

Acquired chromosomal changes in lymphocytes are associated with cognitive dysfunction (CD) prior to chemotherapy in women with breast cancer (BC)

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Background: Improved survival for women with BC is accompanied by the development and persistence of psychoneurological symptoms (PNS) that compromise quality of life. One of the most troublesome symptoms is CD. The underlying mechanisms of CD are unclear, but could reflect, in part, a cascade of biological events in which cancer, its treatments, and/or stress related to its diagnosis/treatment triggers inflammatory activation that, in turn, leads to the acquisition of chromosomal changes. Methods: We have initiated a 2-year longitudinal research study. To date, we have studied 25 women (ages 29-67) with early-stage BC (stage I n=5; IIA n=10; IIB n= 9; IIIA n=1) and have compared their acquired lymphocyte chromosomal abnormalities levels (cytokinesis-block micronucleus assay) at base-line (after surgery yet prior to chemotherapy) to those in age-matched healthy controls. CD was assessed using the Central Nervous System-Vital Signs Test, a computerized neurocognitive battery. Results: The mean micronuclei frequencies (MNF) in women with BC prior to treatment ($5\% \pm 1.6\%$) were significantly higher than those in controls ($1.6\% \pm .87\%$) ($p < .0001$). Several domains of cognitive function including reaction time, complex attention, cognitive flexibility and executive functioning were correlated with MNF ($p < 0.05$). Conclusion: These data suggest that women with BC may have elevated levels of chromosomal instability in lymphocytes prior to chemotherapy and that these genomic alterations may be correlated with a subset of CD domains. Further examination of chromosomal changes as potential mechanisms directly contributing to or mediating the acquisition of PNS is warranted.