

Disappearance of Seborrheic Keratoses Following Treatment With Methotrexate

To the Editor:

A 78-year-old woman was noted to have remarkable disappearance of seborrheic keratoses (SKs) following treatment with oral methotrexate for mycosis fungoides (MF) and Sézary syndrome (SS). On initial presentation, there were multiple 1- to 2-cm, pink, scaly MF patches on the extremities, chest, and buttocks, as well as many large dark SKs on the anterior and posterior trunk (Figure 1). The patient showed complete remission of MF and SS with intravenous doxorubicin without any changes in her SKs. Four months later, the MF relapsed and the patient was treated with oral bexarotene followed by an experimental monoclonal antibody; however, both treatments were discontinued due to drug eruptions. The patient was administered 2 doses of gemcitabine but developed severe capillary leak syndrome and required hospitalization. She started a once weekly dose of oral methotrexate (25 mg), and within 2 months she showed complete remission of MF lesions that also was associated with changes in the SKs, most turning dark and sloughing off, leaving normal skin (Figure 2).

Leser-Trélat sign is a paraneoplastic phenomenon consisting of the sudden appearance and growth of eruptive SKs in association with an internal malignancy, most commonly adenocarcinomas of the stomach or colon, breast cancer, leukemia, and lymphoma. Treatment of the underlying malignancy has been associated with resolution of the SKs. The validity and utility of the Leser-Trélat sign has been questioned, and little evidence exists of an association between eruptive SKs and underlying malignancies.¹ The high frequency of SKs in elderly patients who also have a higher probability of cancer is a confounding variable. The temporal association between development of SKs and diagnosis of malignancy also is subjective and difficult to accurately document.



Figure 1. Posterior trunk with many large dark seborrheic keratoses.



Figure 2. Posterior trunk after 2 months of methotrexate therapy.

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Seborrheic keratoses are common benign cutaneous lesions composed of keratinocytes. They are found most often in older individuals on sun-exposed areas.² The molecular pathogenesis of SKs is proposed to involve a UV-induced mutation of the fibroblast growth factor receptor 3,³ which is a tyrosine kinase receptor that induces verrucous lesions resembling SKs when overexpressed in mice.

Patients with MF that evolves into SS have been reported to develop multiple SKs; the disappearance of the lesions with disease remission also has been reported, but to our knowledge, none of the cases were related to methotrexate therapy.⁴ It is hypothesized that the emergence of SKs was due to secreted factors from the malignant T cells. In a case of SKs that resolved following resection of a nasal carcinoma, there was histologic evidence of a mononuclear cell infiltrate of CD4⁺, CD8⁺, and dendritic cells in the epidermis and dermis of the involuting keratoses.⁵ A similar mononuclear cell inflammatory response has been found in other spontaneously regressing cutaneous tumors. Although our patient's SK regression may be directly related to the remission of her MF and SS, her response to treatment with

methotrexate, and not other drugs, was associated with resolution of multiple SKs.

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