Bilateral ocular deposit of chlorpromazine

Depósito ocular bilateral de clorpromazina

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ABSTRACT

Chlorpromazine is a medication widely used in psychiatry for the treatment of psychoses, especially schizophrenia. Since 1964, published articles have been correlating this medication with the appearance of ocular alterations. In this paper, we report the case of a 65-year-old patient with ocular effects due to long-term therapy with chlorpromazine. Biomicroscopy of both eyes presented diffuse granular brown deposits, most prominent at the deep stroma and corneal endothelium level. Also showed anterior subcapsular brown deposits with a stellate pattern in the lens. The total amount exceeds 2.000g (significant for the ocular alterations described) considering the patient's daily dosage of chlorpromazine of 300mg for ten years. After performing complete ophthalmic evaluation and discarding other causes for the ocular deposits, we diagnosed a secondary corneal deposit and cataract due to the use of chlorpromazine. This case reinforces the importance of periodic follow-up with an ophthalmologist for chlorpromazine users to trace ocular changes, heeding the exposure time and its dosage.

RESUMO

A clorpromazina é uma medicação muito empregada na psiquiatria para tratamento de psicoses, especialmente em casos de esquizofrenia. Desde 1964 existem artigos publicados que correlacionam o uso dessa medicação com o aparecimento de alterações oculares. Neste trabalho, relatamos o caso de um paciente de 65 anos com efeitos oculares devido à terapia de longo prazo com clorpromazina. A biomicroscopia de ambos os olhos apresentou depósitos granulares difusos e de cor marrom, mais proeminente ao nível do estroma profundo e do endotélio da córnea, além de depósitos castanhos subcapsulares anteriores centrais em um padrão estrelado no cristalino. Considerando a dose diária de clorpromazina de 300mg por 10 anos usada pelo paciente, a quantidade total ultrapassa 2.000g (dose considerada significativa para as alterações oculares descritas). Após avaliação oftalmológica completa e descartado outras causas desses depósitos oculares, foram diagnosticados depósito corneano e catarata secundários ao uso de clorpromazina. O caso apresentado reforça a importância do acompanhamento oftalmológico periódico de usuários de clorpromazina para o rastreio de alterações oculares, atentando-se ao tempo de exposição à droga e à posologia da mesma.

INTRODUCTION

Chlorpromazine was synthesized in France in 1950 by Charpentier, introduced as a clinical practice after 2 years by Delay and Deniker; frequent in psychoses treatment, especially schizophrenia.[1-3]

Antipsychotics, like any drug, are capable of producing harmful effects on the body, along with the benefits that we seek when we medicate.[1]

In 1958, adverse ocular effects were noticed in patients using chlorpromazine,[1] but they were only described by Greiner and Berry in 1964.[2,3] Since then, there have been several reports correlating this medicine with lens and corneal opacity.[1-5]

In this paper, we report the case of a 65-year-old patient with ocular deposits due to long-term therapy with chlorpromazine.

CASE REPORT

A 65-year-old Caucasian male attended the outpatient clinic of ophthalmology at *Hospital de Clínicas* in *Universidade Federal do Paraná* (UFPR), in Curitiba (PR), Brazil, complaining of progressive low visual acuity in his left eye. He was under treatment for manic-depressive psychosis with chlorpromazine 300mg per day for 10 years. In addition, he was using 400mg per day of carbamazepine and 10mg per day of diazepam. He did not present previous ophthalmic pathology or surgery.

Ophthalmic examination:

- Uncorrected visual acuity (UCVA) according to the Snellen Chart: 20/25 in the right eye (OD) and 20/40 in the left eye (OS).
- Best corrected visual acuity (BCVA) according to the Snellen Chart: 20/25 in the OD (dynamic refraction of +0.25 -0.25 x105º) and 20/25 in OS (dynamic refraction of +0.50 -1.00 x110º).
- Biomicroscopy of both eyes (OU): diffuse brown granular deposits, most prominent at the deep stroma and corneal endothelium level (Figures 1B, 2A, and 2B) and central anterior subcapsular brown deposits with a stellate pattern in the lens (Figures 1A and 2B); mild corneal edema; no anterior chamber reaction; reactive and regular pupil.
- Intraocular pressure (IOP) measured by the Goldmann applanation tonometer: 14mmHg (OD) and 12mmHg (OS).
- Four-mirror gonioscopy (OU): open-angle up to the ciliary body range in all quadrants, with 2+/4+ pigmentation, and no pigmentary glaucoma.

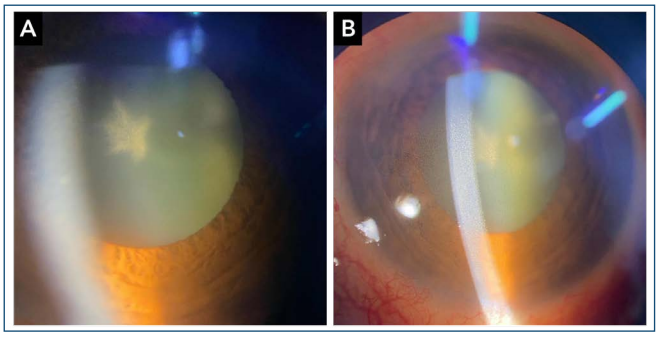

Figure 1. Right eye: slit lamp photograph, (A) shows stellar cataract and (B) shows multiple fine deposits on the cornea.

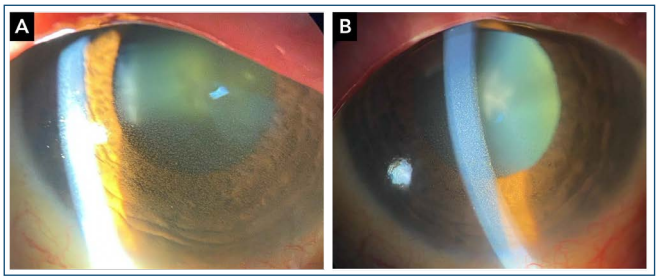

Figure 2. Left eye: slit lamp photograph, (A) multiple fine deposits in the cornea and (B) corneal deposits and stellar cataract.

- Indirect fundoscopy (OU): attached retina, optic nerve, and macula with no alterations, transparent vitreous. Papillary excavation of 0,3x0,3 (OD) and 0,45x0,45 (OS).
- Corneal specular microscopy: 2.183 cells/mm² (OD) and 2.167 cells/mm² (OS). The endothelial mosaic showed cells with ill-defined edges probably because of corneal opacity OU.
- Corneal pachymetry: 592µm (OD) and 578µm (OS).

We requested laboratory tests to discard metabolic, hereditary, and infectious causes. Among these tests, only cytomegalovirus immunoglobulin G (IgG) and toxoplasmosis IgG were positive.

The total amount of oral chlorpromazine exceeded 2.000g (a dosage considered significant for the ocular alterations described) considering the patient's daily dosage of 300mg for ten years. Therefore, the diagnosis of corneal deposits and secondary cataract from the use of chlorpromazine was confirmed. We instructed the patient about the presented alterations and reported the examination findings to his psychiatrist.

We did not suggest surgical treatment due to the improvement of visual acuity wearing eyeglasses at this point. The patient is being followed up every six months at the ophthalmology anterior segment outpatient clinic at *Hospital de Clínicas* at UFPR.

DISCUSSION

Chlorpromazine is derived from phenothiazine and used in the treatment of psychiatric disorders. High doses of this drug for a long period can cause cutaneous and ocular pigmentation. The most affected ocular structures are sun-exposed areas, such as the crystalline lens, cornea, conjunctiva and eyelids. These changes are dose-dependent and are irreversible even with medication discontinuation.[2-4,6-14]

Changes in the anterior segment occur after a cumulative dosage of 500g, with lenticular involvement preceding corneal pigmentation.[2] Alexander and collaborators had discovered that 67% of patients who had used this medication had some alteration of the crystalline lens, while 45% of them presented corneal alteration. However, both conditions rarely reduce the visual acuity, and the patients may occasionally report glare and halos around lights.[3-5]

Thaler and collaborators described lenticular pigmentation as occurring in five stages, ranging from isolated, brownish, dust-like spots on the anterior surface of the lens to stellate cataracts that can impair visual acuity. The stellate pattern, which characterizes the lenticular changes as grade IV, has a dense central area with radiating branches,[4] as seen in our patient.

The germinal zone of the crystalline lens epithelial cells is on the periphery of the anterior lens capsule. Considering the central star-shape of the deposits, it is believed that, when epithelial cells move towards the center of the anterior capsule, they gather the deposits in their cytoplasm and eventually accumulate them in the center of the capsule, where they eventually die. This centripetal movement of lens epithelial cells, as well as aqueous convection, may be a possible mechanism for the star-shaped deposition of the drug in the anterior capsule of the lens. Chlorpromazine accelerates the normal lenticular aging process, which may also contribute to closed-angle glaucoma.[3,8,9,11] Lens pigmentation is rarely evident when the total cumulative dosage is less than 500g, and the prevalence of pigmentary changes increases with a dosage between 1.000 and 2.000g. Since some psychiatric conditions may require daily dosages of over 800mg, lenticular pigmentation can appear in 14 to 20 months of therapy. Dosages consisting of 2.000mg per day caused lenticular changes in 6 months of treatment.[3]

Corneal deposits are generally described as present in the posterior stroma, Descemet membrane, and endothelium, as in our patient's case, suggesting drug distribution from the aqueous humor. Chlorpromazine is believed to denature proteins when exposed to light, which become opaque and deposit on the tissue. The role of receptors is also crucial in explaining the location of deposits on the cornea. It has been postulated that endothelial deposits can be attributed to the binding of chlorpromazine to dopamine D2 receptors to the corneal endothelium.[3,5,6,8,9,13,14]

An experimental study showed that corneal endothelial cells are sensitive to phototoxic reactions of chlorpromazine solution pre-irradiated for 30 minutes with ultraviolet light. Because the cornea is constantly exposed to light and allows for long-wavelength ultraviolet light in, it is a potential concern that patients receiving chlorpromazine may be at risk for corneal endothelial cell damage induced by phototoxic reactions from this drug or its by-products deposited deep in stroma or endothelial cells.[3,5,6,8,9,13,14]

Retinal changes may occur after using chlorpromazine, but they are rare. There were no signs of drug deposition on the posterior segment in our case.[2,3,8,10] The use of eyeglasses to presumably reduce the amount of ultraviolet light entering the eye has not been successful in diminishing the prevalence of ocular toxicity. The use of d-penicillamine was also unsuccessful in reversing the pigmentary changes.[3]

In the case of corneal and lens changes, when visual acuity is not significantly affected and the patient is asymptomatic, drug dosing can continue without modification. If the patient becomes symptomatic we must reduce the dosage or use a different drug.[4] Joint treatment between the psychiatrist and the ophthalmologist is crucial.

This case reinforces the importance of periodic follow-up with an ophthalmologist for chlorpromazine users to trace ocular changes, heeding the exposure time to the drug and its dosage.

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