Koebnerization and generalized spread of vitiligo following radiotherapy

Sir,

Vitiligo is an acquired, idiopathic disorder characterized by circumscribed depigmented macules and patches with absence of melanocytes. It occurs worldwide with a prevalence of 0.12%.\(^1\) Koebner phenomenon (KP) plays a very important role in the pathogenesis of vitiligo, with varying physical and chemical trigger factors. Herein we describe a case of vitiligo developing koebnerization and dissemination following radiotherapy for esophageal carcinoma.

A 60-year-old male presented to our outpatient department with white colored patches over face, back, chest, both hands, and both thighs. Patient was a known case of vitiligo since childhood with small, stable lesions over the periorbital areas. He was diagnosed to have squamous cell carcinoma of middle one-third of esophagus six years ago that was treated with surgical resection followed by chemotherapy. Patient developed recurrence one year ago and was treated with paclitaxel and carboplatin followed by external beam radiotherapy (59.4 Gy in 33 cycles over a period of 43 days). Whilst on radiotherapy, the patient developed mild erythema over the exposure sites that subsided with hyperpigmentation. One month after completion of radiotherapy, the hyperpigmentation resolved and multiple depigmented macules developed over the areas of exposure. Similar macules also developed over both forearms and thighs. There was no subsequent improvement in these depigmented macules till presentation.

On examination, multiple depigmented patches were present in a ‘L’ pattern over the back and chest, conforming to the area of radiotherapy exposure [Figures 1 and 2]. Multiple depigmented patches were also present in bilateral periorbital areas (present since childhood), dorsum of both hands, and thighs [Figure 2]. Wood’s lamp examination of depigmented patches on back showed a milky white florescence.

The patient was advised topical fluticasone propionate (0.05% cream) and tacrolimus (0.1% ointment). Further follow-up is awaited.

Vitiligo is an acquired depigmentary disorder of the skin that results from the selective destruction of melanocytes. KP is seen in at least one-third of patients with vitiligo.\(^2\) The skin injury inducing it may be physical, mechanical, chemical, thermal, allergic or irritant reactions, chronic pressure, inflammatory dermatoses, or therapeutic modalities. In some of these situations, post-inflammatory hypopigmentation may be difficult to distinguish from koebnerization of vitiligo.\(^2\) However, inspection under Wood’s light as also further follow-up can help to differentiate the two conditions in doubtful situations. In our patient, the depigmentation persisted for 6 months after onset. Also the appearance of depigmented patches over non-exposed parts of the body following radiotherapy confirms the diagnosis.

The pathogenesis of KP in vitiligo is not known. It has been suggested that physical or chemical trauma to the skin may lead to increased oxidative stress including accumulation of hydrogen peroxide. In response to prolonged H\(_2\)O\(_2\) exposure, many proteins are affected including stress proteins such as heat shock protein (HSP 70) which prevent premature degradation of cellular proteins. Although initially protective for the cell, once
released into the extracellular environment these stress proteins are very immunogenic, facilitating the presentation of other antigens to dendritic cells and eliciting an immune response.\(^2\)

Koebnerization of vitiligo following radiotherapy is rare and fewer than 15 reports have been described in literature including one from India.\(^3\) Most of the reports describe depigmentation limited to areas of irradiation. There are only two reports of disseminated vitiligo developing after radiotherapy. However, in both the cases, there was no prior history of vitiligo. Polat, et al.\(^4\) reported a case of disseminated vitiligo developing after radiotherapy in a case of nasopharyngeal carcinoma, with no prior history of vitiligo. Abood, et al.\(^5\) reported a case of melanoma, with no prior history, developing generalized vitiligo after radiotherapy.

The mechanism of development of disseminated depigmentation is not known. A "two-hit" hypothesis has been proposed. Localized radiotherapy leads to increased oxidative stress thereby triggering the process of haptenation and resulting in the formation of highly immunogenic neoantigens. This leads to systemic autoimmune response to melanocytes resulting in sites of depigmentation distant to the irradiated field.\(^5\)

Thus, we present a rare case of radiotherapy induced koebnerization and dissemination of vitiligo. Patients should be made aware of such a possibility and appropriately counseled.

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