

Excess granulation tissue and hair loss following acitretin

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Abstract

Retinoids are routinely used in dermatology for various clinical entities including acne vulgaris, rosacea, hypertrophic scars, striae distensae, psoriasis, disorders of dyskeratinization, cancer prevention and other chronic hyperkeratotic disorders. Oral acitretin therapy is effective in the treatment of psoriasis normalizing cellular differentiation and maturation but clinical side-effects are reported. We describe the occurrence of excess granulation tissue in the nails sulcus and noncicatrical universal alopecia in a psoriatic patient receiving oral acitretin.

A 52-year-old white woman presented to our observation because she was affected by moderate psoriasis since the age of 43. Examination revealed red, scaly, disseminated plaques covering a large area of her body. Because of the unresponsiveness to the previous treatments (topical therapies), we started oral acitretin at the dose of 30 mg/day. After 40 days of therapy, psoriasis was well controlled, but an area of granulation tissue was noted in the nail sulcus of both hands (Figure 1). At the same time the patient developed progressive and notable hair loss from the entire body.

The following laboratory studies performed prior to, during and following acitretin therapy, were normal: RBC count, WBC count and differential; sedimentation rate, serum creatinine, LDH, SGOT, SGPT, alkaline phosphatase, total bilirubine, cholesterol and triglycerides, ANA, urinalysis and analysis of thyroid. The histological findings of the granulation tissue included the presence of proliferating microvessels and the dermis contained a dense mixed perivascular cellular infiltrate with numerous plasma cells. Based on these findings, excess granulation tissue and universal alopecia were considered to be acitretin-induced. Acitretin was stopped.

After 4 weeks, her hair growth substantially improved and granulation tissues resolved. To facilitate the healing twice a week silver-nitrate applications were made on granulation tissue. The patient's hair loss completely reversed in 7 weeks.

Retinoids are routinely used in dermatology

for various clinical entities including acne vulgaris, rosacea, hypertrophic scars, striae distensae, psoriasis, disorders of dyskeratinization, cancer prevention and other chronic hyperkeratotic disorders. The most common side effects are mucocutaneous. Most of the side effects of retinoids simulate those of excess vitamin A administration. Vitamin A promotes mucopolysaccharide synthesis in the granulation tissue of skin wounds in rats which is believed to be essential in the early stages of wound healing. Synthetic retinoid administration may exaggerate the usual state of wound healing, however, as we have seen increased granulation tissue production in patients treated with both isotretinoin and acitretin.^{1,2} In fact short-contact tretinoin therapy is a novel modality in which to treat chronic ulcers and stimulate the formation of granulation tissue.³

The excess granulation tissue reported with retinoids usually appear after 3 to 12 weeks of therapy, but there are reports in which the reaction appeared 6 months after beginning therapy,⁴ and even after the withdrawal of the drugs because of the long elimination half-life of etretinate.⁵ In our patient, the lesions developed 40 days after starting the therapy, in accordance with literature.

The granulation tissue response appears to be idiosyncratic and unrelated to either the daily dose of retinoids or the total cumulative



Figure 1. A) Granulation tissue on the first, the second and the fourth nails sulcus of the right hand after 40 days of therapy with acitretin. B) Detail of the granulation tissue of the first nail sulcus.

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dose.² The reaction may resolve spontaneously after the discontinuation of therapy. The formation of excess granulation tissue during retinoids therapy may be explained by several factors:⁶ i) the desquamative reaction at the undersurface of the proximal nail-fold may act a foreign body in the lateral nail groove and incite a clinical inflammatory response; ii) the soft keratin of the nail plate results in fine spicules which emerge from the lateral edges and break through the lateral nail grooves; iii) the fragility of the skin induced by retinoids may allow micro-organism to enter; iv) retinoids significantly inhibits the migration of neutrophils from blood to tissue.⁶

The prevalence and severity of alopecia depend on the drug as well as on individual predisposition.^{7,8} Alopecia occurs less frequently with acitretin than with etretinate,⁹ and such rapid and severe alopecia has not been frequently reported in the literature.

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