Case Report

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Progression of Keratoconus following Hormone Replacement Therapy

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Abstract:

Here we report a rare case of keratoconus in a lady, which was previously stable, but progressed following Hormone replacement therapy (HRT) given for menopausal symptoms. This is to stress on the importance of a close follow up of a keratoconus patient who is placed on HRT

Keywords: Keratoconus, Hormone Replacement Therapy, Estrogen

Introduction:

There are evidences suggesting that female hormonal changes influence keratoconus progression. Puberty and pregnancy can cause a progression in keratoconus, the common factor here being increase or fluctuation in serum levels of estrogen.¹ There is an anecdotal report on the effect of menopause also on keratoconus progression.²

Estrogen receptors have been identified in the cornea³ and the action of estrogen causes a change in the corneal biochemical stability and hence reduces corneal stiffness.^{4,5} Apart from this, estrogen also shows an effect on the pachymetric values by causing a paradoxical increase in the corneal thickness.⁵

Hormone Replacement Therapy (HRT) used to treat menopausal symptoms usually has a combination of estrogen and progesterone supplements.⁶ We report an unusual case of progression of a stable keratoconus when the patient was started on HRT for menopausal symptoms, hitherto largely unreported in literature.

Case Report:

A 35-year-old woman presented to our hospital with frequently increasing refractive error over nine years duration. On examination, her best-corrected visual acuity was 20/180 in the right eye with a refractive error of -11.00DS/ -3.00DC x 10⁰ and 20/30 in the left eye with -3.50DS/-1.00DC x 170⁰. A complete ophthalmic examination was done for her and corneal topography, tomography and

ultrasound pachymetry. The topography was done using the Tomey TMS 4. The pentacam used was Oculus Pentacam HR and the pachymetry was done with the Tomey SP 3000 pachymeter. She was diagnosed with a keratoconus in both eyes which, was worse in the right eye. Her best corrected visual acuity with contact lenses was 20/30 in both eyes. Corneal tomography was used in her follow up after it was available in our hospital from April 2009.

Sim K values were 55.48 x 90⁰ and 49.99 x 10 in the right eye and 48.02 x 73⁰ and 45.38 x 163⁰ in the left eye. Average central corneal ultrasound pachymetry was 435 microns in the right eye and 481 microns in the left eye. The prognosis of keratoconus was explained to the patient and she was followed up every six months. All the parameters of keratoconus in both eyes remained reasonably stable over five years of follow up. The patient was subsequently started on Hormone Replacement Therapy (HRT) for menopausal symptoms elsewhere. It involved a combined estrogen with progestin therapy with conjugated estrogen 0.45 mg once a day and medroxyprogesterone 1.5mg once a day, orally. Six months subsequent to the HRT, the patient showed an increase in the keratoconus parameters in both eyes. Patient had no history or clinical features of tetany or magnesium deficiency which is one of the rarer causes of progression in keratoconus².

The right eye showed progression of the disease with Sim K values

at 56.35 x 103⁰ and 54.14 x 13⁰. Pachymetry values dropped to 401 microns in the right eye and 450 microns in the left eye. The patient was not willing for collagen cross linking treatment in that particular visit.

Six months later, there was a further precipitous drop in pachymetry to 346 microns in the right eye and 387 microns in the left eye. Since the pachymetry in the right eye was too low for collagen cross linking, it was decided to proceed with hypotonic collagen cross linking for the left eye which the patient underwent,

while the right eye remained under observation. A year later, while the patient was still on HRT, the right eye pachymetry showed a marginal increase to 365 microns. The details are elaborated in the table below.

The patient was asked to undergo hypotonic collagen cross linking in the right eye at this stage. Subsequently keratoconus in both eyes has remained stable over six monthly follow up visits, over a three year duration. The HRT was tapered off during this period by the endocrinologist.

Table 1

	Eye	Jan 2002	Feb 2007	April 2009(post HRT)	Feb 2013	Feb 2014	Feb 2015
Sim K reading (TMS)	OD	K1-55.48x 91 K2-49.99x1	K1-55.29x108 K2-52.49x18	K1-56.35x103 K2-54.14x13	K1-56.65x113 K2-51.97x23	K1-60.93x125 K2-57.77x35	K1-58.32x121 K2-53.87x31
	OS	K1-48.02x 73 K2-45.38 x163	K1-47.28x83 K2-44.53x173	K1-47.73x77 K2-45.20x167	K1-49.55x77 K2-46.84x167	K1-50.51x65 K2-46.90x155	K1-47.73x56 K2-45.96x146

	OS	Not available	Not available	K1-46.3x73 K2-44.7x163	K1-46.6x89 K2-47.3x179	K1-47.6x68.1 K2-46.0x158.1	Not done
TMS (Indices)	OD	Keratoconus detected	Keratoconus stable	Keratoconus progression	No progression	Keratoconus progression	No progression
	OS	Keratoconus not detected	Keratoconus detected	Keratoconus stable	Keratoconus progression	No progression	No progression
Pentacam (Indices)	OD	Not available	Not available	Keratoconus +	Keratoconus progression	Keratoconus progression	Not done
	OS	Not available	Not available	Keratoconus +	Keratoconus progression	No progression	Not done
USG Pachymetry	OD	435	401	346	335	365	333
	OS	481	450	426	385	385	341
Pentacam pachymetry (Thinnest)	OD			383	351	372	
	OS			443	414	391	
Pentacam pachymetry (At Apex)	OD						
	OS						

Discussion:

Keratoconus can progress during puberty, pregnancy and hormonal therapy,² due the effect of estrogen. We report progress of stable keratoconus due to oral HRT given for menopause.

Human corneal keratocytes contain estrogen receptors (ER- α , ER- β) where estrogen initiates the biochemical changes in the stroma and also on the endothelial cells.^{3,4} Corneal stiffness is determined by extracellular matrix which mainly consists collagen, proteoglycans and glycosaminoglycans.⁴ Estradiol, the active form of estrogen also stimulates the production of matrix metalloproteinases⁷ and production or activation of other collagenolytic enzymes thus weakening the collagen network.⁸ It also increases prostaglandins secretion which is responsible for activation of collagenase.⁹

Glycosaminoglycans have water binding capacity, which is responsible for tissue flexibility. Estrogen stimulates synthesis of glycosaminoglycans resulting in enriching of the water content and thus increasing corneal thickness which ultimately causes weakening of collagen network.⁴ This may be the cause for the small increase in the pachymetry of our patient in one eye. Thus the overall effect of estrogen on the biomechanics of cornea results a small increase in corneal thickness and distensibility but reduced stiffness.

In a report by Z Gatziofufas et al, a correlation between thyroid levels, pregnancy and progression of keratoconus was suggested.¹⁰ Furthermore pregnancy itself is a documented risk factor for progression of keratoconus due to the altered estrogen levels¹¹. In a study by Fink et al, it was proved that contrary to previous belief, keratoconus can progress even in older age groups.¹² If it did not then hormonal variations like menopause should not make any difference in disease stability.¹²

Oral HRT is one of the modes of treatment for menopausal symptoms. HRT contains estrogen with progesterone to offset the side effects of estrogen.⁶ The serum level of estrogen in a woman on HRT is increased which can have its effect on the thickness, distensibility and stiffness which can be more pronounced in an already weakened keratoconic cornea. This was the effect seen in our patient whose hitherto stable disease progressed while on HRT. Hence, when we ruled out all other factors, we could say that that HRT was the probable cause of progression of keratoconus in this patient, though causal effect is not confirmed.

Conclusion:

Though keratoconus usually does not progress in the menopausal age group, HRT in a woman with keratoconus can affect the biomechanical stability of the cornea. Women with preexisting keratoconus on HRT should be under close monitoring until the completion of HRT to look for progression.

Key words- keratoconus, hormone replacement therapy, estrogen

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