LETTERS TO THE EDITOR

Relapses of CMV retinitis after 2 years of highly active antiretroviral therapy

EDITOR,—Highly active antiretroviral therapy (HAART) can reduce HIV replication and increase the CD4+ cell count.1 Some cytomegalovirus (CMV) disease relapses have been described within the first 3 months of HAART.2 However, after this critical phase, quiescent retinitis and an unusually prolonged relapse free interval suggest restoration of immune functions. Maintenance therapy can be discontinued for the majority of HAART responders.3 The duration of CMV disease remission is actually unknown.

CASE REPORTS

A 29 year old, HIV infected woman was affected by CMV retinitis in the left eye in August 1996. Her CD4+ T lymphocyte count was 15 cells ×10^3 at that time. CMV retinitis was treated with intravenous foscarnet. HAART was initiated in June 1996 (d4T, 3TC, and ritonavir). In June 1997, her CD4+ cell count increased to 400 cells ×10^3 and the HIV viral load became undetectable. CMV maintenance therapy was discontinued in December 1997 without any relapse until May 1999 when a relapse of CMV retinitis, associated with inferior retinal detachment, was noted. At that time, her CD4+ cell count was 380 cells ×10^3, CMV viremia was negative, but HIV viral load had increased to 31 000 copies/mL. The lymphoproliferative test against CMV antigens was negative. The patient was treated with intravenous ganciclovir and vitrectomy surgery was performed. CMV DNA was found in the vitreous by polymerase chain reaction.

A 69 year old HIV infected man was referred to our department in November 1996 for bilateral CMV retinitis. CD4+ T lymphocyte count was 35 cells ×10^3 at onset. Retinitis was treated with intravenous foscarnet. HAART (3TC, d4T, nevirapine) was initiated in September 1997. For 2 years, the HIV-1 viral load remained undetectable, and CD4+ cell count rose to 120 cells ×10^3. In October 1998, the HIV viral load started to increase, reaching 6100 copies/mL. In May 1999, a relapse of CMV retinitis was diagnosed and treated successfully with intravitreal ganciclovir injections. At that time, the HIV viral load rose to 22 000 copies/mL, and CD4+ cell count was 180 cells ×10^3. The lymphoproliferative test against CMV antigens was negative. CMV viremia and pp65 antigenemia always remained negative.

COMMENT

Several studies suggest that selected patients with healed CMV retinitis who have both immunological and virological response to HAART can temporarily discontinue maintenance therapy.4 In our patients on HAART, CMV retinitis was quiet for months, as long as the HIV-1 replication remained under control. CMV relapses occurred when the viral load started to increase even though the CD4+ T lymphocyte count remained stable (mean 280 cells ×10^3). Autran et al have studied in two lymphocyte proliferators to specific antigens such as CMV and reported positive effects of HAART on CD4+ T cell functions.5 The CD4+ T cell reactivity to recall antigens that restore a certain immune competence is linked to the control of HIV replication.6 For our patients, the T cell reactivity to CMV antigens was negative. These immunological tests are not routinely performed and their usefulness in predicting CMV diseases is not established. Casado et al showed that a positive CMV polymerase chain reaction test is the most predictive test associated with the development of CMV diseases.7 In a prospective multicentre study, Mazeron et al showed that HIV viral load is a predictive marker, independent of the CD4+ cell count.8 Our findings suggest that an increase in the HIV viral load increases the risk of CMV retinitis relapse despite a high CD4+ T lymphocyte count.

Our case report emphasises the importance of close ophthalmological follow up in patients on HAART when the HIV-1 viral load starts to increase despite a CD4 T lymphocyte count of over 100 cells ×10^3.

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Figure 1 Large lower lid/cheek tumour visible on left side. Note blue discoloration and small area tethering to skin.
Red-blue or blue discoloration of the skin is a more typical feature of pilomatrixoma and should help to differentiate it from inclusion and dermoid cysts which are the most common misdiagnoses. Inclusion cysts have a diffuse yellow colour when filled with keratin and are more likely to be softer and more fluctuant than pilomatrixoma. They are also rarer in children than in adults. The skin over dermoid cysts looks normal and can be moved freely over the lesions. Capillary haemangiomas that arise in the subcutaneous tissue without involving the skin can have a blue-purple colour similar to pilomatrixoma but that lesion tends to be soft and compressible on palpation and growth is much faster than pilomatrixoma. A chalazion can become inflamed but does not show the red-blue discoloration of pilomatrixoma. Rhabdomyosarcoma is the most common orbital malignancy of childhood that can become inflamed but does not show the red-blue discoloration of pilomatrixoma. A chalazion can have a blue or red-blue discoloration. The disorder has an AR inheritance and is caused by an impaired fibrinolysis related to deficient plasminogen type I. Recently causative mutations in the plasminogen gene have been identified in affected patients. Pathological findings disclose fibrin as the major component within amorphous hyaline-like eosinophilic material, fibrilloglobular proliferation, inflammatory cellular infiltration, and acid mucopolysaccharides.

The treatment of the disorder has generally been unsuccessful, although spontaneous resolution may occur. Excision of the membrane (with cryocoagulation and/or autologous conjunctival graft or scleral graft) often worsens the conjunctivitis within a few days after surgery. Treatment strategies that act on the different constituents found in the ligneous membrane have been proposed; topical proteolytic enzymes (hyaluronidase and chymotrypsin),1 fibrinolytic drops that cause fibrinolysis,2 and topical anti-inflammatory agents (corticosteroids and cyclosporin).3

In 1995 De Cock et al. suggested the administration of topical heparin (antifibrin action) in combination with the above agents. The authors reported efficacy of their treatment although it was not consistent in all patients.

**CASE REPORT**

In an early report we discussed a boy who underwent eight consecutive unsuccessful excisions of a ligneous conjunctival membrane between August 1997 and February 1999.4 Surgery was combined with topical medications—chymotrypsin, hyaluronidase, dexamethasone, and heparin.


**Letters**
Research on type I plasminogen deficiency conducted by Schuster et al disclosed in our patient a decreased plasminogen activity (36% of normal activity) and a causative mutation in the plasminogen gene.

On 12 March 1999 we performed another excision of the recurrent membrane and we applied mitomycin C for 3 minutes followed by an amniotic membrane graft. Adjuvant medical treatment consisted of the administration of systemic prednisone 1 mg/kg/day and topical heparin for 14 days. This treatment was successful (Fig 1) and since then the membrane has not recurred.

On ocular follow up examination we observed the formation of complicated SCP cataract.

On 27 January 2000 we performed a lensectomy with insertion of a PC-IOL and peroperatively we injected 25 µg tissue plasminogen activator (r-tPA) intracameraly, to prevent fibrinous effusion. During the first postsurgical week, slit lamp examinations showed the absence of reaction in the anterior chamber. The child was discharged from hospital on day 7. On control examination (day 9) slit lamp examination revealed multiple fibrin strands emerging from the pupil towards the cornea over 360° (Fig 2). The child was again admitted and received a protective shell to prevent eye robbing. This measure was followed by the disappearance of fibrin after 1 day. The PC-IOL restored the visual acuity.

COMMENT
Up to now strategies that have been proposed for the treatment of conjunctivitis ligneosa act on different aspects in the cascade of wound healing. We added two agents, mitomycin C and r-tPA, that had not yet been applied for this indication.

Mitomycin C is an antiproliferative drug that prevents the development of scar tissue and is widely used in ocular surgery. We propose to use mitomycin C in combination with heparin and corticosteroids in the treatment of ligneous conjunctivitis.

If intraocular surgery is needed in affected patients, we suggest using intracameral re-combinant tissue plasminogen activator in order to stimulate fibrinolysis. The intracameral injection of 25 µg r-tPA has proved to be efficient and safe in the treatment of severe postoperative fibrinous reactions.

Until causative treatment with pharmacological plasminogen is possible we believe that mitomycin C and r-tPA may be useful adjuvant agents respectively in conjunctival and intraocular surgery in patients with ligneous conjunctivitis.

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Annular granular corneal opacity: a rare corneal stromal dystrophy or degeneration?

EDITOR,—Very rare, subtle conditions of the cornea may be infrequently reported but can provide valuable insights into the workings and diseases of the cornea. We report an unusual appearance of corneal rings in an asymptomatic patient with no similar abnormalities detected in first degree relatives.

CASE REPORT
A 56 year old white female emmetrope (20/20 both eyes) presented with photopsia second-
However, in the two other cases, wedge-shaped ring opacities, most dense over Descemet’s membrane are described, a feature common to those we observed. The ages of the patients in these reports range from 25 to 80 and all investigations, sometimes exhaustive, were unremarkable. Where family members were examined, none demonstrated similar features and where patients were followed up (2–9 years), appearances remained stable. However, in one report, the rings were not observed during a ophthalmic examination 14 years previously, suggesting that they are not congenital in origin.

Another report of a unilateral, off-white, anterior, mid-peripheral ring is of note because the patient was found to have elevated serum cholesterol. However, the opacity may have been a unilateral arcus.

Of the six bilateral cases reported, only two described a wedge-shaped corneal opacity in cross section and predominantly in the posterior stroma and closely resemble our case. With so few cases reported, over a wide range of ages, and without affected family members it is unclear whether the condition should be described as a dystrophy or a degeneration. It is important to report such rarities, so that further correspondence and reporting is encouraged which may help to lend insights into causes of more serious corneal abnormalities.

**Comments**

**Idiopathic tractional corectopia**

**Editor:**—Congenital abnormalities of the pupil periphery are uncommon. Slit lamp examination will usually identify which of the various rare anterior segment developmental anomalies has caused the pupil appearance. Possible associations include iris coloboma, Axenfeld-Reiger anomaly, ectopia lentis et pupillae, persistent pupillary membrane, and hyperplastic pupillary membrane. Surgical intervention for the pupil abnormality is not normally required.

Idiopathic tractional corectopia is an isolated unilateral congenital pupil abnormality with a highly characteristic appearance (Fig 1). The four previously reported cases required no intervention or responded well to simple lysis of the fibrous strand that is characteristic of the case.

We report a fifth case, where progression of the tractional process led to failure of initially stable lesions. Conservative management of a surgical pupilloplasty was required as no benefit was obtained by cutting the fibrous strand.

**Case Report**

A healthy male child was referred to the ophthalmology department soon after birth with a unilateral misshapen eccentric pupil. There was no family ocular history. At initial examination he was found to have right corectopia with an oblique oval pupil and a fibrous band extending from the pupil margin to the corneal surface that superficially resembled an incomplete corneal scar: normal: hypoplasia, pterygia, retroillumination defects, or ectropion uvea were not present. The corneal diameter and intraocular pressure were normal. A pupil opening was not possible without the injection of collagen and limited view of the ocular fundus. The pupil did not dilate with topical mydriatic. Examination of the left eye was unremarkable. Ultrasound of the eyes was normal.

Over the next 5 months the pupil in the right eye became smaller and more eccentric. Occlusion therapy was commenced but the right eye became visually unresponsive. The pupil could be seen to offer no optical pathway by this stage (Fig 1). At surgery the fibrous band was cut with intraocular scissors but there was no effect on pupil morphology. Further attempts to mobilise the pupil threatened to disinsert the iris root superonasally. Therefore a central pupil was created by small multiple iris sphincter incisions. Postoperatively the eye settled well and without complication. At 6 months postoperatively the vision in the right eye had improved to 6/24 with aggressive occlusion therapy.

**Comment**

Early reports of isolated corectopia are not particularly useful owing to inadequate examination techniques and equipment. Isolated corectopia was considered by Duke-Elder to be a bilateral condition.

Scott Atkinson et al reported four children with isolated unilateral corectopia, resulting from a white band that extended from the pupil margin to insert in a circumferential condensation of tissue on the endothelial surface of the peripheral cornea that superficially resembled an incomplete corneal scar. The condition was named “idiopathic tractional corectopia” (ITC). The pupil displacement may progress during the first months of life, possibly by further contraction of the fibrous band. The origin of the band is unknown.

Children with ITC need to be monitored closely by monocular vision testing as they are at risk of amblyopia. Prompt laser or surgery may be indicated if vision reduces because of optical pupil occlusion.

**References**

has been described as an alternative to vitrectomy. Ulbig et al recently reported the results of a series of premacular subhyaloid haemorrhages treated with pulsed Nd:YAG laser. Nevertheless, this procedure is not without complications. They reported one case of macular hole formation and one case of retinal detachment after the procedure.

We feel that premacular subhyaloid or sub-ILM haemorrhage caused by factors other than diabetic retinopathy may be managed conservatively in the first few months. Our case demonstrates that a good visual outcome can be achieved with conservative management.

COMMENT

As far as we know, there have been two previously reported cases of subhyaloid or sub-ILM haemorrhage associated with bacterial meningitis. The exact mechanism of this haemorrhagic response is not fully understood. Valsalva retinopathy has been suggested. Coughing and vomiting cause a rapid rise in intravenous pressure within the eyes. This can cause spontaneous rupture of superficial retinal capillaries.

Elevation of intracranial pressure is a potential complication of meningooccal meningitis. A sudden increase in intracranial pressure can rupture the epipipillary and peripipillary capillaries, known as Terson’s syndrome. In this case, lumbar puncture was clinically contraindicated, but raised intracranial pressure may have occurred.

Clotting disorders have been reported to cause sub-ILM haemorrhage. The mild prolongation of the prothrombin time in this patient could be due to the consumption of coagulation factors as a result of the release of bacterial endotoxin. This mild clotting defect may have caused the preretinal haemorrhage in this case.

Spontaneous resorption of subhyaloid or sub-ILM haemorrhage caused by Valsalva retinopathy usually occurs without sequel. Fur’s plana vitreectomy has been recommended for dense preretinal haemorrhage resulting from diabetic retinopathy, as spontaneous resorption is usually prolonged in these patients. Laser puncturing of the posterior hyaloid face or the internal limiting membrane

Figure 1 Right fundus photograph showing a round, cell circumscribed, dome-shaped haemorrhage overlying the posterior pole.

Figure 2 Fluorescein fundus angiography at 16 weeks showing the clearance of the haemorrhage with residual inferior rim of haemorrhage outlining the detached internal limiting membrane.

Figure 1 Right fundus photograph showing a round, cell circumscribed, dome-shaped haemorrhage overlying the posterior pole.

Figure 2 Fluorescein fundus angiography at 16 weeks showing the clearance of the haemorrhage with residual inferior rim of haemorrhage outlining the detached internal limiting membrane.

Reversal and converse ocular bobbing with synkinetic blinking and opcosolus in a child with Epstein-Barr virus encephalitis after bone marrow transplant for MPS I

Editor,—Reverse ocular bobbing is an abnor-

mous spontaneous eye movement in which the eyes move rapidly in opposite directions (fast phase), followed by a slow drift (slow phase) back to the primary position (that is, the reverse of ocular bobbing—fast conjugate downwards deviation, with a slow return up to the midline). This eye movement disorder may be seen in patients with viral encephalitis, metabolic encephalopathy, and in those with pontine lesions. Converse ocular bobbing (also referred to as reverse ocular dipping or slow upward bobbing) consists of a slow phase upwards, followed by a fast phase back to the primary position, and has also been reported in patients with viral or metabolic encephalopathy, and in those with pontine infarction. Opsoclonus, also referred to as “saccadomania” or “dancing eyes”, is characterised by intermittent bursts of large amplitude high velocity multidirectional back to back saccades, and has also been reported in patients with viral encephalitis and metabolic encephalopathy, as well as in those with occult neuroblastoma and myoclonic jerks.

When these back to back saccades occur purely horizontally, they are known as “ocular flutter” and can be a stage of resolving opcosolus. We report a case of converse ocular bobbing, reverse ocular bobbing with synkinetic blinking, opcosolus, and ocular flutter occurring in a patient with Epstein–Barr viral encephalitis.

CASE REPORT

A 2½ year old female with a delayed diagnosis of mucopolysaccharidosis type 1 (MPS I) underwent a bone marrow transplant (BMT). Preoperative assessment revealed hearing loss of 60–65 dB, marked ventricular dilatation, but without evidence of raised intracranial pressure. Her visual acuity was recorded as being 6/24 using Cardiff acuity cards, but it was felt that the vision may be better than this as the child was uncooperative during vision testing. She had moderate corneal haze on her retina and optic discs appeared normal. BMT preparative chemotherapy consisted of fludarabine/melphalan/antilymphocyte globulin, and the patient received an HLA matched unrelated donor bone marrow infusion, with additional graft versus host disease prophylaxis consisting of cyclosporin and methyl prednisolone. Fourteen days post-BMT, the neutrophil count had recovered (the BMT preparative chemotherapy regimen induces a febrile neutropenia in these children, which typically recovers at 2–3 weeks post BMT), but the patient remained febrile on broad spectrum antibiotics and antifungal agents. Twenty nine days post-BMT, she became irritable, her pyrexia persisted, and her upper limbs became hypertonic. Her conscious level then deteriorated and computed tomograph (CT) scan revealed acute hydrocephalus with large ventricles and an emergency external ventricular drain was inserted. Epstein–Barr virus (EBV) was detected in the cerebrospinal fluid by polymerase chain reaction (PCR), EEG showed generalised slowing with occasional sharp waves, and magnetic resonance imaging with gadolinium revealed extensive abnormal signals in the cerebral white matter. A diagnosis of EBV encephalitis was made. The patient was commenced on phenytoin in case there was being underlying seizure activity. On examination of her eyes at that time, she was not fixing or following and had developed abnormally eye movements, which consisted of converse ocular bobbing in the initial phase (that is, slow phase up/fast phase down, see above). Each upward slow phase was accompanied by a blink. On observation 2 days later she had developed reverse ocular bobbing (slow phase up/fast phase down) as opposed to converse bobbing. The upward fast phase was accompanied by a blink which she seemed to be attempting to overcome with her frontalis muscle which was overacting in synchrony with the blinks. A repeat CT scan demonstrated resolving hydrocephalus and persistent cerebral oedema. Repeat lumbar puncture revealed decreasing EBV titres (as measured using quantitative PCR), which eventually became negative. There was a subsequent improvement in her condition, and her parents had noticed much less eye movement activity. However, on examination she was still demonstrating intermittent episodes of re-
verse ocular bobbing with synkinetic blinking, and now intermittent bursts of both opsonolus and ocular flutter.

COMMENT
Ocular bobbing, dipping (also referred to as reverse bobbing)—slow downward movement, followed by a fast upward movement to the primary position), and reverse bobbing have been reported on different occasions in the same patient, as have opsonolus and ocular bobbing. Synchronism of inverse ocular bobbing (slow phase down/fast up) and blinking has been reported in a 7 year old female with severe cerebral trauma; the rapid phase of the eye movement was synchronous with phasic contraction of the orbiculans orbis.

The above case of reverse and converse ocular bobbing with synchronous blinking, together with the later development of opsonolus and ocular flutter in a child with viral encephalitis is the first such combination of eye movement disorders to be reported in one individual. The abnormal eye movements in this child may be a result of her encephalitis, congenital myasthenoidus, or the treatment she received. It is difficult to determine which phenomenon or combination is responsible. When such abnormal eye movements occur either together or in isolation, viral encephalitis should be considered.

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Retinорhinехis in macular translocation

EDITOR.—Age related macular degeneration is one of the leading reasons for legal blindness in the western world. Most therapeutic strategies, however, have so far been unsuccessful in restoring vision for the majority of patients. Recently, Robert Machemer suggested translocating the macula on healthy retinal pigment epithelium, outside the originally central region of the fundus. The method includes a circumferential peripheral retinotomy to mobilise the retina. The retinotomy has usually been performed by cutting the retina close to the ora serrata using scissors or the vitreotomy instrument. Using scissors can lead to complications since the underlying Bruch’s membrane and the uvea can be injured. Using the vitrectomy instrument for cutting the retina leads to a loss of retinal tissue since the vitreotomy instrument works by a combined action of suction and cutting. The purpose of this study was to report on an alternative technique for circumferentially mobilising the retina.

CASE REPORT
A 87 year old woman presented with long-standing rhegmatogenous retinal detachment with proliferative vitreoretinopathy, and an additional age related macular degeneration with a 2 mm by 3 mm large disciform subfoveal membrane. A three port pars plana vitrectomy was performed. After removal of epiretinal membranes and after pars plana phakoemulsification, the detached peripheral retina was grasped with a microforceps, and by gentle and repeated traction, the inner layer of the pars plana epithelium was separated from the outer layer of the pars plana epithelium. Additionally, a tear was produced between the inner pars plana epithelium and the non-pigmented epithelium of the pars plicata. By regrasping and changing the position of the microforceps, the peripheral retina with the pars plana epithelium was attached was circumferentially separated from the inner surface of the eye wall. Further surgical steps included retinal rotation, temporary injection of perfluorcarbon liquid, or to be replaced by silicone oil, and circumferential peripheral endolaser coagulation. The same procedure with peripheral retinorhexis was performed in the next patient aged 75 years and undergoing pars plana vitrectomy for macular rotation as treatment of age related macular degeneration.

COMMENT
One of the major complications of macular translocation for the treatment of age related macular degeneration is the development of proliferative vitreoretinopathy. Some of the reasons are the incision into the retina and the temporary detachment of the retina. Since the risk of proliferative vitreoretinopathy depends on the size of a retinal defect and on the area of exposed retinal pigment epithelium, one tries to perform the circumferential retinal incision with the least possible retinal detachment and least possible loss of retinal tissue. It may be accomplished by a retinorhexis using the technique described here. Retinal tissue is not lost since the tear in the tissue is located in the epithelium of the pars plana peripheral to the ora serrata. Consequently, retinal pigment epithelium is not, or only slightly, exposed. It may reduce the risk of postoperative proliferative vitreoretinopathy.

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The clinical diagnosis of ARN was supported by a rapid increase in the area of retinal whitening over the next 2 days and confirmed by stabilisation in response to intravenous aciclovir treatment. Flurbiprofen 100 mg three times per day did not control her pain, and in view of optic disc swelling prednisolone 80 mg per day was prescribed together with dexamethasone 0.1% four times per day and cyclopentolate 1% twice per day. Betagan 0.5% twice per day was successful in controlling the intraocular pressure.

Three days after starting intravenous aciclovir the area of affected retina stabilised at about 5 disc diameters and argon laser was applied to wall of the area of necrotic retina from the posterior pole. The disc became gradually less swollen and increased vitreous activity dropped vision to 6/24. The dose of prednisolone was reduced slowly as the vitritis cleared. Final vision was 6/12 being limited by an epiretinal membrane.

**COMMENT**

Pain, redness and, sometimes, even scleritis may accompany ARN early in its course which should always be considered when these signs are present. The diagnosis of ARN is clinically defined as one or more areas of retinal necrosis with discrete borders primarily located in peripheral retina, rapid circumferential progression, occlusive vasculopathy with arteriolar involvement, and inflammatory reaction in vitreous and anterior chamber. The one other disease that can have scleritis, high IOP, and retinitis is toxoplasmosis. Although polymerase chain reaction (PCR) for herpes and toxoplasma can distinguish the two, ARN was diagnosed clinically in view of the rapidity of advancement, rendering PCR unnecessary.

Although herpes viruses may become active simultaneously in more than one site, the anterior scleritis was probably a local response to ARN.

ARN should be considered in patients with raised intraocular pressure and scleritis because useful vision can be maintained with prompt treatment.

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