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Short Communication

Didanosine-Associated Toxicity Mimicking Retinitis Pigmentosa in a HIV Infected Patient

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Keywords

- Toxic retinopathy
- *Pseudoretinosis pigmentaria*
- Acquired Immuno Deficiency Syndrome
- Didanosine/adverse effects

Abstract

Objective: To report uncommon Didanosine-associated retinal toxicity in a HIV infected patient.

Method: Case report

Results: A 51-year-old HIV-infected female, treated with didanosine (ddI) for 16 years, with history of decreased night vision, peripheral visual field loss, photopsias, and motor ataxia. Ophthalmologic examination and auxiliary test confirmed the diagnosis of retinal toxicity. Most of symptoms improved after medication discontinuation.

Conclusion: This report highlights the need for constant monitoring of patients using the ddI for early detection of possible retinal toxicity.

INTRODUCTION

Since 1991, there are reports in the literature associating didanosine (ddI), purine analogue and reverse transcriptase inhibitor used in the treatment of acquired immunodeficiency syndrome (HIV) to toxic retinopathy [1,2] and optic neuritis [3,4]. Whitcup et al. [1] conducted a study that demonstrated anatomopathologic lesions in the retinal pigment epithelium (RPE), accompanied by partial loss of choriocapillaris and neurosensory retina mainly in the middle-periphery. The damaged mechanism is still unknown [5]. The first cases were reported in children [1-3], followed by case reports also in adults [6].

Among ocular complications in patients living with HIV, the most commonly described were opportunistic infections, retinal vascular disease, cancer and drug toxicity [7]. Although the RPE is partially protected by the presence of the blood-retinal barrier and scleral isolation, there are many potentially toxic substances that can cause its degeneration [8,9], and have been associated with toxic retinopathy [1,2], optic neuritis [3,4], anterior uveitis and cystoid macular edema [10]. Systemic adverse events include pancreatitis and peripheral neuropathy [1].

Didanosine is an antiretroviral with activity against HIV-1 and HIV-2, including strains resistant to zidovudine (AZT) [5], whose active form dd-ATP (2-3 dideoxyadenosina triphosphate) have activity against the virus *in vitro* attacking T cells and monocytes, increasing CD4+ T cell levels and decreasing HIV p24 antigen [1], functioning as an inhibitor by competing for the substrate of reverse transcriptase enzyme dATP viral [11].

We report a case of an HIV positive patient, who presented DDI-associated toxicity mimicking retinitis pigmentosa after 17 years of continuous treatment.

CASE PRESENTATION

A 51-year-old HIV-infected female caucasian, natural from Sao Paulo, with a 5-month history of decreased night vision in the left eye (OS), peripheral visual field loss, photopsias and motor ataxia examined by a neurologist and diagnosed with Parkinson disease in use of antiretroviral therapy: atazanavir, ritonavir, lamivudine, tenofovir, didanosine, and other medications such as: levodopa, levothyroxine, atorvastatin, risedronate sodium, calcium, vitamin D, ranitidine and olanzapine. CD4+ T cell count was 180 cells/mm3 and viral load undetectable. Patient referred low visual acuity in the right eye (OD) since childhood due to an anisometropic amblyopia. Visual acuity was light perception in OD and 20/20 in OS. Ophthalmic exam showed ptosis in OD and myopic refraction, pupil examination and intraocular pressures were normal in both eyes. Anterior segment evaluation was

normal in OS and showed a dense cataract in OD. Fundus examination disclosed a round, well defined waxy pallor optic disc with a 0,6 cup-disc ratio, arteriolar narrowing with loss of the foveal reflex. The peripheral retina disclosed discrete amounts of bone spicule- like pigment changes in OS. The fundus examination of the right eye was difficult due to the cataract.

Laboratory tests (blood counts, serologies, etc.) chest X-ray, MRI of the spine and abdominal USG were normal. Visual field test Thereshold 30-2 SITA Standard of the OD was impossible and in OS showed a foveal sensitivity of 37 dB, glaucoma hemifield test outside normal limits, concentric constriction, mean deviation (MD) and pattern standard deviation (PSD) graphics highly altered with marked loss of sensitivity in all external points between 10 and 15 degrees, except in some points temporal to the blind spot. Electroretinogram (ERG) demonstrated a multifocal loss of retinal function suggestive of retinal toxicity. Magnetic resonance imaging (MRI) of skull showed: increased signal intensity on T1 in the globus pallidus and subthalamic nuclei.

The diagnosis of toxic retinopathy associated with didanosine was made based on clinical history, examination and ophthalmologic exams. This medication was withdrawal and changed to new antiretroviral regimen: Lopinavir, Ritonavir and Atazanavir. Vitamin A was prescribed. In the follow-up visit after 2 weeks, the patient referred ocular and systemic symptomatic improvement. After 1 year of didanosine discontinuation, all the tests were repeated and demonstrated a visual field improvement of reliability indices and an increased of foveal sensitivity and MD. However glaucoma hemifield test continues outside normal limits, the numerical and graytone graphs showed an improvement in sensitivity of the central points (enlargement of tubular area) and paracentral points in the 4 quadrants.

DISCUSSION

When evaluating patients with suspected retinitis pigmentosa (RP) and a negative family history, causes of acquired retinal degeneration that can mimic RP such as: previous episode of ophthalmic artery occlusion, diffuse uveitis, including infections such as syphilis, paraneoplastic syndromes and retinal toxicity of drugs should be considered [12].

In the present case, the combination of a good clinical history and a complete ophthalmic examination contributed significantly to diagnosis, since many diseases and syndromes entered as differential diagnosis (advanced RP, advanced glaucoma, chronic papilledema, optic disc drusen, vitamin A deficiency, toxic agents, inflammatory processes, genetic diseases featured by the association of pigmentary retinitis fundoscopic aspect and ataxia [12] and bilateral occipital lesion sparing the macular region (though this last cannot be ruled out by the lack of the visual field in the contralateral eye, MRI of the brain showed no injury at this location).

In all cases described in the literature, patients with ddI toxic retinopathy had peripheral pigmentary changes in both eyes, always with clinical and histological sparing of the macula [13]. These secondary injuries are quite rare and more common in children who are treated with high ddI doses [1,2,3]. Fernando et al. [13] observed a marked improvement in electrophysiological function in an adult patient after ddI discontinuation. Similar findings were made in children [3]. It is not yet known the mechanism by which ddI injures the RPE, the neurosensory retina and the choriocapillaris, but appears to be related to the drug's effect on mitochondrial DNA [5]. Neither is well-known mechanism by which retinal dysfunction could revert, but one study suggests that macula, could play a key role on this functional recovery [13].

This report shows the need for constant monitoring of patients using the ddI for early detection of possible retinal toxicity.

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