Comunicações Curtas e Casos Clínicos

Bull´s Eye Maculopathy in a patient treated with efavirenz

Cristina Vaz Pereira[1], Mónica Franco[1], Rita Guerra Pinto[2], Sandra Barrão[3], Helena Prior Filipe[3]

[1]Interno do Internato Complementar de Oftalmologia, Instituto de Oftalmologia Dr. Gama Pinto

[2]Assistente Hospitalar de Oftalmologia do Moorfields Eye Hospital

[3]Assistente Hospitalar Graduado, Instituto de Oftalmologia Dr. Gama Pinto

ABSTRACT

Objective: To report a case of retinal toxicity associated with efavirenz in an adult.
Methods: We describe a case of gradual-onset blurry vision in both eyes in a 37-year-old HIV caucasian woman, on antiretroviral therapy (ART), including efavirenz. Results: The patient presented with a best corrected visual acuity of 20/100 for the right eye (RE) and 20/125 for the left eye (LE). Fundoscopy revealed mottled atrophic changes of the macular retinal pigment epithelium (RPE) in both eyes. Fluorescein angiography revealed an annular pattern of RPE atrophy in both eyes. Full-field electretinography (ERG) was normal.
Conclusions: Based on our patient´s history and on previous reports, efavirenz seems to be the culprit in this case. Our report provides evidence in support of routine ophthalmological evaluation of patients on efavirenz.

Keywords
Efavirenz, retinal toxicity, HIV, retinal pigment epithelium.

INTRODUCTION

Approximately three dozen medications have been associated with retinal toxicity[1].

Efavirenz (EFV) is a non-nucleoside reverse transcriptase inhibitor used in the management of HIV infection. Well-known extra-ocular side effects are headache, sleep disturbances, depression, fatigue and dermatological changes.

We present a case of structural and functional retinal changes in a patient medicated with EFV.

METHODS

A 37-year-old caucasian woman, with HIV-1 and HCV co-infection detected in 1996, presented with complaints of blurry vision, which she had begun to notice 4 years prior.

Adherence to follow-up on systemic infection was poor, and she had only been medicated with antiretroviral therapy (ART) during her pregnancies: in 1996 with zidovudine (ZDV); 2002 with ZDV/lamivudine and nevirapine (NVP) and in 2004 with didanosine, lamivudine and NVP.

In 2007 her CD4+ count was 41 cells/mm^3 (1,8%) and she was initiated on fixed combination tenofovir/emtricitabine and lopinavir/ritonavir, which she had stopped in the first month.

In December 2009 she appeared with a CD4+ count of 238 cells/mm^3 and HIV viral load of 69498 cps/mL, and started tenofovir/emtricitabine and EFV. Since this time CD4+ count have kept above 300 cells/mm^3 and viral load has been undetectable.

After start on EFV she report dizziness in the morning,

trouble sleeping and tiredness and three months later the patient started to notice progressive loss of vision in both eyes and started to have an irregular adherence.

During follow-up the patient had no AIDS-defining illness.

Our first ophthalmological evaluation of this patient occurred in April 2013 and was thus performed after a cumulative period of 24 months with EFV, and 10 months after last ingestion of the drug, according to the patient.

At presentation best corrected visual acuity was 20/100 for the right eye (RE) and 20/125 for the left eye (LE). Biomicroscopy and intra-ocular pressure was normal in both eyes. Dilated fundus examination revealed mottled atrophic changes of the macular retinal pigment epithelium (RPE), in a bull´s eye pattern, more marked in the LE (figure 1), with no other visible abnormalities.

Fluorescein angiography showed early mottled hyperfluorescence in the macula of both eyes, in an annular pattern, consistent with bull´s eye atrophy of the RPE (figure 2).

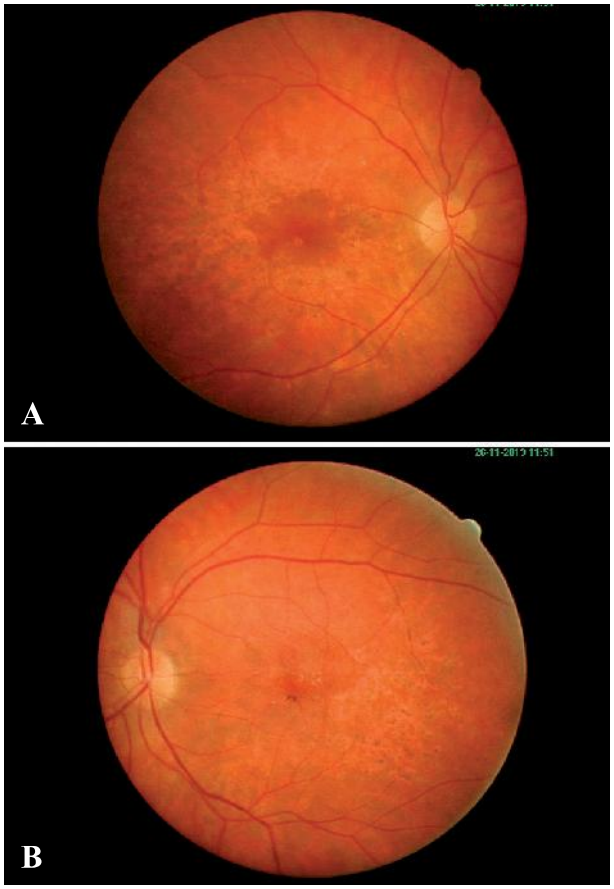

Fig. 1 | (**A**), (**B**) Colour photographs showing mottled atrophic changes of the macular RPE, in a bull´s eye pattern, in both eyes.

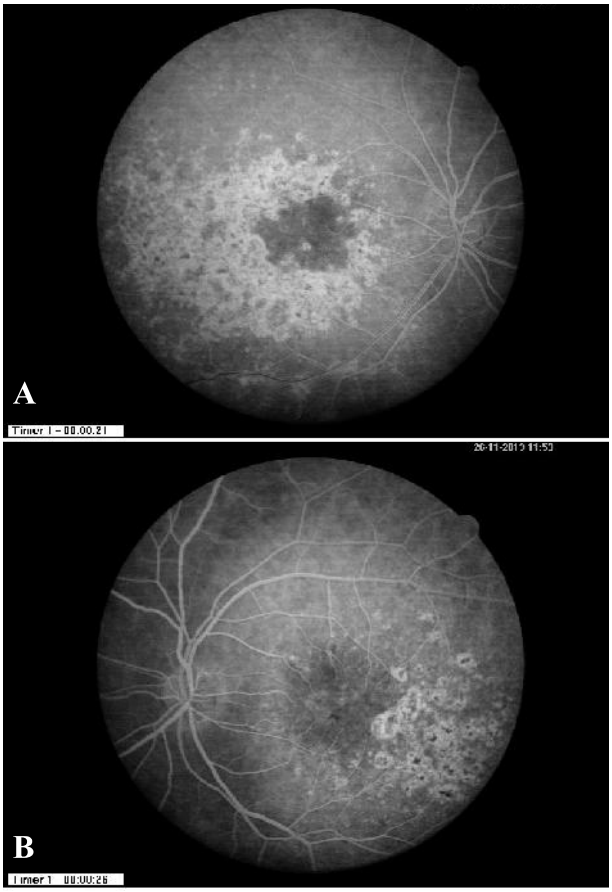

Fig. 2 | (**A**), (**B**) Fluorescein angiography showing a ring-shaped RPE defect in the macula of both eyes.

Macular optical coherence tomography (OCT) revealed thinning of the neuroretina, more evident in the temporal region to the fovea, at the expense of the outer layers of the retina, with almost total absence of the photoreceptors line (figure 3).

Fig.3 (a), (b) Macular optical coherence tomography showing a thinning of the retina, with almost total absence of the photoreceptors line.

Full-field electroretinography (ERG) was normal.

Chest x-ray was normal; VDRL was negative; and cytomegalovirus (CMV) viremia was negative.

The patient refers no family history of retinal disorders.

DISCUSSION

Ocular manifestations in AIDS patients are classically related to low CD4+ counts, especially HIV-related microangiopathy and CMV retinitis[2]. Our patient presented with a low CD4+ count during a short period and many years before the ocular complains, with CMV viremia negative.

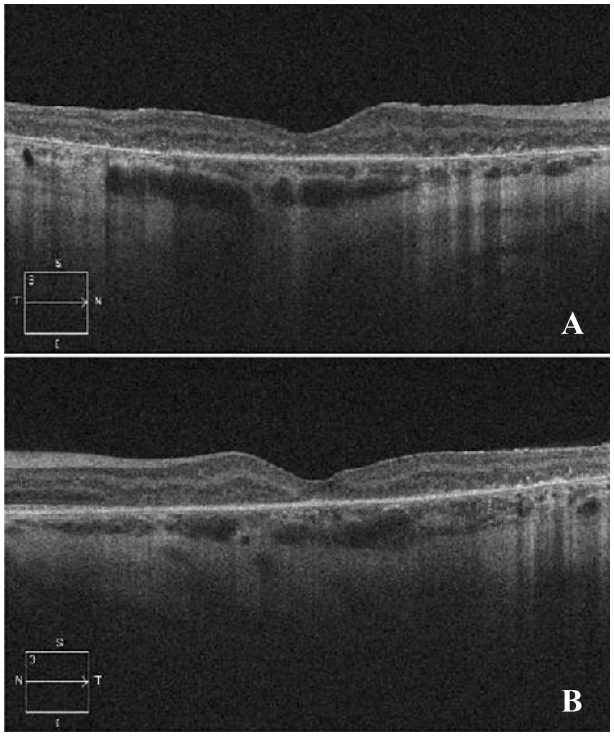

Fig. 3 | (**A**), (**B**) Macular optical coherence tomography showing a thinning of the retina, with almost total absence of the photoreceptors line..

Three drugs used in the treatment of HIV infection have previously been linked with retinal epitheliopathy: didanosine (ddI)[3,4], clofazimine[5], and the protease inhibitor ritonavir[6].

Retinopathy of ddl has a peripheral occurrence and histologically was shown to affect primarily the RPE with secondary damage to the neurosensory retina and to the choriocapillaris[4]. Clofazimine is implicated in pigment epitheliopathy and ritonavir retinal toxicity has being associated with RPE changes without fovea involvement[7].

EFV presents a marked pharmacokinetics and pharmacogenetics inter-individual variability. Central nervous system (CNS) side effects are increased with EFV plasma concentrations>4000ng/mL and more frequent in patients carrying mutation on CYP2B6*6 allele, associated with a significantly greater EFV plasma exposure[8,9]. The mutation on CYP2B6*6 allele frequency is higher in african population (49 and 47% in Ghanaians and African Americans, respectively)[10], when compared to frequencies in Caucasians and Orientals (25 and 18%, respectively)[11,12].

Despite the high frequency of mutation on CYP2B6*6 allele there is only one report of retinal toxicity associated with EFV, appearing to be an idiosyncratic reaction.

The patient exposition to ddI and ritonavir was very short and had no temporal relation to visual complains. Since she was started on EFV she begun to notice serious CNS side effects, followed by the visual complains.

However EFV is the most commonly used medication in ART and there is only one case of epitheliopathy linked with EFV[13].

CONCLUSION

Although it´s an unusual report, despite the huge number of patients on EFV, together with the other similar case reported[13], we believe that the visual deffect it´s due to EFV and could justify the routine evaluation of, at least, some patients with the most serious SNC side effects, believing that those patients have an increased plasma concentration of the drug.

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CONTACTO
Cristina Vaz Pereira
crisvpereira@gmail.com
Tlm:926568598
Rua Américo da Silva Marinho 1, 8º esquerdo.
2835-312 Lavradio - Portugal