



## Retinal toxicity of long term overdose of sildenafil citrate: A case report

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### ABSTRACT

**Purpose:** To report a case of eye structure changes in a patient with long-term overdose of sildenafil citrate.

**Observations:** A 28-year-old male presented to our outpatient clinic with flare sensation in both eyes for 1 year after taking sildenafil citrate at a dose of 200 mg daily for two years. mERG and OCT examination revealed persistent damage of retinal photoreceptor cells. The symptoms did not disappear after 3 months off the medication.

**Conclusions and importance:** Long term excessive use of overdose sildenafil citrate can cause serious damage to retinal photoreceptor cells. The retinal side effects of sildenafil citrate still need to be further investigated, and the administration of systemic overdose also needs to be considered by all physicians, not just ophthalmologists.

### 1. Introduction

Sildenafil citrate, a selective inhibitor of PDE-5, is widely used to treat erectile dysfunction. Overdose of sildenafil citrate can cause some ocular side effects such as impaired blue/green color discrimination and blurred vision. Herein, we report a case of side effects in a male patient with binocular visual disturbance after long term overdose of sildenafil citrate.

### 2. Case report

A 28-year-old man presented with a 1-year history of photopsia in both eyes. The patient had a medical history of taking 200 mg sildenafil citrate every day for 2 years for the treatment of erectile dysfunction (ED). On ophthalmic examination, the best-corrected visual acuity (BCVA) was 20/20 in the right eye and 20/25 in the left eye. Intraocular pressure was normal in both eyes. There was no significant abnormality in the anterior segment and fundus of either eye. Autofluorescence (AF) images in both eyes were normal (Fig. 1B, D). Optical coherence tomography (OCT) revealed hyper reflectivity of the ellipsoid zone in the fovea and discontinuity of the ellipsoid zone in the parafoveal region in both eyes (Fig. 1E and F). Examination of the visual field showed that both eyes had a central scotoma (Fig. 1I and J), and multifocal electroretinogram (mERG) showed abnormal appearances of 3D amplitudes

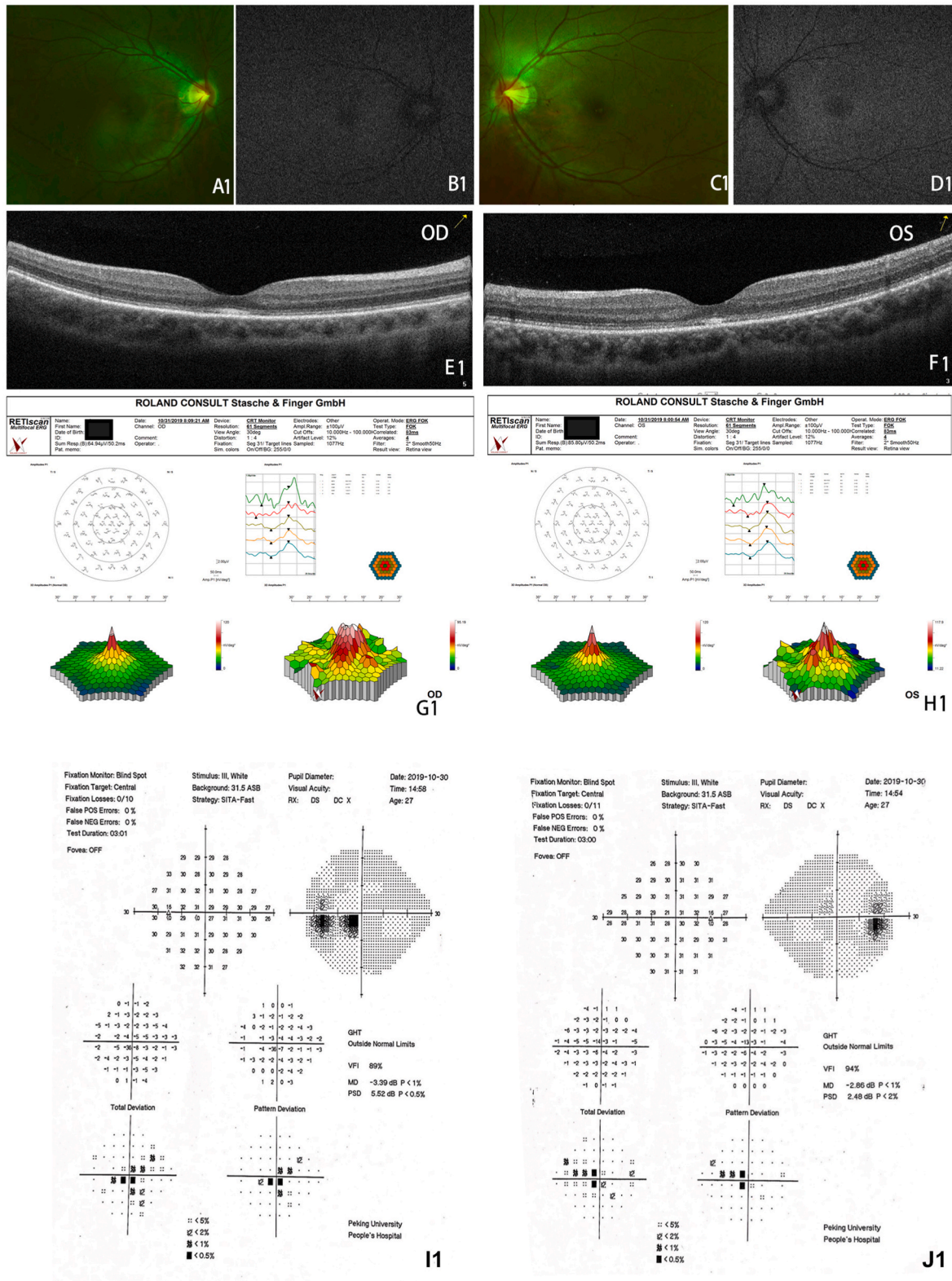
including disappearance of the regular macular peaks in both eyes, even though the retinal response amplitude density of 5 rings were normal (Fig. 1G and H). We suggested that the patient stop taking sildenafil citrate and take vitamin C to promote drug metabolism.

Three months after discontinuing the medication, BCVA was 20/25 in both eyes. The visual field examination showed a central scotoma in both eyes (Fig. 2I2, J2). OCT showed no changes of the hyper reflectivity of the ellipsoid zone in the fovea compared to prior (Fig. 2E2, F2). The mERG showed that the retinal response amplitude density of 5 rings fell sharply and the macular peaks disappeared in both eyes, which indicated that the damage to the photoreceptor outer segments and the interdigitation zone was progressive (Fig. 2G2, H2).

### 3. Discussion

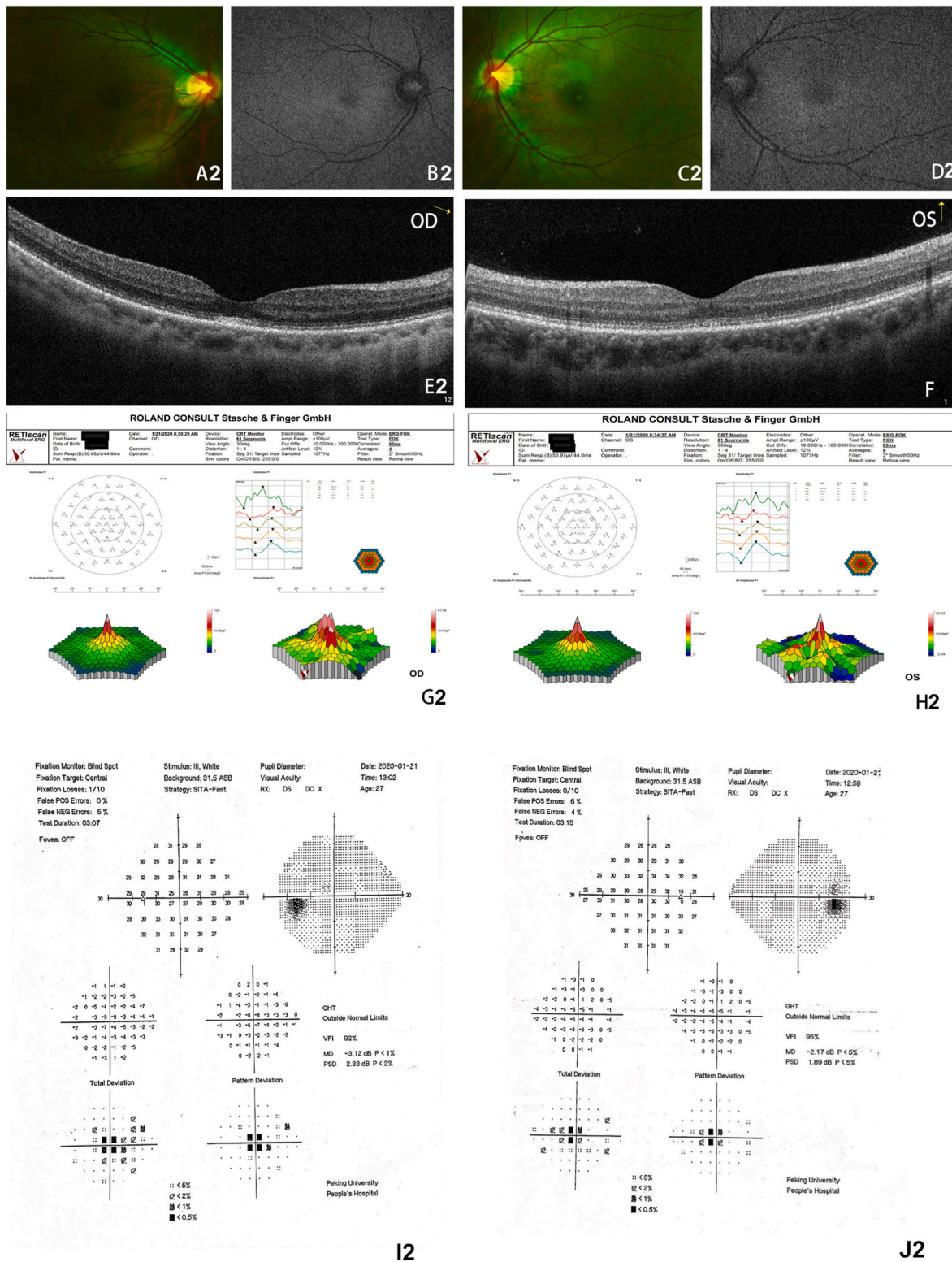
Sildenafil citrate, which was identified during the process of drug development for cardiovascular diseases, is now widely used in the treatment of male erectile dysfunction. It is generally known by its commercial name Viagra. Sildenafil citrate is a selective cyclic guanosine monophosphate-dependent PDE-5 inhibitor. PDE-5 inhibitors can increase the level of cGMP and relax the smooth muscle of arterioles, so sildenafil citrate is used to treat pulmonary arterial hypertension. This medication has some ocular complications associated with PDE-5, such as anterior ischemic optic neuropathy (AION), subretinal hemorrhage,

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**Fig. 1.** Multimodal imaging at presentation of both eyes. **A, B, C and D** : The color fundus photograph and autofluorescence (AF) in both eyes are normal. **E and F**: OCT reveals hyper reflectivity of the ellipsoid zone in the macular fovea and discontinuation of ellipsoid zone of parafovea in binocular. **G and H**: mERG shows the abnormal appearances of 3D amplitudes including disappearances of the regular macular peaks in both eyes. **I and J** : The visual field examination of the patient at the first visit shows that both eyes have central scotoma. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)





**Fig. 2.** Multimodal imaging after withdrawal of both eyes .  
**A2, B2, C2 and D2 :** The color fundus photograph and autofluorescence (AF) in both eyes are still normal. **E2 and F2:** OCT shows hyper reflectivity of the ellipsoid zone in the macular fovea in binocular had no changes compare to 3 months ago. **G2 and H2:** mERG shows retinal response amplitude density of 5 rings fell sharply and still showed the disappearances of macular peaks. **I2 and J2:**The visual field examination of the patient after withdrawal shows that both eyes still having central scotoma. . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

central serous chorioretinopathy (CSC) and extraocular muscle paralysis.<sup>1</sup>

Sildenafil citrate can also inhibit 6-phosphodiesterase (PDE-6) in retina. PDE-6 is an important substance to convert optical signals into electrical signals in the process of vision. PDE-6 can adjust the Na<sup>+</sup> channel of the outer segment of the photoreceptor, resulting in a series of photoelectric conversion activities. Inhibition of PDE-6 can lead to visual abnormalities and color vision defects. An animal study showed that Sildenafil can cause reversible damage to light conduction of monkey rod and cone cells, and showed a high correlation between plasma sildenafil citrate concentration and the degree of function loss.<sup>2</sup> In our case, the patient took an overdose of sildenafil citrate orally for a long time. The abnormality of his visual symptoms and objective auxiliary examination revealed the damage of photoreceptor cells. The damage of the macular area was due to the arrangement of high-density cone cells. Therefore, the patient had visual symptoms after taking the drug for a long time.

A few studies show that sildenafil citrate is safe to use and absorbs rapidly. The blood concentration usually reaches its peak after oral administration for 0.5–1.5 hours; sildenafil citrate has a half-life of about 3–5 hours and can be metabolized by cytochrome P450 3A4 isozyme. Previous studies have shown that the effects of single or long-term high-dose or overdose sildenafil citrate on human visual function are reversible, and these side effects will be completely relieved within 24 hours after drug withdrawal. Karaarslan.C<sup>3</sup> described 17 patients who received the maximum recommended therapeutic dose (100 mg) who developed visual symptoms after taking sildenafil citrate, but their visual dysfunction was relieved within 21 days. Li et al.<sup>4</sup> reported that a young woman developed binocular visual symptoms after taking an overdose (2000mg) of sildenafil citrate, but gradually recovered after 38 days. Yanoga et al.<sup>5</sup> reported a case of persistent retinal toxicity associated with a single high-dose sildenafil citrate intake, with symptoms and photoreceptor structural changes lasting for several months. In our case, sildenafil citrate related ocular symptoms persisted for one year, and damage to the outer segment of the photoreceptors seemed to persist. This outcome may be related to long-term overdose of sildenafil. Therefore, exploring whether there are differences in the sensitivity of cytochrome P450 3A4 isozymes in different individuals may be of great significance to the study of drug toxicity metabolism.

#### 4. Conclusions

In conclusion, although most previous studies have shown that the damage to retinal photoreceptor cells caused by excessive sildenafil

citrate is reversible, in our case, the ocular damage caused by drug toxicity was sustained. Therefore, the mechanism of sildenafil citrate induced retinal toxicity needs to be further studied; long term overdose of sildenafil citrate may cause more unknown damage. Therefore, evaluating the safety of such drugs needs more attention from all physicians.

#### Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

#### Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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#### Declaration of competing interest

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