A young woman with sudden visual field shimmering: A case report

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Clomiphene citrate is a common drug used for the treatment of chronic anovulation, especially in polycystic ovary syndrome (PCOS) patients. The drug potentially has systemic and ocular side effects. Here, we present ocular side effects in a PCOS patient and emphasize the need to pay attention to visual complaints during treatment course with clomiphene citrate.

Key words: Clomiphene citrate, field shimmering, side effect

The article presents a case of peripheral visual field shimmering, a rare ocular side effect of clomiphene citrate, in a young patient of polycystic ovary syndrome (PCOS).

Case Report

A 35-year-old woman presented with a chief complaint of "wavy peripheral vision." The patient was diagnosed before with polycystic ovary syndrome (PCOS) and was scheduled on treatment with clomiphene citrate for chronic oligo-ovulation. The patient had received clomiphene citrate 50 mg tablet for her 5–9th day of menstrual cycle for the first month, with no complications. On the second day of the second treatment cycle with the same dose, she noticed continuous waves of lights coming from the peripheral field, sparing the central vision; the symptoms started suddenly at the time of waking up in the morning after turning on the lights. The symptom lasted for about 3 minutes. In addition, she mentioned temporary flashing when going from dark to light condition throughout the day. No headache was present after the visual symptoms. There was no associated pain, decreased vision, redness, or photophobia. There was no history of any other systemic disease and she had no history of migraine. Drug history was negative except for clomiphene citrate and some vitamin supplements.

On the examination, the best corrected visual acuity (BCVA) was 10/10 for both eyes. Examination of both anterior and posterior segments was within normal limits. No relative afferent pupillary defect (RAPD) was present. Color vision was normal (using an Ishihara color plate). The patient was sent for a 24-2 SITA standard visual field test, which was completely normal; a brain magnetic resonance imaging (MRI) was requested which revealed no abnormality. The patient was diagnosed with visual disturbances due to clomiphene citrate and was requested to stop taking clomiphene and asked for follow-up at 3 months.

After cessation of drug at the 11-month follow up visit, the examination was entirely normal, but the patient had a complaint of prolonged afterimages (palinopsia) and occasional flashes in the peripheral field. Repeat visual field test was normal and according to neurology consult, repeat brain MRI was not requested. The patient is fully informed about the nature of this disorder and asked for regular follow-up visits.

Discussion

Infertility due to anovulation or oligo-ovulation is one of the most common causes for reproductive difficulty in otherwise healthy women, especially in patients with PCOS. Selective estrogen receptor modulators (SERMs) are one of the most commonly used drugs to treat this condition.[1] These are structurally nonsteroidal compounds that bind to estrogen receptors and show tissue-dependent agonist and antagonist effects. For many years, the first line of pharmacologic ovulation induction was the use of SERMs, of which clomiphene citrate has been the most common drug. Clomiphene citrate is characterized by agonistic properties when endogenous estrogen levels are low and acts as a competitive antagonist when levels are high.[2,3] Clomiphene citrate resembles estrogen and binds to the hypothalamic estrogen receptors for a prolonged time, reducing the concentration of intracellular receptors by inhibiting replenishment. Depletion of estrogen receptors in the hypothalamus results in the normalization of gonadotropin-releasing hormone secretion, and hence, secretion of pituitary follicle stimulating hormone levels is optimized and follicular development and ovulation occur.[3]

A study showed different patterns of visually evoked potential latencies during different phases of the menstrual cycle. The latencies are reduced during the follicular and ovulatory phase of the menstrual cycle and increased during the ovulatory phase. Estrogen inhibits the synthesis of gamma-aminobutyric acid. This agent acts as an important inhibitory neurotransmitter in the cerebral and visual cortexes.[4] Thus, the inhibition of gamma-aminobutyric acid increases the excitatory effect on the striate cortex. So, estrogen can stimulate the visual cortex and trigger the development

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of visual concepts such as hallucinations, palinopsias, optic neuropathy, and more.[5-8]

There were previous reports on the visual side effects of clomiphene citrate. The presence of these symptoms frequently results in the immediate cessation of therapy. The visual symptoms include abnormal visual sensations and peripheral scotomas, photophobia, and palinopsia (prolongation of afterimages) such as shimmering and flashes, blurred vision, central and peripheral scotomas, photophobia, and palinopsia (prolongation of afterimages). In the majority of cases, the visual symptoms disappear shortly after the end of treatment.[9] However, one report showed continuation of visual symptoms, even 2–7 years after drug cessation. In that report, three women aged 32–36 years were treated for infertility with clomiphene for 4–15 months and developed palinopsia, shimmering of the peripheral field, and photophobia.[6] In other case reports, evolution of central retinal vein occlusion (CRVO) was observed during treatment with clomiphene citrate.[10-12] Hence, the presence of visual symptoms frequently results in the immediate cessation of clomiphene therapy. A recent observational study was performed to evaluate visual disturbances experienced during clomiphene citrate therapy, and a reversible change in foveal flicker sensitivity was the only statistically significant finding, suggesting that the visual disturbances are more likely due to a transient effect of clomiphene on the visual cortex than to a toxic effect on the retina. They suggest that clomiphene does not have a detectable adverse impact on either the clinical examination or the psychophysical parameters of color vision, visual acuity, contrast sensitivity, or visual fields.[9] There is a report of maculopathy following extended usage of clomiphene, suggesting that there may be a direct effect of the drug on the retina.[13] In our case, the visual side effects started after a relatively short period and low dose of the drug, and there was continuation of some of the symptoms even after 11 months of cessation of the drug. This is inconsistent with the result of Racette *et al*.,[9] and may show that the visual side effects of clomiphene citrate and their persistence is independent of the dose and time of exposure to the drug.

Conclusion

According to above discussion, clomiphene citrate may cause visual disturbances, with indirect effect on the visual cortex or direct retinal toxicity. Hence, candidates for clomiphene citrate therapy should be carefully selected by physicians experienced in the management of gynecological or endocrine disorders. Patients should be informed by the physician about any unusual visual symptoms such as blurring, spots, or flashes, which are totally drug dose and duration of drug exposure independent, and may be persistent even after drug discontinuation.

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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