Repigmentation of Gray Hair in Lesions of Annular Elastolytic Giant Cell Granuloma

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PRACTICE **POINTS**

- Hair repigmentation can be a clinical clue to a subjacent inflammatory disease.
- Hair depigmentation associated with aging may be a reversible condition under proper stimulation.

Hair pigmentation is a complex phenomenon that involves many hormones, neurotransmitters, cytokines, growth factors, eicosanoids, cyclic nucleotides, nutrients, and a physicochemical milieu. We report a case of repigmentation of gray hairs in lesions of annular elastolytic giant cell granuloma (AEGCG) on the scalp of a 67-year-old man.

Cutis. 2015;96:E19-E22.

Hair pigmentation is a complex phenomenon that involves many hormones, neurotransmitters, cytokines, growth factors, eicosanoids, cyclic nucleotides, nutrients, and a physicochemical milieu.[1] Repigmentation of gray hair has been associated with herpes zoster infection,[2] use of systemic corticosteroids,[3] thyroid hormone therapy,[4] or treatment with interferon and ribavirin.[5] We report a case of repigmentation of gray hairs in lesions of annular elastolytic giant cell granuloma (AEGCG) on the scalp of a 67-year-old man.

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The authors report no conflict of interest.
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Case Report

A 67-year-old man presented to the dermatology department for evaluation of pruritic lesions on the face and scalp of 1 year's duration. The patient reported that hairs in the involved areas of the scalp had turned from gray to a dark color since the appearance of the lesions. The patient had a history of hypertension and type 2 diabetes mellitus. His current medications included irbesartan, atorvastatin, metformin, acetylsalicylic acid, omeprazole, and repaglinide.

Physical examination revealed plaques on the scalp and cheeks that were 2 to 10 mm in diameter. Some of the plaques had an atrophic center and a desquamative peripheral border. The patient had androgenetic alopecia. The remaining hair was dark in the areas affected by the inflammatory plaques while it remained white-gray in the uninvolved areas (Figure 1).

A biopsy of one of the lesions was performed. Histopathology revealed a granulomatous dermatitis involving mostly the upper and mid dermis (Figure 2). Granulomas were epithelioid with many giant cells, some of which contained many nuclei. A ringed array of nuclei was noted in some histiocytes. Elastic fibers were absent in the central zone of the granulomas, a finding that was better evidenced on orcein staining (Figure 3). On the contrary, the peripheral zone of the granulomas showed an increased amount of thick elastotic material. Elastophagocytosis was observed, but no asteroid bodies, Schaumann bodies, or mucin deposits were noted. Histochemistry for microorganisms with

Ziehl-Neelsen and periodic acid–Schiff staining was negative. Other findings included a mild infiltrate of melanophages in the papillary dermis as well as a mild superficial dermal inflammatory infiltrate that was rich in plasma cells. Immunostaining for *Treponema pallidum* was negative. The lymphocytic infiltrate was $CD4^+$ predominant. A prominent dermal elastosis also was noted. Hair follicles within the plaques were small in size, penetrating just the dermis. Immunostaining for HMB-45, melan-A, and S-100 demonstrated preserved melanocytes in the hair bulbs (Figure 4). CD68 immunostaining made the infiltrate of macrophages stand out. Based on the results of the histopathologic evaluation, a diagnosis of AEGCG was made.

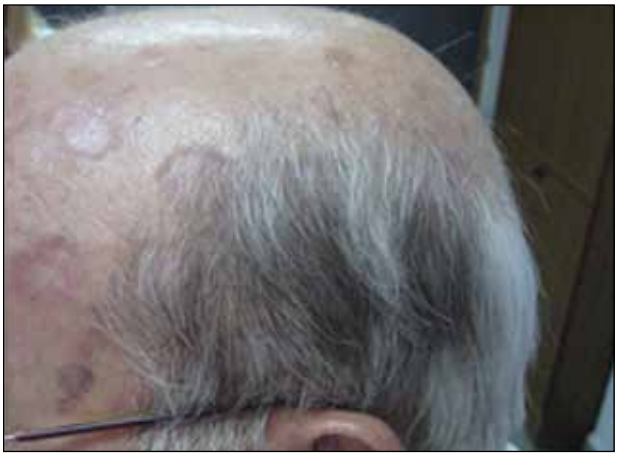

Figure 1. Repigmentation of gray hair in the areas affected by plaques on the scalp.

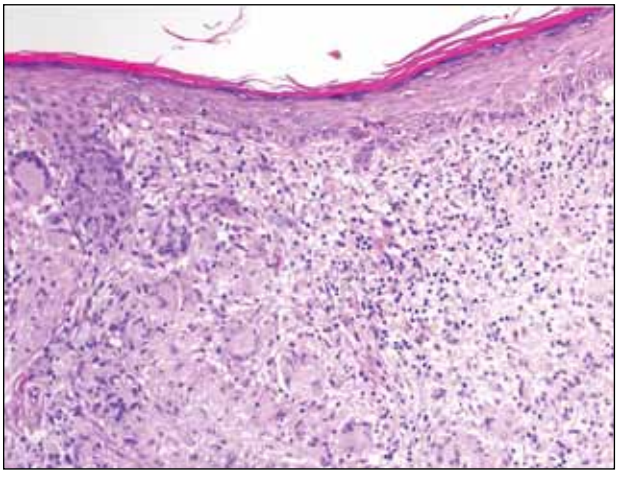

Figure 2. Biopsy showed granulomatous dermatitis in which many giant cells were seen. The latter contained several nuclei, sometimes in a ringed array (H&E, original magnification ×20).

Comment

Annular elastolytic giant cell granuloma is a controversial entity that was first described by O'Brien[6] in 1975 as actinic granuloma. Hanke et al[7] proposed the term

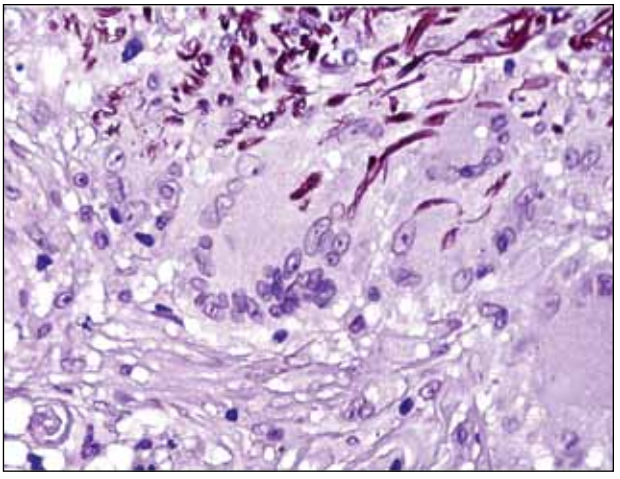

Figure 3. Orcein stain demonstrated a decrease in elastic fibers in the center of the granulomas as well as an increase of elastic fibers in the periphery. Elastophagocytosis was easily observed (original magnification ×40).

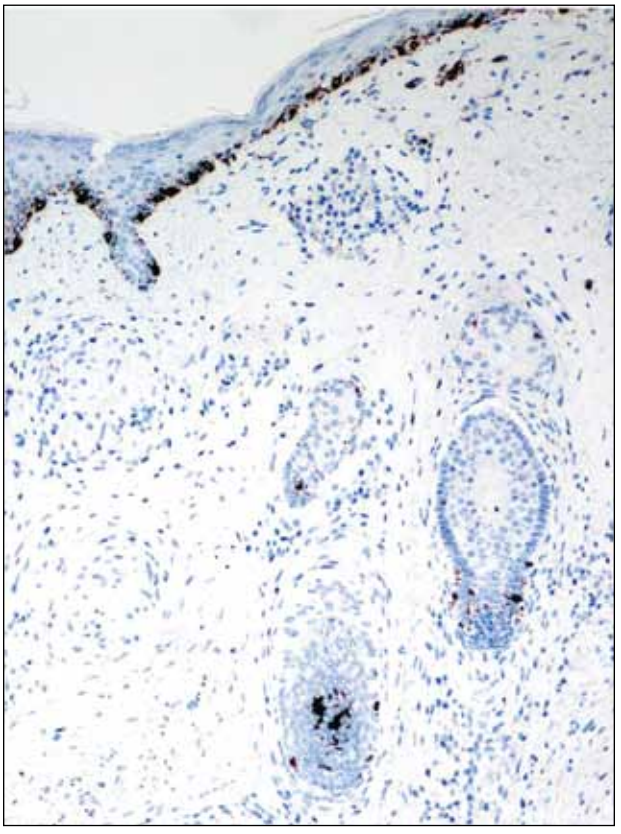

Figure 4. Immunohistochemical staining for HMB-45 showed preservation of melanocytes in the hair bulbs (original magnification ×20).

annular elastolytic giant cell granuloma to encompass lesions previously called actinic granuloma, atypical necrobiosis lipoidica, and Miescher granuloma. Some researchers have claimed that AEGCG is an independent entity, therefore separate and distinguishable from granuloma annulare. Histopathologic clues to distinguish AEGCG from granuloma annulare have been noted in the literature.[7-9] Other investigators believe AEGCG is a type of granuloma annulare that appears on exposed skin.[10] There are several variants of the classic clinical presentation of AEGCG, such as cases including presentation in unexposed areas of the skin,[11] a papular variant,[12] a rapidly regressive variant,[13] a reticular variant,[14] a variant of early childhood,[15] a generalized variant,[16] presentation in a necklace distribution,[17] presentation as alopecia,[18] a sarcoid variant,[19] or presentation as reticulate erythema.[20] However, no variant has been associated with hair repigmentation.

Melanin units from the proximal hair bulb are responsible for pigmentation in adult hair follicles and are integrated by the hair matrix, melanocytes, keratinocytes, and fibroblasts.[21] Hair bulb melanocytes are larger and more dendritic than epidermal melanocytes (Figure 5). The hair only pigments during the anagen phase; therefore, its pigmentation is cyclic, as opposed to epidermal pigmentation, which is ongoing. Hair pigmentation is the result of a complex interaction between the epithelium, the mesenchyme, and the neuroectoderm. This complex pigmentation results from the interaction between follicular melanocytes, keratinocytes, and the fibroblasts from the hair papilla.[22] Hair pigmentation involves many hormones, neurotransmitters, cytokines, growth factors, eicosanoids, cyclic nucleotides, nutrients, and a physicochemical milieu[1,23-25] (Table), and it is regulated by autocrines, paracrines, or intracrines.[21] Therefore, it is likely that many environmental factors may affect hair pigmentation, which may explain why repigmentation of the hair has been seen in the setting of herpes zoster infection,[2] use of systemic corticosteroids in the treatment of bullous pemphigoid,[3] thyroid hormone therapy,[4] treatment with interferon and ribavirin,[5] porphyria cutanea tarda,[26] or lentigo maligna.[27] In our patient, AEGCG might have induced some changes in the dermal environment that were responsible for the repigmentation of the patient's gray hair. It is

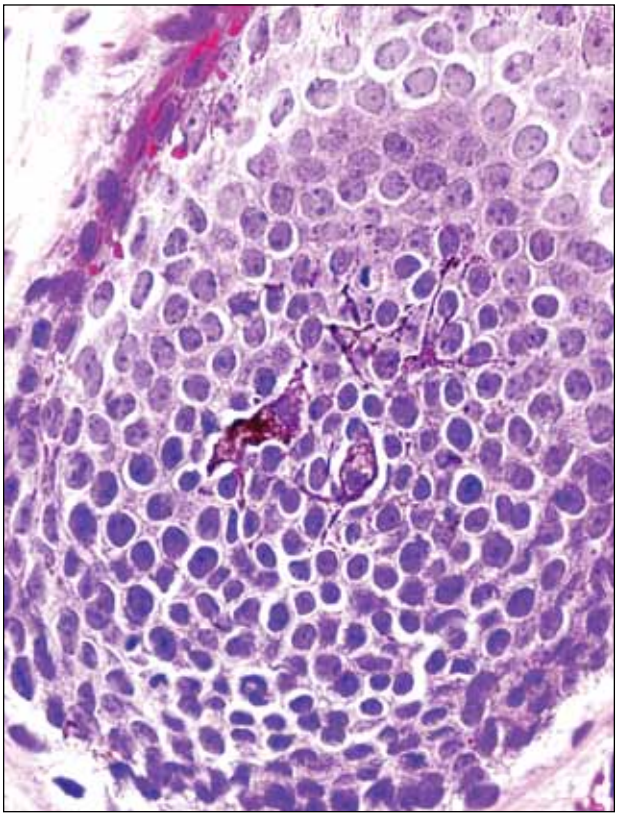

Figure 5. A hair bulb of a normal follicle showing the morphology of melanocytes, which are dendritic and large (H&E, original magnification ×100).

Primary Regulators in Melanogenesis

Positive Regulators (Melanogenesis Stimulators)	Negative Regulators
Adrenocorticotrophic hormone	Agouti protein (in animals, not in humans)
Androgens	Cholinergic agonists
Bone morphogenetic proteins	Dopaminergics
β-endorphin	Glucocorticoids
Endothelin-1	IFN-γ
Endothelin-3	IL-1
Estrogens	IL-6
Histamine	Melatonin
L-3,4-dihydroxyphenylalanine	Tumor necrosis factor α
Leukotrienes	Transforming growth factor β
L-tyrosine	Triiodothyronine
α–Melanocyte-stimulating hormone	
Prostaglandins	
Stem cell factor	
Vitamin D_3	

speculated that solar radiation and other factors can transform the antigenicity of elastic fibers and induce an immune response in AEGCG.[12,15] The lymphocytic infiltrate in these lesions is predominantly $CD4^+$, as seen in our patient, which is consistent with an autoimmune hypothesis.[15] Nevertheless, it most likely is too simplistic to attribute the repigmentation to the influence of just these cells.

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