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A Case of Metastatic Melanoma in a Female Patient with Vitiligo

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ABSTRACT

Patients with metastatic melanoma occasionally develop de novo hypopigmentation, pathologically indistinguishable from Sutton's nevus and common vitiligo, respectively. The case of a 68-year-old female with vitiligo of 2 years of evolution is documented, presenting a left inguinal mass and a para-aortic lymph node conglomerate. In the left inguinal region, a ganglion with thickened cortex and liquid content was identified. The laboratory results report hemoglobin of 8.30 g/dL, leukocytes 19.12 u/L, albumin 2.2 mg/dl, DHL 1222 Ul/L, alpha-fetoprotein 2 ng/ml, Ca-125 14.30 U/ml, Ca-19.9 8.60 U/ml and carcinoembryonic antigen of 2.14 ng/ml. Upon inspection, hypochromic, bilateral, and symmetrical lesions can be seen on the back of the hands, wrists, scalp, facial region, and neck. Biopsy showing malignant metastatic melanoma is performed. Starting management with Pembrolizumab 1 mg/kg every 21 days. Currently in follow-up and adjuvant treatment. Melanoma is the most aggressive form of skin cancer. The association of malignant melanoma with de novo hypopigmentation has been found, synchronously or following the diagnosis of the tumor. In recent years, it has led to the development of monoclonal antibodies. However, its diagnosis has implications for life prognosis due to high mortality.

KEYWORDS: melanoma, vitiligo, neoplasm metastasis

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INTRODUCTION

Cutaneous melanoma represents the most aggressive form of skin cancer, and its incidence is constantly increasing in the Western population. In Europe, more than 100,000 cases of melanoma are recorded every year[1].

BACKGROUND

Skin depigmentation, such as that which occurs in vitiligo, has been associated with cutaneous melanoma since the 1970s. Most antigens recognized by cytotoxic t lymphocytes (CTL) isolated from melanoma patients are expressed on both cells melanoma as in normal melanocytes, which explains why the autoimmune responses against melanocytes that lead to vitiligo or Sutton's nevus could also be present in patients with melanoma, resulting in leukoderma or melanoma-associated halo[2].

Melanoma represents 4% of all malignant skin tumors, although it is responsible for 80% of deaths from this type of tumor. Most melanomas are located on the skin (95%) and less frequently (5%) on the mucosa (oral, digestive tract, genital), retina, or meninges. Approximately 3% of patients develop occult melanomas (metastatic disease without evidence of a primary tumor) [3.4]. Vitiligo is an acquired skin disorder characterized by depigmentation secondary to the loss of melanocytes in the epidermis, which gives rise to well-defined achromic spots that can develop at any age, with a peak incidence between 10 and 30 years of age. Although the etiology of vitiligo is uncertain, humoral, and cellular immune phenomena, as well as a non-immunological mechanism, play important roles in its pathogenesis[4]. Patients with metastatic melanoma occasionally develop de novo hypopigmentation, synchronously or following tumor diagnosis, either surrounding the melanoma (Sutton's phenomenon) or distantly, being pathologically indistinguishable from

Sutton's nevus and common vitiligo, respectively. association has been called “melanomaassociated vitiligo” or “melanoma-associated leukoderma” [4,5].

The most accepted hypothesis to explain the mechanism of vitiligo-type hypopigmentation in malignant melanoma considers that it is the result of an autoimmune response against antigens shared by melanocytes and melanoma cells, such as antityrosinase antibodies, involved in a haptenization process[5]. The case of a patient in 3rd level of care is presented.

CLINICAL CASE

A 68-year-old female with systemic arterial hypertension, type 2 diabetes mellitus under treatment, and vitiligo of 2 years' evolution. She presented a left inguinal mass (fig. 1A). The simple abdominal-pelvic tomography (fig. 1B) shows a para-aortic lymph node conglomerate with approximate dimensions of 57 x 39 mm in its major axes. Towards the left inguinal region, a thickened cortical ganglion with liquid content measuring 21 x 12 mm was identified. The laboratory results report hemoglobin of 8.30 gr/dL, hematocrit 91.20%, VCM 91.26 fL, leukocytes 19.12 u/L, absolute neutrophils 17.25%, urea 17.1 mg/dl, creatinine 0.38 mg/dl, albumin 2.2 mg/dl, DHL 1222 Ul/L, alpha-fetoprotein 2 ng/ml, Ca-125 14.30 U/ml, Ca-19.9 8.60 U/ml and carcinoembryonic antigen 2.14 ng/ml. Upon inspection, hypochromic, bilateral, and symmetrical lesions were observed, predominantly on the back of the hands, wrists, scalp, facial region, and neck, with sharp, curvilinear boundaries, and the presence of ephelide-shaped macules. A lymph node biopsy was taken, obtaining 100 ml of sallow fluid with necrotic lymph node complex and liquefaction tissue. Histopathological report shows malignant metastatic melanoma (fig. 1C). Starting management with Pembrolizumab 1 mg/kg every 21 days. The patient is currently under follow-up and adjuvant treatment.

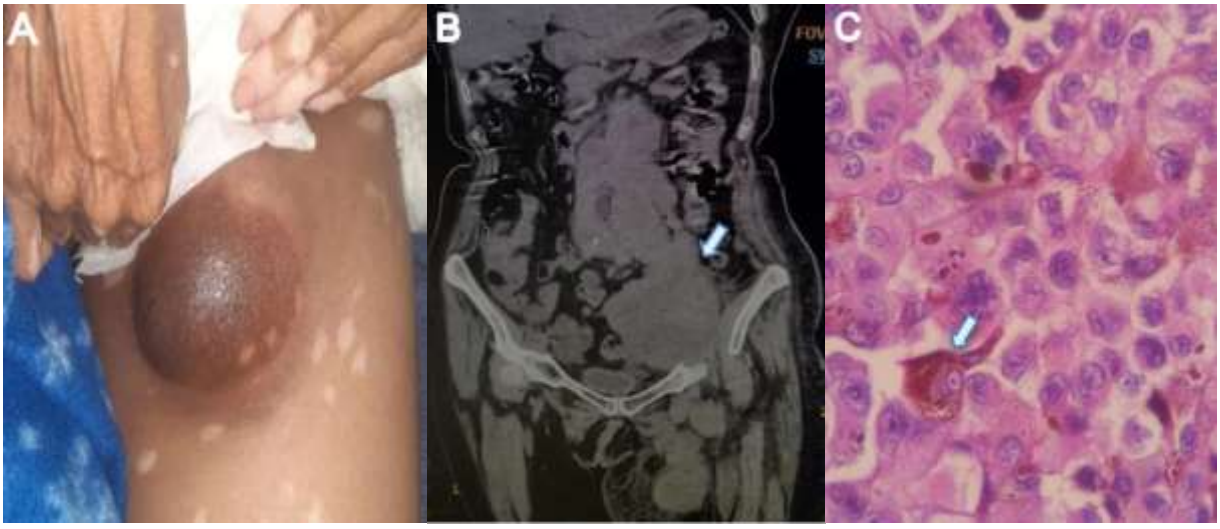

Figure 1. A) Non-mobile, soft, painful tumor in the left inguinal region of approximately 5 x 8 cm in diameter, hyperchromic with satellite hypochromic macules, B) Simple abdominalpelvic tomography, with irregular tumor (arrow) that extends to structures kidneys and left iliac fossa, with lobulated edges, adjacent to the aorta, C) Histopathological specimen with fibrofatty tissue, remnants of lymphoid tissue and infiltrated by solid neoplasia, with balanoid groups and perivascular stratified layers, with large cells with pleomorphic nuclei ,polymorphous, multinucleated, lobed, with lumpy chromatin and prominent nucleolus, atypical mitoses with extensive eosinophilic cytoplasm. Some cytoplasms show melanin pigments (arrow) and extensive areas of tumor necrosis.

DISCUSSION

Melanoma is a malignant tumor that develops from melanocytes, it is the most aggressive form of skin cancer, in 2018 according to Globocan data this disease accounted for 3.1% of all new cases in the world[6].

Depigmentation of the skin, such as that which occurs in vitiligo or Sutton's nevus, has been associated with cutaneous melanoma since the 1970s, with a reported frequency of 216%, with a survival of 21% in patients with vitiligo and melanoma with regional metastasis, compared to patients without this association where survival was 3%[3,7].

The association of malignant melanoma with de novo hypopigmentation has been found, synchronously or following the diagnosis of the tumor, however, there are case reports in which hypopigmentation has developed before the diagnosis of malignancy8. Melanoma is considered a highly immunogenic tumor due to its high mutation load, and it has also been found that the antigens recognized by cytotoxic T lymphocytes isolated from patients with melanoma are expressed both in melanoma cells and in normal melanocytes, which explains why they could also be present in autoimmune responses against melanocytes that lead to vitiligo[3,8]. Until 2010, the main treatment for patients with unresectable locally advanced and metastatic melanoma consisted of chemotherapy; however, the responses obtained were short-lived and associated with high toxicity. In recent years, better knowledge of the biology of immune checkpoints has led to the development of monoclonal antibodies to activate the antitumor immune response, including those directed against the programmed cell death proteins PD1 or CD279, located

in the membrane of tumor cells and other cells of the organism[8].

The monoclonal antibody Pembrolizumab has been extensively studied, as it has been shown to potentiate the T cell-mediated immune response by blocking the interaction between PD1 and its ligands. In addition, it has been found to be superior to standard 1st or 2nd line therapy in advanced melanoma in all efficacy parameters, as well as with a better safety profile[9].

CONCLUSIONS

The finding of metastatic melanoma in the context of a patient with vitiligo is usually a rare case. However, its diagnosis has implications for life prognosis due to high mortality. The comprehensive approach to these patients is key to their survival.

CONFLICTS OF INTEREST

None reported.

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