Case report

Bilateral cystoid macular edema misdiagnosed as pars planitis in a patient on sertraline therapy

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ABSTRACT

Purpose: To describe the presentation, clinical course and management of a patient with bilateral maculopathy associated with sertraline.

Observations: We report a rare case of bilateral cystoid macular edema and subretinal fluid in a 78-year-old Asian Indian female who was on chronic sertraline therapy. The patient was initially misdiagnosed as intermediate uveitis and started on oral corticosteroids. However, multimodal imaging with fluorescein angiography and optical coherence tomography ruled out ocular inflammation. There was symmetrical bilateral macular involvement and changes on macular electroretinography, which provided clues to the diagnosis of toxic maculopathy. After cessation of sertraline therapy, the retinal pathology reversed with improvement in visual acuity.

Conclusions and Importance: Development of cystoid macular edema due to sertraline is a very rare adverse event and must be considered by psychiatrists and ophthalmologists. Our case demonstrates this rare toxicity along with its imaging features, and reversal on cessation of sertraline therapy.

1. Introduction

Sertraline hydrochloride is one of the most commonly used, first-line selective serotonin reuptake inhibitor (SSRI) used in the management of several psychiatric conditions such as major depression, obsessive-compulsive disorder, panic attacks, post-traumatic stress disorder and anxiety disorders.¹,² Since this drug obtained the United States Food and Drug Administration (US FDA) approval in 1991, it has become one of the most widely prescribed psychiatric medications for management of depression worldwide.³ Due to its affinity for various receptors, including serotonin transporter, dopamine transporter, and σ1 receptor, it may be associated with a number of undesirable systemic side effects such as extrapyramidal features of rigidity, resting tremor, dyskinesia, dysgraphia, weight gain and dry mouth.⁴,⁵

The ocular side effects of sertraline are very rarely reported. Some of the rare manifestations of sertraline toxicity include acute angle closure glaucoma⁶ and optic neuropathy.⁷ In the literature, two cases presumed sertraline maculopathy and a single case of bull’s eye maculopathy related to sertraline use have been previously published.⁸⁻¹⁰ In this case report, we have described the course of bilateral maculopathy and its reversal in a lady with psychotic depression who was started on sertraline therapy a few months ago.

2. Case report

A 78-year-old Asian Indian lady presented with complaints of gradual progressive diminution of vision in both the eyes (OU) for the past 1 month. The patient had been evaluated elsewhere and a diagnosis of intermediate uveitis with bilateral cystoid macular edema (CME) was made. She underwent detailed laboratory work-up for uveitis including tuberculin skin test, treponema pallidum hemagglutination assay (TPHA), and chest radiography to rule out infectious etiology, and antinuclear antibodies (ANA), anti-double-stranded DNA (DdDNA), and anti-neutrophilic cytoplasmic antibody (ANCA) to rule out autoimmune etiology. All her laboratory tests were within normal limits. With the diagnosis of pars planitis with bilateral CME, her treating ophthalmologist initiated her on oral corticosteroids (30 mg/day prednisone) for 2 weeks, which were subsequently tapered to a dose of 20 mg/day.

The patient presented to the ophthalmology department at our institution for a second opinion. At the time of presentation, her best-corrected visual acuity (BCVA) was 6/18 in the right eye (OD) and 6/12 in the left eye (OS). Anterior segment examination was unremarkable with a clear cornea, no anterior chamber inflammation and bilateral pseudophakia. Posterior segment examination revealed a clear media, with no vitreous cells or haze. The foveal reflex was blunted in both the eyes (Figs. 1 and 2). Fluorescein angiography (FA) and indocyanine...
green angiography (ICGA) did not reveal any evidence of posterior segment inflammation or optic disc hyperfluorescence/leakage. There was presence of a symmetrical macular hyperfluorescence (due to leakage of small deep vessels especially those seen temporal to the fovea in the left eye) suggestive of accumulation of fluid. Fundus autofluorescence imaging (FAF) showed a subtle central macular hypoautofluorescence due to the presence of overlying fluid above the retinal pigment epithelium (RPE). Swept-source optical coherence tomography (SS-OCT) revealed presence of bilateral intraretinal and subretinal fluid suggestive of macular edema (Fig. 3). Since there was no clinical or imaging feature suggestive of intraocular inflammation/uveitis, the diagnosis of pars planitis was considered unlikely. Multifocal electroretinography showed unevenly distributed, moderately reduced and abnormal waveforms especially in the inner two rings in both the eyes signifying cone-mediated functional loss of the posterior pole (Fig. 4). A detailed drug history revealed that the patient had been started on sertraline 50 mg/day after the diagnosis of psychotic depression was established 7 months ago. Review of her previous ocular examination records (prior to initiation of sertraline) showed a visual acuity of 6/6 in OU, without any positive fundus findings. Therefore, sertraline-induced maculopathy was suspected and patient was advised to seek psychiatrist consultation in order to consider an alternative medication. Simultaneously, her oral corticosteroids were tapered and stopped over the next 2 weeks.

Fig. 1. Fig. 1 shows multimodal imaging of the right eye of the patient diagnosed with sertraline maculopathy. Fundus photography shows clear media and a blunted foveal reflex (A). Fundus autofluorescence imaging shows subtle increase in the macular hypo-autofluorescence (B). The early frames of combined fluorescein angiography (FA) and indocyanine green angiography (ICGA) (C) do not show significant disc or vascular leakage. There is subtle early hyperfluorescence of the macula in the right eye in the late phase (D). ICGA does not reveal any abnormality of the right eye in the late phase.

Fig. 2. Fig. 2 shows multimodal imaging of the left eye. Similar to the right eye in Fig. 1, fundus of the left eye also showed clear media and blunted foveal reflex (A). There was subtle increase in hypo-autofluorescence of the macula on autofluorescence imaging (B). Early and late frames of fluorescein angiography (C and D) showed presence of hyperfluorescence in the macula suggestive of macular edema. There were no abnormalities noted on indocyanine green angiography imaging.

Fig. 3. Serial swept-source optical coherence tomography (SS-OCT) of right (A, C and E) and left eyes (B, D and F). At baseline, SS-OCT of both eyes revealed subretinal fluid with elevation of the retinal pigment epithelium (RPE) (A and B for the right and left eyes, respectively). Left eye also showed intraretinal cystoid spaces in the line scan shown. At 2 week follow-up after cessation of sertraline, there was an interval decrease in the subretinal fluid in both the eyes and improvement in visual acuity (C and D). At 12 week follow-up visit, there was complete resolution of subretinal fluid in both the eyes (E and F). The left eye showed residual intraretinal cystoid spaces.
Fig. 4. Multifocal electroretinography of the right (A) and left eyes (B) shows abnormal responses in both the eyes. Both eyes shows responses that are unevenly distributed across the tested field with predominantly unformed averaged waveforms (especially in the central fields of the right eye; A). The responses are moderate-to-severely reduced without significant changes in the implicit times. In summary, the multifocal electroretinography shows severely abnormal cone-mediated function of the posterior pole in both the eyes.
Four weeks after the initial visit, the patient was symptomatically better and her BCVA improved to 6/12 in OD and 6/9 in OS. There was interval reduction in the CME in OU (Fig. 3). Sertraline was stopped and replaced with quetiapine (an atypical anti-psychotic). At 3-month follow-up, her BCVA further improved to 6/9 in OD and OS. The OCT scan showed a near complete resolution of CME with only few residual cystoid spaces in OS (Fig. 3). The subretinal fluid had completely resolved in both the eyes. The patient was tolerating quetiapine well and maintains a regular follow-up with the psychiatrist.

3. Discussion

Sertraline is an extensively used SSRI in the management of various psychiatric conditions including psychotic depression. Ocular adverse events are rare with sertraline and among the reported cases, reports of rise in intraocular pressure, optic atrophy, and scotomas have been more commonly described. Macular involvement of sertraline is not well known, with only three cases in published literature. The National Registry of Drug-Induced Ocular Side Effects also does not provide detailed description of maculopathy associated with sertraline in the current edition. Previous reports have described distinct features of sertraline maculopathy either in the form of well circumscribed yellowish hypopigmented areas of RPE atrophy involving the macula with a few surrounding satellite lesions consisting of RPE atrophy, or Bull’s eye maculopathy. However, the OCT features of these lesions have not been described previously. In addition, there is paucity of information on the reversal of toxic manifestations after withdrawal of sertraline therapy.

In our case, the abrupt onset and rapid progression of signs and symptoms with the intake of sertraline therapy, the mfERG changes, and bilateral CME were observed. This is a new finding which has not been previously reported. Although a diagnosis of intermediate uveitis was considered elsewhere, a thorough clinical examination and fundus imaging ruled out ocular inflammation in this case.

The exact mechanism leading to the development of macular changes in sertraline toxicity is not clear. Researchers at the University of Oxford have greatly helped in advancing the knowledge regarding the role of serotonin in the mammalian eye. Sertraline, by inhibiting the neuronal uptake of serotonin, increases the levels of serotonin in the central and peripheral nervous system, including the eye (cornea, sclera, iris, ciliary body, RPE and choroid). Despite low levels of serotonin in the mammalian retina, a number of serotonin receptors exist in the photoreceptors and RPE. Apart from its role in visual processing, serotonin is linked to ganglion cell apoptosis. In the RPE, serotonin potentiates cAMP production and adipogenesis. Serotonin also modulates several functions using a messenger system of cyclic adenosine monophosphate (cAMP). Therefore, by adversely affecting the macular RPE function, sertraline may be responsible for development of maculopathy as a rare adverse event. Additional research on serotonin receptors and its effect on RPE will shed more light on this subject and the possible mechanisms of sertraline toxicity.

The goal of this index case report and previously published cases in the literature is to determine the possible association of sertraline with bilateral maculopathy. Since sertraline is a very commonly used drug, additional cases developing CME must be studied so that a real association can be established. It is imperative to sensitize physicians and patients to the possibility of these adverse effects with sertraline use. When examining patients with macular edema, a note must be made of the history of its intake. Further research into the mechanisms of ocular adverse events resulting from sertraline are may help in highlighting this association.

Patient consent

The consent to publish has been obtained from the participant in writing to report individual patient data.

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Conflicts of interest

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Authorship

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

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.06.021.

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