Genetic markers in surrounding tissues linked to breast cancer tumor grade, presence of metastases

May 15 2007

Researchers have identified genetic markers on several chromosomes in the tissue surrounding tumor cells that are associated with breast cancer tumor grade and the presence of lymph node metastases, according to a study in the May 16 issue of JAMA.

A high degree of variability is observed in both biological behavior and clinical outcome in sporadic breast cancer, and this diversity may increase the difficulty in determining the appropriate treatment for a patient, according to background information in the article. "It has been recognized for decades that identical chemotherapeutic regimens for similar stage and grade in patients with, for example, breast cancer (or virtually any malignancy) respond differently. The complexities of genetic alterations in breast cancer may provide a primary basis for these consequent (secondary) clinicopathological features, an idea supported by prior positive correlations between certain breast cancer genotype and phenotype [visible characteristics of an organism]."

Charis Eng, M.D., Ph.D., of the Cleveland Clinic Genomic Medicine Institute, Cleveland, and colleagues tested the hypothesis that cell genomic alterations in tumor stroma (the cells and tissues surrounding the tumor) significantly alter tumor behavior, as reflected in clinicopathological features at the time of diagnosis. The researchers conducted a cross-sectional analysis of DNA from the epithelium (membrane tissue) and stroma of 220 primary sporadic invasive breast

carcinomas for genomic alterations. Data were collected from October 2003 through June 2006.

"Eight significant associations were found between compartment-specific, chromosome-specific loss of heterozygosity [having dissimilar pairs of genes for any hereditary characteristic]/allelic [one of two or more alternative forms of a gene] imbalance [LOH/AI], and clinicopathological features. Although only two markers on chromosome 14 in the epithelium were significantly associated with any clinicopathological feature at all (in this case, progesterone receptor), genomic instability within 7 chromosomes in the stroma of primary invasive breast carcinomas were significantly associated with tumor grade (chromosome 11) and the presence of regional lymph node metastases (chromosomes 1, 2, 5, 18, 20, and 22)," the authors write.

"These results support a model in which genetic changes in both stromal and epithelial compartments occur during tumorigenesis, and progression is codetermined by local interaction between these cell populations within the primary tumor," they write. "… as with any patient-oriented study, our data should be validated, perhaps with emerging novel technologies, in larger series especially those with event-free survival data and therapeutic trials with longer follow-up."

Source: JAMA and Archives Journals