Presumed sertraline maculopathy

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ABSTRACT.

Purpose: **To report a unique case of a woman who developed simultaneous bilateral maculopathy presumed to result from intake of sertraline hydrochloride, a serotonin reuptake inhibitor.**

Methods: **Full clinical ocular examination, color vision testing, automated static perimetry, electroretinography, electrooculography and fundus fluorescein angiography were performed. Living members of her family were also examined.**

Results: **The patient had normal electroretinography and electrooculography results. Automated static perimetry showed generalized reduction of sensitivity and central scotomas. Macular lesions resolved 6 months after discontinuation of sertraline, however, during twenty months of follow-up her visual acuity and abnormalities in other psychophysical tests did not improve.**

Conclusion: **Patients started on sertraline should be informed of the potential risk of developing maculopathy, and they should be examined regularly to detect possible early alterations.**

Key words: sertraline – retinal pigment epithelium – maculopathy – toxicity.

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Sertraline hydrochloride is a selective serotonin reuptake inhibitor in the central nervous system with the chemical name of (1S-cis)-4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalamine, $C_{17}H_{17}Cl_2N$ (Budavari 1989). This drug is currently prescribed to patients with depression, obsessive compulsive and panic disorders (PDR 1999). Sertraline hydrochloride is marketed in the form of tablets or capsules which contain dibasic calcium phosphate dihydrate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, polyethylene glycol, micro-cristalline cellulose, polysorbate 80, titanium dioxide (E171), sodium starch glycolate and synthetic yellow iron oxide (PDR 1999). Ninety-eight percent of the drug is bound to serum proteins and the primary site of elimination is liver through N-demethylation (PDR 1999).

A woman who was on sertraline for more than a year and who developed bilateral simultaneous and symmetric maculopathy is described in this report. We presume that this maculopathy or more specifically, macular retinal pigment epitheliopathy, is related to the use of sertraline and to the best of our knowledge, there has been no previously published observation in the literature pointing out this particular side effect.

Case Report

In November 1998, a 58-year-old woman was referred with the complaint of gradually decreasing vision in both eyes. She could clearly trace the beginning of her symptoms back to May 1998 when she suddenly realized that she could not read the newspapers with her usual +2.00 D near glasses. She did not experience any night vision difficulties. In January 1998, she had her last regular once-a-year ocular check-up with her local ophthalmologist who has been following her for 5 years. Office records indicated that her uncorrected visual acuity then was 20/20 each eye. A dilated fundus examination was reportedly normal. Four months prior to this, she was started on oral sertraline 50 mg per day for signs of depression.

On our examination, her best corrected visual acuity was 20/60 RE and 20/40 LE. Pupils measured 3.5 mm bilaterally with brisk light reaction and no afferent pupillary defect. Her color vision was 0/15 OU using Ishihara pseudoisochromatic plates. The anterior segments were normal and her intraocular pressures measured 15 mmHg bilaterally. Fundoscopy revealed a yellow-cream colored area of retinal pigment epithelial atrophy, measuring 2 disc diameters and whose epicenter was the fovea in both eyes (Fig 1A and B). This relatively well-circumscribed area appeared minimally elevated, and there were distinct clumps of retinal pigment epithelium (RPE) in the inner layers of the retina. The lesion was surrounded by several small satellite-like areas of RPE atrophy. The peripheral fundi were entirely normal. Intravenous fluorescein angiography revealed early fuzzy hyperfluorescence which steadily increased through the late phases of the study (Fig. 1C and 1D). The linear and centrifugal arrangement of RPE agglomerations and the small surrounding atrophic areas were better demonstrated on angiography. Her electroretinographic (ERG) work-up revealed normal dark adapted rod response, normal maximum combined response, and normal cone response according to our laboratory normals. The electrooculography (EOG) test results were also normal with Arden ratios of 2.06 and 1.97 for the right and left eyes, respectively. The Goldmann perimeter showed normal peripheral fields and central scotomas detected on II-4 and I-4 settings. Her automated static perimetry test results (Humphrey Field Analyzer, central 30.2 treshold test) were highly reliable, indicated by the short term fluctuation of 1.71 DB OD and 1.62 DB OS. There was a general reduction of sensitivity compared to age-matched controls (MD for OD and OS were −7.80

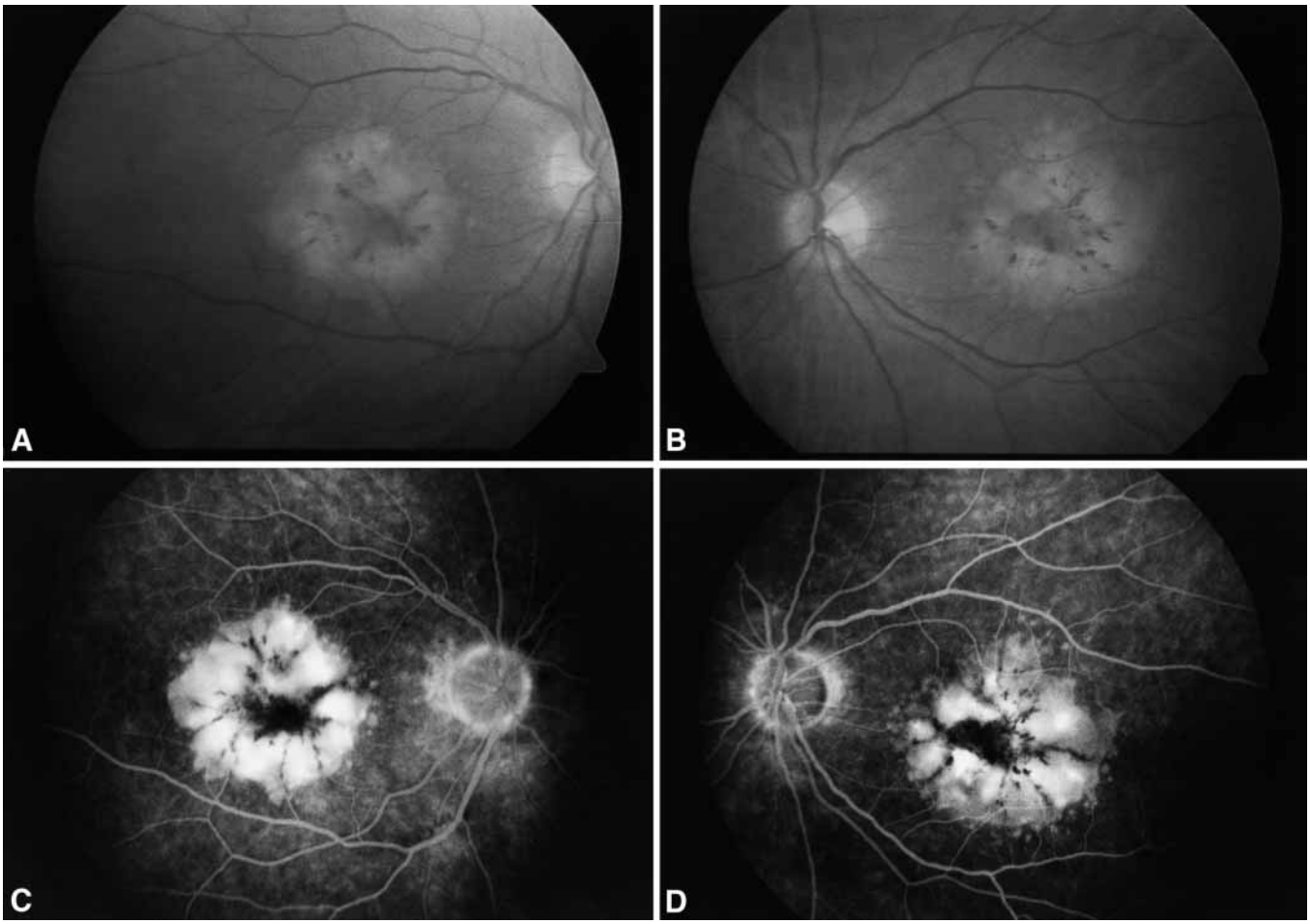

Fig. 1. A: Fundus view of the right at initial presentation **B**: left fundus. **C**: Recirculation phase fluorescein angiogram demonstrating staining and focal pooling of the dye. Satellite areas of retinal pigment epithelial loss adjacent to the main lesion are more evident on angiography, **D**: left fundus.

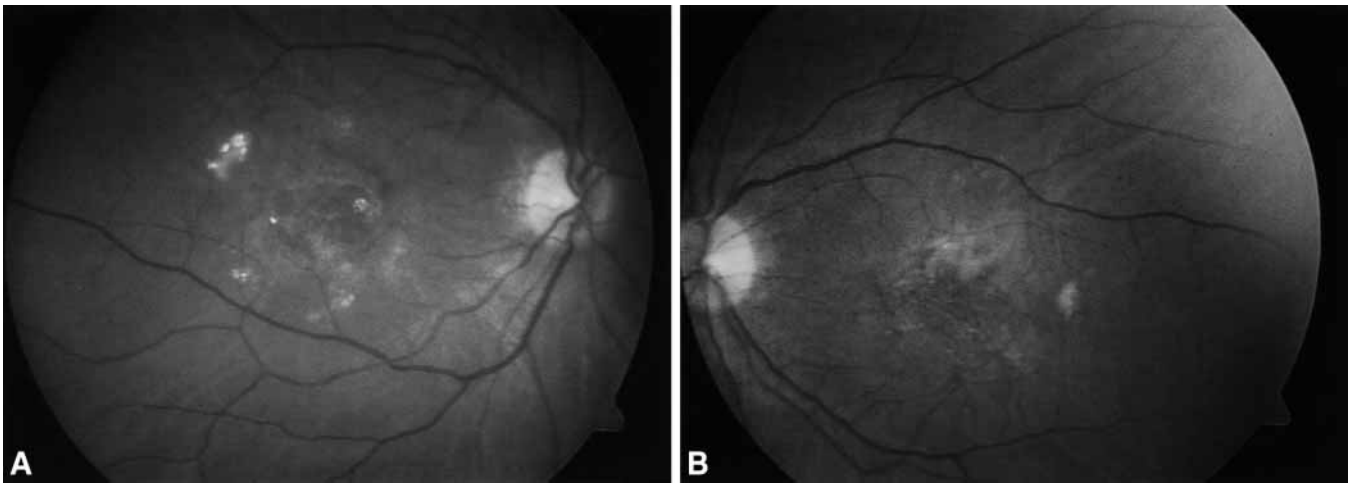

Fig. 2. Fundus view 6 months after discontinuation of sertraline **A**: right eye, **B**: left eye.

DB, $p<0.5\%$ and –7.30 DB, $p<0.5\%$, respectively). There was also central scotoma in each visual field (PSD for OD and OS were 4.12 DB, $p<5\%$ and 7.31 DB, $p<10\%$; CPCD for OD and OS were 3.64 DB, $p<5\%$ and 2.76 DB, $p<10\%$, respectively).

Her daughter and mother, who were her only living blood relatives, were examined and found to be normal. The drug was discontinued. Six months later, the macular lesions had resolved gradually leaving a faint scar (Fig. 2). She was followed for twenty months and during this period there has been no improve-

ment in her visual acuity and other psychophysical test results.

Discussion

Treatment-emergent adverse effects, which are defined as any event occuring for the first time or worsening while receiving the particular drug following a baseline evaluation, have been amply described with the use of sertraline (PDR 1999). Ocular signs and symptoms, however, are infrequently encountered and include periorbital edema, exophthalmus, ptosis, nystagmus, diplopia, abnormal lacrimation, hyphema, xerophthalmia, conjunctivitis, accommodation problems, photophobia, visual field defects and scotomas (PDR 1999). There is no detailed information concerning the latter two side effects. A 28-year-old male patient suffering uneven pupillary dilation following sertraline use has been reported (Barret 1994). More recently, a case of a 42-year-old woman taking 100 mg sertraline daily for 4 years and developing blurred vision, central scotoma, decreased color vision has been described. The symptoms in that particular patient emerged two months after she started concommitant melatonin and a high-protein diet but resolved six months following the discontinuation of the latter two (Lehman & Johnson 1999). Another patient who received sertraline 50 mg daily, experienced visual hallucinations persisting 30 to 40 seconds and consisting of blue-green central discs with annular surrounds. These hallucinations developed within 3 weeks after the start of sertraline treatment (Bourgeois et al. 1998).

The macular lesions of our patient are quite similar to those seen in butterfly dystrophy, which is characterized by normal visual acuity at presentation, intact color vision and diminished central sensitivity with normal peripheral visual fields. Also, there are densely packed pigment granules at the level of RPE (Deutman et al. 1970; Gutman et al. 1982). Our patient had a relatively rapid deterioration of visual acuity, absent color vision and central scotomas, all developing within six months following an entirely normal ocular examination. The abrupt onset and rapid progression of signs and symptoms in our patient would be unexpected in butterfly dystrophy. The pigmentation over the lesions would be coarser and located deeper in butterfly dystrophy in a patient who is almost 60 years old. Finally, complete disappearance of macular lesions within six months is not a feature of butterfly dystrophy.

The diagnosis of sertraline-related maculopathy will certainly remain controversial until further evidence of cause and effect relationship emerges in a greater number of patients. However, we believe that patients and physicians should be warned against this potential adverse effect and regular follow-up schedules be offered to those taking sertraline.

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