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SHORT COMMUNICATION

Progressive severe visual loss after long-term withdrawal from thioridazine treatment

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PURPOSE. *To report advanced thioridazine-induced retinopathy in a 50-year-old woman with evidence of progressive severe loss of vision over 30 years after withdrawal from thioridazine treatment.*
METHODS. *The ocular fundus examination revealed areas of retinal pigment epithelium (RPE) clumping as well as generalized atrophy of the RPE and choroid. The patient experienced visual loss to the level of no light perception in both eyes despite the fact that the funduscopic appearances of her optic nerves and retinal vasculature remained relatively normal.*
CONCLUSIONS. *This case demonstrates that severe progressive visual loss can occur several years after the cessation of chronic thioridazine treatment. (Eur J Ophthalmol 2006; 16: 651-3)*

KEY WORDS. *Vision loss, Progressive, Thioridazine, Treatment*

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INTRODUCTION

Thioridazine (Mellaril) is a phenothiazine commonly used in the treatment of psychoses. Soon after its introduction into clinical practice in the late 1950s, thioridazine was found to cause a pigmentary retinopathy associated with visual loss (1). Drug doses up to 2000 mg/day were common before the dose-related retinal toxicity was recognized (2). Currently, the recommended maximum daily dose of the drug is 800 mg (2). In general, after discontinuing the thioridazine treatment, retinal toxicity progresses for a few years, after which the visual acuity and visual fields improve and remain stable (3). This report describes a patient with progressive severe loss of vision and clinical evidence of thioridazine retinopathy who had been treated more than 30 years earlier with thioridazine.

Case report

In 1972, a 20-year-old woman with a history of psychosis was treated with 2000 mg/day thioridazine, over a period of 6 weeks. The patient complained of blurry vision and impaired color and decreased night vision. She denied having any family history of eye disease and there was no parental consanguinity. On examination, the patient was noted to have constricted visual fields and fundoscopy revealed fine pigmentary changes. Based on clinical findings, thioridazine-induced retinal toxicity was suspected and the treatment was discontinued. Her visual acuity improved but the visual fields remained constricted. In 1992, the patient complained of a further decrease in her vision and a retinal examination revealed coarse pigmentary changes. The visual fields were constricted to

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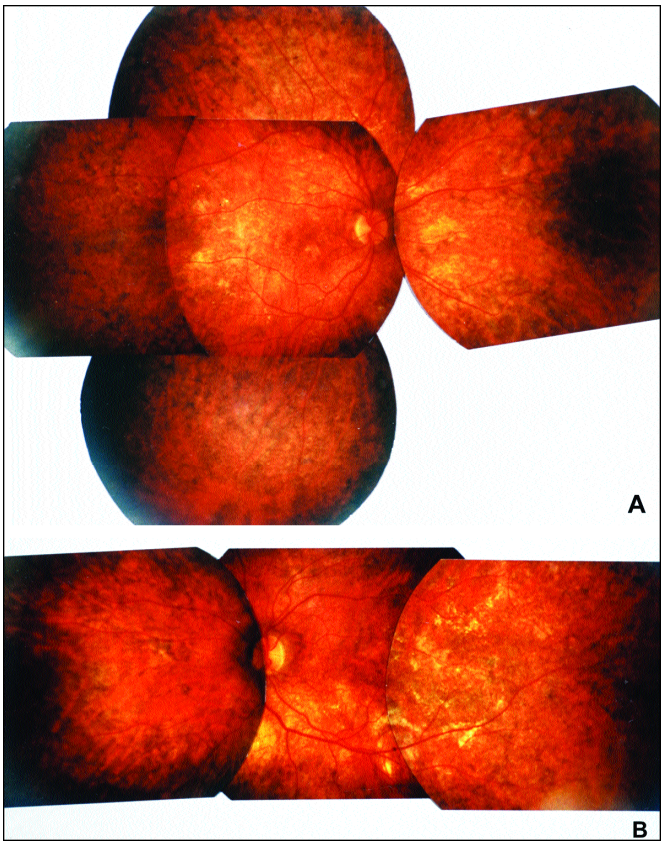

Fig. 1 - *Composite photograph of the right eye (**A**) and the left eye (**B**), showing areas of retinal pigment epithelium (RPE) clumping and generalized RPE and choroidal atrophy. The changes are more prominent in the macular area than in the periphery.*

less than 10 degrees in the right eye and less than 6 degrees in the left eye. An electroretinogram (ERG) revealed decreased amplitude of rod and cone-mediated responses. Progressive delayed visual loss was attributed to thioridazine-caused retinal toxicity. In 1996, the patient's vision decreased to 20/400 in the right eye and hand motion in the left eye. The patient received low vision rehabilitation and was able to function independently. After the patient reported a further decline in her visual function, she was seen again in December 1998. Her vision was 20/800 in the right eye with a very constricted visual field and no light perception (NLP) in the left eye. Dilated examination revealed clear vitreous media, sharp optic disks with pink color, and slight temporal sloping. There were areas of retinal pigment epithelium (RPE) clumping and generalized RPE and choroidal atrophy, which were more pronounced in the macular area than in the periphery (Fig. 1). Both the ERG and electro-oculogram were flat and fluorescein angiogram revealed a normal filling time. The patient's total loss of vision in the left eye was attributed to progressive delayed thioridazine-caused retinal toxicity. The patient was lost to follow-up for the next 4 years until later when she reported a total loss of vision in her right eye to NLP without any further changes in her fundus examination.

DISCUSSION

Patients with acute thioridazine retinopathy typically report blurred vision, dyschromatopsia, or nyctalopia, usually several weeks after receiving the drug. This most commonly occurs with doses in excess of 800 mg/day, but has been reported with doses as low as 200 mg/day (4). Visual acuity may be normal or variably reduced. Color vision is often subnormal with constricted visual fields. Initially it was thought that if the drug was discontinued promptly, the patient may have a good recovery of visual function. Later reports revealed that despite the discontinuation of thioridazine, progressive retinopathy with deterioration of visual acuity, visual fields, and dark adaptation might occur in patients who had received high doses of the drug (5). Our patient received 2000 mg of thioridazine a day for 6 weeks, the total dosage of 84 gm. This dosage is well under the doses reported by Meridith in his 3 patients (5), in whom he showed progression of drug induced retinopathy after withdrawal of thioridazine.

Fundus of our patient showed clinical appearance typical of late, advanced thioridazine retinopathy (6). The loss of RPE and choriocapillaries corresponding to atrophic changes of fundus were visible by fundus fluorescein angiography. The ultrastructural examination of the multiple atrophic areas has revealed a sequence of degenerative changes from the margin to the center of these lesions (6). Near the margin, shortening and loss of photoreceptor outer segments overlying morphologically intact RPE appears to be the initial degenerative event followed by central loss of RPE cells and choriocapillaries. Miller at al (6) reported histopathological and ultrastructural study of early thioridazine retinopathy in a 61-year-old male who had clinical evidence of advanced thioridazine retinopathy associated with progressive severe visual loss who had received high dosages of thioridazine 18 years earlier. Marmor (7) reviewed clinical findings in 7 patients with thioridazine retinopathy and found that fundus appearance in thioridazine retinopathy evolved with in the first year from the coarse granular retinopathy of acute toxicity to the patchy or nummular retinopathy of late thioridazine

damage. All these patients showed significant visual improvement and some had recovery of ERG during the first year after cessation of high doses of thioridazine, despite an increasingly atrophic fundus appearance. He argued that thioridazine retinopathy does not progress functionally during the change from granular to nummular retinopathy, although there was a risk for late functional decompensation.

Based on the patient's progressive loss of vision and characteristic fundus appearance, we believe that thioridazine was the primary cause of our patient's retinopathy. The patient had no family history of eye disease, and her visual symptoms started after several weeks of thioridazine treatment. Thioridazine may have damaging effects on the RPE/photoreceptor complex and choriocapillaris, which may progress even after the drug is discontinued. Because thioridazine is bound to melanin, thioridazine may persists in eyes for a long time (5). This report emphasizes the importance of eliciting a careful drug history in any patient with acute or progressive visual loss. This report emphasizes the importance of eliciting a careful drug history in any patient with acute or progressive visual loss.

None of the authors has any propriety interest in this manuscript.

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