Complete regression of mycosis fungoides after ipilimumab therapy for advanced melanoma

Gil Bar-Sela, MD,[a] and Reuven Bergman, MD[b]
Haifa, Israel

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INTRODUCTION

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL).[1] Immunostimulatory approaches, such as interferon administration, are well established in the treatment of CTCL.[2] In the last years, several new antibodies that enhance the immune system activity have entered the field of cancer immunotherapy. Ipilimumab (a cytotoxic T-lymphocyte antigen−4 [CTLA4]- blocking antibody, Yervoy, Bristol-Myers Squibb, Princeton, NJ) was the first one of its class to receive an approval for treatment of melanoma.[3] Whether ipilimumab might be effective in CTCL is not known. We describe a case of complete remission of cutaneous MF during ipilimumab treatment for advanced melanoma.

CASE REPORT

A 44-year-old man presented in 1992 with scaly plaques on the trunk and extremities with histopathology of parapsoriasis. In 2002, 2 biopsies in 2 separate medical centers showed MF, stage IA. He was treated with ultraviolet B phototherapy until complete remission, but the MF recurred clinically and histopathologically 14 months later. The patient was followed up but chose to avoid further intervention. In 2011 he had melanoma on the scalp diagnosed for the first time, Breslow 4.2 mm, without ulceration and with negative sentinel lymph node biopsy, stage IIb. He underwent wide local excision and a sentinel lymph node biopsy. One year later, he had regional in-transit melanoma recurrence requiring further surgery. Eventually in 2013, he presented with biopsy-proven metastasis in the right parotid gland and left cervical lymph node, without any other metastasis according to positron emission tomography−computed tomography scan. Molecular genetic test result for BRAF mutation was negative. MF patches and plaques were present on his chest and arms. The patient started treatment with ipilimumab in January 2014, given every 21 days for a maximum of 4 treatments. After the third treatment, all the cutaneous MF lesions disappeared. Positron emission tomography−computed tomography after the fourth and last ipilimumab treatment showed mixed response, with a new fluorodeoxyglucose-avid palpable lymph node in the left side of the neck. Second-line treatment with pembrolizumab (anti-program death−1−blocked antibody, Keytruda, Merck, Sharp Dohme Corp, Whitehouse Station, NJ) was started with partial response. Currently, the patient is still in complete remission from his MF.

Abbreviations used:

CTCL:	cutaneous T-cell lymphoma
CTLA4:	cytotoxic T-lymphocyte antigen-4
MF:	mycosis fungoides

DISCUSSION

CTLA-4 is a negative costimulatory molecule that inhibits T-cell activation by binding to CD86 in the immunologic synapse, and its expression is highly regulated. A significant increase in CTLA-4 expression was seen in malignant T cells from patients with MF, while exhibiting a correlation between higher expression and the grade of the disease.[4] Also, inhibition of proteasome function in normal T cells with bortezomib caused sustained expression of CTLA-4 in normal $CD4^+$ T cells, mimicking the expression pattern observed in Sézary syndrome.[5] This finding suggests that targeting this pathway may be beneficial in CTLA-

From the Division of Oncology[a] and Department of Dermatology,[b] Rambam Health Care Campus and Rappaport Faculty of Medicine, Technion-Israel Institute of Technology.
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Correspondence to: Gil Bar-Sela, MD, Director, Integrated Oncology and Palliative Care Unit, Rambam Health Care Campus, POB 9602, Haifa 31096, Israel. E-mail: g_barsela@rambam.health.gov.il.

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4—overexpressing T-cell neoplasms. Another possible explanation for the regression of MF in our case was that CTLA-4 blockade decreased regulatory T-cell activity, which enhanced the anti-tumoral immunologic activity against MF.

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