

Cognitive Effects of Chemotherapy and Cancer-Related Treatments in Older Adults

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Advances in cancer treatment are producing a growing number of cancer survivors; therefore, issues surrounding quality of life during and following cancer treatment have become increasingly important. Chemotherapy-related cognitive impairment (CRCI) is a problem that is commonly reported following the administration of chemotherapy treatment in patients with cancer. Research suggests that CRCI can persist for months to years after completing treatment, which has implications for the trajectory of normal and pathologic cognitive aging for the growing number of long-term cancer survivors. These problems are particularly relevant for older individuals, given that cancer is largely a disease of older age, and the number of patients with cancer who are aged 65 years or older will increase dramatically over the coming decades. This review will briefly summarize empirical findings related to CRCI, discuss CRCI in older patients with cancer, propose potential causative hypotheses, and provide a canonical patient case to illustrate how CRCI presents clinically. Finally, potential intervention strategies for CRCI will be highlighted and issues to consider when evaluating older patients with a history of cancer will be discussed. (Am J Geriatr Psychiatry 2017; 25:1415–1426)

Key Words: Chemotherapy-related cognitive impairment, chemotherapy, cognitive impairment, subjective cognitive decline

Advances in cancer treatment are producing a growing number of cancer survivors; therefore, issues surrounding quality of life during and following cancer treatment have become increasingly important. Chemotherapy-related cognitive impairment (CRCI) is one such quality of life issue that is commonly reported following the administration of chemotherapy in patients with cancer.¹ Although studies reporting cognitive impairments associated with

chemotherapy have been reported in patients with non-central nervous system (non-CNS) cancers since the 1980s,² the phenomenon commonly referred to as “chemobrain” or “chemo fog” is poorly understood and, until relatively recently, was largely unacknowledged.³ Research suggests that CRCI can persist for months to years after finishing treatment,⁴ which may have implications for the trajectory of cognitive aging for the growing number of long-term cancer survivors.⁵ These

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implications are particularly relevant for older individuals as risk for not only cancer, but cognitive impairment increases with age. As of January 2016, 62% of cancer survivors (9.61 million) are currently 65 years or older,⁶ and this number is expected to increase dramatically over the coming decades.⁷ Therefore, as the number of older cancer survivors who will have to cope with CRCI is likely to increase, it is crucial to understand how CRCI presents clinically and to screen for symptoms of cognitive impairment. This article will briefly provide an overview of CRCI, discuss risk factors for CRCI, and will highlight potential intervention strategies and therapeutic targets for CRCI. A typical patient case summary is included to illustrate how CRCI often presents clinically, as well as to provide context for how current research can inform clinical practice.

CASE SUMMARY

The patient is a 68-year-old, married woman employed as a teacher at a high school with a history of breast cancer. At 65 years of age, she presented with an abnormal routine mammogram screening; subsequent diagnostic imaging revealed a suspicious abnormality in her right breast. She underwent lumpectomy with axillary lymph node dissection, and pathology revealed stage IIa (pT1c, pN1, cM0), estrogen receptor-positive and progesterone receptor-positive (ER + /PR+), human epidermal growth factor receptor 2-positive (HER-2/neu+), invasive ductal carcinoma. The patient received chemotherapy and targeted therapy consisting of six cycles of docetaxel, carboplatin, and trastuzumab, as well as radiotherapy to the right breast and underarm. Chemotherapy and radiotherapy were followed by adjuvant endocrine therapy with letrozole and completion of 1 year of maintenance trastuzumab to reduce risk of breast cancer recurrence. During chemotherapy, the patient reported worsening fatigue and cognitive complaints, including greater difficulty with memory, attention, concentration, and ability to multitask. The patient was advised that cognitive complaints during chemotherapy are not uncommon and would likely improve following completion of chemotherapy.

Follow-up with the patient 2 years post-chemotherapy revealed that the patient's cognitive complaints have not improved. She has stated that her symptoms have negatively impacted her job as a teacher. She denies

receiving complaints about her work performance, but suspects that her coworkers are aware of changes. Upon questioning, she states that she has difficulty with word finding, needs reminders and notes to complete tasks, frequently loses paperwork, reports being easily distracted, has forgotten events and conversations, has trouble learning new work-related tasks, and reports that it takes greater cognitive effort to complete work-related tasks. She denies trouble recognizing faces, getting lost while navigating in familiar places, or any change in ability to manage household chores. She ambulates, dresses, bathes, drives, and shops independently. She states that she has been less interested in socializing, due to anxiety and distress surrounding her cognitive functioning.

She stated that at a breast cancer support group, the topic of "chemobrain" was discussed, prompting her concerns that the changes in her cognitive functioning were a consequence of her breast cancer treatment. She was referred for neuropsychological evaluation by her primary care physician. Neuropsychological testing revealed that she performs below expectations for age and education level on measures of memory, executive function, and attention, although her performance was within the normative range. Despite performance within the normative range on objective cognitive testing, subjective cognitive (self-report) measures reveal endorsements of cognitive complaints.

OVERVIEW OF CRCI

The American Cancer Society defines CRCI as: increased forgetfulness, trouble concentrating and remembering details, difficulty with multitasking and word finding, and taking longer to finish tasks.⁸ Although changes across various domains on objective testing have been reported for CRCI, effects have been reported most prominently in the domains of attention, working memory, executive function, and processing speed.⁵ To date, the majority of CRCI research has involved women with breast cancer,^{1,9} who (as of January 2016) represent approximately 23% (3.6 million) of the 15.5 million cancer survivors in the United States alone.¹⁰ Although it is likely that patients who receive chemotherapy for any type of cancer may experience CRCI, much of the literature in populations other than breast cancer is preliminary;¹¹ research in patients with other types of cancer reveal similar results.^{4,12-17}

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