Inflammatory melanoma in transit metastases with complete response to talimogene laherparepvec

Jonathan T. Blackmon,[a] Michael S. Stratton, MD,[b] Young Kwak, MD,[b] Peter G. Pavlidakey, MD,[c] Andrzej T. Slominski, MD,[d] Svetlana B. McKee, RN, BSN,[e] Toni M. Viator, RN,[f] Ju Young Kim, PhD,[g] Conway C. Huang, MD,[h] and Robert M. Conry, MD[e]
Lookout Mountain, Georgia; Birmingham, Alabama; and Carlsbad, California

Key words: dermal intercalation; dermal lymphatics; erythematous plaque; immune phenotype; inflammatory melanoma; talimogene laherparepvec.

INTRODUCTION

Inflammatory melanoma was first described in 1984 in 2 patients presenting with nodular cutaneous melanomas resected from the back followed 4 to 12 months later by recurrence in the form of diffuse, indurated, erythematous skin 20-25 cm in diameter with scattered nodularity.[1] Microscopic examination found melanoma cells in the dermis and dermal lymphatics. Both patients died of hematogenous metastases within 6 months of their inflammatory melanoma recurrences.[1] Although histopathologic examination of melanoma frequently finds an associated inflammatory cell infiltrate, gross clinical inflammation is extremely rare.[1] A search of PubMed and Google Scholar performed on August 5, 2016 found 3 additional case reports of inflammatory melanoma, 2 of which involved direct dermal lymphatic extension from grossly involved lymph nodes.[2-4] Here we report the first, to our knowledge, successfully treated case of surgically incurable inflammatory melanoma with emphasis on molecular and immunophenotypic characterization.

Abbreviation used:

TVEC: Talimogene laherparepvec

CASE REPORT

A 79-year-old white man presented with an ulcerated, epithelioid, melanotic melanoma of the left dorsal forearm, 1.6 mm deep, that was widely excised with negative margins and a negative sentinel lymph node biopsy from the left axilla (T2b, N0, M0). Beginning a year after his primary excision, and over a period of 23 months, 6 separate satellite melanoma nodules within 2 cm of the original scar were excised. Eight months later, a surgical oncologist aggressively excised additional satellite melanoma nodules, and repeat sentinel lymph node biopsy found melanoma in 1 of 3 left axillary nodes. The *BRAF* gene was wild-type. Positron emission tomography/computed tomography found no evidence of metastatic melanoma. Melanoma again recurred locally 2 months later with 6 pigmented dermal satellite nodules. Radiotherapy consisting of 36 Gy in 6 fractions over 2 weeks was delivered to the left forearm encompassing all previously affected sites with a 2-cm margin. Four months later, he had a clinical complete response to radiotherapy with all satellite nodules becoming macular, but 2 months thereafter he presented with 60 new punctate, black, dermal nodules affecting most of the left forearm with a confluent, erythematous plaque extending from the dorsum of the left hand and thumb to the mid upper arm (Fig 1, *A*). Skin

From Covenant College[a]; the Deparment of Dermatology[b] and Divisions of Dermatology and Pathology,[c] Dermatopathology,[d] Hematology Oncology,[e] and Dermatology[h]; and Comprehensive Cancer Center,[f] University of Alabama at Birmingham; and Navigate BioPharm Services, Inc, a Novartis company, Carlsbad.[g]

Funding sources: None declared.

Conflicts of interest: Supported by Navigate BioPharm Services, Inc, a Novartis company, through manpower and materials. Dr Kim is an employee of Navigate BioPharm Services, Inc, a Novartis company. The other authors have no conflicts of interest to declare.

Correspondence to: Robert M. Conry, MD, Melanoma Program Director, Associate Professor, Division of Hematology Oncology, University of Alabama at Birmingham, 2145 Bonner Way, Birmingham, AL 35243. E-mail: rconry@uabmc.edu.

JAAD Case Reports 2017;3:280-3.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2017.02.011

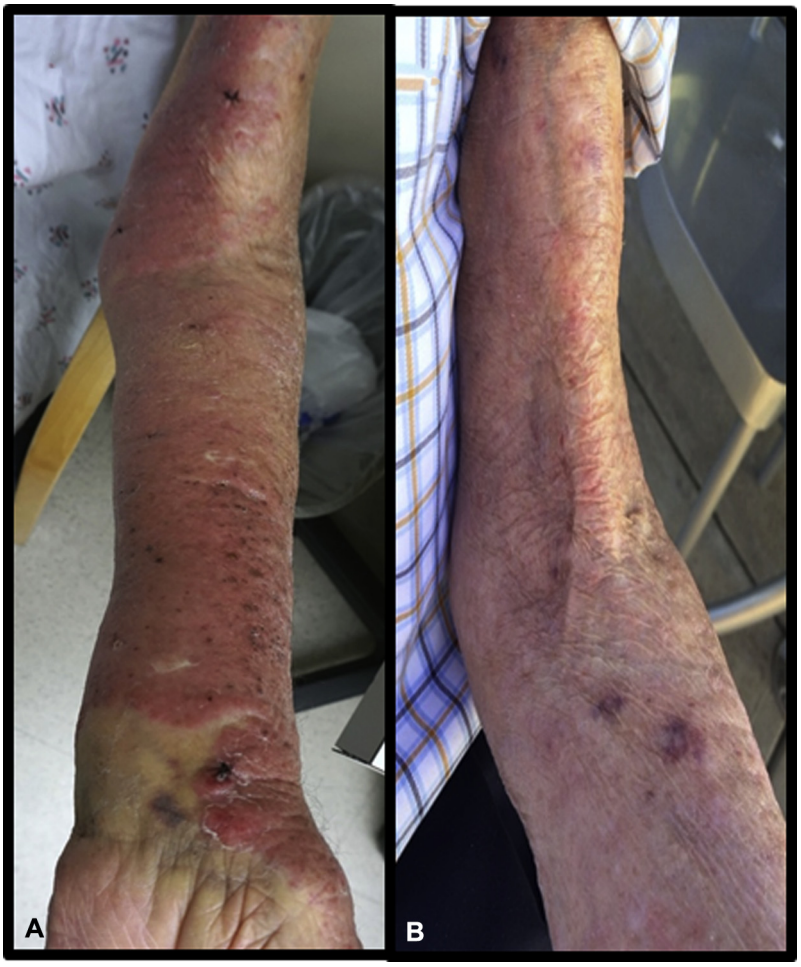

Fig 1. **A**, Sharply demarcated red plaque with intermixed dark brown to black papulonodules from the volar wrist proximal to the upper arm. **B**, Posttreatment improvement in inflammatory plaque.

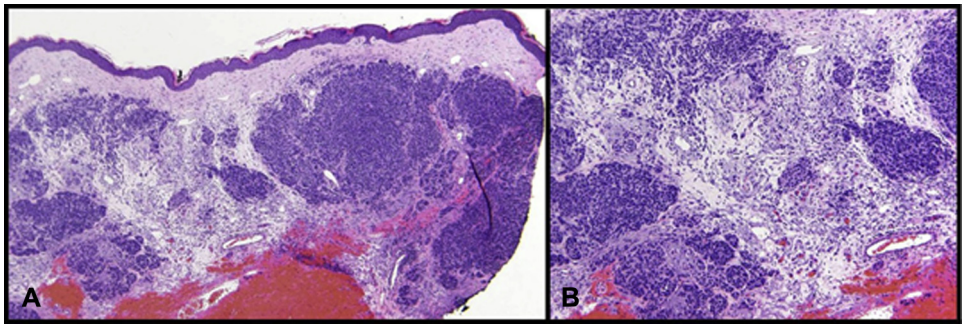

Fig 2. **A**, Large nodules of atypical melanocytes present within the dermis intercalating between solar elastosis. **B**, Nodules of atypical melanocytes intercalating between solar elastosis with both nests and single cells. (Original magnifications: **A**, ×4; **B**, ×10.)

punch biopsies from the left biceps; volar wrist; and the medial, lateral, and volar forearm all found a diffuse inflammatory plaque with widespread dermal intercalation by predominantly amelanotic melanoma cells (Fig 2, *A* and *B*). Quantitative multiplexed immunohistochemistry for expression and proximity of PD1 and PD-L1 from 4 tumor biopsy sections over the left forearm conducted by Navigate BioPharm Services Inc (Carlsbad, CA) using AQUA technology found that PD-L1 expression in melanoma cells varied from 1% to 70% depending on the biopsy location, and there was an average