Eruptive Seborrheic Keratoses Restricted to Plaque/Patch-Stage Mycosis Fungoides

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Abstract
Eruptive seborrheic keratoses (ESK) are rare in dermatology. They are usually inflammatory in nature and may be encountered as Leser-Trélat sign. ESK may also be simultaneously observed with hepatic angiomas, chemotherapy, segmental neurofibromatosis, HIV or erythrodermic pityriasis rubra pilaris, psoriasis, and drug eruption. ESK may be transient and self-healing. Others recede after successful treatment of the underlying disease. In some instances, seborrheic keratoses may follow an isotopic response and remain strictly restricted to sites of previous eczema, photo-exposition or tattoos. A patient with patch/plaque lesions of classic-type mycosis fungoides (MF) presented sudden ESK that were exclusively limited to the MF lesions. In conclusion, this patient combined an isotopic response and ESK.

Introduction
The most frequent type of eruptive seborrheic keratoses (ESK) is the Leser-Trélat sign, a paraneoplastic dermatosis characterized by the rapid appearance of multiple, often pruritic and inflammatory seborrheic keratoses (SK) in a symmetrical pattern on the back, mimick-
ing a Christmas tree [1]. Occasionally, ESK can be observed simultaneously with chemotherapy [2], segmental neurofibromatosis [3], HIV [4], or erythrodermic forms of pityriasis rubra pilaris [5], psoriasis, and drug eruptions [6]. They may be transient and present self-resolution. Others recede after a successful treatment of the underlying disease [6].

Furthermore, SK may remain restricted to sites of previous eczema and tattoos [7]. Wolf’s isotopic response is a subtype of the Köbner phenomenon, in which one skin disorder occurs at the site of a second one [8].

Case Report

A 77-year-old male patient had suffered for several years from classic-type mycosis fungoides (MF). Two biopsies confirmed the clinical suspicion, immunohistochemistry revealed CD3, CD4 but no CD8+ atypical lymphocytes. Monoclonal TCR rearrangement was evidenced. An internal workup including a PET scan was unremarkable. Lymphocyte typing was normal. No circulating Sézary cells were observed. His usual medication consisted of metformin, atronase nasal spray, losartan, simvastatin, and gliclazide. He never presented remarkable lymphadenopathies.

Previous treatments included topical steroids inducing short remission periods. Subsequently, the patient underwent UVB and PUVA light therapies with longer complete remission periods. Due to progressive resistance to light therapies, a treatment with oral methotrexate was initiated at 20 mg/week. After a nearly complete remission, the dosing regimen was further reduced to 12.5 mg/week. Currently, the patient is staged as T2N0M0B0 disease.

Unexpectedly, he suddenly presented an appearance of several warty-like lesions, but only restricted to the center or the periphery of MF skin lesions (Fig. 1). The lesions were asymptomatic, nonpruritic, small, unique, and around 10 lesions were identified. At the time of diagnosis, his mSWAT score was 45 and the disease stage T2N0M0B0. A skin biopsy was performed under local anesthesia and revealed papillomatous hyperplasia, compatible with SK of the acanthotic and hyperkeratotic type (Fig. 2). An immunohistochemical search for human papilloma virus (HPV) antigens was negative and in situ hybridization for low-risk and high-risk HPV was also negative. Further skin examination did not reveal the presence of other SK outside the patch/plaque MF lesions.

Although initially not symptomatic, the progressive growth of the lesions incited to use topical cryotherapy that was successful after 2 monthly sessions.

Discussion

The sudden appearance of single SK restricted to the center or the periphery of patch/plaque-stage MF lesions has, as far as we are aware of, not been reported previously. Several hypotheses could be advanced for this special type of ESK. It is currently not known whether ESK are of a particular SK subtype [1].

First, this manifestation could represent a particular form of MF, similar to MF with unusual epidermal hyperplasia [9]. However, histology did not reveal the presence of atypical T-cells in the SK. On the other hand, ESK could be an adverse effect of methotrexate, although this was never reported previously. In contrast, methotrexate has been described as rather beneficial against SK [10].
Another possibility is an increased infectious risk of MF-affected skin. Indeed, as MF lesions progressively change their immunological profile from a Th1 to a Th2 profile, the risk of microbial infestations increases, in particular bacterial and viral infections [11]. In fact, longstanding MF has been demonstrated to be prone to high-risk HPV, retrieved several times over longer time periods. The presence of high-risk HPV was also demonstrated using nested PCR in verrucae occurring in 3 patients with MF [12]. However, in our case, no HPV DNA was retrieved by PCR.

Paracrine promotion of SK growth might have been induced by the MF lesion. Indeed, genetic evidence suggests that SK may be induced by a combination of both growth-promoting mutation and an additional stromal paracrine promotion [13].

The Leser-Trelat sign with rapid-growing SK has been described in only 3 patients with MF [13, 14]. In 1 patient, ESK preceded the appearance of MF for several weeks. PUVA therapy was a successful treatment and coincided with the healing of ESK [14]. In our case with ESK, the diagnosis of Leser-Trelat cannot be excluded, particularly in the light of the underlying MF.

Exceptionally, ESK may remain strictly localized to a specific skin site, such as a decorative tattoo [7]. Furthermore, ESK can be reversible, as has been described after the healing of the underlying dermatoses [6].

Another hypothesis is that SK could induce the MF lesions, like a Köbner phenomenon [15, 16]. However, the MF lesions in our case were present long before the appearance of the SK.

In conclusion, ESK restricted to MF lesions is a not previously mentioned phenomenon, probably linked to a Th2 environment of the MF lesions favoring the growth of ESK, just as observed with viral warts.

Statement of Ethics

Ethical approval has been obtained.

Disclosure Statement

The authors declare no competing interests. There was no funding for this work.

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Fig. 1. Eruptive seborrheic keratoses centered in mycosis fungoides skin lesions (black arrows).
Fig. 2. Histological presentation of the seborrheic keratos. Note the absence of atypical lymphocyte infiltration.