RE: How Many Etiological Subtypes of Breast Cancer: Two, Three, Four, or More?

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In their recent article in the Journal, Anderson et al. have argued that there must be at least two different causes of breast cancer (1). This is based on the well-known bimodal peak frequencies at age of breast cancer diagnosis. The first breast cancer type tends to arise early in life, with modal age at diagnosis near 50 years, and generally behaves aggressively. The second breast cancer type occurs later in life with modal age near 70 years and usually follows a more indolent course. The authors then speculate that these two types of cancer arise from two main cell types. In the same issue of the Journal, Weigelt and Reis-Filho indicate that this speculative cell-based idea is not supported by evidence (2).

Surprisingly, given past reviews in the Journal that encouraged researchers to revisit oncogenic viruses as potential causes of various types of breast cancer (3), neither Anderson et al. (1) nor Weigelt and Reis-Filho (2) consider the substantial evidence that breast cancer may have viral origins. There are currently four viruses with well-documented oncogenic potential that may have roles in breast cancer. These are high-risk human papilloma viruses (HPVs), Epstein-Barr virus (EBV), mouse mammary tumor viruses (MMTVs), and bovine leukemia virus (BLV) (4). Some of these viruses are dependent on sex hormones for their replication, as is breast cancer. Of particular relevance to the Anderson et al. (1) hypothesis that young-age breast cancer appears to have different etiology from late-age breast cancer is the evidence that HPV-positive breast cancer appears more commonly in young women (5). This parallels the high frequency of HPV genital infections in young women. Unfortunately, in recent years there has been an increase in seriously aggressive young-age breast cancer (6). The evidence is not robust, but high-risk HPVs could be the reason.

In addition is the evidence that MMTV-positive breast cancer has similar histological and molecular characteristics to mouse mammary cancer (7,8). These may be an additional subset of breast cancers as referred to by Weigelt and Reis-Filho (2,3).

References

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