

Quetiapine associated Central Serous Chorioretinopathy: Implicit role of serotonin and dopamine pathways

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A 30-year-old insomniac, an off-label user of quetiapine, presented with blurring of central vision, eventually diagnosed as central serous chorioretinopathy. A potential association was suspected based on the drug's actions on the autonomic nervous system. He showed improvement on drug withdrawal; then he unwittingly resumed quetiapine and had a recurrence. Possible underlying mechanisms that include alteration in choroidal perfusion through serotonin and dopamine receptors

are discussed. Although retinal vein occlusions and pigment epithelial detachment have been described with quetiapine, to the author's knowledge, this is the first case report of quetiapine-associated central serous chorioretinopathy.

Key words: Adverse drug reaction, central serous chorioretinopathy, dopamine, quetiapine, serotonin

Central serous chorioretinopathy (CSCR) is characterized by subretinal accumulation of fluid leading to central blurring of vision and metamorphopsia. Apart from corticosteroids and sympathomimetic agents, phosphodiesterase inhibitors and mefloquine are other drugs associated with the condition.^[1-3] Quetiapine is an atypical antipsychotic drug with affinity for multiple receptors including those for dopamine and serotonin. Ocular adverse effects include blurring of vision, retinal vein occlusion, oculogyric crisis, ocular pain, transient myopia, narrow angle, halos around lights, hallucinations as in Charles-Bonnet syndrome, and photopsiae.^[4-6] A case of CSCR associated with quetiapine is presented. He had a marked regression on drug withdrawal and recurrence on inadvertent re-challenge.

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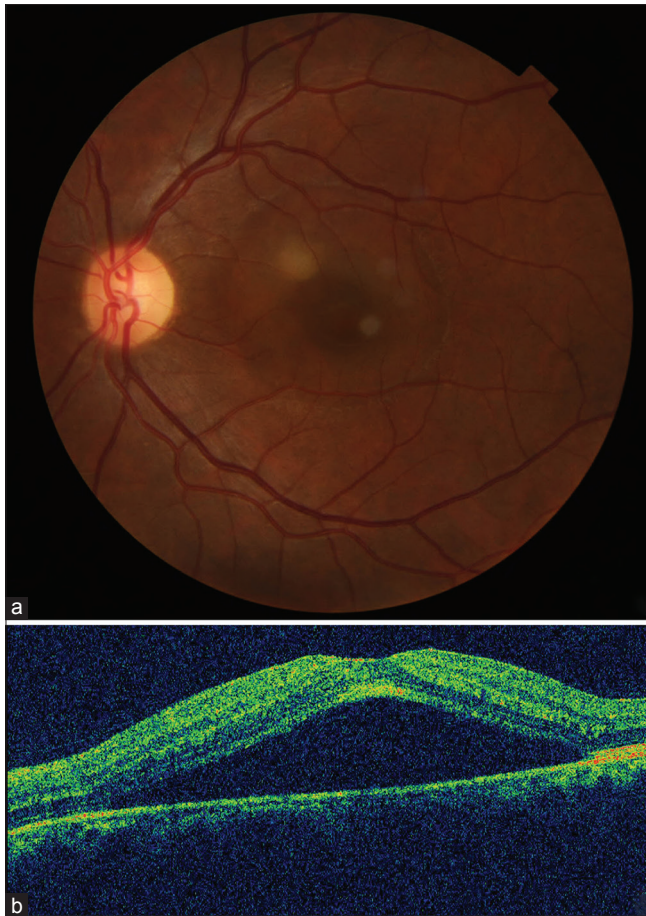


Figure 1: (a and b) Initial fundus picture and corresponding serous elevation (641 μ) on OCT

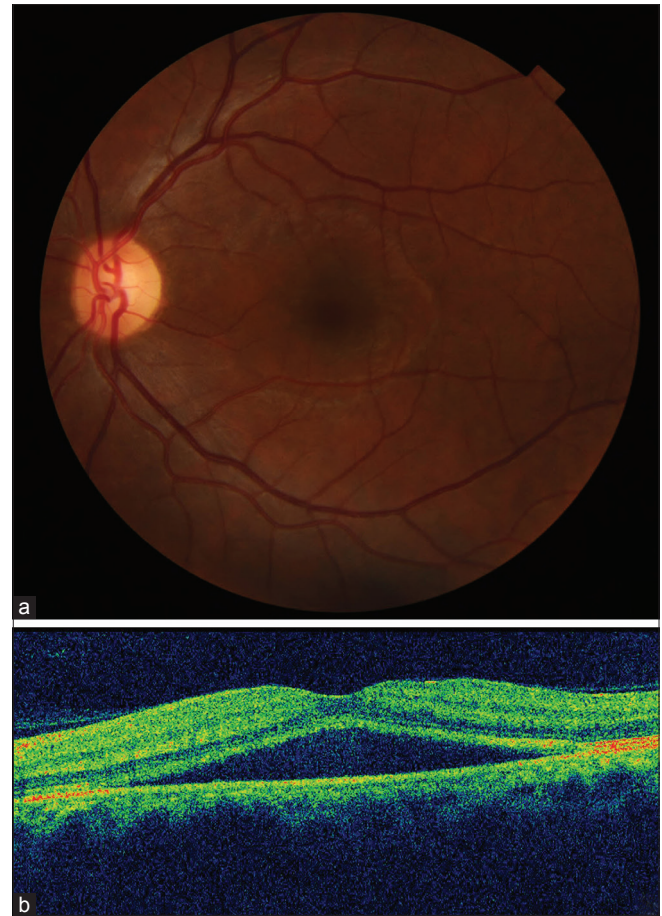


Figure 2: (a and b) Partial resolution (401 μ) on day 9 on withdrawal of quetiapine

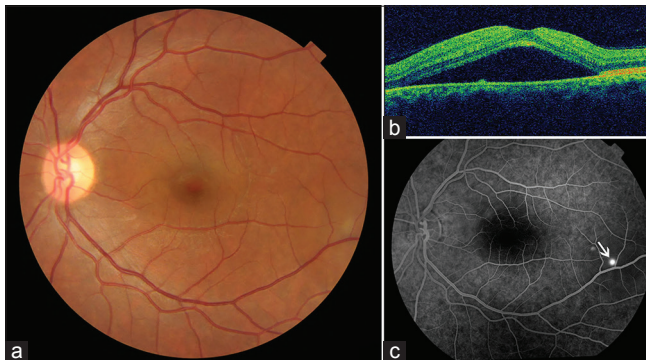


Figure 3: (a-c) Recurrence after resumption of quetiapine. Two distinct areas of serous elevations (637 μ) were noted - the temporal one is a fresh lesion. Angiogram shows an ink blot pattern (solid arrow)

Case Report

A 30-year-old man presented with acute diminution of vision in the left eye without metamorphopsia. His previous medical history included insomnia, gastroesophageal reflux, hemorrhoids, pharyngitis, and seborrheic dermatitis. Dermatitis was treated with mometasone furoate 0.1% ointment for 5 days 10 months ago without any visual symptoms. For insomnia, he used quetiapine (Seroquel 200 mg) off label for an unspecified duration. He had no other addictions.

His best corrected visual acuity (BCVA) was 6/6 and 6/15. Intraocular pressure was 13 and 12 mmHg in right and left eye, respectively. On fundus examination, a large neurosensory elevation of approximately 3-disc diameters in size involving the fovea was seen in the left eye resembling CSCR with a distinct pale area. Optical coherence tomography (OCT) showed undulation of the retinal pigment epithelium at the nasal parafoveal area and subretinal fluid [Fig. 1a and b]. He declined to undergo fluorescein angiography apprehending hypersensitivity.

Patient was asked to discontinue quetiapine. Nine days later, there was a marked reduction in the serous elevation and the extent of the lesion; the pale lesion within the dome had disappeared [Fig. 2a and b]. His BCVA improved to 6/9. He was then lost to follow-up only to return 10 months later, with 1 week history of recurrent blurring of vision in left eye with distortion (BCVA 6/18); slit lamp biomicroscopy revealed two distinct areas of serous elevations – one corresponding to the initial location, and a fresh one along inferotemporal arcade approximately 1.5-disc diameter in size, with a distinct pale-colored area. This time he agreed to undergo fluorescein angiography. A single area of leak was noticed corresponding to the pale area within the fresh lesion; it enhanced in the late phase as an ink blot [Fig. 3a-c]. He admitted resuming quetiapine 3 weeks earlier. He was advised to discontinue quetiapine. A medical advisory against use of quetiapine

and steroids was added in his records. The patient did not revert; nevertheless, informed that he has been asymptomatic 25 months after the recurrence.

Discussion

Prima facie, this CSCR patient had multiple risk factors identified by a CSCR-specific questionnaire developed in view of high prevalence. Further, the natural history of CSCR can be waxing and waning.

However, a reasonable temporal sequence to quetiapine intake, amelioration of serous elevation on day 9 after withdrawal, and recurrence on inadvertent re-challenge after a 10 month remission with a Naranjo algorithm score of 5, implies a probable association. Classical association with stress, steroids, and activation of hypothalamus–pituitary–adrenal axis aside, recent insights suggest that psychobiological influences from the prefrontal cortex govern the terminal events at the levels of choriocapillary endothelium, retinal pigment epithelium/Bruch's membrane interface leading to CSCR via dopamine, and serotonin pathways.^[3,7] Angiographic evidences suggest that CSCR arises when increased hydrostatic pressure in the choroid associated with choroidal hyperpermeability reverses the normal physiologic flow of fluid from the retina to the choroid.

Quetiapine operates through multiple neurotransmitter receptors including serotonin (5-HT_{1A}, 5-HT_{2A}, 5-HT_{2C}), dopamine (D₁ like, i.e. D₁ and D₅ and D₂ like, i.e. D₂, D₃, and D₄), histamine (H₁), and adrenergic (α ₁ and α ₂) receptors.^[8] D₁-like receptors are excitatory heteroreceptors located on nondopamine neurons, whereas D₂-like receptors are inhibitory, presynaptic autoreceptors. Serotonin receptors modulate emotions (5-HT_{1A}) in the limbic system, as well as regulate release of serotonin from presynaptic terminals and other neurotransmitters such as acetylcholine in the hippocampus and dopamine in the prefrontal cortex (5-HT_{1B} and 5-HT_{1D}). Reduced blood serotonin level has been demonstrated in chronic CSCR compared to age-matched controls.^[9]

Indeed, mammalian choroid with its rich distribution of dopamine receptors has a network of neurons called intrinsic choroidal neurons and nonvascular smooth muscles beneath the Bruch's membrane that regulates the choroidal thickness and vascular flow through autonomic innervations.^[8]

Choroidal vasodilatation in response to dopamine infusion is mediated through D₁-like (D₁/D₅) receptor activation.^[10] Altered vascular perfusion is a known feature of CSCR associated with phosphodiesterase inhibitors (tadalafil, sildenafil); and a possible factor in mefloquine-associated CSCR.^[2,11]

Serotonin-mediated ciliochoroidal effusion has been proposed as a mechanism for transient myopia associated with atypical antipsychotics, including quetiapine and aripiprazole.^[4] Hyperlipidemia and thromboembolism that indirectly affect vascular perfusion have been considered as underlying factors in quetiapine-associated retinal venous occlusions; one of these cases had a concurrent pigment epithelial detachment, a frequent concomitant feature of CSCR.^[5,6]

In this case, we did not have access to enhanced depth imaging or swept source OCT to assess the possibility of pachychoroid. However, a host factor such as pachychoroid and environmental triggers such as steroids/quetiapine may not be mutually exclusive given the previous reports of concurrent presence or progression of one or more disorders of pachychoroid spectrum.

Conclusion

Although this is the first such association to the author's knowledge, a more circumspect, preventive ophthalmological approach to explore possible pharmacological triggers is strongly recommended especially with current off label use of psychobiological drugs.^[2,3] Apparently, quetiapine modulated choroidal perfusion and thickness through dopamine and serotonin receptors in autonomic nervous system.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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