NOTES & COMMENTS

Hidradenitis suppurativa after radiotherapy for uterine adenocarcinoma: A typical example of an isoradiotopic response

To the Editor: We read with great interest the case report by Haber et al[1] in the May 2017 issue of *JAAD Case Reports* which described a 57-year-old woman who developed radiation-induced hidradenitis suppurativa (HS) after radiotherapy (RT) for uterine adenocarcinoma. In this patient, HS appeared 1 year after the last cycle of RT and, interestingly, the lesions were strikingly contained within the distinct margins of the radiation treatment, clearly indicating induction by ionizing radiation.

The onset of primary skin cancers on previously irradiated areas has been considered the sole long-term cutaneous side effect of RT for a long time. Actually, an irradiated area is prone to the development not only of tumors, but also of opportunistic infections and immune-mediated skin disorders, representing a typical example of an immunocompromised cutaneous district (ICD).[2-4] The ICD is a novel concept, delineated by Ruocco et al,[3,4] that applies to an area of diseased or injured skin where local immune control has been altered, thereby permitting the development of a dysimmune reaction, infection, or tumor confined to the diseased or injured site. In the ICD, the locoregional immune dysregulation is caused by an obstacle to the normal trafficking of immunocompetent cells through lymphatic channels or an interference with the signals that the neuropeptides and neurotransmitters, released by peripheral nerves, send to membrane receptors of immunocompetent cells.

In the radiation dermatitis, the lymph network is deeply disrupted with abnormal dilation of some vessels and obstruction of others, which results in an obvious obstacle to the trafficking of immune cells. Moreover, peripheral nerve fibers are compressed by dermal fibrosis. Therefore, the dysregulation of the immune control occurring in irradiated areas may well be explained by the impaired lymph flow on one hand and the fibrotic constriction or reduction of peptidergic nerve fibers on the other hand. Both changes locally alter the interplay between immune cells conveyed by lymph vessels and neuromediators running along peripheral nerve fibers,[2,3] resulting in a locoregional immune default. We do not know which immunologic pathways could have been enhanced by RT and would have led to HS in this patient. Both T_H1 and T_H17 lymphocytes have been claimed to play a role in the pathogenesis of HS, as well as in perianal Crohn's disease and several inflammatory diseases.[5] In particular, a dysregulated cytokine expression with enhanced release of interleukins (ILs)-1β and -17 has been demonstrated in both lesional and clinically normal perilesional skin of patients with HS.[6] Moreover, T_H17-derived cytokines can induce massive tissue inflammation and autoimmunity.[7] Bearing in mind that ionizing radiation has profound effects on the composition and function of T-cell populations for a prolonged time after exposure, with selective inhibition or depletion of adaptive regulatory T cells,[3] it is not risky to assume that an imbalance of the T cell population in the irradiated area could have caused the locoregional immune dysregulation leading to HS in this patient.

A recent classification of isomorphic and isotopic skin reactions has proposed a newly coined terminology to indicate each specific cause responsible for the occurrence of an ICD.[8,9] According to this new categorization, the report by Haber et al can be considered an example of an "isoradiotopic response." This definition, first proposed by Shurman et al,[10] indicates the onset of a new skin disease (HS in the case about which we are discussing) on a skin area previously exposed to ionizing radiation (RT for uterine adenocarcinoma in this case).

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REFERENCES

1. Haber R, Gottlieb J, Zagdanski AM, Battistella M, Bachelez H. Radiation-induced hidradenitis suppurativa: a case report. *JAAD Case Rep*. 2017;3:182-184.
2. Ruocco V, Brunetti G, Puca RV, Ruocco E. The immunocompromised district: a unifying concept for lymphoedematous, herpes-infected and otherwise damaged sites. *J Eur Acad Dermatol Venereol*. 2009;23:1364-1373.
3. Ruocco E, Di Maio R, Caccavale S, Siano M, Lo Schiavo A. Radiation dermatitis, burns, and recall phenomena: meaningful instances of immunocompromised district. *Clin Dermatol*. 2014;32:660-669.
4. Ruocco V, Ruocco E, Piccolo V, Brunetti G, Guerrera LP, Wolf R. The immunocompromised district in dermatology: a unifying pathogenic view of the regional immune dysregulation. *Clin Dermatol*. 2014;32:569-576.
5. Giudici F, Maggi L, Santi R, et al. Perianal Crohn's disease and hidradenitis suppurativa: a possible common immunological scenario. *Clin Mol Allergy*. 2015;13:12.
6. Kelly G, Hughes R, McGarry T, et al. Dysregulated cytokine expression in lesional and nonlesional skin in hidradenitis suppurativa. *Br J Dermatol*. 2015;173:1431-1439.
7. Schlapbach C, Hänni T, Yawalkar N, Hunger RE. Expression of the IL-23/Th17 pathway in lesions of hidradenitis suppurativa. *J Am Acad Dermatol*. 2011;65:790-798.
8. Caccavale S, Kannangara AP, Ruocco E. Categorization of and comments on isomorphic and isotopic skin reactions. *Clin Dermatol*. 2017;35:105-110.
9. Caccavale S, Kannangara AP, Ruocco E. The immunocompromised cutaneous district and the necessity of a new classification of its disparate causes. *Indian J Dermatol Venereol Leprol*. 2016;82:227-229.
10. Shurman D, Reich HL, James WD. Lichen planus confined to a radiation field: the "isoradiotopic" response. *J Am Acad Dermatol*. 2004;50:482-483.

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