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SHORT COMMUNICATION

Case report

Clonazepam associated retinopathy

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PURPOSE. *To report a case of retinopathy associated with the longterm intake of the antiepileptic drug clonazepam.*
METHODS. *Case report.*
RESULTS. *A 36-year-old woman, with a history of long-term use of the antiepileptic drug clonazepam developed subtle visual disturbances. Funduscopy revealed areas of mild depigmentation of the retinal pigment epithelium throughout the posterior pole bilaterally corresponding to transmission hyperfluorescence on fluorescein angiography. There was no history of any inherited retinal degenerative disease and no other known agent responsible for retinal toxicity had been used.*
CONCLUSIONS. *The longstanding intake of the antiepileptic drug clonazepam may be associated with the development of toxic retinopathy. (Eur J Ophthalmol 2003; 13: 813-5)*

KEY WORDS. *Clonazepam, Retinopathy*

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INTRODUCTION

A large variety of pharmacological agents may have toxic effects on the human retina (1). Clonazepam is a widely used antiepileptic agent belonging to the family of benzodiazepines. No retinal side-effects of clonazepam have been described to the best of our knowledge. We report a case of retinopathy associated with the longstanding intake of clonazepam.

Case report

A 36-year-old woman was referred to us complaining of ill-defined visual disturbances. She had been suffering from juvenile myoclonic epilepsy since the age of fifteen which was treated with clonazepam administered orally for 21 years (8 mg per day for 8 years, then 6mg per day for 13 years); the patient's body weight was 48 kg. The rest of her medical and ophthalmological history was unremarkable. No other medications had been used and there was no family history of retinal degenerative disease.

The last ophthalmological evaluation, including fundoscopy after pupil dilation, which was performed 10 years ago, was normal. On our examination best-corrected visual acuity was 20/20 OD and 20/30 OS. She had a small central scotoma OS on the Amsler grid test, although central visual fields (Humphrey 10-2 program; Humphrey-Zeiss, San Leandro, CA) tested with both red and white targets were normal. At

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the photostress test there was increased recovery time with both eyes; the left eye was more pronouncedly affected. Color vision tested by the Ishihara plates was normal with both eyes. Slit lamp biomicroscopy was unremarkable. Dilated funduscopy revealed mild depigmentation of the retinal pigment epithelium (RPE) throughout the posterior pole bilaterally (Figs. 1 and 2). Fluorescein angiography revealed extensive areas of transmission hyperfluorescence, corresponding to the areas of RPE depigmentation that had been observed clinically. The areas of depigmentation consisted of two concentric rings, one surrounding the fovea and the other more peripherally, containing the temporal arcades (Fig 3). Photopic and scotopic Ganzfeld electroretinography and electro-oculography recorded a normal response bilaterally. Flicker responses were not taken due to the patient's history of light-induced epileptic seizures.

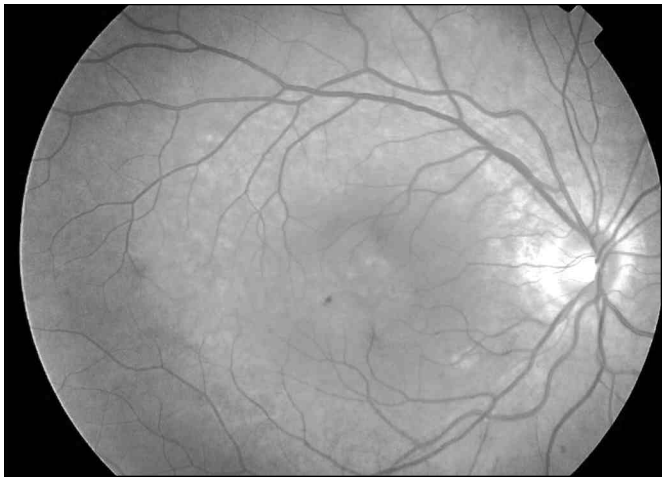

Fig. 1 - *Fundus photograph of the right eye.*

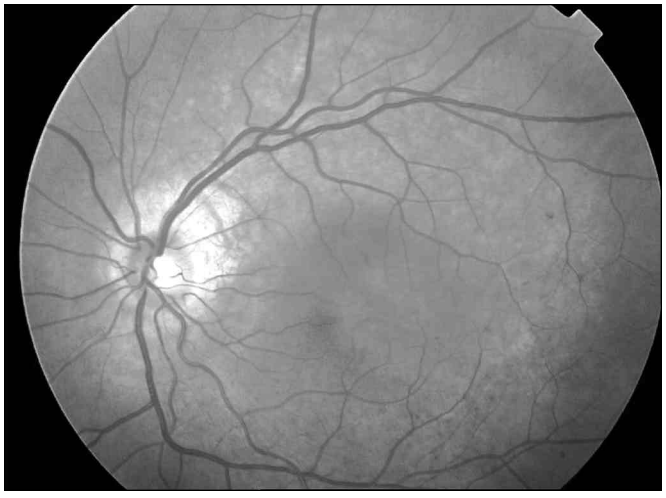

Fig. 2 - *Fundus photograph of the left eye.*

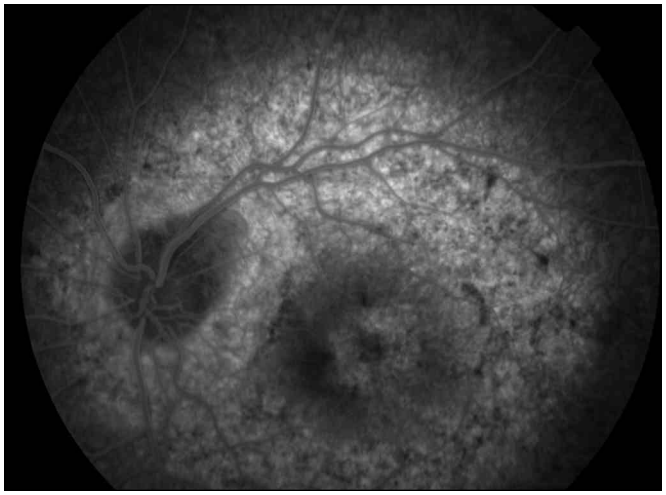

Fig. 3 - *Fluorescein angiography of the left eye showing an extensive area of transmission hyperfluorescence.*

DISCUSSION

We report the case of a patient who had been treated with clonazepam for a prolonged period of time and developed a bilateral retinopathy with discrete RPE changes at the posterior pole and subtle visual disturbances. Clonazepam was used for 21 years and was still in use when visual disturbances evolved.

A great variety of systemically or topically administered drugs such as quinine, chloroquine, chlorpromazine, thioridazine, ethambutol, cyclosporin, α-interferon, tamoxifen, indomethacine, digitalis, deferoxamine, clofazimine, synthetic retinoids, didanoside, canthaxanthin, methoxyflurane, topical epinephrine or gentamycin, etc. may induce different forms of toxic retinopathy (1). None of these drugs had been used by our patient. Moreover, the patient had no family history of an inherited retinal degenerative disease. Consequently, we can speculate that the retinopathy which occurred in our patient was due to the prolonged intake of clonazepam.

Although there is no known retinal toxicity by clonazepam, it is of interest that there is a report of a case with similar retinal findings after a 7-year use of relatively high doses of diazepam, a drug that belongs to the same pharmacological family as clonazepam (2). The mechanism by which clonazepam may cause toxic retinopathy is unclear. The antiepileptic action

of benzodiazepines is primarily due to the modulation of gamma-aminobutyric acid (GABA) receptors in the brain. It is of interest that similar receptors have been identified at the RPE and at the retina of both humans and mammals (3), while a special affinity of clonazepam with these receptors has been described in the mammalian retina (4).

In conclusion, we present a case of retinopathy that developed in a patient treated by the antiepileptic drug clonazepam. This possible side-effect of clonazepam should be confirmed by reports of similar cases.

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