Cognitive Complaints After Breast Cancer Treatments: Patient Report and Objective Evidence

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The report by Ganz et al. in this issue of the Journal is an ambitious study that adds to the body of work assessing the neurocognitive effects of cancer and cancer treatment (1). Cognitive dysfunction, although frequently subtle, occurs in many cancer patients before, during, and long after diagnosis and treatment. There are now more than 12 million cancer survivors in the United States. One out of six people aged 65 years or older is a cancer survivor; 1.4 million of these survivors were diagnosed more than 20 years ago. With advances in early detection and treatment, cancer is becoming a chronic illness. However, cancer patients experience a number of adverse symptoms, including cognitive impairment, fatigue, pain, and sleep disturbance, most frequently in combination. This has been documented in a number of clinical human studies and animal models and has been investigated long enough to generate a number of meta-analyses and review articles (2–6). There are two issues to keep in mind regarding cognitive symptoms related to cancer treatment, which at first may seem contradictory. First, it is likely that scientific studies of this syndrome underestimate the true incidence in the overall cancer population. Second, applying these research data to individuals in the clinic with cognitive complaints is complex and requires a differential diagnosis.

As is always the case in studies that pool subject data, individual differences are obscured, suggesting that the true incidence of cognitive symptoms in cancer patients may be underestimated. First, a newly diagnosed person with cognitive impairment before treatment and a baseline evaluation may not experience much noticeable decline during therapy but still remain below their previous level of function. Second, as Ganz et al. acknowledged (1), the exclusion criteria for their study were extensive, including daily alcohol use (a glass of wine at dinner would have excluded many from their study), although their rigor was justified by their associated mechanistic biological endpoints. However, this suggests that their findings may not reflect the symptom burden of the larger population of cancer survivors who did not meet their criteria. Third, formal neuropsychological testing to confirm patient reports, as used in this article, is usually conducted in a one-on-one distraction-free setting, which is not representative of the individual’s real-world home and work environment. Thus, the cognitive test results may underestimate the effect of cognitive inefficiencies on the person’s daily routine.

Cognitive dysfunction in cancer patients is multifactorial, a result of the interaction between the cancer itself, individual (host) factors such as genetic susceptibility and immune reactivity, and the effect of specific treatments (7). In addition, the real-life impact of cognitive dysfunction on cancer patients depends upon their preillness level of function, the type of work they do, their developmental stage of life (eg, working parents with small children vs retired persons), and their overall ability to manage and cope with changing life circumstances. Furthermore, “chemobrain” is a diagnosis of exclusion because a number of factors may be responsible for or contribute to patient-perceived cognitive inefficiencies besides cancer treatment. These include the influence of systemic cancer on the central nervous system, central nervous system spread of disease, other cancer-related symptoms such as fatigue or pain, effects of adjuvant medications such as steroids and immunosuppressants, co- or preexisting neurologic and psychiatric illnesses, and even secondary gain. Thus, appropriate referrals and diagnostic work-ups are essential to guide treatment strategies.

Fortunately, symptom assessment is increasingly incorporated into clinical trials of new agents and routine patient care because cancer treatment can only be considered successful if these symptoms are managed. Successful management is guided in part by...
our evolving understanding of the mechanisms by which these symptoms develop, including inflammation (8,9), autoimmune phenomena (10), hormonal influences (11), and neurotoxic effects of specific agents (12,13). However, although research into mechanisms of cognitive dysfunction related to cancer therapy is clearly important and needed, a full understanding of the biology of cancer-related symptoms is not necessary for effective interventions to be employed.

First, identification and treatment of underlying medical and psychological conditions, including endocrine dysfunction, anemia, sleep disturbance, diabetes, and depression, is necessary but sometimes overlooked in the battle against cancer. Second, there are a number of behavioral strategies that are often helpful, including relaxation training to focus attention and reduce stress, exercise, cognitive rehabilitation, and compensatory strategies such as using personal electronic mobile devices or daily planners. Lifestyle changes, including alterations of the work environment, reasonable accommodations in the scholastic environment, and vocational retraining are often very effective. However, mental exercises that are designed and marketed to improve cognitive function, which perhaps provide mental stimulation in general and likely result in improved performance on the specific task, have not been definitively proven to generalize to other aspects of the person’s ability to function. Third, pharmacologic treatments, particularly psychostimulants, have been shown to be useful for people with attentional problems and fatigue, if not medically contraindicated. Research into other pharmacologic strategies, including agents that attenuate inflammation or reduce oxidative stress, is ongoing. However, it is important that such agents do not undermine the primary antineoplastic therapy and “feed” the tumor.

A large number of cancer survivors suffer from neurocognitive, emotional, and behavioral symptoms that interfere with their academic, vocational, and social pursuits. These impairments, as demonstrated in the Ganz et al. study (1), commonly involve problems with memory, multitasking, speed of cognitive processing, and the need to use more mental effort to perform routine tasks (all of which also contribute to fatigue and depression). However, many cancer survivors can enjoy improved levels of functioning if properly diagnosed and provided with the right support. Symptom assessment coupled with effective and proactive intervention strategies are a critical component throughout and after cancer treatment.

References

Note
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Can We Identify Predictive Biomarkers for Antiangiogenic Therapy of Cancer Using Mathematical Modeling?

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Angiogenesis (the term referring generically to new blood vessel formation) is a hallmark of all solid tumors (1), and vascular endothelial growth factor (VEGF) is the most prevalent and potent angiogenic growth factor in these tumors (2,3). For this reason, there have been