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Pathology of radiation toxicity and its implication on quality of life

Radiation plays an important part in the multidisciplinary management of head and neck cancer and is associated with acute and late effects in the irradiated tissues, which in turn affect the quality of life. The ability to predict and identify normal tissue responses may pave the way toward appropriate and timely management of these sequelae.

Acute changes produced by radiation include mucositis, decreased acuity of taste, skin erythema, and desquamation. Tissues receiving radiation exhibit degrees of dysplasia and atrophy, atrophy and ectasia of salivary glands, epithelial desquamation, ulceration, fistula formation, and rupture of major vessels.

Some of the late effects of radiation are xerostomia, osteoradionecrosis, soft tissue fibrosis, carotid artery injury, trismus, dysphagia, thyroid disease, ocular toxicity, and ototoxicity.[1] Increased collagen synthesis secondary to cytokine and growth factor mediated process leads to tissue fibrosis. Fibrosis of skin and muscles could lead to restricted mouth opening; torticollis, and other impaired physiological functioning. There is sparse literature on the effects of delayed radiation changes in the oral mucosa.

This study by Pandya *et al*. on 27 patients may be considered a step in this direction. It is one of the few to study the histological nature of the collagen fibers in radiation-induced fibrosis. There is a preponderance of thick and mature fibers in the irradiated tissues.[2] Though they have spoken about the pathological features of the irradiated tissue, they have done this in all samples, postrecurrence, where there may be other factors at play. Despite this, it is an important study since it talks about the underlying pathology of late radiation effects. This may be utilized in the clinic to identify substances that could inhibit the process and help ameliorate the intensity of such effects.

Several categories of drugs have been tried for managing the fibrotic sequelae of radiation such as corticosteroids, nonsteroidal anti-inflammatory agents, zinc, interferon, pentoxifylline (PTX), and tocopherol. Delanian *et al*. evaluated the role of PTX and tocopherol in radiation-induced fibrosis. They showed that an objective response to treatment at 12 months was recorded in 83%, with a mean decrease of two-thirds in their surface areas and of half in their SOMA scores.[3] Okunieff *et al*. demonstrated that use of PTX 400 mg TID for 8 weeks improved the active and passive range of movements, muscle strength and decreased limb edema and pain associated with decrease in circulating levels of fibroblast growth factor-2.These agents have been available for some time, but the results are mostly equivocal.[4]

Patients with head and neck cancers are known to have higher degrees of physical symptoms and emotional distress pre- and post-treatment compared to other cancers.[5] In the pretreatment phase higher levels of distress can be attributed to body image changes and impaired physical functioning such as breathing, speaking, eating, etc., in addition to symptoms that can be directly attributable to the disease.[6] In the posttreatment phase, physical symptoms and distress can be attributed to treatment-related acute and late effects. Studies have shown a positive correlation between radiation treatment for head and neck cancer and increase in pain and distress scores. Hence, patients with head and neck cancer should be routinely screened for distress and quality of life.[7] In addition to disease and treatment-related factors, the patient's environment, family and other psychological factors have a significant contribution to the overall sense of well-being in the individual.

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Majority of patients in head and neck undergo surgical intervention of various forms ranging from diagnostic to therapeutic. Treatment interventions impair patients physical and psychological well-being, caused by facial disfigurement and physical disability; for example, impaired basic functions, such as communication (speaking), breathing, chewing, swallowing, eating (dysphagia), and drinking.[8]

Studies have shown that psychological morbidity is higher in head and neck cancer patients undergoing both curative and palliative intent of treatment. Mixed anxiety and depression compounded with spiritual and existential distress is commonly seen in these patients,[9] and incidence is high during the treatment phase.[10] Honest and open communication, explanation of the disease process and treatment, shared decision-making, good symptom control and early recognition of anxiety and depressive symptoms can improve the psychological morbidity. Facilitation of hope, spiritual mentorship and strong family ties will help patients to tide over these.

Early detection of distress and timely institution of remedial interventions help in patient's adaptation and completion of treatment and patient rehabilitation. Advances in radiation treatment have improved loco-regional control and decreased toxicity. There is a paradigm shift from radical ablation to organ preservation, restoration of physiological function and rehabilitation.[11] This has translated into less physical symptoms, less distress, minimal interference with the physiological functioning and improved health-related quality of life. Clinical and histopathological characterization of toxicity helps in development of rational toxicity interventions and improvises treatment regimens to minimize toxicity by modifying fractionation. Knowledge of higher prevalence of psychological distress and increase in all modalities of distress during treatment should enable the clinicians to anticipate, be prepared and plan interventions to decrease psychological distress.

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