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10 1 Association Between Confocal Morphologic Classification and Clinical Phenotypes of Multiple Primary and Familial Melanomas.

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## **ABSTRACT**

Importance: The improved knowledge of clinical, morphologic, and epidemiologic heterogeneity of melanoma in the context of multiple primary and familial melanomas may improve prevention, diagnosis, and prognosis of melanoma. Objective: To characterize reflectance confocal microscopy (RCM) morphologic patterns of melanomas in multiple primary and familial melanomas. Design, Setting, and Participants: In this cross-sectional, retrospective study, patients in a hospital-based referral center were recruited from March 1, 2010, through August 31, 2013; data analysis was conducted from September 1, 2013, through May 31, 2014. Consecutive primary melanomas, documented by dermoscopic and confocal examination, from multiple primary and familial melanomas with known CDKN2A mutational status were studied. Main Outcomes and Measures: Epidemiologic, genetic, dermoscopic, and histologic data were evaluated according to an RCM morphologic classification: dendritic cell, round cell, dermal nest, combined, and nonclassifiable types. Results: Fifty-seven melanomas from 50 patients (28 women [56%] and 49 white patients [98%]) were included: 23 dendritic cell (40%), 21 round cell (37%), 2 dermal nests (4%), 2 combined (4%), and 9 nonclassifiable (16%). The median (SD) age of the participants was 53.0 (16.9) years (interquartile range, 41.8-71.2 years), and the median (SD) age at the first melanoma was 46.0 (17.1) years (interquartile range, 35.8-61.5 years). Dendritic cell melanoma was characterized by older age at diagnosis, phototypes 2 and 3, more intense solar exposure, and moderate to severe solar lentigines; it was the most prevalent confocal type in facial lesions and was associated with the lentigo maligna histologic subtype. Round cell melanomas were identified more often in the familial context and in individuals with phototype 1 skin types; RCM features, such as junctional thickening, dense dermal nests, and nucleated cells within papillary dermis, were more frequently found in this subtype. Dermal nest and combined melanoma were associated with the absence of pigmented network on dermoscopy and thicker tumors on histologic analysis. Nonclassifiable type was associated, by RCM, with the absence of pagetoid cells on confocal examination and lower frequency of marked atypia on melanocytes in the basal cell layer; it presented with lower ABCD Total Dermoscopy Scores and RCM scores compared with the other types. CDKN2A mutation carriers may develop any RCM type of melanoma. Conclusions and Relevance: Different routes to develop melanoma can be identified according to RCM morphologic classification, with dendritic cell melanomas being associated with chronic sun damage and round cell melanoma with early age at onset and phototype 1 in the context of multiple primary and familial melanomas. The morphologic expression of melanomas via dermoscopy and confocal examination varies according to differences in tumor stage and biological behavior. PMID:27579522 DOI:10.1001/jamadermatol.2016.1189