Successful treatment of recurrent dermatophytosis with isotretinoin and itraconazole

Sir,
Dermatophytosis is among the most common skin diseases affecting millions of people worldwide. We are facing an unprecedented increase in the number of recurrent tinea infections in our daily practice. In the absence of susceptibility tests and studies, it is difficult to comment whether these recurrences represent true resistance to common antifungals or are due to other reasons.

A 23-year-old man presented with a 2-year history of recurrent, reddish itchy lesions involving the face, neck, trunk, lower extremities, gluteal and inguinal regions. Initially, the lesions were limited to the gluteal and inguinal regions and used to resolve following treatment with oral fluconazole and topical steroid-antifungal combination therapy. During subsequent episodes, similar lesions appeared on the trunk, lower extremities and face; these were treated with over-the-counter medications, only to recur. He underwent therapy with systemic terbinafine and topical eberconazole for 2 weeks at a local hospital and achieved complete remission but his lesions recurred after partial resolution. Finally, oral isotretinoin (20 mg/day) and itraconazole (200 mg/day) along with topical sertaconazole was given for a period of 1 month. Following this treatment, the skin lesions resolved completely [Figure 4] and a repeat potassium hydroxide mount showed no fungi. A follow-up examination 6 months later showed no recurrence of lesions.

In the absence of antifungal susceptibility testing on isolated strains of fungi, it is inappropriate to label this patient as a case of drug-resistant dermatophytosis. The mechanism of therapeutic success with isotretinoin,
from the pathogenesis of dermatophyte infection and the effects of retinoids on human skin.

The successful initiation of infection is a process closely related to the capability of the infecting dermatophyte to overcome host resistance mechanisms. Cutaneous barriers against dermatophyte adherence, germination of arthroconidia and hyphae penetration into the stratum corneum include the intact keratinized layers of the skin and mucosal surfaces, the presence of fungistatic fatty acids on the skin and other effectors such as skin pH. Once installed, the dermatophytes must scavenge for nutrients for growth, a process based on the induction of structural proteins, permeases and enzymes of the cell wall, in addition to the secretion of a variety of proteins and hydrolytic enzymes such as nucleases, lipases, non-specific proteases and keratinases that occur in response to a short supply of essential nutrients in the host.

Following adherence, successful installation of dermatophytes requires rapid germination of arthroconidia and penetration of hyphae into the stratum corneum. Failure to do so will result in elimination by the continuous desquamation of the epithelium. Retinoids act as modulators of epidermal growth and supervisors of differentiation. Although they act toward normalization in hyperproliferative epithelia as in psoriasis; in normal epidermis, they promote cell proliferation. Therefore, increased cell turnover in the epidermis may halt the spread of ongoing infection by eliminating the growing dermatophyte.

Retinoids are also known to alter terminal differentiation towards a non-keratinizing, metaplastic

Figure 1: (a and b) Multiple erythematous papules and plaques with minimal scaling on lower abdomen, bilateral groins, upper thigh and buttocks

Figure 2: (a and b) Multiple erythematous papules and plaques with minimal scaling over lower abdomen, bilateral groins, upper thighs, buttocks, neck and legs

Figure 3: Septate hyphae seen on KOH mount of skin scraping
and mucosa-like epithelium. The glycosylation pattern of normal skin treated with retinoic acid resembles that of mucosal epithelium with a reduction of tonofilaments, decreased corneocyte cohesiveness, impaired function of the permeability barrier and increased transepidermal water loss, thus explaining the keratolytic effect of retinoids in hyperkeratotic disorders.

Dermatophytes de-repress non-specific proteolytic enzymes and keratinases which have optimum activity at acidic pH and are important virulence factors. Thus, growth is dependent on the pH of the skin which being acidic gives an ideal ambient environment for the fungus. High transepidermal water loss values and impaired barrier function of the skin are correlated with high skin pH which being increased with retinoid therapy raises the skin pH, thereby possibly inhibiting dermatophyte growth.

Finally, retinoids are generally thought to stimulate humoral and cellular immunity. Retinoids can enhance antibody production, stimulating peripheral blood T helper cells. Cell surface antigens of T cells and natural killer cells have been reported to increase after retinoid exposure in vitro. On the other hand, dermatophytes have mechanisms that allow them to evade the host response such as the immunosuppressive action of fungal mannans that causes reduction of inflammation and phagocytosis. Retinoids may counteract some of these immunosuppressive effects of the dermatophyte.

The occurrence of such recalcitrant recurrent dermatophyte infections is bordering on endemicity. Although we do not recommend oral isotretinoin for the routine treatment of dermatophytes, our observation opens avenues of further research to establish the use of isotretinoin in recurrent dermatophytosis.

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Conflicts of interest
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