Cystoid macular oedema in patients with AIDS and cytomegalovirus retinitis on highly active antiretroviral therapy

EDITOR.—Between 16% and 40% of patients with AIDS develop cytomegalovirus retinitis (CMVR). 1,2 This typically presents when the CD4+ count drops below 75 cells/µl. Visual loss is usually due to retinal detachment, macular or optic nerve infection, or vascular occlusion. Typically a minimal inflammatory response is mounted. Patients with CMVR not associated with HIV infection may develop a vitritis with cystoid macular oedema (CMO) during immune restoration.1

With the advent of highly active antiretroviral therapy (HAART) patients with AIDS are enjoying improvement in their immune status, with falling HIV viral loads and rising CD4+ counts. Such patients may mount a significant inflammatory response against CMVR, causing a regression of the CMV infection but a paradoxical visual loss due to the inflammation. We describe two such patients with CMVR and vitritis, who lost vision as a result of CMO.

CASE REPORTS

Patient 1 was diagnosed with zone 2 CMVR affecting the left eye in May 1996. He was induced on intravenous ganciclovir 5 mg/kg twice daily for 2 weeks and maintained on intravenous ganciclovir 5 mg/kg once daily for 5 months until progression of CMVR occurred. He was then induced on intravenous cidofovir 5 mg/kg/week followed by intravenous cidofovir 5 mg/kg twice a month maintenance. At the same time he was started on HAART therapy consisting of D4T, 3TC, and indinivir. There was a rapid resolution of active CMVR with a rise in CD4+ count and a fall in the HIV viral load (Fig 1). However, 2 months later his vision dropped to from 6/12 to 6/24 and vitritis, optic nerve swelling, and CMO were noted (Figs 2 and 3). Vision in the right eye was maintained with no sign of CMVR.

Patient 2 was diagnosed with zone 2 CMVR affecting the right eye in October 1996 (Fig 4). He was induced on intravenous ganciclovir 5 mg/kg twice daily for 2 weeks followed by maintenance on ganciclovir by mouth 3 g/day for 4 months until progression of the CMVR occurred into zone 1 in the right eye and zone 3 in the left eye. He was treated with bilateral ganciclovir implants with no systemic cover. Treatment of HIV with AZT and 3TC was continued. Immune recovery followed the successful treatment of pulmonary tuberculosis. In May 1997 his CD4+ count had risen to 250/µl with a low HIV viral load. Vision in the right eye fell from 6/9 to 6/24 due to macular oedema and mild vitritis. Treatment with topical prednisolone four times daily and with acetazolamide 250 mg twice daily, produced a sustained two line improvement in visual acuity (Figs 5 and 6). Vision in the left eye was maintained at 6/5 with stable zone 3 disease and no CMO.

COMMENT

The picture of CMV retinitis is changing with the advent of effective retroviral therapy. CMVR has recently been diagnosed in patients with relatively high CD4+ counts (197–270/µl) following the initiation of HAART. A syndrome of macular serous exudation has recently been described, and there are reports of iritis in patients with intra-ocular cidofovir. However, only a few cases with CMO have been described.1,2

Both patients in this study developed macular oedema. In patient 2 use of a ganciclovir implant may have contributed to macular leakage. However, in both patients only the eye with extensive disease developed CMO.

Further analysis of the rate of immune recovery, viral load levels, and other immune markers may help to predict which eyes may become affected by CMO.

The question of treatment causes a dilemma. The systemic use of immunosuppressive agents may be contraindicated; however, the use of topical or sub-Tenon’s steroid may have some benefit. One of our patients benefited from acetazolamide 250 mg twice daily, although the side effects when combined with antiviral drugs made this treatment unsustainable. Others have used NSAIDS topically and systemically with some effect.

Cystoid macular oedema in HIV+ patients with CMVR retinitis may represent a healing phase of the disease, which sadly still causes visual loss and presents physicians and immunologists with new clinical challenges.

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Figure 1 Progression of CMVR in the left eye of patient 1 (right eye unaffected). HAART therapy was started at month 6 and macular oedema with reduced vision was noted by month 8. CMVR activity was suppressed from month 6. CMO = cystoid macular oedema, VA = visual acuity. Shaded area indicates: CMVR activity. CMVR treatment, or the presence of CMO.

Figure 2 Fundus photograph of patient 1 showing vitritis and a swollen disc.

Figure 3 Fundus fluorescein angiogram of patient 1 demonstrating macular oedema with optic disc leakage.
Acicardi syndrome

EDITOR,—Acicardi syndrome is a congenital disorder characterised by severe epilepsy, agenesis of the corpus callosum, typical chorioretinal lacunae, and learning disabilities. Normally it carries a poor prognosis. We present a case in which these symptoms have been found in a 49 year old woman, suggesting a “forme fruste” of the disorder.

CASE REPORT

A 49 year old woman previously thought to have cerebral and retinal toxoplasmosis was referred because of visual deterioration, poor balance, and obvious visual field restriction. On examination her corrected visual acuity was right 0.2 (6/9.5) and left 0.8 (6/38). The discs and smaller rounded pale yellow areas of pigmentation around the fovea. (A) Right eye showing large rounded chorioretinal defect and hypoplastic disc with marginal pigmentation. (B) Left eye, showing colobomatous hypoplastic disc and smaller typical chorioretinal lacunae (arrowed). There are three areas of pigmentation around the fovea.

Figure 1

Figure 2

COMMENT

Acicardi syndrome is thought to be an X linked dominant disorder.1 Females are exclusively affected, the disorder being lethal in males. There is heterogeneity of clinical severity. Most patients have severe learning disability, intractable epilepsy, agenesis of the corpus callosum, and reduced life expectancy. However, recently a 10 year old girl has been described with a mild form of the disorder.2

Previous necropsy studies on the chorioretinal lacunae have shown focal thinning and atrophy of the retinal pigment epithelium and choroid.3 We suggest that the pigmented para macular lesions seen in our case may have been caused by choroidal new vessels penetrating a break in Bruch’s membrane, as has been described in choroideremia, Best’s disease, and rubella retinopathy.4

The fundal appearances are atypical of chorioretinitis due to toxoplasmosis and there is no intracranial calcification to support that diagnosis.

Our case suggests that there may be a wide spectrum of Acicardi syndrome. She is not severely mentally disabled and her epilepsy has been well controlled. However, she does have the typical chorioretinal lacunae present from childhood, and dysgenesis of the corpus callosum. The striking feature is that she was diagnosed in middle age, providing further evidence that a mild form of the disease does exist.5

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Paucity of signs in X linked ocular albinism with a 700 kb deletion spanning the OAI gene

EDITOR,—X linked ocular albinism (XLOA) shows great variability in clinical expression between affected males as well as in heterozygote females, even within one sibship.1 So far, we have found mutations in the OAI gene in only 15% of the X linked ocular albinism patients (unpublished). Also Schiaffino et al2 revealed mutations in only one third of XLOA patients. Here, we report normal 46XX karyotype. Radiology reveals no evidence of costovertebral abnormality.


5 Garano RF, Cooney EL. Uveitis following administration of the cytotoxic inhibitor indinavir to a patient with AIDS. Clin Infect Dis 1997; 24:529.

on the clinical features of a person with XLOA in which the entire OA1 gene was missing due to a submicroscopic interstitial deletion in the distal short arm of the X chromosome. The detailed molecular findings were published elsewhere. 1 As Winship et al. 2 suggested that XLOA and late onset (fourth and fifth decades) sensorineural deafness are allelic variants, or that both entities may be due to contiguous gene defects, we examined our patient for hearing loss.

CASE REPORT
A man, born in 1956, was seen at our department for genetic counselling because of XLOA. Genealogical examination could not reveal consanguinity or a link with other families with XLOA. He had dark blond hair, moles and freckles, and tanned with difficulty. Visual acuity on the right eye was 20/80 with S +3.5 C −4.25 10 −6 and on the left eye 20/80 with S + 3.75 C −4.75 0. On ophthalmic examination we found congenital pendular horizontal nystagmus, iris transillumination and absent macular reflexes, and an albinotic fundus periphery. Visual evoked potentials showed abnormal neuronal crossing at the optic chiasma, as in albinism. Macromelanocytes were visible by electron microscopy in a skin biopsy taken from the forearm.

A neurological test set revealed no anosmia or hyposmia, nor could we find kidney abnormalities or hormonal disturbances as in Kallmann syndrome. Audiograms in 1996 showed normal results. In addition, our case was examined because he complained of fertility problems. In this examination only a reduced number of spermatozoa were found (22.5 × 107/milliliter). Molecular genetic investigation revealed a deletion of 700 kb in the Xp22.2 region of the X chromosome. All nine exons of the OA1 gene were tested in the DNA of our case and were found to be deleted. 3

COMMENT
The ophthalmic features of this case are comparable with those of the affected males described by Charles et al. 4 and van Dorp. 5 The albinism in patients described by these authors is most probably caused by a variety of distinct mutations in the OA1 gene. Clinical variability between families may be due to different OA1 mutations in male patients, but can also be accounted for by other genetic factors, such as preferential X inactivation in female carriers. Variation in clinical expression within one sibship is probably not caused by different mutations but by environmental factors or modifying genes.

Since the molecular defect in our case spans the entire OA1 gene we expected relatively severe clinical or functional abnormalities. However, only relatively ‘mild’ XLOA symptoms were found.

The audiograms in our patient showed normal patterns indicating that a separate gene for sensorineural deafness may exist in the genomic vicinity of the OA1 gene but outside the DNA deletion in our case. The fact that we found mutations in only 15% of the XLOA patients may indicate that either the OA1 gene has not been cloned in its entirety, or that a separate, closely linked and as yet not discovered albinism gene exists in the distal part of the X chromosome.

In conclusion, our case, with this 700 kb deletion, showed the mild and classic form of XLOA, in addition to infertility. It is as yet uncertain if this infertility was due to a genetic factor.

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Intracranial plasmacytoma masquerading as Gradengo’s syndrome

EDITOR,—Maini and MacEwen recently published a report in the BJO of intrabulbar optic nerve compression secondary to an intracranial plasmacytoma. Although rare, extradural plasmacytomas usually present in the head and neck region, and with improved methods of intracranial imaging, it is likely that more of these tumours will be detected at an early stage by the ophthalmologist. Here, we report a similar case of intracranial plasmacytoma but presenting as a rare disorder of ocular motility normally associated with middle ear infection.

CASE REPORT
A 45 year old man presented to his general practitioner with a sudden onset of horizontal diplopia after blowing his nose vigorously. He was noted to have a mild pyrexia, left frontal sinus pain, and left sided otaiga but was otherwise well. Two years earlier the patient had been diagnosed as having myeloma following the detection of serum and urinary paraproteins in association with lytic lesions of the sternum and femur. At that time he received total body irradiation and a peripheral blood stem cell transplant. Subsequently, the paraproteinaemia and symptoms regressed and the patient was considered to be in remission.

He was referred immediately for an ophthalmological opinion with a provisional diagnosis of middle ear infection. Orthoptic assessment revealed a moderate left esotropia for near (20 prism dioptries) and distance (16 prism dioptries) and a diagnosis of incomplete left lateral rectus palsy was confirmed by a Hess chart examination. Examination was otherwise unremarkable: visual acuity was normal and no afferent pupillary defect or papilloedema could be detected. Close follow up was organised in conjunction with the haematology department, but the following week he re-presented with left sided trigeminal neuralgia, left sided deafness, and dysarthria. Neurological examination suggested involvement of the left V, VI, VIII, X, and XII cranial nerves. A computed tomogram (Fig 1) showed a lytic lesion at the apex of the petrous temporal bone, and subsequent magnetic resonance imaging confirmed the presence of an intracranial lesion extending caudally from the left middle cranial fossa to involve the affected cranial nerves (Fig 2).

The lesion was diagnosed as an extradural plasmacytoma and the patient underwent posterior fossa radiotherapy. He fortunately made a rapid improvement, but still had a slight residual diplopia which allowed by a prismatic correction. There was no evidence of relapse of his myeloma.

COMMENT
In 1904 Gradengo described a syndrome of sixth nerve palsy with pain in the distribution of the upper divisions of the trigeminal nerve caused by otitis media and mastoiditis in the region of the apex of the petrous temporal bone. He complained of sudden horizontal diplopia on eye movements. In 1930 Gradengo’s case was reported by McLeod and his patient had similar symptoms. He also noted pain radiation to the face but no cranial nerve palsies. Clinically the case can be described as a ‘true’ Gradengo’s syndrome.

Another case report was published by Lessi in 1944. He described a 31 year old man with a probable Gradengo’s syndrome. The patient had a right facial nerve palsy with pain on eye movements. The pain also radiated to the eye but no other cranial nerve palsies were noted.

We describe a case of a 45 year old man with a similar clinical presentation to Gradengo’s syndrome which led to the diagnosis of an intracranial plasmacytoma. Intracranial plasmacytomas are rare tumours which are usually found within the head and neck region of patients with myeloma. As such, they are usually diagnosed in a rather advanced stage of the disease. Intracranial plasmacytomas can present as a perineural meningioma, sinus thrombosis, or a cranial neuropathy. A diagnosis of intracranial plasmacytoma can be challenging and therefore a multidisciplinary approach is necessary. In our case, the plasmacytoma was confirmed by biopsy of the temporal bone and the patient’s myeloma was subsequently diagnosed.

Our report highlights the similarity of intracranial plasmacytomas with Gradengo’s syndrome. Although these tumours are usually diagnosed in a late stage of the disease, the clinical symptoms can mimic a Gradengo’s syndrome. Therefore, a high index of suspicion should be maintained in patients with a clinical presentation similar to Gradengo’s syndrome.

Figure 1 A computed tomogram (bone settings) through the base of the skull showing destruction of the air cells within the left petrous temporal bone (A). The lytic lesion has eroded through the wall of the petrous temporal bone (arrows) and into the posterior cranial fossa (B).

Figure 2 T1 weighted post gadolinium magnetic resonance image showing the extent of the intracranial plasmacytoma. The mass is seen at the apex of the petrous temporal bone medially and within the middle ear air cells laterally (arrows).
bone. In recent times, however, other causes have been recognised—for instance, meningioma, fractures, and T cell lymphoma. To our knowledge, this is the first report of Gradengio’s syndrome caused by an extramedullary plasmacytoma, and almost certainly the first to be confirmed with magnetic resonance imaging.

The possible pathogenesis of this particular case is interesting, since the diplopia occurred soon after a vigorous nose blowing. In Gradengio’s original paper, the cranial nerve involvement was thought to occur as a result of gradual spread of middle ear infection upwards to cause inflammation of the meninges at the apex of the petrous temporal bone. In this report we believe that the osteolytic plasmacytoma eroded into the apex of the petrous temporal bone, thus weakening the roof to the underlying air cells. The abrupt rise in intra-auricular pressure with nose blowing caused a sudden upward eruption of cells, or dural tear, affecting the sixth nerve and allowing rapid progression of the tumour into the posterior cranial fossa as far caudally as the hypoglossal canal over the following week (Fig 1).

The involvement of the sixth nerve in myeloma is more often an indirect result of raised intracranial pressure or diffuse meningeal infiltration. It is important to underline the difference between that condition and the much rarer isolated intracranial extramedullary plasmacytoma described in this report. In the latter, systemic indicators of myeloma are absent, and the prognosis following radiotherapy is far better.

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Use of ultrasound biomicroscopy in the localisation and management of an anteriorly situated intraocular foreign body

**Editor,—** The precise imaging of anteriorly located intraocular foreign bodies (IOFBs) is possible with present techniques—namely, computed tomography (CT) scanning, and A and B scan ultrasonography. In this case, ultrasound biomicroscopy (UBM) proves itself to be an excellent imaging technique for these IOFBs and therefore useful in clinical practice.

**CASE REPORT**

A 79 year old man presented to the eye casualty department complaining of a painful, red left eye with reduced vision. Two weeks previously he had been hit in that eye by the end of a nail which he had been pulling out of a table. He believed he had removed the piece of metal from his eye at the time. On examination, visual acuity (VA) was 6/9 in the right eye and 6/60 in the left eye. There was a nasal subconjunctival haemorrhage, though the entry wound was found at 5 o’clock, extending radially from the cornea to the scleral border of the limbus and was siedle negative. There was an anterior uveitis with cells ++ and flare +++, and 360 degree posterior synechiae. There was brisk vitreous activity, cells +++, and poor fundal view. Intraocular pressure was 12 bilateral. Gonioscopy revealed iris tissue up to the wound but no foreign body in the anterior chamber. Plain skull x-ray (Fig 1A) showed an intraocular radio-opaque foreign body. The patient was admitted for intense dilatation and steroid treatment before surgery. Superotemporal posterior synechiae were broken and some fundal view was obtained—BIO 3, though the IOFB was not seen. Conventional A and B scan ultrasound failed to localise accurately the foreign body, although it was identified on extreme peripheral sections (Fig 1B). CT scan showed a densely radio-opaque IOFB but accurate localisation was not possible.

The wound had been present for 2 weeks, was self sealing, and it was considered safe to perform UBM using a standard eyecup, which had been disinfected using Milton. This identified a foreign body (Fig 1C,D) adjacent to pars plana, 4 mm posterior to the angle recess (that is, 5 mm posterior to limbus) at the 5 o’clock meridian. When surgery was performed, a scleral trap door was constructed and a giant magnet was then placed with its point 5 mm from the limbus at the 5 o’clock meridian. The metallic foreign body was removed with ease. The scleral flap was then sutured. Cryotherapy was then applied to the entry site and the peripheral retina was inspected for any evidence of tears. In addition, perioperative systemic and topical steroids were administered to control intraocular inflammation and prevent proliferative vitreoretinopathy (PVR). Unfortunately, 6 weeks later he developed a total retinal detachment with inferior PVR, despite perioperative control of intraocular inflammation with systemic steroids, and further surgery was required.

**COMMENT**

The accurate localisation of IOFBs is essential for the optimum management of patients. This enables the surgeon to plan the mostatraumatic method of removing the IOFB during surgery. Anteriorly located foreign bodies are particularly problematic as it may be impossible to visualise them directly although indention can aid direct visualisation of those located at the retinal periphery. At present, imaging of these IOFBs is possible with conventional A and B scan ultrasonography, plain x ray and CT scanning. CT scanning has its limitations owing to image obscuration from eye movement and the quality of images reconstructed by computers, although newer methods have been developed in an attempt to overcome these factors. A and B scan ultrasonography, although sensitive in detection and localisation of posterior segment IOFBs, does not provide good resolution of the extreme retinal periphery, ciliary body, posterior chamber, and drainage angle whereas UBM has good resolution of these areas. UBM can prove a useful tool to pinpoint the location of anteriorly located IOFBs as has been shown in experimental

Figure 1 (A) Lateral skull x ray showing appearance of foreign body. (B) Extreme peripheral B scan ultrasonography at 5 o’clock meridian showing foreign body (arrow) with shadowing posterior to it. (C) Ultrasound biomicroscopy at 5 o’clock meridian, sagittal view. Line measures distance from angle recess to foreign body, 4 mm. (D) Transverse view, ultrasound biomicroscopy showing foreign body adjacent to pars plana.
Intravitreal phaco fragment missed by computed tomography

EDITOR,—A phacoemulsification (phaco) chop- per was accidentally damaged by a phaco handpiece during a phaco cataract surgery. A small fragment was suspected to have dropped into the vitreous cavity. The presence of this tiny intravitreal foreign body (IOFB) was missed by the orbital x rays and the computed tomography (CT) scan, but was clearly shown on ultrasound biomicroscopy (UBM). Paracentral vitrec- tomy was performed and the foreign body (FB) was found and removed. This case demonstrates the potential hazard caused by the powerful phaco energy as well as the usefulness of the B-scan in detecting small size IOFBs, which may be missed by the standard CT scan.

CASE REPORT
A 72 year old Chinese woman underwent right phaco cataract extraction in December 1996. In the middle of the phaco process, the phaco chopper accidentally came into contact with the tip of the phaco handpiece briefly. No obvious breakage was seen on the chopper and the phaco process was continued. However, when the nucleus removal was completed and the chopper was removed from the eye, it was noted that the chopper had two loose points with two tiny pieces of the instrument easily breaking off from the main body. When these two loose pieces were put back to the breaking points, the instrument appeared to be intact. Missing fragments, however, could not be entirely excluded. A thorough search for any residual fragments in the anterior chamber under the operating microscope did not reveal anything. The residual cortex was then removed with the standard automated irrigation and aspiration technique. Near the end of cortical removal, the vitreous pressure was high and the posterior capsule was accidentally ruptured at a site between the 3 and 6 o’clock positions. In addition to some vitreous loss, the tear extended to beyond the equator resulting in a linear radial tear in the anterior capsule at the 6 o’clock position. Anterior vitrectomy was thus performed. The capsular remnants were thought to be inadequate for a stable placement of a posterior chamber intraocular lens (IOL). The wound was thus closed without IOL implantation but a second stage scleral fixation of IOL was planned.

In order to make sure that no metallic fragments from the chopper were left in the eye, we performed a B-scan study on the eye. A small piece of IOFB was clearly shown (Fig 1). However, there were no vitreous haemorrhage or retinal detachment. An orbital x rays (anteroposterior and lateral views) was done but no radio-opaque FB was found. We went on to evaluate the case further with an orbital CT scan. A spiral CT scan was performed (3 mm collimation, 3 mm/s table speed, 120 kVp, 80 mA) and the images were reconstructed into 1 mm images. No FB could be identified. Subsequently, the patient received a pars plana vitrectomy and removal of residual lens material. The surgeon was also able to visualise and remove the metallic FB (0.1 x 0.3 x 0.6 mm) from the vitreous cavity. The capsular remnants were found to be adequate for suture fixation of IOL without suturing. Postoperatively the patient did well with no complications. The CT films were reviewed again retrospectively by the radiologist and no radio-opaque FB was suspected. This eye achieved a visual acuity of 6/9 at the latest follow up, which was 6 months after the incident.

COMMENT
In recent years, phaco surgery has grown to become one of the standard methods of removing cataract in many parts of the world. Many ophthalmologists are using the two handed technique to perform phaco. This technique has been proved to be effective and is well tolerated by the eye. However, there are times when the lens manoeuvre instrument, such as the phaco chopper, comes into contact with the phaco handpiece while the ultrasound is being applied. Small metallic fragments may break off from such instruments. The possibility of the presence of metallic fragments from these instruments left in the eye should not be overlooked. Braunstein et al reported six cases of intraocular metallic FBs after cataract extraction by the two handed phaco technique. Similar findings have also been produced in vitro by applying ultrasound power from phaco handpiece to a cycloidalysis spatula.

The above case demonstrates this risk and the way it was managed afterwards. There are several important aspects. Firstly, the phaco surgeon has to be alert and aware of the potential damage to the phaco instruments that may arise when these instruments come into contact with the phaco tip. It would be advisable to take precautions to avoid such contact. Secondly, if such contact occurs during the surgery, the eye as well as the instruments needs to be carefully examined. In our case, although the loose pieces of the phaco chopper seemed to be all present, a tiny piece was in fact still left intraocularly.

Thirdly, it is essential to employ multiple imaging modalities to increase the sensitivity of the detection.

CT scan, in most settings, is preferred to B-scan for the demonstration and localisation of FBs in the globe. Lindahl recommended CT scans as the primary diagnostic tool in the detection and localisation of IOFBs. In most cases, a 5 mm cut CT scan is already effective enough to diagnose a IOFB and an x ray may show to manage the radio-opaque FB. A 3 mm cut is recommended if the plain x rays is negative or equivocal. Reconstruction into 1 mm cut might enhance the chance of detecting small FBs. However, we choose to remove the FB surgically as the metallic FB was part of the surrounding structure. As demonstrated in our case, the tiny IOFB was clearly shown in the B-scan but missed by the CT scan, despite the fact that the chopper material is metallic and has a CT number of 590. Besides, ultrasound could be extremely useful for localisation of FB when it is anterior to the globe wall, intramural or extracapsular. Additionally, it can also help delineate the extent of associated soft tissue injury.

There are reports describing tiny metallic fragments breaking off from the phaco handpiece in which conservative treatment was recommended. We opted to remove the FB surgically as the metal part of the fragment was from the chopper in our case is much larger.

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Absence of relative afferent pupillary defect and pupillary hemiakinesia in a child with homonymous hemianopia due to (retro-)geniculate porencephaly

EDITOR,—Relative afferent pupillary defect (RAPD) is important in diagnosing lesions of the anterior visual pathways. RAPD is almost always present in unilateral optic nerve disease. Optic tract lesions are characterised by a combination of homonymous hemianopia and RAPD contralateral to the side of the lesion with subsequent, specific, asymmetric optic atrophy. In acute homonymous hemianopia RAPD has been used to differentiate between infrageniculate and suprageniculate lesions, since neither optic atrophy nor RAPD should occur in the presence of acquired affections of optic radiation or visual cortex.

Pupillary hemiakinesia—that is, reduced or absent pupillary light reaction after stimulus presentation in the blind field, is typical of optic tract lesions. However, we examined a young boy with unilateral involvement of postchiasmal visual pathways, homonymous hemianopia, and asymmetric optic atrophy due to a porencephalic substance defect, but without RAPD or pupillary hemiakinesia.

CASE REPORT

The 7 year old boy has been in ophthalmological care since shortly after birth because of horizontal nystagmus, strabismus, head posture (left head rotation), bilateral optic atrophy, and defective exploration of his right hemifield. Paediatric examination revealed a marked latent nystagmus; ocular motility is unimpaired; pursuit is slightly jerky; optokinetic nystagmus (OKN) is not clearly triggered by targets moving to the patient’s right but is normal in the contralateral direction. Goldmann perimetry shows left homonymous hemianopia and a distinct constriction of the right hemifield on 26 September 1996 (Fig 1). The pupils are equal in size, react sluggishly to light, and show no RAPD. This can be confirmed by infrared pupillography showing bilaterally reduced amplitudes and prolonged latencies. Hemifield stimulation finds no difference between the nasal and temporal fields (Fig 2). The anterior segments are normal. Funduscopy shows a pronounced, bilateral optic atrophy which is somewhat band-shaped in the left disc.

Magnetic resonance imaging confirmed a huge, supratentorial porencephalic substance defect of the right cerebral hemisphere reaching the lateral geniculate nucleus (LGN) of that side (Fig 3).

COMMENT

Partial, asymmetric, bilateral optic atrophy with a faint horizontal band-shaped configuration in the left optic disc and left homonymous hemianopia indicate a lesion of the right optic tract, probably caused directly or indirectly by trans-synaptic (transgeniculate) degeneration due to an intraparenchymal or perinatal postgeniculate lesion. OKN asymmetry suggests that the lesion includes the right occipito-parieto-temporal region. Neuroimaging confirms that the right LGN is involved in the porencephalic process.

However, the pupillary findings in this case are puzzling. Although RAPD contralateral to the lesion is to be expected, neither a careful swinging flashlight test nor pupillography show any side differences. A slight RAPD as found in amblyopia might compensate for an RAPD caused by a tract lesion. However, if amblyopia were present in this boy it should be found on the left side, thus not balancing but even amplifying the RAPD.

Wilhelm et al found that RAPD occurred in approximately half of all patients with lesions closer than 10 mm to the LGN or involving it. In lesions further away than 18 mm from the LGN it did not occur at all. Thus, optic tract lesions can exist without RAPD if the connections between anterior visual pathways and midbrain remain unaffected. These axons do not seem to be just branches of the retinogeniculate pathways. This may explain the absence of RAPD in spite of clear signs of a (transgeniculate) optic tract lesion which has also been described by Tychsen et al.


Letters

Figure 1 Visual fields (Goldmann perimetry). Note the marked constriction of isoptres in the right hemifield.

Figure 2 Infrared pupillographic recording with hemifield stimulation results, latency times (upper), and constriction amplitudes (lower). Each value represents the mean of 20 measurements. Stimulus conditions: size 15° half circle, 2° offset to the vertical meridian; duration 200 ms; stimulus illumination 4.6 cd/m²; background illumination 1.0 cd/m². The visual field defect cannot be demonstrated pupillographically, and no significant difference between right and left eye is present. The latency times are unusually high and the constriction amplitudes very small.

Figure 3 Magnetic resonance image: porencephalic defect of the right hemisphere involving optic radiation and reaching the lateral geniculate nucleus.
Even more puzzling, however, is that hemifield stimulation demonstrates no pupillary hemianoikia, which should be present in cases with optic tract atrophy. It is unlikely that the pupillary behaviour is caused by a stray light artefact because the stimuli were very dim. Compared with pupillary responses in the same age group, those of the patient appear very small and the latencies unusually long. This may be interpreted as a general loss of pupillary motor input to both sides of the midbrain caused by this widespread cerebral lesion. This would support the view of Clarke and Gamlin derived from primate experiments, interpreting the pretectal area as an integrator of all afferent pupillomotor input rather than a simple relay station.

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Expression of transforming growth factor β superfamily and their receptors in the corneal stromal wound healing process after excimer laser keratotomy

EDITOR.—Corneal stromal clouding (corneal haze) develops after excimer laser keratotomy. During the corneal wound healing process after excimer laser keratotomy, abnormal subepithelial fibrous tissue is formed just under the abraded area, where keratocytes proliferate and extracellular matrix (ECM) components, including collagens (type III, IV, and VII), fibronectin, laminin, and tenasin, are deposited.1 This abnormal ECM deposition is thought to correspond to the corneal haze.

The transforming growth factor β (TGF-β) superfamily contains many multifunctional proteins, including TGF-βs, activins, and bone morphogenetic proteins (BMPs).2 They regulate cellular proliferation, differentiation, migration, and ECM production.3 Through these functions, TGF-β is known to regulate the wound healing process in many tissue. For example, TGF-β accelerates the abnormal ECM deposition and scar tissue formation in the skin wound healing process in vivo.4 TGF-β also accelerates the proliferation and ECM production of the cultured skin fibroblasts in vitro.5 In the corneal cells, TGF-β and TGF-β receptors are expressed in resting status and in the wound healing process after injury.6 TGF-β is reported to stimulate ECM production of keratocytes. These facts suggest that TGF-β is involved in corneal haze formation. In the present report, we tried to investigate the role of the TGF-β superfamily in the corneal stromal wound healing process and the corneal haze formation after excimer laser keratotomy.

CASE REPORT

The central areas measuring 6 mm in diameter of 20 corneas of European cats were abraded to 100 µm depth using an EC 5000 excimer laser (Nidek, Aichi, Japan). After excimer laser keratectomy, corneal haze was quantitated using a newly developed device (EAS-1000, Nidek, Aichi, Japan) that measures scattered light intensity of the cornea.7 In parallel with the haze measurement, the expressions of TGF-βs, TGF-β type I and II receptors, activin type I, IB, and II receptors, BMP type IA, IB, and type II receptors, collagens (types I, III, and IV), fibronectin, and laminin were immunohistochemically observed in the cryosections of the corneas without treatment and 3 days, 1 week, 4 weeks, and 10 weeks after excimer laser keratotomy.

COMMENT

Table 1 shows the intensity of the corneal haze and the expression of the TGF-βs, TGF-β superfamily receptors, and ECM components in the corneas before and after excimer laser keratotomy.

Table 1

<table>
<thead>
<tr>
<th>Time</th>
<th>Control</th>
<th>1 week</th>
<th>4 weeks</th>
<th>10 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean corneal haze (SD)</td>
<td>7838 (1568)</td>
<td>14690 (1952)</td>
<td>34953 (3258)</td>
<td>16328 (2031)</td>
</tr>
<tr>
<td>Type I collagen</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>±</td>
<td>±</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Type IV collagen</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Fibronectin</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>Laminin</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>TGF-β1, β2, β3-LAP</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>TGF-β receptors (type I and II)</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>BMP receptors (type IA, IB, and II)</td>
<td>±</td>
<td>±</td>
<td>±</td>
<td>±</td>
</tr>
</tbody>
</table>

— = Undetectable; ± = very weak; ±± = moderate; ++ = strong.

Figure 1 (A) Expression of TGF-β3 without treatment. TGF-β3 is detected in the corneal epithelial cells. Expression of TGF-β3 in keratocytes is very weak. (B) 4 weeks after the excimer laser keratotomy. The expression of TGF-β3 increases in the keratocytes which proliferate in the subepithelium of the laser irradiated area. Expression of TGF-β3 does not change in corneal epithelial cells (bar = 100 µm).

Table 1

The intensity of corneal haze, and expression of extracellular matrix components, TGF-βs, and TGF-β superfamily receptors.
keratectomy. The corneal haze gradually increased and reached the peak 4 weeks after treatment. In the subepithelial tissue of the laser irradiated area, the keratocyte proliferation and expression increase of type III and type IV collagens, fibronectin, and laminin were observed. Among the TGF-β family and the TGF-β superfamily receptors, only the TGF-β1, β2, β3 (Fig 1), and TGF-β type I and type II receptors were significantly upregulated in the activated keratocytes under the regenerating epithelium 4 weeks after the treatment. The expression of activin receptors and BMP receptors were only slightly increased. The synchronised increase in the expression of TGF-βs, TGF-β receptors, the abnormal extracellular matrix deposition, and corneal haze formation suggests that TGF-β is involved in the activation of keratocyte function during the corneal stromal wound healing process and could affect corneal haze formation after excimer laser keratectomy.

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