macular region, compatible with a transmission defect at the level of the RPE in both eyes (Fig. 2). A visual field test (Humphrey 30-2) failed to reveal any specific abnormality. In September 1999, in spite of the similarity of the retinal findings, his visual acuities were 6/36 in the right eye and 6/9 in the left. His $CD4^+$ count was 450 cells/mm^3 and his viral load was 36 000 RNA copies/ml.

Two months later (November 1999) the macular lesions were unchanged, and despite the fact that Efavirenz had been discontinued for 5 months vision had dropped to hand movements in the left eye. Electrodiagnostic tests were performed, with the pattern and focal ERGs showing no response. The rod ERG and electro-oculogram were normal. The cone ERG was mildly delayed. The conclusion was of a profound bilateral maculopathy. The following baseline serological investigations were negative: toxoplasma serology, VDRL/TPHA, cryptococcal antigen and CMV IgM.

At his last assessment the patient presented the same changes in the macula and his visual acuities were 6/60 in both eyes.

Comment

Ocular manifestations in AIDS patients are classically related to low $CD4^+$ counts, especially the HIV-related microangiopathy and the cytomegalovirus retinitis.[2] Our patient never presented with very low $CD4^+$ counts, which makes the possibility of an opportunistic disease in his case very unlikely.

Few cases have been published regarding retinal drug toxicity in patients with AIDS. A well-established correlation between didanosine (DDI) and peripheral retinal changes has been shown. Didanosine toxicity is related to high doses of the drug and affects children more frequently; however, cases in HIV-positive adults have been reported.[3,4] Didanosine lesions produce electroretinographic and visual field defects without changes in visual acuity because of their peripheral occurrence. Histologically DDI was shown to affect primarily the RPE with secondary damage to the neurosensory retina and to the choriocapillaris.[5] Although no histopathological information was available, we can, based on the clinical appearance, the angiographic and electroretinographic findings, conclude that the damage in our patient was also primarily to the RPE.

As the other drugs used by the patient, including azathioprine and 3TC (Combivir), have been available for a long time and no cases of retinal toxicity have been associated with their use, we believe that retinal damage in this case was due to Efavirenz. Since the experience with Efavirenz is still limited it is possible that more cases will appear and physicians should be aware of this possible side-effect, which may have devastating effects on vision.

References

1. Staszewiki S, Morales-Ramires J, Tashima K, *et al*. Efavirenz plus ziduvudine and lamivudine, efavirenz plus indinavir, and indinavir plus zidovudine and lamivudine in the treatment of HIV-1 infections in adults. N Engl J Med 1999;16:1865–73.
2. Kupperman BD, Petty JG, Richman DD, *et al*. Correlation between $CD4^+$ counts and the prevalence of cytomegalovirus retinitis and human immunodeficiency virus-related noninfectious retinal vasculopathy in patients with acquired immunodeficiency syndrome. Am J Ophthalmol 1993;155:575–82.
3. Whitcup SM, Butler KM, Caruso R, de Smet MD, Rubin B, Husson RN, *et al*. Retinal toxicity in human immunodeficiency virus-infected children treated with 2' ,3' -dideoxyinosine. Am J Ophthalmol 1992;113:1–7.
4. Cobo J, Ruiz MF, Figueroa MS, Antela A, Quereda C, Perez-Elias MJ, *et al*. Retinal toxicity associated with didanosine in HIV-infected adults. AIDS 1996;10:1297–300.
5. Whitcup SM, Dastgheib K, Nussenblatt RB, Walton RC, Pizzo PA, Chan CC. A clinicopathologic report of the retinal lesions associated with didanosine. Arch Ophthalmol 1994;112:1594–8.

Andre L. L. Curi
Gwenyth Freeman
Medical Retina Department
Moorfields Eye Hospital
London, UK

Moses Kapembwa
Northwick Park & St Mark's Hospitals
London, UK

Carlos Pavesio ✉
Moorfields Eye Hospital
London, UK

Carlos Pavesio ✉
Moorfields Eye Hospital
City Road
London EC1V 2PD, UK

Sir,

Angle closure risk from proprietary medicines

Acute angle closure glaucoma is uncommon in the Caucasian population with a prevalence of 0.1%. However, it must be diagnosed and managed quickly and effectively to prevent permanent visual loss.[1,2] Pharmacological agents capable of causing mydriasis and cycloplegia can precipitate acute angle closure glaucoma in a predisposed patient with pre-existing narrow angles. These patients are usually unaware of their risk of angle closure glaucoma so that drug data sheets advising patients to 'speak to your doctor if you have glaucoma' are likely to go largely unheeded. The appropriate advice should be to stop the preparation and seek medical review if blurred vision is associated with significant eye pain, headache, or nausea and vomiting.

Case report

A 48-year-old man presented to eye casualty with a 3 day history of pain, redness and blurred vision of the right eye. In the previous 2 months he had experienced several episodes of ocular pain whilst watching television. There was no other significant history. For

2 days before the start of his symptoms, he had been treating symptoms of 'flu with the recommended dose of the proprietary medications Day Nurse and Night Nurse.

On examination, the visual acuities were right HM, left 6/6. The right eye manifested ciliary injection, corneal epithelial oedema, folds in Descemet's membrane, aqueous cells, and a fixed mid-dilated pupil. The anterior chambers were shallow bilaterally. Applanation tonometry found an intraocular pressure of 42 mmHg on the right and 14 mmHg on the left. Gonioscopy of the left eye revealed a Schaffer grade 0–1 angle. When the acute attack had settled gonioscopy of the right eye revealed a Schaffer grade 0 angle.

The patient was initially treated with intravenous acetazolamide and topical pilocarpine, timolol and Maxidex to the right eye, and topical pilocarpine to the left eye. A left YAG peripheral iridotomy was performed the same day and the right eye was similarly treated following normalisation of the intraocular pressure and clearing of the cornea.

Comment

This patient presented with an attack of acute angle closure glaucoma after treating an episode of 'flu with the proprietary medications Night Nurse and Day Nurse (Smith Kline Beecham) containing paracetamol, dextromethorphan and promethazine, and phenylpropanolamine. The data sheet for both products advise 'talk to your doctor first if you have glaucoma'. The Night Nurse data sheet also states that '...blurred vision may also occasionally occur, and occasionally people get an upset stomach'.

This episode raises the possibility that these proprietary medications played a role in the onset of this patient's attack of acute angle closure glaucoma. A completed yellow card has therefore been sent to the Committee on Safety of Medicines. The components of the two products that are implicated in this case are promethazine in Night Nurse and phenylpropanolamine in Day Nurse. Promethazine is used here for its antihistamine properties with the intention of reducing nasal secretions. However, it also has sedative, anti-emetic, and weak antitussive effects by acting as a peripheral and central H_1 receptor antagonist, an anticholinergic, a local anaesthetic and a weak α-adrenergic.[3] Phenylpropanolamine is included for its decongestant properties, which facilitate nasal breathing. However, it also is an indirectly acting sympathomimetic with mainly α_1-agonist and also some β_1-agonist activity.[3]

Both anticholinergics and α-adrenergics can cause mydriasis and cycloplegia, the former by acting on the sphincter pupillae and the ciliary muscle, and the latter by stimulating the dilator pupillae muscle. It is not unreasonable to postulate that the combined effects could result in closure of an already narrow angle susceptible to this, as we believe happened in this case. The blurred vision referred to in the data sheet is presumably the result of mydriasis and cycloplegia rather than corneal oedema. In the absence of any additional warning, cases of angle closure glaucoma precipitated by this medication could present late because a patient may consider this to be a harmless side-effect. Although patients with glaucoma are advised to talk to their doctor first, typically patients will not be aware that they are 'at risk' of angle closure. Perhaps the problem of late presentation might be avoided if reference were made to the importance of pain as a symptom, for which advice should be sought immediately. We have suggested to the manufacturers that the advice contained in the leaflet 'Will Day/Night Nurse suit you' should include the following statement: 'If blurred vision is associated with significant eye pain, headache, or nausea and vomiting the preparation should be stopped and medical advice should immediately be sought.' As a result of this suggestion the manufacturing companies Regulatory Affairs Department are now in the process of rewording the patient information leaflet.

Since July 1963 the Committee on Safety of Medicines has received one report of glaucoma and three reports of abnormal vision associated with use of promethazine. In the case of phenylpropanolamine there have been five reports of glaucoma, two of mydriasis and 15 of visual abnormalities.[5] Many other products contain the ingredients that are implicated in this case. Promethazine is a constituent of Avomine, Medised, Pamergan, Phensedyl, Ronpirin, Phenergan, Phenhalal, Q Mazine, Sominex, and Tixylix Night-time, and Phenylpropanolamine is contained in Allereze, Benylin Day and Night, Contac 400, Dimotapp, Mu-cron, Nirolex prolonged release, Sinutab, Triogesic, Triominic and Vicks Coldcare.[4,5] If the Committee on Safety of Medicines felt it appropriate it could recommend that the Medicines Control Agency request similar patient advice on other products containing promethazine and phenylpropanolamine.

References

1. Congdon N, Wang F, Tielsch JM. Issues in the epidemiology and population based screening of primary angle closure glaucoma. Surv Ophthalmol 1992;36:411–23.
2. Fingeret M, Kowal D. Acute glaucoma: diagnosis and treatment. Optom Clin 1991;1:165–91.
3. Therapeutic Drugs, vol. 2. Edinburgh: Churchill Livingstone, 1991.
4. Martindale. 32nd ed. London: Pharmaceutical Press, 1999.
5. OTC directory. 1999–2000 Treatments of common ailments. Proprietary Association Great Britain.

Victoria Barrett
Tim Jordan
Southampton Eye Unit
Southampton General Hospital
Southampton, UK

Victoria Barrett, MBChB(Hons), BSc(Hons) ✉
Southampton Eye Unit
Southampton General Hospital
Tremona Road
Southampton SO16 6YD, UK