Letter to the Editor

Transverse Melanonychia After Radiation Therapy

To the Editor:

Nail changes have been commonly associated with chemotherapy and radiation therapy for cancer. Transverse melanonychia is a less common nail finding that has been associated with conventional radiotherapy, infliximab, zidovudine, antimalarials, and several chemotherapeutic agents, among other agents. However, according to a PubMed search of articles indexed for MEDLINE using the terms *transverse melanonychia and radiation* as well as *transverse melanonychia*, only one case series from 2005 reports transverse melanonychia secondary to total skin electron beam radiation (TSEBR).[1]

We report a 72-year-old man who was sent to the dermatology department for a consultation on nail changes. He had been treated at an outside institution and received TSEBR for systemic and disseminated lymphoma. The patient underwent 8 weeks of treatment, which was well-tolerated throughout. Primary adverse events included fatigue and exhaustion. Approximately 6 weeks into treatment, the incidental finding of gradual darkening of the fingernails was noted. Transverse hyperpigmented bands started at the proximal nail and extended to affect half of each fingernail on both hands (Figure). The finding was consistent with transverse melanonychia. No surface changes or other abnormalities of the nails were noted. None of his medications were known to cause nail changes. Furthermore, his history revealed no new medications in the last year.

The skin adnexa, including the hair and nails, can provide important diagnostic clues to a patient's health. Systemic disease and malignancy may impact a number of parameters such as nutrition, inflammation, and profusion, leading to local effects on the adnexa. Cancer treatment with chemotherapy and radiation therapy also has been found to induce hair and nail abnormalities that generally are due to cytotoxic effects of the chemotherapeutic agent or the direct physical damage caused by radiation.[2]

Melanonychia, or development of melanin pigmentation of the nail plate, may be a normal variant in darker-skinned individuals but also has been associated with cancer and its treatment. Three patterns of melanonychia exist: longitudinal, transverse, and diffuse. More than one pattern of melanonychia may be observed in a single nail plate.[2]

Longitudinal melanonychia is a common and well-documented finding associated with numerous etiologies. The longitudinal pigmented streaks generally are associated with discrete pigmented lesions in the nail matrix.[3] These streaks may be acquired without an association to disease but also have been reported with Addison disease,

Transverse hyperpigmented bands on the fingernails.

AIDS, hyperthyroidism, pregnancy, breast cancer, metastatic melanoma, and Peutz-Jeghers syndrome, among other causes.[2]

Chemotherapeutic agents known to cause melanonychia include vincristine, doxorubicin,[4,5] dacarbazine, 5-fluorouracil, and methotrexate. Postinflammatory events such as lichen planus and fixed drug reactions also have resulted in melanonychia. Our patient developed transverse melanonychia following TSEBR.

Transverse melanonychia is a rare finding, particularly in cases of treatment with TSEBR.[1] Total skin electron beam radiation has been used for more than 50 years to treat cutaneous malignancies.[6,7] Only 4 cases (including our case) of associated transverse melanonychia have been reported using the search criteria previously described,[1] all believed to be caused by a transient phenomenon with unknown long-term consequences. After completion of TSEBR, resolution of the hyperpigmentation occurs, though the bands remain until the nail grows out.[2]

The etiology of transverse melanonychia remains unclear. It is known, however, that any pattern of melanonychia results from aberrations of the nail matrix.[8] Melanonychia from chemotherapeutic agents occurs from nail matrix melanocyte activation by the drug. This mechanism of melanocyte activation is unclear and has been found to be independent of melanocyte-stimulating hormone and corticotropin as well as UV light.[9]

The use of TSEBR in skin disease is advantageous because of the relatively superficial deposit of energy. However, electron beams can cause contamination if x-rays are produced and penetrate more deeply.[10] Given that radiation therapy results in DNA damage, it is plausible to assume that the DNA damage could lead to melanocyte activation; however, it is interesting that melanocyte growth terminates after radiation therapy is completed. It is unclear why activated melanocytes cease replicating and do not go on to form larger melanocytic lesions. It also has not been determined if the development of melanoma should be a concern. A possible explanation is an unknown internal or external suppression signal mechanism or suppression cell type that inhibits melanocyte activity. This suppression may be unlocked as the target of chemotherapy or radiation therapy, and once the insult is removed, suppression reoccurs.

Longitudinal melanonychia, the focal activation of melanocytes, is a common occurrence and often a normal variant, especially in black and Asian populations.[11] The focal nature of longitudinal changes raises the possibility that certain melanocytes are more prone to activation than others based on matrix location including sites such as the mid matrix, which is relatively unprotected by neighboring fingers, that are more prone to trauma.[12] Transverse changes may be observed if radiation bypasses the focal trauma effect that may normally affect the most exposed/elevated medial part of the matrix and is thus able to activate the entire matrix simultaneously, thereby causing transverse melanonychia.

An increased sensitivity of certain melanocytes further accounts for the common occurrence of longitudinal melanonychia. Some authors also have suggested an individual genetic predisposition to localized increases in melanocytic pigmentation as a cause.[13] Similar theories have been studied and proposed for the origin of other transverse nail changes. For example, transverse nail depression in times of stress or transverse leukonychia are believed to be due to systemic transient insult that produces simultaneous transverse deregulation. One theory of the pathogenesis of transverse leukonychia due to chemotherapy and congenital causes involves alteration in nail plate keratinization.[14] The potential of different compartments within the distal matrix also has been emphasized by exploring active and inactive melanocyte compartment cell populations that exist in the distal matrix.[15]

Nail hyperpigmentation caused by TSEBR is seen without hyperpigmentation of the skin, particularly because the hands and feet are shielded 50% of the time during TSEBR therapy.[11] In fact, hypopigmentation of the skin tends to be seen post–radiation treatment,[1] which suggests a potential systemic suppression that is deactivated. Alternatively, melanonychia may be caused by postinflammatory activation of melanocytes in the nail matrix, as sometimes seen with postinflammatory hyperpigmentation after irritation.

The lack of information regarding radiation-induced melanonychia, particularly transverse melanonychia, leads to many questions. Further research and more cases of melanonychia are likely needed to elucidate the etiology.

Sincerely,
Brenda L. Pellicane, MD
Rashid M. Rashid, MD, PhD
Houston, Texas

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