

Case Study

Phenothiazine group drug induced corneal and lenticular deposits in a patient of severe depression – a case report

ABSTRACT :

A 50-yr-old man, who had been taking medication for severe depression with psychosis, presented to eye OPD of UPRIMS & R with a chief complaint of visual disturbance of 8 months duration. He was continuously taking chlorpromazine unsupervised in double the dose and doubles the frequency. Slit-lamp examination revealed fine, discrete, and brownish deposits on the posterior cornea (Fig. 1). In addition, bilateral star-shaped anterior sub capsular lens opacities, which were dense, dust-like granular deposits, were noted (Fig. 1). Best-corrected visual acuity was 6/36 in the right eye and 6/24 in the left eye. Other ocular findings were normal. Dark pigmentation on face was present. The deposition was not reversible even after stopping the drug.

Keywords: - corneal deposits, drug induced lenticular opacity, phenothiazine induced deposits

Key Message:-

This case report shows that Phenothiazine group drug if taken in excess dose and for long duration can lead to visually disabling corneal deposits and star shaped lenticular opacification.

Phenothiazine group drug must be used with caution and under slit lamp ophthalmic monitoring and strictly under psychiatric monitoring.

The pigmented deposits in cornea are not reversible even after stopping the drug.

INTRODUCTION

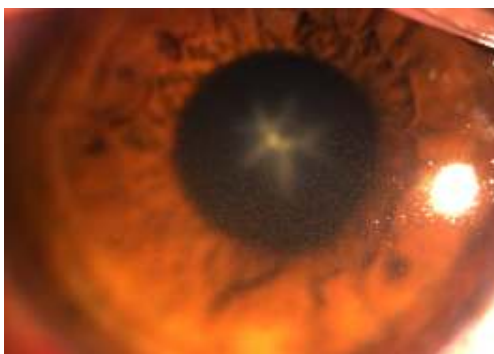
In 1960s phenothiazine was widely used for the chronic treatment of schizophrenia¹. However despite its extremely effective antipsychotic action, there is significant decline in the usage of phenothiazine over the last decade due to its tendency to produce ocular complications¹. In 1964 Greiner and Berry first described the ocular toxicity of phenothiazine over the cornea, conjunctiva and lens². One of the hypothesis for the ocular manifestations of

long term phenothiazine therapy is the property of phenothiazine to get deposit in the ocular tissues and to denature the proteins when exposed to light making them opaque³⁻⁴. Even after the discontinuation of the drug, these ocular changes persist.

Several case reports of chlorpromazine-induced corneal deposits and cataracts have been published till now (references from the literature to be written); however, Chlorpromazine and trifluoperazine-induced corneal deposits and cataract are unusual and rare. Herein, we report the case of Chlorpromazine and trifluoperazine-induced corneal deposit and cataract in a case of severe depression. Here we also report severe phototoxic pigmentation of skin in our case which occurs due to binding of phenothiazine to melanin granules¹⁻⁴

CASE

A 50-yr-old man, (race of patient to be written) who had been taking medication for severe depression with psychosis, presented to eye OPD with complaints of visual disturbance of 8 months duration. He was taking chlorpromazine unsupervised in double the dose and double the frequency. Slit-lamp examination revealed fine, discrete, and brownish deposits on the posterior cornea (Fig. 1). In addition, bilateral star-shaped anterior subcapsular lens opacities, which were dense, dust-like granular deposits, were noted (Fig. 1). Best-corrected visual acuity was 6/36 in the right eye and 6/24 in the left eye. Other ocular findings were normal. (any dark pigmentation in the retina to be written) Dark pigmentation on forehead was present (Fig 2). Rest systemic examination was within normal limits. (any pigmentation on the hands and fingers?)



63 Fig 1A

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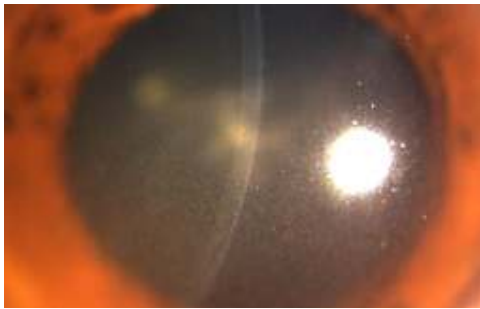


Fig 1B



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66 Fig 1C

Fig 1D

67 Fig 1A Right eye showing diffuse brownish coloured deposits in the inferior
68 2/3 rd of cornea with anterior sub capsular star shaped cataract.

69 Fig 1B Left eye showing diffuse brownish coloured deposits in the inferior 2/3
70 rd of cornea with anterior sub capsular star shaped cataract.

71 Fig 1C and 1D showing the level of brownish pigment deposit in right eye and
72 left eye, respectively.

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75 Fig 2 shows blackish pigmentation of the forehead of the patient.

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77 According to the information provided by his chemist, the patient had received
78 T. Trinicomforte (Trifluoperazine 5mg, Trihexphenidyl 2 mg, T. chlorpromazine
79 50 mg) and T. Alprex (Alprazolam 0.25mg) . Patient took these drugs for 6
80 years and now off drugs since 2 months. Psychiatry consultation done which
81 provided information that patient took these drugs in double the dose
82 prescribed and in double the frequency for 6 years without any supervision
83 and suffering from severe depression.

We have done dermatology consultation for pigmentation on face which correlated with Phenothiazine drug induced photo toxicity, causing dark pigmentation.

Patient was counselled and the intake of phenothiazine group drug stopped. Patient is shifted to newer safe anti-psychotic Risperidone after psychiatric consultation.

~~This case report shows that Phenothiazine group (chlorpromazine + trifluoperazine) drug if taken in excess dose and for long duration can lead to visually disabling corneal deposits and star shaped lenticular opacification. The deposits are not reversible even after discontinuation of drug.~~

DISCUSSION

Phenothiazines such as chlorpromazine or methotrimeprazine were introduced to the psychiatry clinics in 1953 and have been widely used for the treatment of psychiatric illnesses since then. Multiple studies have been conducted over the phenothiazine for their potential side effects of overdose and their complications^{1,3-5}. On chronic use, phenothiazine were found to have level 50 times higher than blood concentration in the ocular tissues in comparison to that of other tissues of the body⁶. Greiner and Berry were the first to describe the effect of long term medication of chlorpromazine in 70 patients as brownish granular pigmentation in the parenchyma of the cornea and a central star shaped opacity in the centre of anterior capsule of lens². McCarty et al reported that the ratio of anterior capsular opacity in cataract patients not on phenothiazine medication was 0.2%, while the ratio was 26% for the schizophrenics on phenothiazine medication⁷. A study conducted by Ruiz Gomez et al on the incidence of rate of cataract in Schizophrenics and control group subjects showed that the rate was 8.8 times higher in patients under long term medication of over 300mg chlorpromazine daily than that of the control group⁸. Many authors have reported that long term medication of phenothiazine increases the risk of cataract. It is believed that the clinical changes in the ocular tissues in patients who received a specific dosage of phenothiazine could be due to an increase in number and melanin content of melanin cells on the exposure of eyes to harmful ultraviolet rays and the accumulation of abnormal metabolites from photosensitization of chlorpromazine which is present in high concentration in the eyes. Still

118 controversy regarding the toxic levels of phenothiazine exists. According to
119 Delong et al, characteristic changes in the eyes were generally observed in
120 patients receiving chlorpromazine dosage of over 1000mg, and in more than
121 90% of patients receiving dosage of over 2,500mg; however these changes
122 were rare when the total dosage was 500mg⁹. Thaler et al reported that if
123 daily dosage of chlorpromazine exceeding 800mg, lenticular pigmentation can
124 begin to occur as early as within 14 to 20 months of treatment. A daily dosage
125 of 2000mg has caused these changes to appear as early as within 6 months
126 of therapy. As the dosage is increased, the ocular changes became more
127 distinct and remain continued even after stopping the medication¹⁰. Lal et al
128 reported the pigmentation in the skin and corneal endothelium due to long
129 term usage of phenothiazine and other neuroleptics like haloperidol,
130 trifluoperazine, levomepromazine and thioproperazine. They also reported
131 that skin pigmentation is reversible and might have different mechanism of
132 pigmentation than that of cornea¹¹.

133 Very few cases of corneal and lenticular drug deposits reported so far from
134 use of Phenothiazine group drug and none of them from India. Although
135 corneal and lenticular deposits have been present in literature after
136 Phenothiazine group drug¹⁻⁷.

137 The purpose of this case study is to highlight the visually disabling corneal
138 and lenticular deposits after the use of Phenothiazine drug which are not
139 reversible after stopping the drug in a patient of severe depression. This case,
140 may represent just the tip of the iceberg, and hence calls for establishment of
141 stringent ophthalmic screening protocols for the identification of corneal and
142 lenticular deposits at early stage when patient is on these drugs. This report
143 also re-iterates the fact that ophthalmic manifestations of drugs need to stop
144 of these drugs and their replacement by safer anti-psychotic drugs. Patient
145 will need cataract surgery with intraocular lens implantation to clear lenticular
146 deposits for visual rehabilitation.

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