Extensive “halo naevi” phenomenon and regression of melanin during nivolumab treatment in metastatic melanoma: a predictor of a better outcome?

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Objective

Vitiligo-like depigmentation in stage III-IV melanoma patients, treated with immune checkpoint inhibitors (ICI), has been associated with improved overall survival, pointing to depigmentation phenomena as a proxy of response to immunotherapy (1,2). Conversely, halo nevus, or Sutton phenomenon, is a rarer clinical manifestation and its prognostic value, as well as any differences from the classical form, remains undefined. As of today, descriptions on extensive halo nevus development (defined as involvement on more than 50% of pre-existing naevi) during ICI treatment are lacking.

Methods and materials

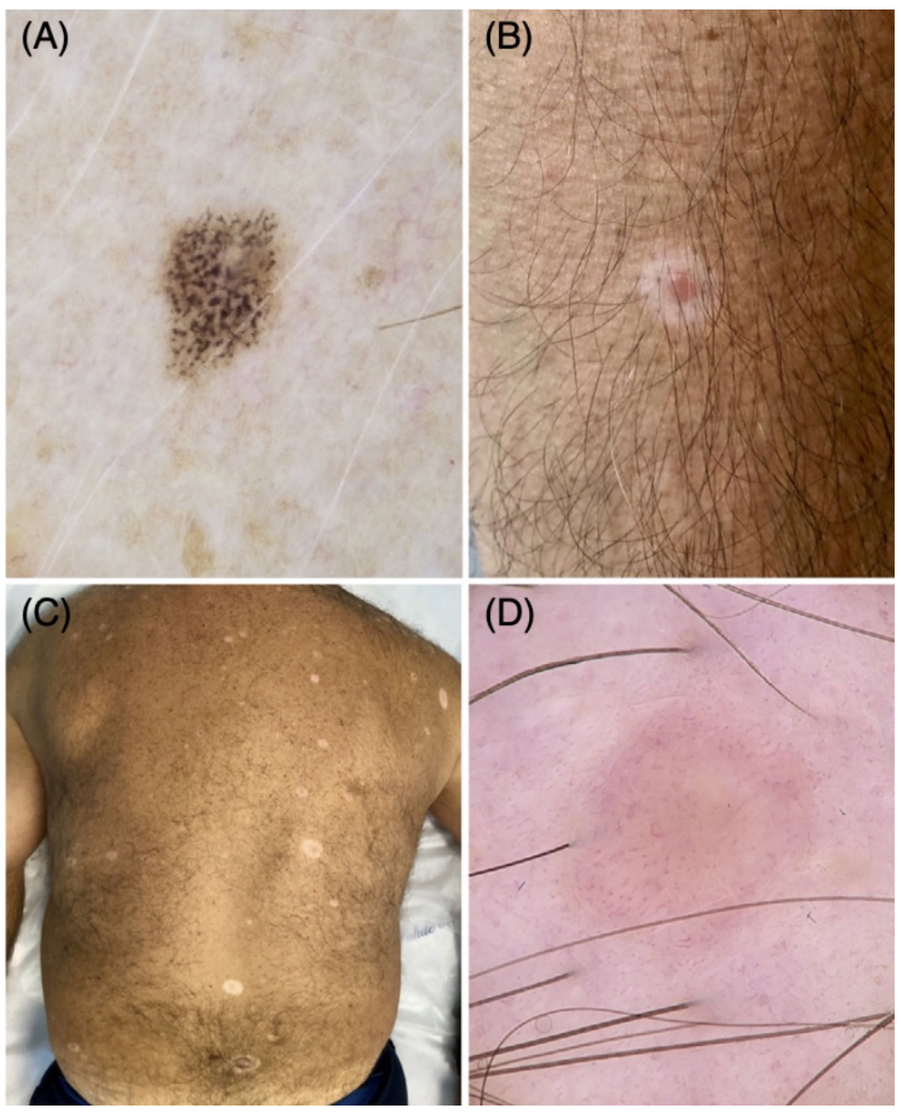
The case of a 63-year-old man with metastatic melanoma in treatment with anti-PD1 nivolumab is herein presented along with a comprehensive overview on the current knowledge on ICI-related halo phenomena.

Results

After 12 weeks on anti-PD1 nivolumab (480 mg every 4 weeks), an achromic halo appeared on our patient’s left arm around a pre-existing nevus. The halo phenomenon progressively involved more than 50% of naevi on the body during the following months. In few cases, the sudden disappearance of pre-existing naevi was observed, resulting in achromic macules only. The dermoscopic evaluation revealed complete regression of the melanin in some other naevi. The patient has remained progression-free after 120 weeks of immunotherapy.

Conclusion

Extensive halo phenomenon has been previously reported during pembrolizumab and ipilimumab treatment (3,4). In both cases, complete remission of metastatic melanoma was later obtained. This first case of extensive Sutton phenomenon during treatment with nivolumab supports the hypothesis that extended Sutton phenomenon and melanin regression may be associated with a better prognosis, as it has been previously observed for vitiligo-like depigmentation. Immune-mediate responses against shared melanocytic antigens (i.e., MART-1, gp100, and tyrosinase-related proteins 1 and 2) are likely responsible for the observed phenomenon (5,6).



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Panel. (A) Multiple gray dots, indicative of an ongoing immuneprocess of regression, in a patient's nevus treated with nivolumab.(B) Achromic halo involving a pre-existing nevus on the right arm after12 weeks of nivolumab treatment in a metastatic melanoma patient.(C) Extensive Sutton's phenomenon involving multiple naevi on the back, including intradermal naevi. In some cases, the disappearance of the pre-existing nevus left an achromic macule only. (D) Dermoscopic features of a halo nevus on the right arm showing complete regression of melanin.