Genotype Linked to Early Melanoma in Women

BY DAMIAN McNAMARA

The discovery of a genotype associated with a higher risk for cutaneous melanoma in young women could lead to development of an early screening test, according to findings from a pilot study.

Incidence of melanoma is higher among women than men younger than age 40, generally equivalent between men and women aged 40-50, and affects more men than women in people older than 50, according to data from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database.

Investigators proposed that modulation of estrogen levels through a MDM2 single nucleotide polymorphism (SNP) 309 might explain these epidemiologic differences. Dr. Elnaz F. Firoz, of New York University, and his associates assessed MDM2 SNP309 from DNA samples in a prospective study of 227 patients newly diagnosed with melanoma at New York University Medical Center (Clin. Cancer Res. 2009;15:2573-80).

They chose to evaluate this specific genetic polymorphism because, among other research findings, the presence of a specific G allele of MDM2 SNP309 was associated with earlier onset of colorectal cancer, non–small cell lung cancer, and squamous cell carcinoma of the head and neck, compared with patients lacking this allele (Int. J. Cancer 2006;119:718-21; J. Med. Genet. 2005;42:694-8).

Participants were enrolled between August 2002 and November 2006. The study patients were 98% white, a typical percentage for the melanoma population. In addition, the gender distribution in the study—59% men and 41% women—was representative of the melanoma population in the United States (SEER Cancer Statistics Review, 1975-2005).

Of the patients, 75% had stage I disease, 17% had stage II, and 8% had stage III. Median overall age at time of diagnosis was 58 years. However, women with the GG genotype MDM2 SNP309 were diagnosed a median 13 years younger, at 46 years, compared with women with either the TG or TT genotype (diagnosed at a median of 59 years). Median age at diagnosis for men was approximately equal regardless of genotype (60 years for GG, compared with 58 years for TG or TT).

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Put another way, women with a GG genotype had a 3.9 times greater chance of being diagnosed before age 50, compared with women with TG or TT genotypes. The greatest likelihood of a diagnosis for women with the GG genotype was before age 40 (odds ratio, 4.6).

"The decrease in the odds ratio from 4.6 to 3.9 as the age cut point increased from age 40 to age 50 may reflect the fact that it is not uncommon for women to undergo menopause prior to the age of 50, but it is rare for this to occur prior to the age of 40," the authors wrote. "These findings, combined with the SEER epidemiologic observation that prior to the age of 40 melanoma is more common among women than men (but not after the age of 50), support the hypothesis that active estrogen signaling in combination with the GG genotype may contribute to melanoma onset in women."

The researchers also assessed histopathologic features of the melanoma tumors and found no associations between MDM2 or p53 genotypes and tumor thickness, histopathologic subtype, anatomic site, or tumor ulceration. In addition, they found no associations between these polymorphisms and recurrence or overall survival.

The lack of a control group of patients who were unaffected by melanoma and patient ancestry data were limitations of the study, as was not having information on patients' menopausal status at the time of diagnosis. ■

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