PALLIATIVE CARE
CASE OF THE MONTH

"Lifting the Fog of Chemobrain: Understanding Cancer Related Cognitive Impairment"

by

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Case: Ms. C. is a 38-year-old woman with stage IV ovarian cancer with metastatic disease involving the pleura, omentum and uterus who was referred to palliative care for symptom management. She completed three cycles of chemotherapy with carboplatin and paclitaxel followed by two cycles of doxorubicin along with tamoxifen and leuprolide. Since starting chemotherapy, she notes having word finding difficulty, frequent word substitution, difficulty recalling names and trouble remembering written material or conversations. She finds these symptoms distressing as she holds two master's degrees and was working full time prior to her cancer diagnosis.

Discussion: In recent years, cancer-related cognitive impairment (CRCI) has been increasingly acknowledged and studied in patients with malignancies that do not involve the central nervous system. CRCI is frequently associated with impairments in domains of cognitive functioning including memory, attention, processing speed and executive function. These symptoms greatly affect quality of life as they hinder occupational and social functioning.[1]

While estimates of prevalence vary, roughly 40% of patients with cancer have evidence of CRCI even before initiating therapy, up to 75% have some cognitive decline during treatment and 60% continue to exhibit CRCI after treatment. The severity of cognitive impairment is typically mild to moderate and can persist for years after treatment.[2] Common symptoms include difficulty recalling names or dates, slower processing speed and trouble concentrating or multitasking. While factors influencing prevalence remain poorly understood, patients with lower premorbid cognitive function or presence of an ApoE4 allele may be at higher risk.[2]

Neurotoxicity from chemotherapy has been felt to be the underlying mechanism, thus the commonly used term "chemobrain" was coined. However, CRCI has also been documented in the absence of chemotherapy suggesting there may be more to the story. Hypothesized mechanisms of action include neurotoxic pro-inflammatory cytokine cascades associated with stress and cancer itself, as well as underlying risk factors that predispose to both cancer and cognitive impairment such as poor DNA repair mechanisms.[3]

While the etiology of CRCI is likely multifactorial, there are certain chemotherapeutic agents that tend to be associated with more cognitive decline and have a dose-response relationship. Methotrexate and 5-fluorouracil are two such agents and have been shown to cause diffuse white matter changes on imaging.[4]

It is important to assess for depression, anxiety and prior trauma, as these disorders can impact cognitive functioning[5]. Additional symptoms such as pain, fatigue and insomnia can also contribute to cognitive performance and should be screened for and treated if present.

Although there is no gold standard test to diagnose CRCI, three methods are commonly used to document cognitive function.[6] First, objective cognitive testing provides useful insight into the severity of cognitive impairment. Second, patient self-reported cognitive function measures, such as the Functional Assessment of Cancer Therapy – Cognitive Function scale (FACT-Cog), are often utilized and are less burdensome than formal cognitive testing in terms of time and cost.[7] Of note, perceived deficits often exceed the severity measured by objective means.[8] Finally, research studies have used functional neuroimaging studies to understand the mechanisms underlying cognitive impairment. New research suggests clinical tools using resting functional magnetic resonance imaging (fMRI) may reliably predict which patients are vulnerable to CRCI.[9] More research on resting fMRI is needed for it to be validated for clinical use.

With regards to treatment, behavioral strategies such as cognitive rehabilitation have been studied, primarily with small samples of patients who have undergone treatment for breast cancer, and have shown significant improvements in cognitive performance and quality of life.[2] Additionally, a cognitive behavioral therapy known as Memory and Attention Adaptation Training (MAAT) has been designed to treat patients with CRCI. MAAT involves teaching stress management and self-regulation, as well as training in cognitive compensatory strategies. It consists of sessions with a trained clinician which can be delivered via videoconference, as well as completion of workbook exercises.[10] Physical activity has also been associated with improved cognitive function and the combination of physical activity and cognitive training may result in greater cognitive benefit.[11] Pharmacologic treatment with psychostimulants or donepezil has been trialed, though their effectiveness remains uncertain as studies have produced mixed results.[12] There have been no effective preventative strategies identified as of yet.

Resolution of case: Ms. C. demonstrated subtle impairments in attention and processing speed upon neurocognitive testing and was referred to behavioral medicine. She expressed interest in a cognitive behavioral therapy plan using the MAAT program. She is currently undergoing therapy and notes she found the first visit helpful. She continues to follow with the supportive care clinic for symptom management.

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