Bilateral Intraocular Pressure Rise During the Therapy of Breast Cancer by Tamoxifen in a Patient with Primary Open Angle Glaucoma

Primer Açık Açılı Glokomu Olan Bir Olguda Tamoksifen ile Meme Kanseri Tedavisi Esnasında Bilateral Göz İçi Basıncı Yükselişi

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Case Report *Olgu Sunumu*

ABSTRACT

Tamoxifen is an anti-estrogen agent used in therapy of the breast cancer. A number of ocular complications such as maculopathy have been described secondary to tamoxifen therapy. We report a case of bilateral intraocular pressure rise observed during tamoxifen therapy in a 50-year-old woman with primary open angle glaucoma which has not been previously reported. Rapid decline of intraocular pressure in both eyes was achieved by means of cessation of tamoxifen and administered oral acetazolamide therapy. Here, we aim to attract attention among ophthalmologists and oncologists a possible adverse effect of tamoxifen therapy.

Key Words: Intraocular pressure, primary open angle glaucoma, tamoxifen, estrogen, breast cancer.

ÖZ

Tamoksifen meme kanseri tedavisinde kullanılan antiöstrojen bir ajandır. Tamoksifene bağlı makülopati gibi birtakım oküler komplikasyonlar tanımlanmıştır. Biz primer açık açılı glokomu olan 50 yaşında bir kadın olguda tamoksifen ile meme kanseri tedavisi esnasında bilateral göz içi basıncı yükselişini sunacağız. Bu durum daha önce bildirilmemiştir. Tamoksifenin kesilmesi ve oral asetazolamid tedavisi başlanmasıyla her iki gözde de hızlı göz içi basıncı düşüsü elde edildi. Biz burada göz ve onkoloji hekimleri arasında tamoksifen tedavisinin olası bir beklenmeyen etkisi hakkında dikkat çekmek istiyoruz.

Anahtar Kelimeler: Göz içi basıncı, primer açık açılı glokom, tamoksifen, östrojen, meme kanseri.

Glo-Kat 2010;5:51-53

INTRODUCTION

Tamoxifen is a selective modulator of estrogen receptors (ER) that competitively inhibits the binding of estradiol and disrupts a series of mechanisms that regulate cellular replication and proliferation. In ER positive breast cancer patients, the use of tamoxifen therapy resulted in absolute improvement in the 10 year survival of 12.6% for node positive patients, and 5.3% for node negative patients, independent of patient's age, menopausal status, progesterone receptor status, and the use of adjuvant therapy.[1,2]

Tamoxifen penetrates intraocular fluids to varying degrees. Tamoxifen was found into both vitreous (range 0.5-7.8 ng/ml) and aqueous (range 0.5-3.9 ng/ml) humor from patients undergoing elective ocular surgery during the tamoxifen therapy.[3]

Corneal opacities, posterior subcapsular cataract, maculopathy, optic disc swelling, superior ophthalmic vein thrombosis, proptosis and acute angle closure glaucoma with choroidal detachment have been reported with use of tamoxifen.[4] We are unaware of previous reports regarding intraocular pressure (IOP) rise during the therapy of breast cancer by tamoxifen in a patient with primary open angle glaucoma (POAG).

Geliş Tarihi : 26/11/2009
Kabul Tarihi : 16/12/2009

Received : November 26, 2009
Accepted : December 16, 2009

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CASE REPORT

A 50-year-old woman, in perimenopausal status, who was diagnosed on July 2006 a left breast cancer. The patient undergone lumpectomy and axillary dissection for this lower external left tumor that was an invasive ductal carcinoma, pT1, SBR II, with free margins, without axillary invasion among 13 nodes, positive estrogen (100%) and progesterone (80%) receptors, HER 2 not over expressed. Lumpectomy was followed with breast radiation therapy, and then an anti-estrogen therapy with tamoxifen, 20 mg daily, was started on October 2006 for 5 years duration.

This woman had a history of POAG, diagnosed on December 2004, stabilized after trabeculectomy for right eyes, and she used topical timolol, dorsolamide therapy bilaterally. After 10 months of tamoxifen therapy, she only began feeling some anti-estrogen effects: hot flashes, cutaneous, mucous and corneal dryness but IOP remain stable. She was admitted with sudden severe conjunctival hyperemia, and blurring of the vision after 12 months of tamoxifen therapy. On ocular examination, her best-corrected visual acuity (BCVA) was 20/400 in the right eye and 20/200 in the left eye. The IOP with Goldmann applanation tonometry was 48 and 45 mmHg in right and left eye, respectively. Slit-lamp biomicroscopic examination revealed bilaterally, conjunctival hyperemia, minimal central microcystic corneal epithelial edema, normal anterior chamber depth, open irido-corneal angle. There was no peripheral anterior synechia and neovascularization on the irido-corneal angle and no aqueous flare and cell in the anterior chamber.

Tamoxifen was ceased because it was suspected for these ocular features and oral acetazolamide 250 mg 4 times a day was added to her medications. One day after, her BCVA was 20/100 and 20/25 in right and left eye, IOP was 23 and 19 mmHg in right and left eye, respectively. Conjunctival hyperemia, corneal epithelial edema were regressed. Figure shows the HRT images of the patient. The target IOP of this patient was <15 mmHg especially for right eye but her IOP was not de-

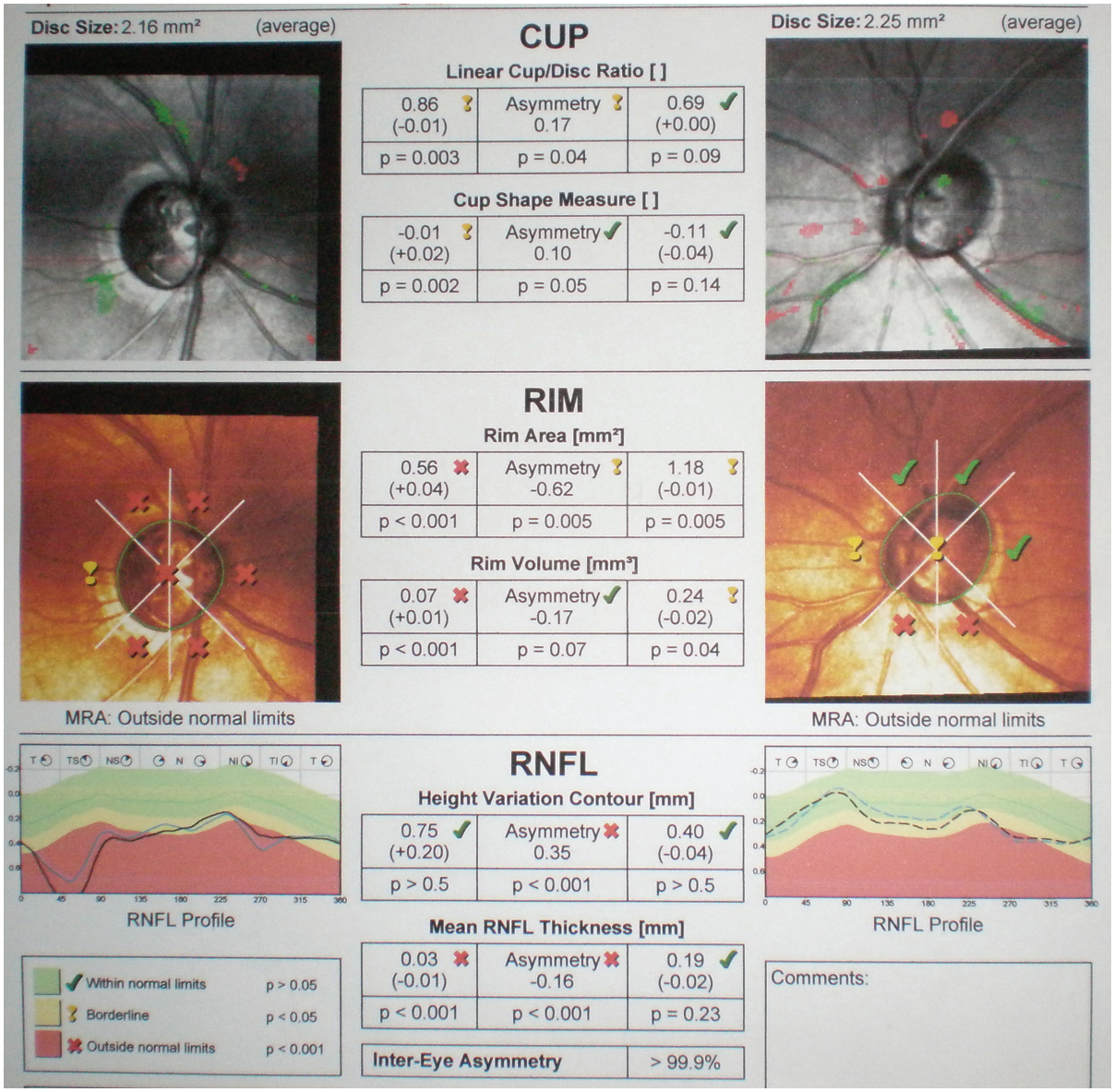

Figure: HRT images of the both eyes.

cline below this level with medical treatment. Hence, second trabeculectomy were performed in right eye after a week. IOP was 15 mmHg in right eye without medical treatment one month after the tabeculectomy.

DISCUSSION

POAG is characterized by a progressive loss of ganglion cells and their axons, resulting in glaucomatous optic neuropathy in combination with corresponding visual field defects. POAG is the third largest cause of irreversible visual deterioration in the Western world. Pathogenesis of POAG is not clearly understood however, elevated IOP is the most important risk factor.

The presence of ER alpha in the epithelium of several ocular tissues such as retina, lens, ciliary body, iris stroma, brings up the possibility that ER could be regulating the transcriptional expression of different target genes in those tissues.5 IOP is higher among postmenopausal women than among men of the same age and premenopausal women; women who had a natural menopause before the age of 45 have a significantly higher risk of POAG than those who had a natural menopause at age 50 or above.[6] In addition, significant decrease in IOP were reported in women taking postmenopausal hormone replacement therapy which consist of estrogen.[7] All these facts suggest the hypothesis of a possible protective effect of estrogen for the IOP elevation and POAG. Tamoxifene has first an estrogene like effect, and then when the estrogen receptors are full, it has an anti-estrogen effect.

Nitric oxide, as a vasodilator, induces a decrease in trabecular pressure in the anterior segment by relaxation of the trabecular meshwork, and may have an effect on the blood supply of the optic nerve and the basal vascular tone retinal and choroidal circulation. Estradiol increases vascular endothelial nitric oxide levels by strongly enhancing the activity of the enzyme nitric oxide synthetase III.[8] Therefore, anti-estrogen agents can increase the resistance of the trabecular meshwork, and may lead to increase the IOP.

In a European study about patients' knowledge and experience of adjuvant endocrine therapy for early breast cancer, near half of the women are worried about the long term effects of endocrine therapy.[9] However, follow up care by oncologists for these patients is overall focused on well known complications from tamoxifen as thromboembolic disease, cerebrovascular events and the increased risk of endometrial cancer.[10]

Breast cancer and POAG are very common disorders in the worldwide. In the light of these observations and concerning this risk of IOP rise occurrence, it seems that the greatest care would be taken by oncologists and ophthalmologists in adjuvant tamoxifen prescription and care for women with ER positive breast cancer and glaucoma diagnosis. So, we aim to attract attention among ophthalmologists and oncologists a possible adverse effect of tamoxifen therapy.

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