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LEUKODERMA AS A PROGNOSTIC FACTOR IN PACIENTS UNDERGOING IMMUNOTHERAPY FOR MELANOMA

Dermatology

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ABSTRACT

Melanoma is a malignant tumor which develops from melanocytic cells. Leukoderma, which is defined as reduction or absence of skin pigmentation, and is often associated either to the melanoma itself or to its treatment. Immunotherapy with checkpoint inhibitors is one of the treatments currently available for metastatic melanoma, and its use frequently causes the development of leukoderma. In this manuscript we report the cases of 4 patients which developed leukoderma following immunotherapy treatment for melanoma and explore the role of leukoderma as a prognostic factor following this modality of treatment.

KEYWORDS

Leukoderma, Immunotherapy, Melanoma

INTRODUCTION

Melanoma is a malignant tumor which develops from melanocytic cells.[1] It occurs most frequently on the skin and has a worldwide annual incidence of 232,000 cases.[2] Leukoderma is defined as reduction or absence of skin pigmentation, and is often associated either to the melanoma itself or to its treatment.[3,4]

Immunotherapy with checkpoint inhibitors is one of the treatments currently available for metastatic melanoma, being able to prolong the overall survival of the patients.[5] Ipilimumab, Pembrolizumab and Nivolumab are immunotherapy treatments which used for melanoma, and their use frequently causes the development of leukoderma.[6]

In this manuscript we report the cases of 4 patients which developed leukoderma following immunotherapy treatment for melanoma and explore the role of leukoderma as a prognostic factor following this modality of treatment.

Case Studies

Case 1: A 74-year-old woman presented with a tumoral lesion in the upper eyelid of her right eye, which was diagnosed as metastatic melanoma in the pathological examination. No primary lesion was found even after extensive clinical evaluation and diagnostic imaging. Three years after the initial diagnosis, the patient presented a second lesion in her right shoulder, which was also compatible with metastatic melanoma. The patient was treated for metastatic melanoma with immunotherapy (Ipilimumab followed by Nivolumab) and developed achromic patches of skin in her legs (Figure 1). No progression of disease was evidenced after 2 years of follow up.

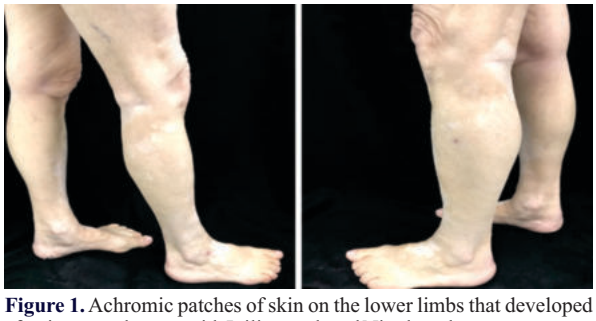

Figure 1. Achromic patches of skin on the lower limbs that developed after immunotherapy with Ipilimumab and Nivolumab

Case 2: A 64-year-old male was diagnosed with a superficial spreading melanoma on his back. Diagnostic evaluation revealed lung metastasis and the patient started immunotherapy treatment with Ipilimumab for 4 months. After 5 years, the patient presented a pericardiac effusion which was positive for malignant cells, compatible with melanoma metastasis. The patient was then treated with Pembrolizumab for 2 years. After the end of this treatment, the patient presented leukoderma in many areas of his body, as well as poliosis (whitening of the hairs) in his head (Figure 2). After one year of follow up the patient didn't show signs of disease progression.

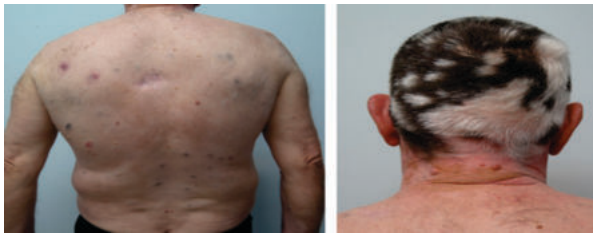

Figure 2. Hypochromic patches on the back of the patient and discoloration of hair shafts on the head.

Case 3: an 81-year-old woman presented with a nodular melanoma of 2,5cm in her left calf. At the moment of the diagnosis, the patient also presented satellitosis near the primary lesion and a skin nodule in her left inguinal region, which upon anatomopathological examination was found to be a metastasis of melanoma. After molecular analysis, which was negative for BRAF V600E mutation, the patient was treated with Pembrolizumab for 6 months. Two months after completing the treatment, the patient developed hypochromic patches of skin in her lower limbs and a hypochromic halo around the metastatic skin lesion on her legs (Figure 3). The patient didn't show signs of disease progression for about 18 months after the treatment was finished.

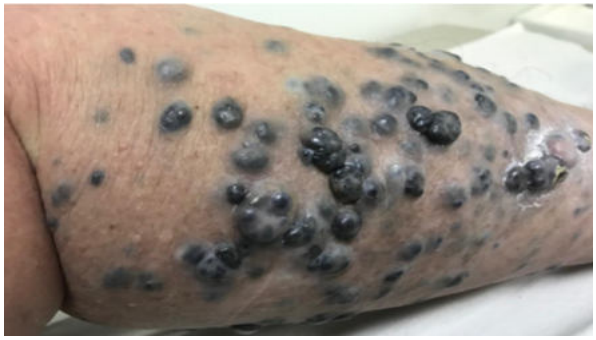

Figure 3. Purple skin nodules (metastatic melanoma) with hypochromic halos following treatment with Pembrolizumab

Case 4: a 61-year-old male presented with a superficial spreading melanoma in his right thoracic area. Diagnostic imaging revealed hepatic metastasis, which lead to the patient being treated with Nivolumab for 14 months. After the treatment, positron emission tomography (PET) scan showed complete regression of the hepatic lesions. One year after the treatment, the patient developed achromic lesions in his thorax, neck, back, and arms (figure 4). There was no disease progression even after 4 years of follow up.

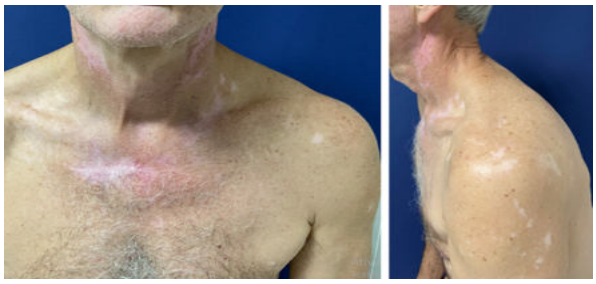

Figure 4. Achromic lesions developed in multiple skin sites after treatment with Nivolumab

DISCUSSION

Immunotherapy includes Pembrolizumab (Anti-PD-1) and Ipilimumab (Anti-CTLA-4). These medications, by means of different signaling pathways, are able to elicit cellular responses against melanoma cells. It is speculated that the leukoderma that may follow the treatment with these medications arises as a cross reaction against healthy melanocytes, due to similar antigens shared between these different population of cells.[7]

The role of leukoderma as a prognostic factor of good response to immunotherapy has been explored in the literature. All of the cases reported in this manuscript showed a good response after immunotherapy, especially the patient from case 4, which showed a complete regression of the hepatic metastasis and didn't show disease progression for 4 years following the treatment. Studies have shown that skin depigmentation following immunotherapy is significantly associated with a favorable prognosis.[7] About 3,4% of patients undergoing immunotherapy develop some kind of skin depigmentation, and those patients were reported as having 2 times lower risk of disease progression and 4 times lower risk of death during the follow up period.[8]

Understanding the skin reactions associated to melanoma and its treatment is important to have a throughout comprehension of the evolution and of the prognostic of the disease. Leukoderma associated with immunotherapy treatment has been shown to be a positive prognostic variable regarding disease progression and mortality.

Conflict of interest disclosures:

The authors state they have no conflicts of interest of any kind in the presented case.

The authors declare that this is an original work which has not been published and is not under consideration for publication in any other journals or media

REFERENCES

1. Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Spatz A, Grob JJ, Malvehy J, Newton-Bishop J, Stratigos A, Pehamberger H, Eggermont AM; European Dermatology Forum; European Association of Dermato-Oncology; European Organization of Research and Treatment of Cancer. Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline--Update 2012. Eur J Cancer. 2012 Oct;48(15):2375-90. doi: 10.1016/j.ejca.2012.06.013. Epub 2012 Sep 13. PMID: 22981501.
2. Schadendorf D, van Akkooi ACJ, Berking C, Griewank KG, Gutzmer R, Hauschild A, Stang A, Roesch A, Ugurel S. Melanoma. Lancet. 2018 Sep 15;392(10151):971-984. doi: 10.1016/S0140-6736(18)31559-9. Erratum in: Lancet. 2019 Feb 23;393(10173):746. PMID: 30238891.
3. Ezzedine K, Eleftheriadou V, Whitton M, van Geel N. Vitiligo. Lancet. 2015 Jul 4;386(9988):74-84. doi: 10.1016/S0140-6736(14)60763-7. Epub 2015 Jan 15. PMID: 25596811.
4. Taïeb A, Picardo M. Clinical practice. Vitiligo. N Engl J Med. 2009 Jan 8;360(2):160-9. doi: 10.1056/NEJMcp0804388. PMID: 19129529.
5. Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nature. 2011;480(7378):480-489. Published 2011 Dec 21. doi:10.1038/nature10673
6. Hua C, Boussemart L, Mateus C, et al. Association of Vitiligo With Tumor Response in Patients With Metastatic Melanoma Treated With Pembrolizumab. JAMA Dermatol. 2016;152(1):45-51. doi:10.1001/jamadermatol.2015.2707
7. Failla CM, Carbone ML, Fortes C, Pagnanelli G, D'Atri S. Melanoma and Vitiligo: In Good Company. Int J Mol Sci. 2019;20(22):5731. Published 2019 Nov 15. doi:10.3390/ijms20225731
8. Teulings HE, Limpens J, Jansen SN, Zwinderman AH, Reitsma JB, Spuls PI, Luiten RM. Vitiligo-like depigmentation in patients with stage III-IV melanoma receiving immunotherapy and its association with survival: a systematic review and meta-analysis. J Clin Oncol. 2015 Mar 1;33(7):773-81. doi: 10.1200/JCO.2014.57.4756. Epub 2015 Jan 20. PMID: 25605840.