More Evidence for Divergent Pathways of Early- and Late-Onset Melanoma

A new study supports different models of tumorigenesis for early- and late-onset melanoma, while additional data implicate genetics in early disease.

The phenomenon of early- versus late-onset melanoma has been recognized for some time, and there has long been speculation that divergent pathways may account for the different clinical presentations. A recent review of data has identified specific patient characteristics associated with early- and late-onset cutaneous malignant melanoma (CMM), and these findings support the notion of divergent pathways and a possible genetic susceptibility for early-onset tumors.

Identifying Pathways

Data from the Surveillance, Epidemiology, and End Results Program (SEER) of the National Cancer Institute were collected and assessed to determine the impact of advancing age on CMM incidence by sex, histopathologic classification—superficial spreading melanoma (SSM) or lentigo maligna melanoma (LMM)—and anatomic site (face, head, and neck or lower extremity). Results revealed that all three factors differed for late- versus early-onset CMM, supporting a role for divergent cancer pathways.

According to researchers, early-onset melanomas were more common in women, tended to be SSM, and were more often found on the lower extremities. In contrast, men were more likely to develop late-onset melanoma on the face, head, and/or neck. LMM was more common among late-onset lesions.

These findings suggest a genetic component for early-onset melanoma. It is possible that certain susceptible patients (predominantly female, based on these findings) may be at higher risk for early or intermittent melanomas. While UV exposure is implicated in the development of these tumors, findings suggest that chronic or significant cumulative exposure may not be necessary to initiate tumorigenesis in these predisposed patients. Chronic or significant cumulative UV exposure may be of greater importance for late-onset melanoma.

A study published earlier this year suggests that the MDM2 SNP309 genotype may identify women at higher risk for developing early-onset melanoma. SNP309 has been associated with early onset of other cancers in women, so researchers ascertained the SNP309 status of 227 melanoma patients enrolled in the prospective study. Results showed that women with the SNP309 genotype were significantly more likely to be diagnosed at any age under 50 compared to those age 50 or older. In fact, they were 3.89 times more likely to be diagnosed before age 50. No such associations were found for men.

Down the Road

Mounting evidence supports the role of divergent cancer pathways in early- and late-onset melanoma, and researchers are already seeking to uncover genetic susceptibilities that may place certain patients at higher risk for early onset of disease. Genetic screenings of patients with a suggestive history may one day allow dermatologists to identify and monitor those patients susceptible to early-onset melanoma.

Meanwhile, clinicians should continue to keep in mind the different distribution patterns of melanoma, which data show is more common on the lower extremities in younger women and more common on the face, head, and neck of older men. Full skin exams of patients may emphasize these particular anatomic sites.

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