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The First Case of Ustekinumab-Associated Hair Repigmentation and a Proposed Mechanism of Action

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Dear Editor:

While hair loss is a common side effect of many drugs, drug-associated repigmentation of hair is uncommon. To date, hair repigmentation associated with ustekinumab, an anti-interleukin (IL)-12/23 p40 monoclonal antibody, has not been described. We report the first case of ustekinumab-associated hair repigmentation.

A 52-year-old male, who had completely grey hair for 10 years, began ustekinumab treatment for psoriasis vulgaris. He presented to our clinic describing the return and regrowth of black hair in the temporal area after three months of initiating ustekinumab (two injections per protocol; Fig. 1A, B). He had a 20-year history of psoriasis. Upon physical examination, hair repigmentation was observed symmetrically across the temporal and posterior occipital regions. At the next follow-up, hair repigmentation appeared to have progressed with increased hair density (Fig. 1C), and a 75% improvement was achieved in the Psoriasis Area and Severity Index.

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Hair greying is a sign of aging in humans[1]. But the mechanism is not yet fully understood. Unlike white hair follicles that have no differentiated melanocytes, grey hair follicles have a reduced number of these cells in the hair bulbs, which indicates that greying hair has more reversible properties than white hair. Furthermore, several studies suggested that defective melanosomal transfer or melanin incontinence due to melanocyte degeneration may contribute to hair graying[2].

To date, hair color changes have been reportedly associated with several drugs, including brentuximab, nivolumab, secukinumab, and adalimumab[1].

Many authors who have reported drug-induced hair repigmentation propose that these drugs may inhibit anti-melanogenic cytokines, including tumor necrosis factor (TNF)-α, IL-1, and IL-6[1]. In this case, we propose two mechanisms that may trigger repigmentation: a direct mechanism and an indirect mechanism (Fig. 1D). First, ustekinumab may contribute to hair repigmentation through the inhibition of type 17 T helper (Th17) cells, which in turn inhibits the production of IL-6, an anti-melanogenic cytokine. IL-23, the target of ustekinumab, is involved in maintaining the effector function of Th17 cells, an important subtype that produces other inflammatory cytokines including IL-6[3]. Thus, ustekinumab, an anti-IL-12/23 p40 monoclonal antibody, may induce melanogenesis by inhibiting the anti-melanogenic cytokine, IL-6. Second, IL-23 may contribute more directly to melanogenesis. In a previous study, Nasti et al.[4] confirmed that normal melanocytes express both IL-12 and IL-23 receptors and suggested that IL-23 is associated with maintaining melano-

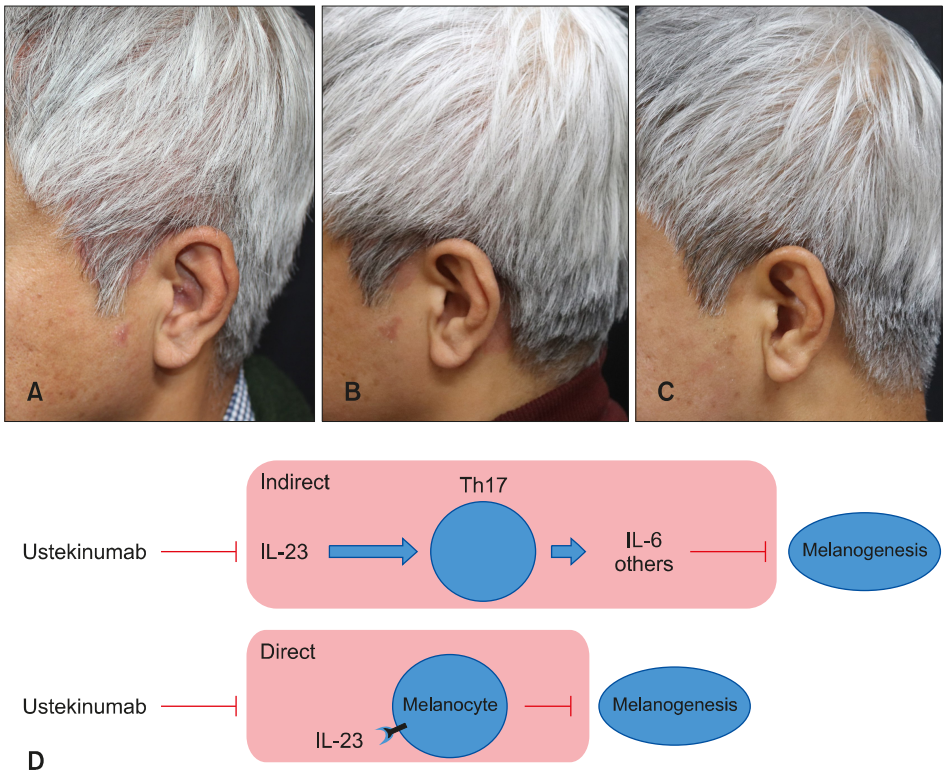

Fig. 1. (A) The hair of a patient who has been completely grey for 10 years. (B) Hair repigmentation is observed symmetrically across the temporal and posterior occipital regions 3 months after the initiation of ustekinumab treatment (two injections per protocol); (C) at the follow-up visit six months after the initiation of ustekinumab treatment, hair repigmentation appears to have progressed. (D) Illustration of the proposed mechanism. IL: interleukin, Th17: type 17 T helper. We received the patient's consent form about publishing all photographic materials.

cyte homeostasis. As proof of this, a patient treated with a biologic agent has an increased risk of a higher nevus count[4]. Vaccaro et al.[5] also reported increased serum levels of IL-23 in vitiligo patients compared to the normal population, which may implicate IL-23 involvement in melanogenesis.

In conclusion, this finding suggests that cytokines are important in the hair-follicle microenvironment for melanocyte production and provides the potential mechanism for IL-23-associated hair follicle melanogenesis. Further study is required to elucidate the mechanism involved in hair repigmentation and regrowth. We believe that this case expands our knowledge regarding hair follicle melanogenesis.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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