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Multimodal Assessment of Chlorpromazine Ocular Deposits in a Patient on Long-Term Chlorpromazine Therapy

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Abstract

Introduction: Chlorpromazine is a widely used antipsychotic medication, known for its potential ocular side effects with prolonged use. Ocular deposits are a well-documented manifestation, typically affecting the cornea, lens, and other anterior segment structures. The presentation of these deposits may be subtle and often go unnoticed unless specifically sought during routine ophthalmologic examinations. We describe a case of anterior ocular segment involvement in a patient with long-term Chlorpromazine therapy.

Case Report: A 68-year-old male with a 20-year history of oral Chlorpromazine therapy for schizophrenia presented for a routine eye examination. His medical history revealed no other significant ocular issues. On examination, the patient had visual acuity of 20/50 in both eyes, and there were no complaints of visual disturbances, but slit-lamp evaluation revealed fine, golden-brown deposits in the corneal endothelium. Additionally, the anterior lens capsule displayed similar pigmentations, indicative of Chlorpromazine deposition. The confocal images demonstrated hyper-reflective, round to oval deposits localized within the central and peripheral regions of the corneal epithelium, stroma and endothelium. Gonoscopic examination revealed pigmentary deposits in the Schwalbe line. The patient denied any subjective visual disturbances, and his intraocular pressure was within normal limits, with OCT images of the optic nerve demonstrating no alterations.

Discussion: Chlorpromazine has been known to accumulate in the cornea and lens with long-term use. The corneal deposits are typically non-progressive, but they can lead to visual disturbances in some cases, particularly if the pigment accumulation is extensive. In the presented case, the ocular findings were characteristic of drug-induced deposition without significant visual impairment, emphasizing the importance of monitoring patients on prolonged Chlorpromazine therapy. Regular ophthalmologic assessments are essential to detect these deposits early and manage any potential complications. Further research is needed to better understand the underlying mechanisms of Chlorpromazine-induced ocular changes and to determine the long-term implications of these deposits on visual health.

Conclusion: Chlorpromazine deposits in the anterior segment of the eye are a recognized but often underreported phenomenon. Clinicians should maintain a high index of suspicion for these changes in patients with long-term use of this medication, especially in the elderly. Regular ophthalmic evaluations should be integrated into the care of patients receiving long-term antipsychotic therapy to detect and manage any ocular side effects.

Keywords: Chlorpromazine Deposits; Anterior Segment; Confocal

Introduction

Chlorpromazine, a widely used first-generation antipsychotic, has been a cornerstone in the management of psychiatric conditions such as schizophrenia for several decades. While it remains effective in treating these disorders, prolonged use of chlorpromazine is associated with a range of ocular toxicities, including the deposition of drug-related pigments in the cornea and lens. The effect is dosedependent and it is not uncommon to identify anterior segment pigmentary deposits in the patients on chronic chlorpromazine treatment [1]. These deposits are commonly observed in the corneal epithelium and stroma but may also affect the corneal endothelium and anterior lens capsule, leading to potential long-term visual consequences [1,2]. Although these deposits are often asymptomatic in the early stages, they can cause visual disturbances if they accumulate or affect critical ocular structures [3].

The ocular deposits are believed to be composed of melanin and chlorpromazine metabolites that accumulate in sun-exposed areas through a phototoxic reaction [2]. The mechanisms behind

these deposits remain poorly understood, but it is believed that chlorpromazine interacts with corneal cellular structures, leading to pigmentary accumulation over time [4]. In vivo studies using advanced imaging techniques, such as confocal microscopy and the HRT II Rostock corneal module, have provided valuable insights into the location and characteristics of these deposits [5]. Despite the relatively benign nature of these deposits in many cases, their presence in the corneal endothelium and anterior lens capsule warrants careful monitoring, as it may lead to endothelial dysfunction or cataract formation [6].

Slit-lamp examination reveals granular white-grey opacities diffusely scattered across the entire corneal endothelium, with the highest concentration in the central area, gradually decreasing in density toward the periphery. Ocular toxicity may also be associated with corneal edema. A stellate-shaped opacification is observed in the central anterior cortex of both crystalline lenses. Corneal changes are typically seen after a cumulative low-dose treatment (>300 mg/day) over two years, or with high-dose administration (>2 g/day) over a short period of time (a few months). The corneal pigmentary deposits are generally irreversible, although there have been reports of slowly reversible epithelial keratopathy in some cases [2].

In this case report, we present a 68-year-old male patient with a 20-year history of oral chlorpromazine therapy, who developed characteristic deposits in both the corneal endothelium and the anterior lens capsule. This case emphasizes the importance of early recognition of chlorpromazine-induced ocular changes, especially in patients with long-term use of this medication, and the need for regular ophthalmic evaluations to manage potential complications effectively. By documenting this case, we aim to further explore the clinical implications of chlorpromazine-induced ocular toxicity and contribute to the growing body of knowledge on this important issue.

Consent

This study adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from the patient for publication of this report and its related images.

Case Presentation

A 65-year-old Caucasian male presented to the ophthalmology outpatient clinic at Hospital de Olhos - CRO in Guarulhos (SP), Brazil, with complaints of progressive low visual acuity in both eyes. The patient had been receiving treatment for schizophrenia for the past 20 years, taking 500mg of chlorpromazine daily, along with 20mg of quetiapine and 20mg of haloperidol per day. He had no prior history of ocular conditions or surgeries. On ophthalmic examination, his uncorrected distance visual acuity (UDVA) was 20/40 in both the right eye (OD) and left eye (OS) according to the Snellen Chart. His corrected distance visual acuity (CDVA) was 20/25 in the OD and 20/30 in the OS with dynamic refraction of +1.75 -1.25 x90º and +1.50 -1.00 x95º, respectively.

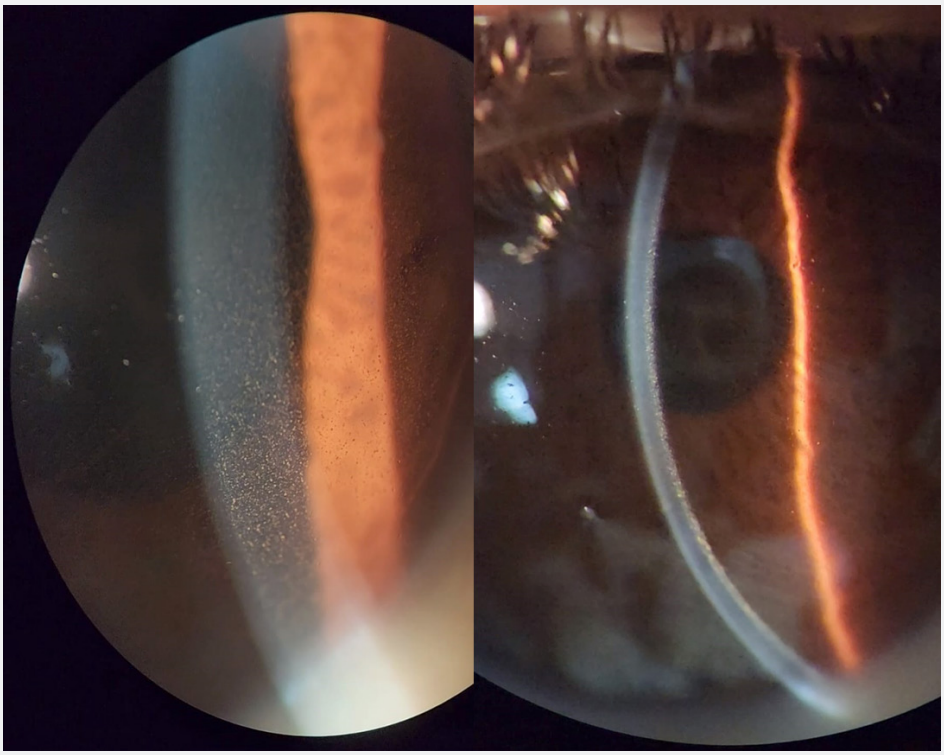

Figure 1: Biomicroscopy revealing Diffuse corneal pigmentary deposits.

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Biomicroscopy (Figure 1) revealed diffuse brown granular deposits, primarily located in the deep stroma and corneal endothelium, along with central anterior subcapsular brown deposits exhibiting a stellate pattern in the lens (Figure 2). Slit-lamp examination showed multiple fine, discrete white deposits scattered across the entire surface of the cornea, most notably in the interpalpebral region. The crystalline deposits were more prominent in the deeper layers of the cornea. The anterior chambers appeared quiet, and star-shaped opacity was observed on the anterior lens capsule, along with nuclear sclerosis in both eyes. Additional tests showed normal intraocular pressure (12mmHg in both eyes), open-angle gonioscopy with 2+/4+ pigmentation and the presence of deposits in the Schwalbe line (Figure 3), with no evidence of glaucoma.

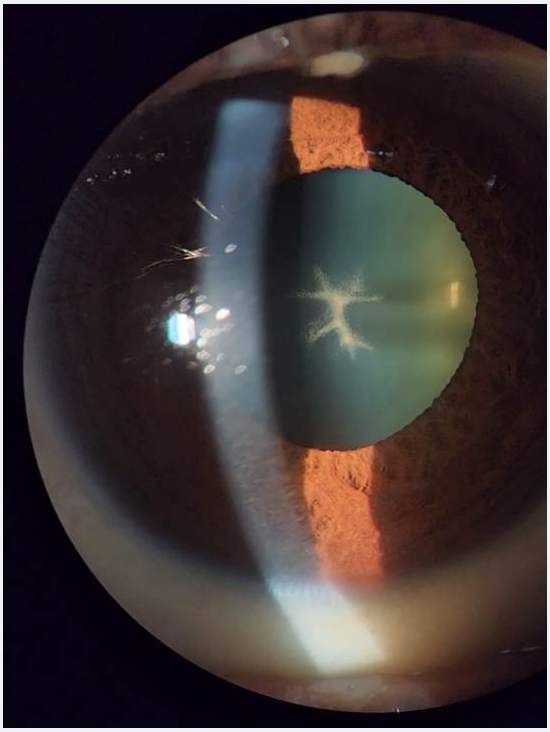

Figure 2: A Star-shaped anterior capsular lens opacity.

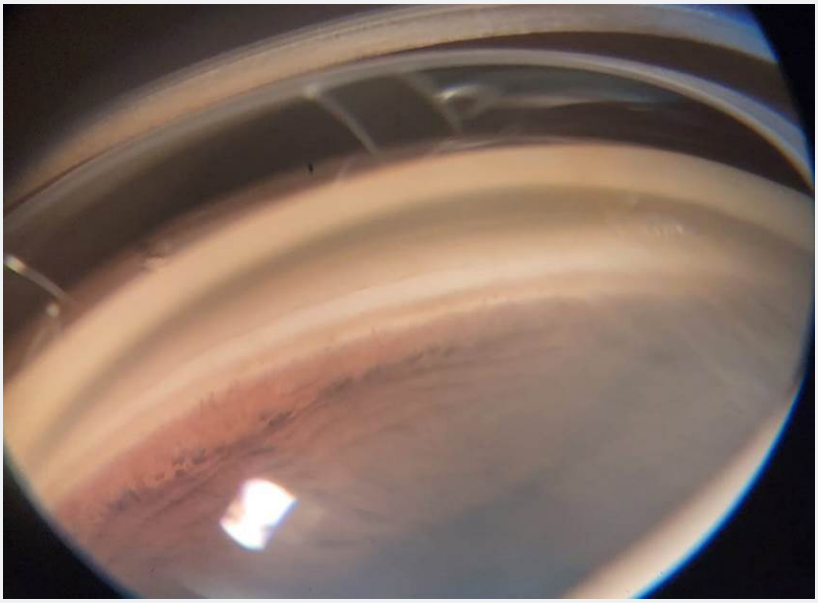

Figure 3: Presence of deposits in the Schwalbe line.

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Corneal specular microscopy (Figure 4) showed endothelial cell changes, likely due to deposits, and pachymetry revealed a central corneal thickness of 527µm in the right eye and 539µm in the left eye. Anterior segment optical coherence tomography (Tomey Corporation 2-11-33 Noritakeshinmachi, Nishi-Ku, Nagoya, Aichi, 451-0051, Japan) showed the presence of depositions involving mainly the endothelium (Figure 5).

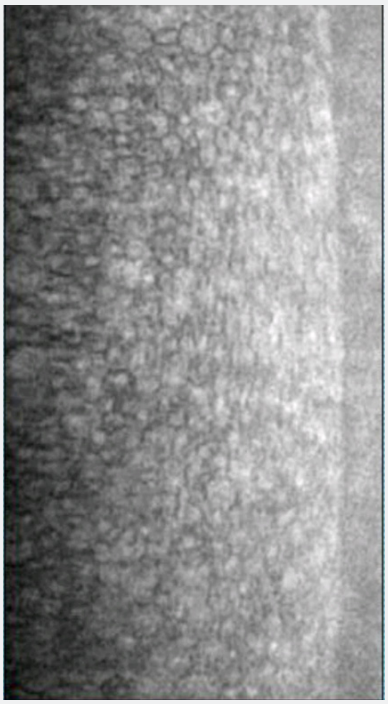

Figure 4: Corneal specular microscopy showing endothelial cell changes.

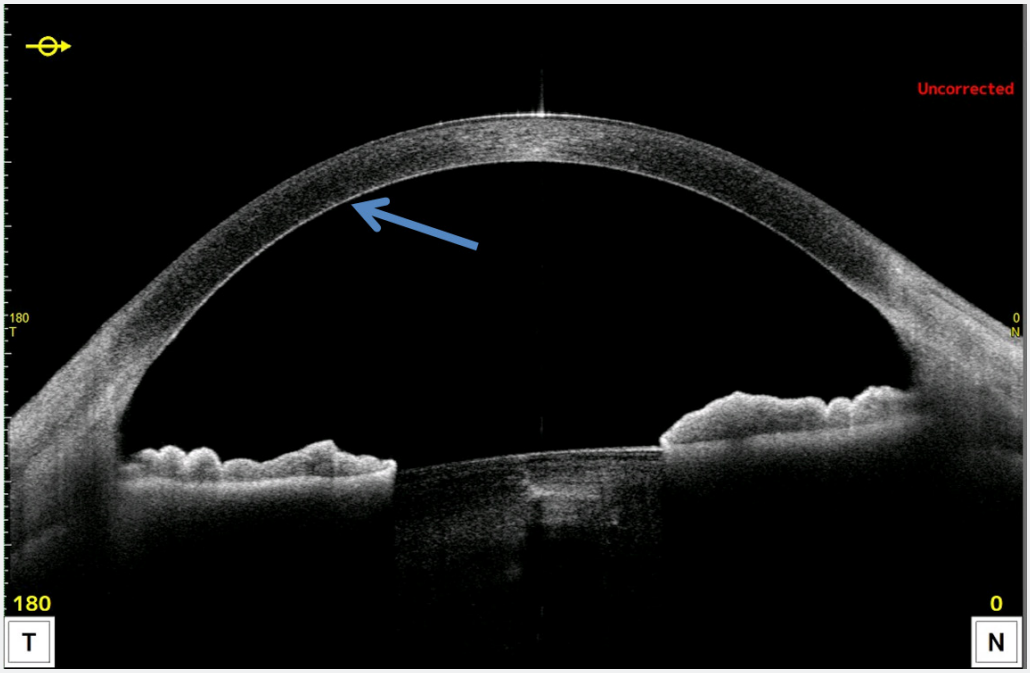

Figure 5: Anterior segment optical coherence tomography showing the presence of deposition involving the full thickness of córnea, mainly the endothelium (blue arrow).

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In vivo confocal microscopy (Figures 6 and 7) was conducted on both corneas using the Confocal Scan 3.0 (Nidek Technology, Padova, Italy). The confocal imaging revealed distinct hyper-reflective deposits present in each layer of the corneal epithelium, along with numerous white granular deposits located in the subepithelial superficial stroma of the cornea. Additionally, granular deposits were detected in the deeper layer of the stroma extending to the endothelium, which showed significant accumulation of deposits.

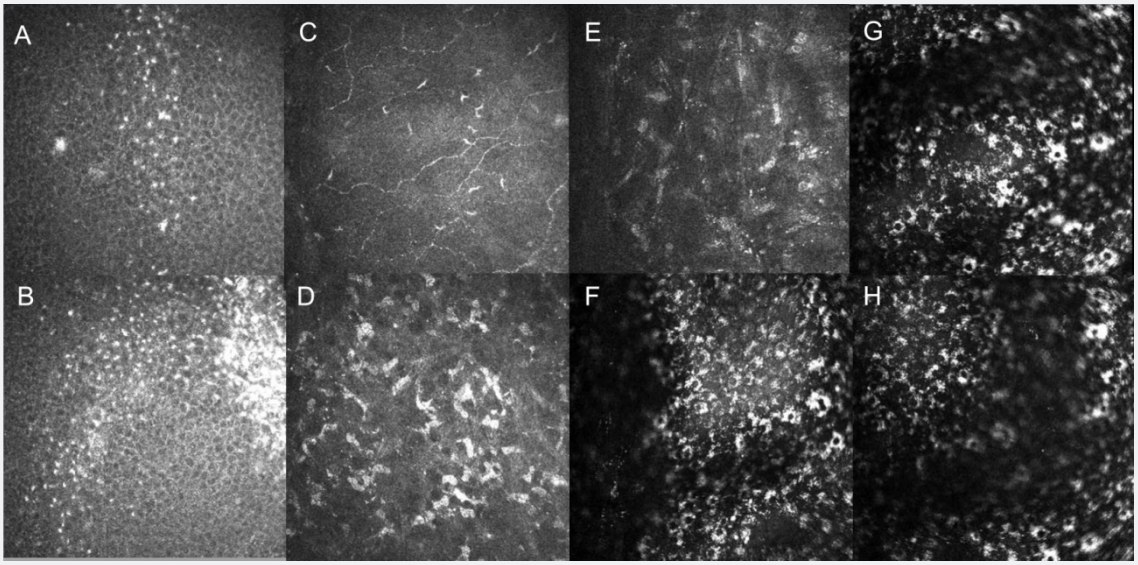

Figure 6:

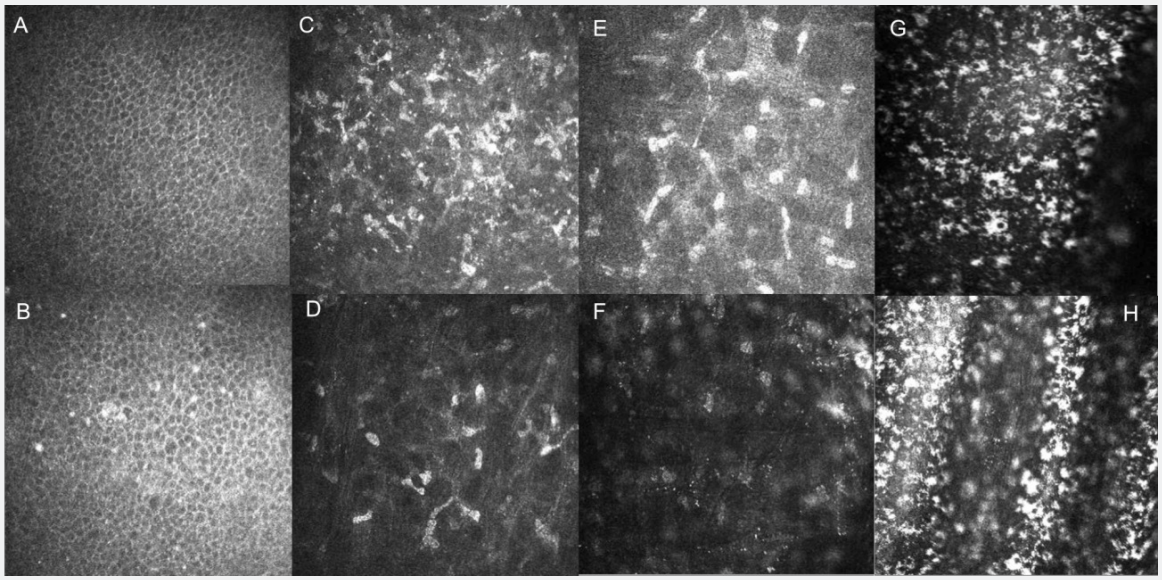

Figure 7:

The cumulative chlorpromazine dose exceeded 2,000g over 20 years, which is considered significant in contributing to the ocular changes observed. As a result, the patient was diagnosed with corneal deposits and secondary cataracts due to long-term chlorpromazine use. In view of the likely antipsychotic agent related ocular toxicity, a letter explaining the ocular clinical findings was issued to his psychiatrist to alert about the use of the anti-psychotic agent.

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No surgical intervention was recommended since the patient's visual acuity improved with corrective eyewear. He is now scheduled for regular follow-ups every six months at the ophthalmology anterior segment outpatient clinic at Hospital de Olhos – CRO in Guarulhos (SP), Brazil.

Discussion

Chlorpromazine, a commonly used first-generation antipsychotic, is associated with ocular toxicity, particularly in patients on long-term therapy. The ocular effects of chlorpromazine toxicity typically include drug deposition in various corneal layers, the anterior lens capsule, and occasionally other structures of the anterior segment [1]. In this case, a 68-year-old male with a 20-year history of oral chlorpromazine therapy presented with deposits in the corneal layers, specially in the endothelium, and anterior lens capsule-an uncommon but recognized finding in such patients [3].

Chlorpromazine has long been linked to ocular pigmentary deposits, a phenomenon first described in 1964 when 70 patients on chronic chlorpromazine therapy (lasting 3 to 5 years) had pigment deposits in the skin, cornea, and lens capsule. Since then, numerous reports have documented chlorpromazine-induced ocular pigmentary deposits, particularly affecting the cornea and lens capsule. Additionally, chlorpromazine is cytotoxic to the corneal endothelium. Other antipsychotics, such as levomepromazine, fluphenazine, trifluoperazine, and clozapine, have also been implicated in ocular pigmentary deposits.

It is proposed that chlorpromazine binds to serotonin and dopamine receptors in the cornea, leading to pigment deposition. Previous studies have highlighted ocular pigmentary deposits in patients receiving chlorpromazine treatment. Although the exact mechanism behind chlorpromazine-induced ocular pigmentary deposition is not fully understood, it is believed to be linked to drug decomposition triggered by ultraviolet light exposure, with deposits occurring more frequently in the interpalpebral region.

As a phenothiazine derivative used in treating psychiatric disorders, chlorpromazine, when used long-term or in high doses, can result in both cutaneous and ocular pigmentation. Ocular structures exposed to sunlight, such as the crystalline lens, cornea, conjunctiva, and eyelids, are most affected. These pigmentary changes are dose-dependent and irreversible, even if the drug is discontinued. Changes in the anterior segment generally occur after a cumulative dose of 500g, with lenticular involvement preceding corneal pigmentation [1-3].

Thaler and colleagues categorized lenticular pigmentation into five stages, ranging from isolated, brownish dust-like spots on the anterior lens surface to stellate cataracts that impair visual acuity. The grade IV stellate pattern, characterized by a dense central area with radiating branches, was seen in our patient. The germinal zone of crystalline lens epithelial cells is located at the periphery of the anterior lens capsule. The star-shaped nature of the deposits suggests that as epithelial cells move toward the center of the anterior capsule, they accumulate deposits in their cytoplasm, which then gather centrally, eventually leading to cell death. The centripetal movement of lens epithelial cells, along with aqueous convection, may help explain the star-shaped deposition pattern in the anterior capsule [4].

Lenticular pigmentation is rarely seen with a cumulative dose of less than 500g. However, pigmentary changes become more common with doses between 1,000 and 2,000g. In patients requiring daily doses over 800mg, lenticular pigmentation may develop within 14 to 20 months of therapy. At doses of 2,000mg per day, lenticular changes can appear within 6 months [1,3].

Corneal deposits typically localize in the posterior stroma, Descemet membrane, and endothelium, as seen in our patient, indicating drug distribution via the aqueous humor. It is believed that chlorpromazine denatures proteins when exposed to light, causing them to become opaque and deposit in the tissue. The drug's interaction with receptors may also influence where deposits form on the cornea. It is suggested that endothelial deposits result from the binding of chlorpromazine to dopamine D2 receptors on the corneal endothelium.

An experimental study demonstrated that corneal endothelial cells are sensitive to phototoxic reactions when chlorpromazine is pre-irradiated with ultraviolet light for 30 minutes. Since the cornea is constantly exposed to light and allows for the penetration of long-wavelength ultraviolet light, there is concern that chlorpromazine-treated patients may be at risk for corneal endothelial cell damage induced by phototoxic reactions from the drug or its by-products.

While chlorpromazine-induced ocular deposits are usually benign and do not always result in visual impairment [6], their presence underscores the importance of regular ophthalmologic evaluations for patients on long-term chlorpromazine therapy. Early detection of such deposits can help prevent or manage potential complications like endothelial cell loss, cataract formation, or other structural changes that may affect vision. Advanced imaging techniques such as confocal microscopy and the HRT II Rostock corneal module have become invaluable tools for accurately diagnosing and monitoring drug-induced corneal deposits in vivo [4,5].

Although chlorpromazine-related deposits are generally not associated with significant visual impairment, their detection has important clinical implications. Regular ophthalmologic exams should be part of standard care for patients on prolonged chlorpromazine therapy to facilitate the early identification of ocular side effects. This proactive approach enables clinicians to monitor deposit progression, educate patients, and intervene if necessary to prevent irreversible corneal damage or other complications [1].

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Moreover, while visual disturbances are rarely significant, patients may report subtle vision changes that can be traced back to drug-induced ocular toxicity. Comprehensive eye examinations, including slit-lamp biomicroscopy and imaging technologies, should be used to detect these deposits and evaluate their impact on ocular health. This case highlights the need for a multidisciplinary approach in managing patients on long-term antipsychotic medications, with regular ophthalmic follow-ups being a crucial aspect of their overall healthcare strategy [2].

In this case, corneal deposits were more clearly visible using HRT II RCM (High-Resolution Tomography II Confocal Microscopy) compared to slit-lamp microscopy. Not only were corneal endothelial deposits observed, but many deposits were also found in the epithelium and diffusily in the stroma. This imaging technique may become essential for assessing the onset or progression of drug-related adverse reactions in vivo.

In summary, this case highlights the ocular toxicity associated with long-term chlorpromazine use, specifically the deposition of the drug in all structures in the anterior segmento f the eye. These deposits are often asymptomatic but have the potential to lead to complications that can affect vision. The findings underscore the importance of regular ophthalmologic examinations in patients on long-term chlorpromazine therapy. Early detection of ocular changes through slit-lamp biomicroscopy and advanced imaging techniques can prevent or manage potential visual disturbances and improve patient outcomes. Regular eye screenings should be considered standard care in these patients to monitor for potential toxic effects on the ocular structures.

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