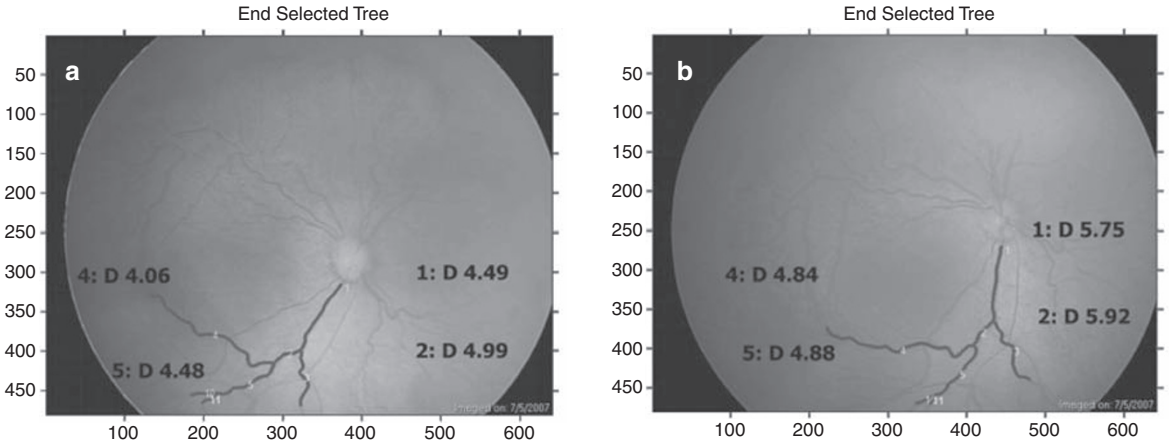

Figure 2 Retinal vascular tree analysis using RISA software. (a) Initial examination: with 'subtle' arterial changes at lower temporal inferior quadrant vessels. (b) same branch tree analysed when this picture was taken with no RetCam handheld lens pressure was applied upon the eye. Note how arterial diameter (D), expressed in pixels, consistently decreases when pressure is applied over the eye.

(RISA) was performed (Figure 2).[3] The vessels were narrower in the image with the compression artifact than in the subsequent images. Those findings confirm the impression of a less severe picture of plus disease in Figure 1a.

Comments

Variations in pressure induced by inadvertent indentation with the RetCam lens could compress, decrease intra-arterial diameter or even collapse retinal vessels.[4] Evaluation of images of plus disease may then be misinterpreted giving a false-negative result, with a subsequent delay detection of serious retinopathy. Careful attention to technique is essential to eliminate blanching of the retina or absence of the arterial blood column at the nerve head that might indicate excessive pressure during imaging.

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The authors do not have any commercial or proprietary interest in the device mentioned in the article.
The authors have no competing interests to declare.
This case report was approved by the local ethics committee.

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Sir,

Retrobulbar optic neuritis after Hepatitis A vaccination in a HIV-infected patient

Opportunistic infections increase morbidity and mortality in human immunodeficiency virus

(HIV)-positive patients. Prophylaxis, including Hepatitis A vaccination (HAV), is recommended for all HIV-positive/Hepatitis A virus seronegative patients.[1,2] Here we describe the occurrence of unilateral autoimmune retrobulbar optic neuritis after HAV in a HIV-infected patient on anti-retroviral therapy (ART) with immune recovery.

Case report

Our patient is a 39-year-old HIV-infected Chinese male on ART (Lamivudine and Efavirenz). His CD4 count was 471 cells/mm^3 (range 500–1600 cells) 3 weeks before receiving the first dose of attenuated HAV. He had not received any previous vaccinations after being diagnosed to be HIV positive. He found his vision in the left eye brighter than his right, 6 days after receiving HAV. This persisted until he developed sudden decreased central vision in his left eye, 12 days after vaccination. There was no associated pain on eye movements. Vision in the affected eye was counting fingers closely with a left relative afferent pupillary defect (RAPD), defective colour vision (0/15 Ishihara colour plates), and a central scotoma. There was no associated uveitis or optic disc swelling. Magnetic resonance imaging revealed left optic nerve enhancement with no compressive lesions (Figure 1). Infective (opportunistic) and autoimmune workup were negative. Lumbar puncture showed lymphocytic pleocytosis with otherwise no evidence of tuberculosis, syphilis, cryptococcus, or viral infection. He was treated with intravenous methylprednisolone for 3 days, with improvement of visual acuity (6/60) and colour vision (6/15 Ishihara plates) by day 3 of treatment. This was followed by a tapering course of oral prednisolone over 2 weeks with further improvement of visual acuity to 6/15 by 1 week and subsequently to 6/9, colour vision (15/15 Ishihara plates), and significant resolution of the central scotoma by 3 weeks (Figures 2 and 3). He has remained stable after a 14-month period of observation with a residual mild left RAPD, interval development of mild temporal disc pallor, and final visual acuity of 6/12. His CD4 counts remained stable at 444 cells/mm^3 after 1 year.

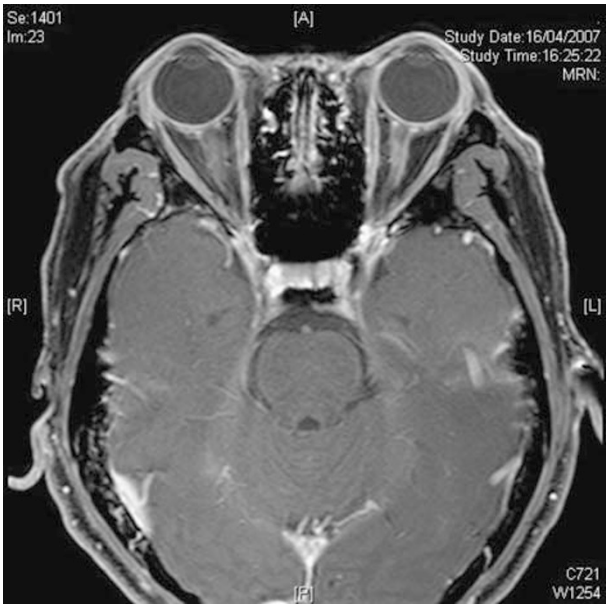

Figure 1 MRI of brain using gadolinium; T1-weighted image showing enhancement of the intra-conal segment of the left optic nerve, sparing the pre-chiasmal portion.

Comment

This is the first report in published literature of optic neuritis after HAV in a HIV-positive patient. Antibody response after vaccination is reduced in HIV-infected patients.[1,3] ART-induced increase in CD4 counts has resulted in improved vaccination response rates.[4] Higher CD4 counts and lower viral load at the time of vaccination have been associated with higher rates of antibody response and seroconversion after vaccination.[1,5] The immunological recovery also means an increased predisposition to immune-mediated reactions.

Considerable controversy surrounds the question of the presence of a causal link between vaccinations and the development of multiple sclerosis (MS) or optic neuritis, and many differing opinions have been heard. Post-vaccination optic neuritis has been reported with vaccination against influenza, hepatitis B, anthrax, and meningococcus infection in non-HIV-infected patients as case reports.[6–11] It is, however, difficult to distinguish a coincidental temporal association from a true causal association merely based on individual case reports. A multicenter, randomised, double-blind, placebo-controlled trial of influenza vaccination in patients with MS found no increased exacerbation rate, nor a change in disease course over a period of 6 months post-vaccination.[12] Payne *et al*[13] reported no statistically significant association between optic neuritis and vaccination against anthrax, influenza, hepatitis B, or smallpox in his study of 1131 cases and 3393 controls. A case–control study published in 2001 found no association between hepatitis B vaccination and the development of MS.[14] However, the study was limited to cohorts of nurses making the findings only applicable to women. A retrospective case–control study[15] published by Destefano *et al* in 2003 refuted the causal association between vaccination against hepatitis B, influenza, tetanus, measles, or rubella and the development of multiple sclerosis or optic neuritis. The authors attempted to minimise the limitations of its retrospective study by modifying inclusion criteria to reduce recall bias and by using data analysis to reduce the error that may result from their differential participation rates of case subjects and controls. In conflict, a more recent prospective case–control study published in 2004 in *Neurology*, involving 163 cases of MS and 1604 controls, reported an increased risk of MS associated with recombinant hepatitis B vaccination.[16] No increased risk was found with influenza or tetanus vaccinations in the study.

To date, there have been no case–control study or randomised trial with regard to HAV in HIV-infected patients. The workup for opportunistic infection in our patient was negative. He responded well to steroid

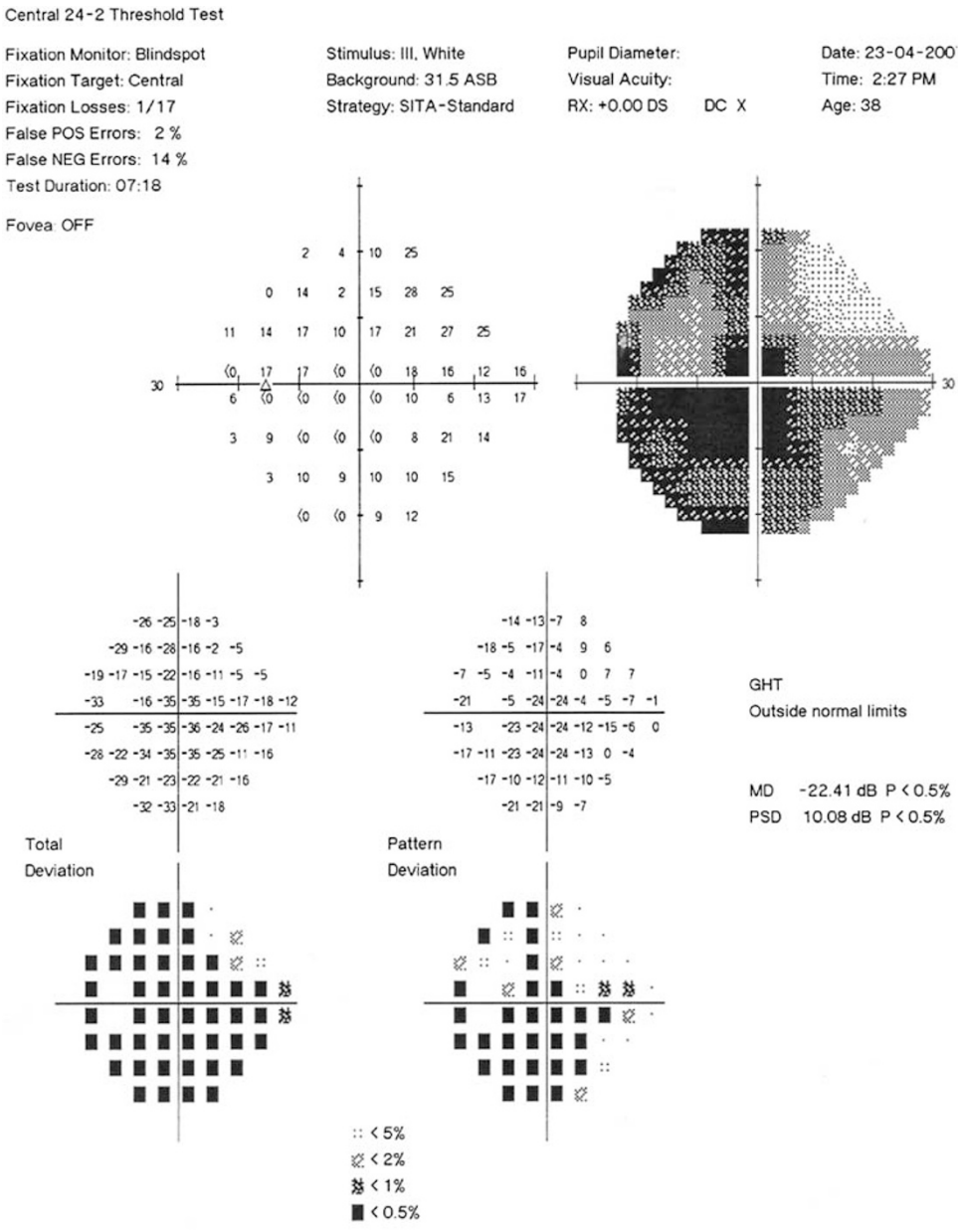

Figure 2 HVF at presentation showing a dense scotoma.

therapy, with a rapid course of recovery beginning from day 3 of treatment and achieving significant visual improvement by 1 week. The marked response to steroids lends weight to an immune-mediated aetiology as the underlying cause. Although immunologically mediated conditions are usually bilateral, up to 20% have a unilateral presentation in previously reported cases of post-vaccination optic neuritis.[11] The course of steroid therapy (initial intravenous with subsequent oralisation) did not result in exacerbation of the HIV infection and had no adverse effect on CD4 counts. The ART regimen that he was on (lamivudine and efavirenz) has no reported causal association with optic neuritis.

The aetiology of the optic neuritis cannot be conclusively determined, but the temporal relationship between the HAV and the development of optic neuritis suggests a possible association. Systemic steroid therapy was useful in achieving prompt recovery of vision and optic nerve function, and did not exacerbate HIV infection or lead to progression to clinical AIDS.

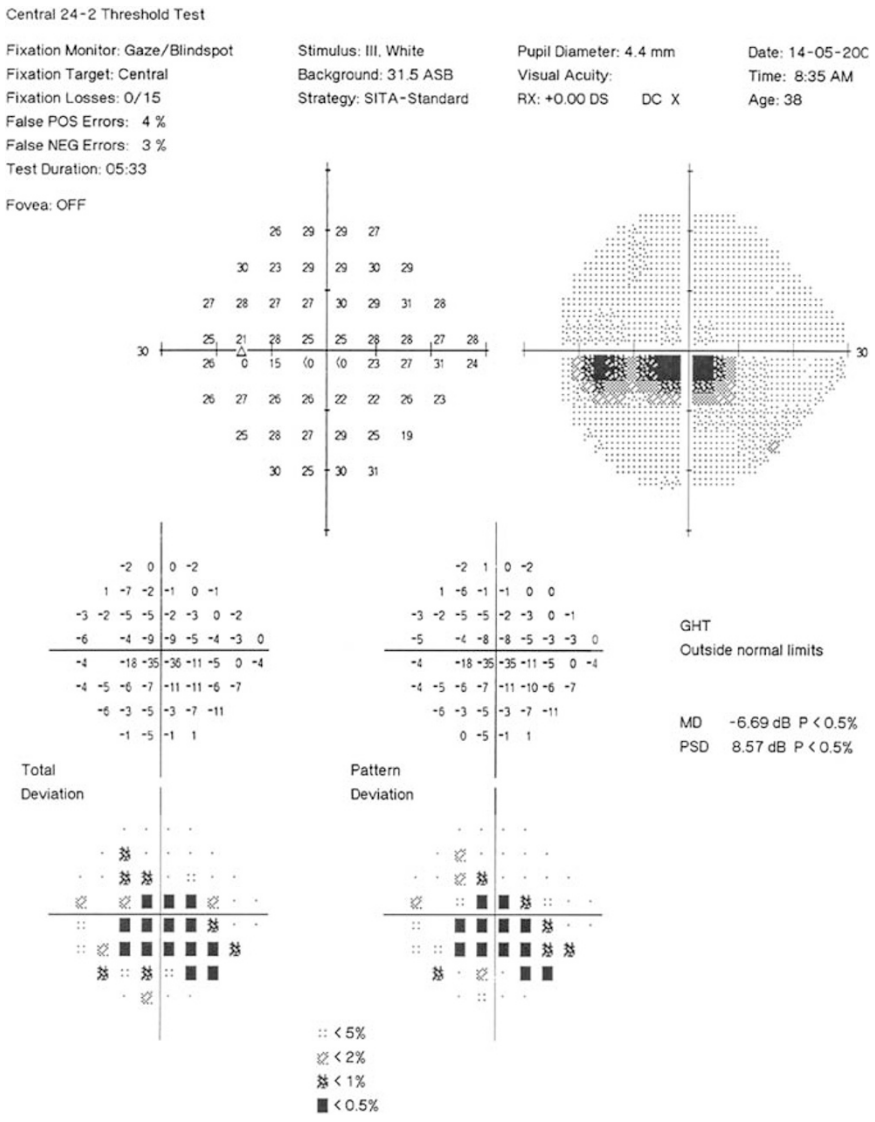

Figure 3 HVF 3 weeks post-treatment showing significant resolution.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Benefits of early awareness in age-related macular degeneration

We commend the fresh perspectives offered by Cervantes-Castaneda *et al*[1] on the possible lack of benefit of early awareness in age-related macular degeneration (AMD).

However, the basis of such a conclusion is questionable in view of several limitations and inadequacies of the study design. Fundamentally, the determination of early awareness of AMD may be biased as it was solely based on the patients' recall of having been previously diagnosed of AMD, given oral supplementation or advised Amsler monitoring. More details could also be provided with regards to the source of such diagnosis and recommendations as clinical competencies and management of AMD may be variable across the spectrum of general practitioners, optometrists and ophthalmologists. Furthermore, we agree that even in patients who were aware of their condition, it is difficult to assess their compliance to treatment and self-examination regimens, which could then influence the rate of detection of neovascular AMD. Lastly, the single-centre design and the associated geographical bias, although minimised by the peculiar referral pattern in the study region, preclude the generalisation of findings to the population.

Contrary to what the authors had suggested, we believe that the benefits of early awareness of AMD are far reaching.[2] Awareness of diseases promotes positive health-seeking behavioural changes in patients; patient education[3] and a prior diagnosis of chronic eye diseases, such as AMD,[4] are associated with increased utilisation of eye-care services. Coupled with effective counselling by clinicians, an early awareness of AMD allows the patient to take an active approach towards self-monitoring (with the Amsler chart remaining as a simple and inexpensive home-based test of choice despite its low sensitivity[5]) and regular eye follow-up. These may also facilitate the detection of other age-related eye diseases such as cataract and glaucoma as well.

As such, it may be premature to disprove the benefits of early awareness in the long-term management of AMD.

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Sir,

Reply to Woo *et al*

We thank Woo *et al* for their insightful comments. Our study aimed to evaluate how many patients with age-related macular degeneration (AMD) are aware of their disease beore developing choroidal neovascularization (CNV) and to assess whether such awareness confers benefit. Unfortunately, we found that many patients were not aware that they had AMD, and that prior awareness did not confer benefit for patients who develop CNV.