

Diagnosis and Treatment of Radiation Therapy induced Ocular Surface Disorders

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Editorial

Radiation therapy (RT, external beam, plaque or proton beam) is being widely used to treat the head and neck malignancies (such as paranasal sinus, oropharynx tumors, thyroid cancers), ocular adnexal tumors (orbital and conjunctival lymphomas), choroidal melanoma/metastasis, retinoblastoma and few benign orbital conditions such as Graves ophthalmopathy and ocular inflammatory syndromes [1-5]. RT may cause acute ophthalmic complications such as dry eye syndrome (also known as “ocular surface disorder” and/or “keratoconjunctivitis sicca”), conjunctivitis, keratitis or chronic complications such as cataract, secondary glaucoma, radiation optic neuropathy, retinopathy, maculopathy, retinal vascular occlusions, and chorioretinal atrophy. Precautions to protect the eye with advanced/modern radiation techniques are still not preventing the ocular morbidity due to radiation [2-9].

In this editorial, we will discuss briefly the clinical features, diagnosis and treatment of radiation induced dry eye syndrome (ocular surface disorder-OSD).

Lacrimal glands and ocular surface provide adequate tears (tear film comprises of 3 layers- aqueous, mucous and lipid layers) to lubricate eyes and protect the ocular surface tissues. Damage/dysfunction or disruption to either of the systems will lead to abnormalities in the tear film thereby leading to ocular symptoms. Radiation causes damage to the lacrimal glands leading to cell damage, necrosis and apoptosis thereby releasing the inflammatory mediators which decrease the tear production and induce dry eyes [6,7,10]. Usually, dry eye symptoms are experienced by many patients during or after treatment by radiotherapy. Radiation induced side-effects on the eye depends on the dose of radiation used (based on the disease site, histology like lymphoma versus squamous cell carcinoma of the head and neck regions), RT duration, technique of RT (3 dimensional conformal versus intensity modulated radiation therapy (IMRT) with either conventional fractionation schema or stereotactic ablative radiation therapy doses, SABR), and type of malignancy [1-9]. Low doses of radiation (20-24 Gy (Gray) given in 10-12 fractions over 2 weeks) are used for treating conjunctival lymphomas for a short duration and are associated with less ocular morbidity. Whereas high doses of RT, 40 Gy in 20 fractions over 4 weeks for orbital lymphoma and RT doses more than 60 Gy for choroidal melanomas or paranasal sinus tumors are associated with significant ophthalmic complications such as severe keratitis, corneal opacities, limbal stem cell deficiencies, radiation retinopathies and painful blind eye [2,7,11]. Lead shields are used for protection of cornea and lens from the radiation [9-11]. Apart from

external beam radiotherapy, plaque brachytherapy and proton beam therapy, radioactive ablation also can cause significant ocular surface dysfunction. In a comparative study of 3 dimensional conformal proton beam therapy (3DCPT) with IMRT for paranasal sinus carcinomas, the ipsilateral lacrimal gland, lens and retina received above normal tolerance doses leading to marked ophthalmic complications. With 3DCPT alone, the contralateral ocular structures received low doses causing less ophthalmic complications [3]. When uveal melanoma was treated with fractionated stereotactic radiotherapy at a doses of 50 Gy over 5 days, there was significant lacrimal gland damage (dose range to lacrimal gland was 7-10 Gy/fraction) that lead to moderate to severe dry eye syndrome after 6 months of RT. A median dose of 7 Gy per fraction to the lacrimal gland caused a 50% risk of low Schirmer results [4]. Radioactive Iodine (131I) ablation to treat the thyroid cancers also caused lacrimal gland dysfunction causing dry eye symptoms in patients after 1.5 years of therapy [8].

The common symptoms of ocular surface disorder are burning, tearing, redness, foreign-body sensation, mucus discharge, ocular discomfort, frequent blinking, photophobia, contact lens intolerance, and blurry/diminution of vision. Dry eyes can be categorized into different grades as mild, moderate and severe depending on the severity of symptoms and ocular signs. The physical examination should include visual acuity measurement, external ocular examination, slit lamp biomicroscopy and tear film assessment tests. Slitlamp biomicroscopic examination will show lid changes such as erythema, madarosis (loss of eyelashes), trichiasis, & blepharitis, decreased tear meniscus height, conjunctival chemosis, excess mucus or debris, corneal filaments, erosions, and superficial/deep vascularization of the cornea, corneal ulcers and opacities. Fluorescein staining of the cornea shows punctate epithelial defects (common location is interpalpebral area and inferior cornea), corneal filaments, corneal ulcer and limbal stem cell defects. There will be scanty tear meniscus at the lower eyelid margin.

Tear film abnormalities are assessed by Schirmer's test, tear break-up time (TUB), and tear osmolality. Normal tear break-up time is less than 10 seconds. Decreased TUB is noted by measuring the blink to the appearance of first tear film defect with fluorescein staining. Schirmer's test is performed with or without topical anesthetic drops. This test measures the basal and reflex tearing. Schirmer filter paper is placed at the junction of the lateral and middle one third of the lower eyelid in the inferior conjunctival fornix. Filter paper wetting of at least 15 mm in 5 minutes is considered normal. Fluorescein, rose Bengal and Lissamine green stains are used to detect the tear meniscus and conjunctival and corneal abnormalities. Ocular surface disease index (OSDI) is a useful tool to measure the severity of the dry eye, vision-related function and response to treatment of the chronic dry eye

patients. OSDI score is a 12 item scale with scoring ranging from 0 to 100. Patients with higher scores have more ocular disability due to dry eyes [12].

American academy of ophthalmology (AAO) preferred practice pattern has formulated guidelines for evaluation and treatment of dry eye syndromes [13-15]. Mild dry eye is treated with frequent artificial tears (thera tears, refresh tears, genteal), lubricant gels (celluvisc, refresh liquigel) and ointments (refresh PM, tears natural PM, hypo tears). For treating the moderate dry eye symptoms, along with the above medication, topical anti-inflammatory agents such cyclosporine (restasis) 0.05%, omega3-fatty acid supplements, punctal plugs and eye shields or moist chambers are used. Topical antibiotic medication is used if there is associated secondary infection. In patients with severe eye symptoms, in addition to the above treatment methods, other measures used are systemic medications (cholinergic agonists, anti-inflammatory agents and mucolytic agents), autologous serum tears, bandage contact lenses, permanent punctal plugs, tarsorrhaphy (temporary or permanent) and stem cell therapy.

Despite of standard multimodality treatment measures, due to the chronicity and recurrence of the dry eye symptoms treatment of ocular surface syndrome secondary to any etiology including radiation therapy is challenging. Timely intervention and addressing the dry eye symptoms can give better quality of life to the patients on radiation therapy by decreasing the ocular discomfort thereby preventing the visual disabilities.

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