
<td>Anti-toxoplasmonic IgG (U/HSDA/ml)</td>
<td>6400</td>
<td>Presence of serum IgM-Ab; no intracellular IgM-Ab synthesis</td>
</tr>
<tr>
<td>Specific IgM (ICT-M)</td>
<td>11/12</td>
<td>Presence of serum IgM-Ab; no intracellular IgM-Ab synthesis</td>
</tr>
<tr>
<td>Specific IgA (ICFA)</td>
<td>10/12</td>
<td>Presence of serum IgA-Ab; no intracellular IgA-Ab synthesis</td>
</tr>
</tbody>
</table>

ND = not done.
laser (488–514.5 nm). This is due to the lower absorption within melanin of the longer diode laser wavelength. Hence there is potentially a greater risk of choroidal nerve damage from the diode laser, particularly with an excessively intense burn. The burn size associated with indirect laser tends to be larger than that achieved with direct laser, particularly if the working distance increases during PRP, thus causing thermal damage to a greater area of retina. Indeed, the post PRP fundus photographs of both patients show large burns tending towards confluence (Fig 2).

Diabetics with and without retinopathy have significantly increased epithelial fragility when compared with normal controls. Diabetics also have reduced corneal sensitivity when compared with normal controls. However, before laser treatment, neither of our two patients had ever had any symptoms or signs of corneal disease. All the corneal problems started post laser and were associated with a total lack of corneal sensation. As the corneal sensation recovered over the months the frequency of the epithelial erosions diminished.

The optics of the diode laser beam mean that it is possible to clip the edges of the iris in the laser beam during treatment. It is possible that this could account for some of the pupillary abnormalities post PRP, but taking into account the corneal anaesthesia and reduced accommodation, it would seem more likely to be a result of damage to a common denominator.

We hypothesise that the large area involved in performing an indirect PRP, and the depth of the burn achieved with diode laser, damaged a large number of choroidal nerves causing the pupillary and corneal abnormalities.

We propose the following measures to avoid choroidal nerve damage when performing indirect diode laser PRP. Grade 1 to 2 burns should be discreetly placed so as to prevent confluence certainly avoiding high intensity grade 3 burns. Under peribulbar and general anaesthesia, it is particularly important to use less intense burns as the painful feedback from choroidal nerve damage is absent. Care should be taken with the working distance of the laser indirect to avoid unduly large burns. Particular caution should be exercised when treating in the horizontal retinal meridia, the typical location of the long ciliary nerves. Finally, the patient should be warned of possible effects on the anterior segment which may occur after indirect diode laser PRP.

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