Hair darkening after treatment with acitretin followed by narrow-band UVB

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Summary
There are several situations in which gray hair partially becomes pigmented, usually after intake of some drugs (3). We report here a patient with psoriasis who experienced localized darkening of white hair and diffuse hyperpigmentation of the skin after treatment with acitretin followed by narrow-band UVB.

KEY WORDS: hair; acitretin; pigmentation; psoriasis.

Introduction
Hair graying is one of the most obvious manifestations of ageing, and starts at different age in the various races: the first gray hair is seen in Whites in the mid-30s, in Asians in the late 30s and in African-Americans in the mid-40s. Half of all people has a significant amount of gray hair by the time they turn 50 (1). In men, graying usually begins at the temples and in the sideburns. Women will usually start around the perimeter of the hairline. Having gray hair is one of the factors that makes a person look older, together with having a more extensive arcus senilis and being bald (2). Up to now, there are no drugs or other substances able to reverse hair graying and hair colorants are the mainstay of recovering lost hair color. There are several situations in which gray hair partially becomes pigmented, usually after intake of some drugs (3). We report here a patient with psoriasis who experienced localized darkening of white hair and diffuse hyperpigmentation of the skin after treatment with acitretin followed by narrow-band UVB.

Case report
A 63-year-old man presented with a history of severe psoriasis, diagnosed at the age of 30. In the previous years he had been treated with steroids, cyclosporine, acitretin and UVB therapy with few benefits. He had a personal history of colectomy for ulcerative colitis and suffered from mild hyperuricemia, not under drug treatment, and hypertension in therapy with ramipril. He habitually smokes about 20 cigarettes per day. The patient experienced hair darkening after 2 months of therapy with acitretin 25 mg/die, followed by cycles of narrow-band UVB. The patient referred that his hair had been white for 20 years (Figure 1A, B) and then during acitretin treatment it had started growing dark and thicker on the frontal and lateral sides (Figure 2A, B). In the same period, under the action of narrow-band UVB, he became tanned, but when the treatment was discontinued the skin remained widely darker. Repigmentation of the hair involved the sideburns and the frontal-temporal area and was not associated with hair loss. Treatment with acitretin had been interrupted due to poor efficacy on the skin psoriasis, but the hair pigmentation persisted in time and was still present. A trace of diffuse brownish colour of the skin still remained.

The patient underwent a 4-mm punch biopsy of abdominal skin. Histology showed moderately dense perivascular and interstitial infiltrate of lymphocytes in the papillary dermis, dilated capillaries in the dermal papillae, increased number of emosiderophages in the mid dermis. Psoriasiform hyperplasia, slight spongiosis, absence of granular zone, parakeratosis with collection of neutrophils in the epidermis were also evident. Normal complement of epidermal melanocytes was seen (Figure 3). PAS stain was negative for hyphae and spores in the stratum corneum. These histological features were consistent with psoriasis. No histological aspects related to diffuse brownish colour of the skin were noted. On admission, porphyrins, cortisol and ACTH were
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within the normal range, as were the rest of the laboratory tests, so we excluded porphyria and Addison’s disease. Mycosis fungoides and Sézary syndrome were also excluded due to normal immunophenotype.

Discussion

Hair repigmentation has been described in several circumstances in the literature, due to local and systemic causes (Table 1) (4-16). Drugs are the most frequent cause of hair repigmentation (Table 2) (10, 15, 17, 18). Most of the reports of drug-induced hair repigmentation are single case reports and hair darkening associated with retinoids, and particularly with acitretin, represents the most frequently described (17, 19, 20). Acitretin has replaced etretinate in the treatment of psoriasis because of its better pharmacokinetic properties (21). Hair loss is one of the most common dose-dependent mucocutaneous side effects and can occur in up to 75% of patients (21), but alterations of pigmentation have been only rarely described and are not mentioned in the drug label. Cases of darkening and modifications of hair texture, both by etretinate (22, 23) and acitretin, have been reported in the literature. In 2007, Clarke first reported a case of generalized hair kinking in a female patient after a 3 months treatment with 50 mg/die of acitretin (19). Similar findings were reported in 2009 in a 70-year-old woman who experienced darkening and curling of the hair.
after 6 months of therapy with acitretin at a dosage of 25 mg/die. The darkening was mainly located in the occipital region, but black hairs were even present between the other white hairs (17). In 2014 Ward et al. described a 61-year-old-man affected by pityriasis rubra pilaris whose hair turned from white to gray and became thicker and wavier after 1 year of treatment with 25 mg/die of acitretin (20). On the contrary, we also found a case report describing full-body poliosis associated with alopecia after a few months of therapy (24). Our patient’s hair had been white for more than 20 years and we can not find any other association apart from the use of acitretin, especially because the hair darkening began in concomitance with the start of therapy. However, the repigmentation persisted despite the cessation of treatment. The irreversibility of the darkening is difficult to compare with the other three case-reports (17, 19, 20) since the other patients were still on medication with acitretin. We hypothesize that acitretin may interfere with the complex pathway of signals controlling melanogenesis, reversing some patterns of pigmentation and growth. According to Slominski et al. gray hairs show a much reduced, but detectable, dopa oxidation reaction (indicator of tyrosinase activity), whereas white hair bulbs are broadly negative. We therefore suggest that acitretin may stimulate the reduced dopa oxidation reaction (before it turns off completely) (25). Indeed retinoid acid receptor genes have been found in most parts of the hair follicles (26), so the exogenous administration of acitretin may have upregulated the gene expression and proteins synthesis, including cellular RA-binding protein.

Conclusions

As reported in the literature, some drugs can rarely induce hair repigmentation and changes in texture. Our aim is to describe our experience in this clinical case and suggest a possible connection between acitretin and hair darkening. Considering the other cases reported in the literature we propose that this concomitant effect should be added to the list in the drug label.

References

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