retention cyst. The echographic characteristics of retained PFO have been described by Hasenfratz *et al*.[5] Delayed display of the echo signal results in a hypoechogenic image due to slower sound conduction in PFO. The lesion presented here is unusually large. On the basis of clinical history and echographic findings, we believe this cyst is likely to contain PFO. It has had no functional effect on vision and no attempt should be made to remove it.

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Sir,

Uveitis associated with concurrent administration of rifabutin and lopinavir/ritonavir (Kaletra)

Case report

A 41-year-old HIV-infected man received lamivudine/zidovudine and nevirapine therapy. He also took isoniazid/rifampicin/pyrazinamide and ethambutol for pulmonary tuberculosis. Because skin rash appeared, nevirapine was replaced by lopinavir/ritonavir 400/100 mg twice daily. The antituberculosis regimens were replaced by rifabutin 300 mg/day and methaniazide 600 mg/day because of known interactions between lopinavir/ritonavir and rifampicin.[1]

Panuveitis was found in his left eye after receiving rifabutin for 86 days (Figure 1). The uveitis resolved following the discontinuation of rifabutin with the administration of topical steroids and cycloplegics. The final visual acuity recovered from hand motion to 1.0.

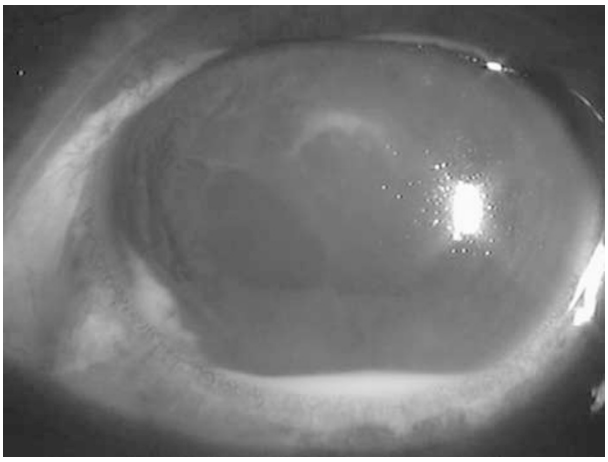

Figure 1 A slit-lamp photograph shows severe cell reaction, fibrin, and a hypopyon in the anterior chamber.

Comment

Conditions associated with uveitis in HIV-positive patients include opportunistic infection, neoplasms, inflammation due to HIV infection itself, and drug toxicities.[2] The patient was negative for HLA-B27 and syphilis. Uveitis did not recur after discontinuing rifabutin for one year. Refabutin was suspected as the cause of uveitis by evidences of timing condition, lack of other causes, and resolution after stopping the implicated drug.

Rifabutin associated uveitis has been described in AIDS patients and identified as a dosage-dependent side effect.[3] Adverse effects are unusual at the recommended dose of 300 mg/day.[4] Clarithromycon or fluconazole was known to increase concentration of rifabutin and the incidence of rifabutin toxicities, including uveitis.[5] Neither clarithromycon nor fluconazole was given to our case.

Ritonavir is a potent inhibitor of CYP3A4 and has been shown to substantially increase rifabutin concentration. Co-administration of rifabutin with ritonavir increased area under the concentration–time curve (AUC) of rifabutin and its 25-*O*-desacetyl metabolite by four times and 35 times, compared with administration of rifabutin alone.[6] Patients receiving rifabutin and ritonavir without the reduction of dosages increased the risk of developing leucopenia, arthralgia, joint disorder, uveitis, and skin discoloration.[6,7] Because of the increased likelihood of rifabutin toxicities, the dosage of rifabutin should be reduced by at least 75% of usual dosage (300 mg once daily) or 150 mg 2–3 times a week when given with lopinavir/ritonavir.[8,9]

To our knowledge, this is the first report of uveitis associated with concurrent administration of rifabutin and lopinavir/ritonavir. Our finding suggests that the dosage of rifabutin should be reduced when it is administered with lopinavir/ritonavir.

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Sir,

Intravitreal bevacizumab (Avastin) causing acute glaucoma: an unreported complication

We report a case where intravitreal bevacizumab, an antivascular endothelial growth factor (VEGF) agent caused an acute intraocular pressure (IOP) rise in an ocular hypertensive patient. This complication, to our knowledge, has not been reported before.

Case report

A 75-year-old Caucasian, with ocular hypertension and using guttae latanoprost and brinzolamide, was found to have classic juxtafoveal choroidal neovascularisation (CNV). After a written informed consent, the patient underwent intravitreal bevacizumab injections (1.75 mg/0.07 ml) at monthly intervals. Vision was checked immediately after each injection (at least counting fingers) to confirm ocular perfusion. Three days after the fourth injection, the patient developed corneal oedema with the IOP rising to 56 mmHg. He had a quiet anterior chamber and vitreous, and gonioscopy showed an open angle. The IOP was initially controlled on maximal medical treatment including oral acetazolamide. Acetazolamide was stopped after 3 weeks. Eleven weeks post-injection, the IOP is controlled on guttae latanoprost, cosopt (dorzolamide–timolol fixed combination), and apraclonidine.

Comment

Intravitreal bevacizumab, increasingly being used for CNV[1] and retinal vascular disorders,[2] is believed to be extremely safe with no association reported with glaucoma.

IOP elevation following an intravitreal injection can be explained by several theories. A temporary vitreous volume increase causes an IOP spike. Studies with pegaptanib, another anti-VEGF, have shown such a spike normalizes within one hour.[3]

Drug-induced trabeculitis is unlikely in the absence of anterior chamber inflammation which generally accompanies viral trabeculitis.[4]

A probable explanation is the blockage of the trabecular meshwork in an ocular hypertensive patient by bevacizumab, a 148 kDa full-length antibody. Mordenti *et al*[5] have shown the clearance of the high-molecular weight antibody from the vitreous is slow (half-life 5.6 days) with the internal limiting membrane acting as a barrier, and it also diffuses from the vitreous to the anterior chamber. Hence, the drug might have accumulated in the trabeculum increasing the aqueous outflow resistance causing the IOP to rise acutely. Now, this effect has lasted for three months; long after the drug is cleared from the vitreous.

In conclusion, bevacizumab should be used with caution in patients with glaucoma or ocular hypertension. Further studies are required to identify any predisposing risk factors in patients susceptible to developing acute glaucoma following intravitreal bevacizumab injection.

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