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Case Report

Clomiphene Citrate Induced Maculopathy

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ABSTRACT

A 26 year old woman presented to an ophthalmology department with defective vision in both eyes gradual in onset and progressive in nature for 6 months duration. Her visual acuity was 6/18 in both eyes not improving with pinhole. Anterior segment examination was normal. There was no relative afferent pupillary defect. Fund us examination showed normal disc and maculopathy with dull foveal reflex. She denied usage of systemic agents that may induce maculopathy, but reported using Clomiphene Citrate (100 mg/day, 5 days per cycle) for one year for primary infertility. Clomiphene is a widely used drug in the treatment of infertility. Patients are usually warned of the side effects such as breast tenderness, bloating, hot flashes and migraine. However, visual disturbances secondary to this drug are not mentioned as these are very uncommon. Therefore when it occurs, the patient can be alarmed and distressed by this unexpected side effect.

Keywords: Clomiphene, Maculopathy, Infertility.

INTRODUCTION

Clomiphene is a widely used drug in the treatment of infertility. Patients are usually warned of the side effects such as breast tenderness, bloating, hot flashes and migraine by the gynaecologist. However, visual disturbances secondary to this drug are not mentioned as these side effects are very uncommon.[1] Therefore, when it occurs, the patient can be alarmed and distressed by this unexpected side effect. In our extensive literature search we have found only less than 10 cases with maculopathy due to clomiphene citrate and it an extremely rare presentation and both ophthalmologist and gynaecologist should be aware of this side effect.

CASE REPORT

A 26 year old woman presented to an ophthalmology department with defective vision in both eyes gradual in onset and progressive in nature for 6 months duration. Her visual acuity was 6/18 in both eyes not improving with pinhole. Colour vision by Ishihara chart was defective in both eyes. Anterior segment examination was normal. The extra ocular movements were normal. There was no relative afferent pupillary defect. Fund us examination showed normal disc and maculopathy with dull foveal reflex. (FIGURE 1)

Fund us fluoresce in angiogram was done which revealed window defect seen at macula with no leakage. (FIGURE 2) Optical coherence tomography showed thinning of the retinal pigment epithelium. (FIGURE 3) Visual field was done.

She denied usage of systemic agents that may induce maculopathy, but reported using Clomiphene Citrate (100 mg/day, 5 days per cycle) for one year for primary infertility. She was known to have polycystic ovarian disease. She had no prior history of systemic or familiar retinal

disease. She was advised to stop the drug and was followed up for one year.

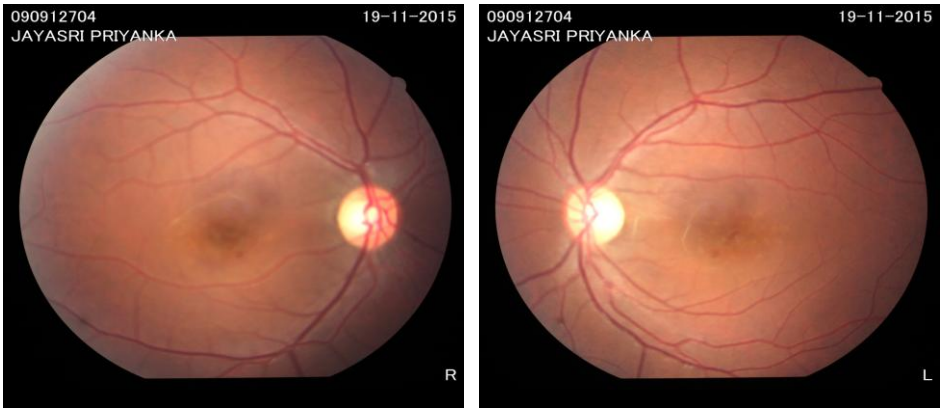

Figure 1: Fundus Photo Showing Maculopathy

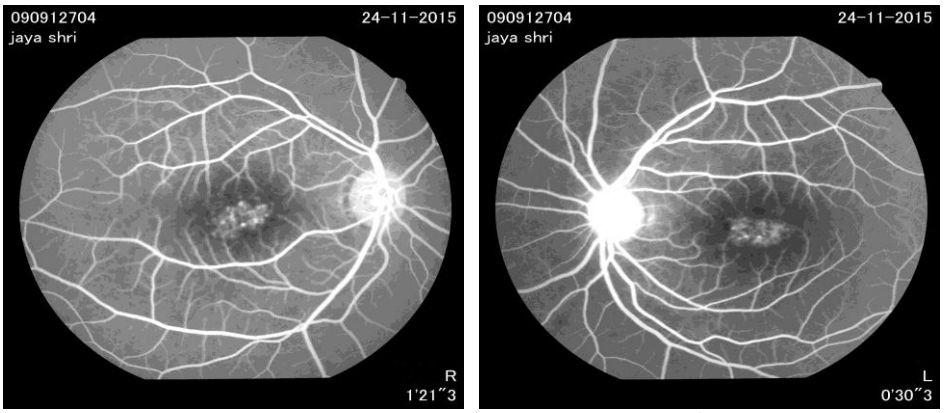

Figure 2: Fundus Fluoresce in Angiogram Showing Window Defect In Macula

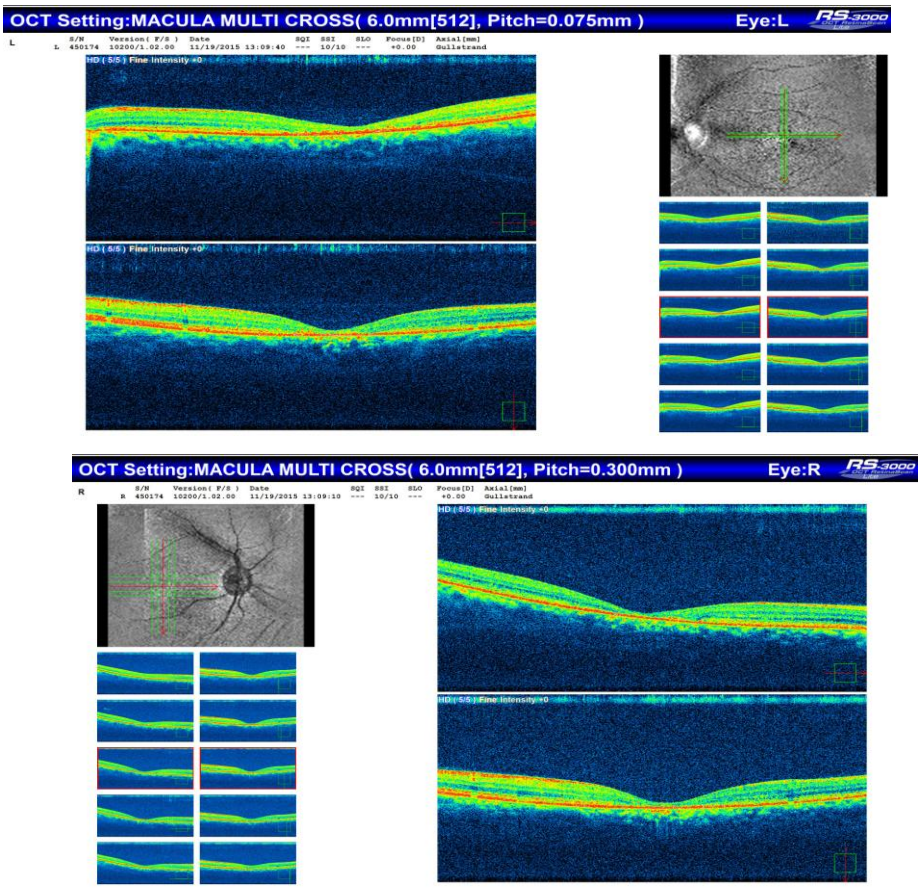

Figure 3: Optical Coherence Tomography

DISCUSSION

Clomiphene citrate (CC) is a selective estrogen receptor modulator mostly used for treatment of infertility associated with polycystic ovarian disease. Unlike Tamoxifen, which is also a selective estrogen receptor modulator, maculopathy has not been reported in association with CC in previous reports. Diplopia, photophobia, temporary visual impairment, and retinal vein occlusion. Although these adverse ocular effects generally disappear within a few days to weeks following discontinuance of therapy, shimmering after-images (palinopsias) and photophobia have been reported to be symptomatic in three cases for 2-7 years. [2]

Clomiphene is a synthetic drug used in the treatment of infertility. Some women do not secrete enough Luteinizing hormone (LH) and Follicle stimulating hormone (FSH) at the right time during the menstrual cycle and as a result, they do not ovulate. For these women, the first drug doctors often prescribe is clomiphene citrate. This synthetic drug stimulates the hypothalamus to release more Gonadotropin releasing hormone (GnRH), which then prompts the pituitary to release more LH and FSH, and thus increasing the stimulation of the ovary to begin to produce a mature egg.

As with any other drug, the patient should be warned of potential side effects. Adverse events reported during a clinical trial by Merrell Dow Pharmaceuticals Inc. involving 8029 anovulatory women include ovarian enlargement 13.6%, vasomotor flushes 10.4%, abdominal-pelvic discomfort, distention, bloating 5.5%, nausea and vomiting 2.2%, breast discomfort 2.1%, visual symptoms 1.5%, headache 1.3%, and abnormal uterine bleeding 1.3% (package insert for Clomid). [3]

As visual symptoms are uncommon, the doctor prescribing clomiphene may neglect to mention this side effect. However if visual side effects occur, it can be very alarming to the patient who has not been forewarned of this. Visual symptoms include blurring of vision, lights, floaters, photophobia, diplopia, scotoma and phosphenes. The aetiology of these is not well understood.

These visual symptoms increase in incidence with increasing total dose or therapy duration and generally disappear within a few days or weeks after clomiphene is discontinued (package insert for Clomid).

Some reported adverse visual disorders that have been reported associated with the use of clomiphene include abnormal accommodation, eye pain, macular edema, optic neuritis, photopsia, posterior vitreous detachment, retinal hemorrhage, retinal thrombosis, retinal vascular spasm and temporary loss of vision (package insert for Clomid). [4]

Patients therefore should be warned of visual symptoms that can occur with clomiphene. They should discontinue this drug and seek complete ophthalmologic evaluation. Ophthalmologists should also be alert to the fact that clomiphene can cause unusual visual disturbances. The patient may not always give the information that she was on clomiphene. She may have stopped using the drug and therefore may not suspect that the visual disturbances are linked to this drug. Therefore the patient should be asked specifically about the use of infertility drugs.

In the past visual disturbances with clomiphene were thought to be reversible, however persistent visual disturbances was seen in this case. The clinician prescribing clomiphene should therefore not take the side effect of visual disturbances lightly, thinking that these symptoms will be reversible and persisting with prescribing clomiphene. [5]

Maculopathy associated with CC was not reported in previous series. Our case was taking CC for an overextended period and developed irreversible visual impairment with maculopathy. Although CC has a similar molecular structure to tamoxifen, CC-associated retinopathy differs from tamoxifenretinopathy as there

are no blocking crystals in FA, but atrophic maculopathy. Our case indicates that CC may induce irreversible retinal damage and visual deterioration if used for an overextended period.

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