

## Biobehavioral and Sociocultural Dimensions of Cancer-Related Fatigue

### Case Study

Mrs. L is a 40-year-old woman who was born in Korea and relocated to Los Angeles, CA, two years ago with her husband and two young children. The transition has been difficult for Mrs. L because she feels isolated from the family and friends she left behind. Despite this, she was in her usual state of good health when, while in the shower, she felt a pea-sized, firm mass on her right breast. An ultrasound revealed a 1.3 cm irregularly marginated hypervascular mass suspicious for malignancy. Biopsy confirmed a poorly differentiated infiltrating ductal carcinoma of the right breast, estrogen receptor-negative, progesterone receptor-positive, Ki-67/3% (i.e., a molecular tumor marker predictive of tumor division and a prognostic factor being evaluated in breast cancer recurrence). Further staging workup was negative for metastatic disease. Mrs. L began neoadjuvant chemotherapy with doxorubicin 50 mg/m<sup>2</sup> and docetaxel 75 mg/m<sup>2</sup> every 21 days for six cycles. On completion of the adjuvant chemotherapy, she underwent a lumpectomy of the right breast with complete axillary lymph node dissection. Pathology confirmed a poorly differentiated infiltrating ductal adenocarcinoma, 2.4 cm in greatest dimension, with 7 out of 12 positive axillary lymph nodes. Subsequently, Mrs. L was scheduled to receive radiation to the right chest wall, with a boost to the mastectomy scar and supraclavicular field. Following radiation, she will receive leuprolide 22.5 mg intramuscularly every three months.

At the time of diagnosis, the nurse taking Mrs. L's history and assessment noted a shy and anxious but sweet young woman who appeared overwhelmed with her circumstances. She spoke English and appeared to understand her treatment situation, but her husband did the majority of speaking for her. During her second cycle of chemotherapy, Mrs. L began to appear tired and anxious during her clinic visits but always denied problems or concerns. After completion of chemotherapy, Mrs. L was tearful during a follow-up clinic visit after her lumpectomy. Laboratory work demonstrated the following: hemoglobin 10.0 g/dl, hematocrit 30%, platelets 140,000 mm<sup>3</sup>, and white blood cells 3,200 mm<sup>3</sup>, with an absolute

neutrophil count of 1,500 cells/mm<sup>3</sup>. Upon questioning, Mrs. L hesitated but did admit to feeling slightly short of breath on activity and stated that she had no energy.

Mrs. L always was accompanied by her husband and two children, ages 4 and 5 years. The nurse noticed that questions directed to the patient were answered most frequently by Mr. L. Giving culturally sensitive care, the nurse included the husband in the assessment process but repeated questions directly to Mrs. L when necessary. The nurse also looked to Mrs. L to reaffirm the husband's perceptions. Using a 0 (no fatigue) to 10 (severe fatigue) scale, Mrs. L quantified her fatigue level as 7. The nurse also asked the following question to help the patient further quantify her energy level: "What is your 0–10 level on awakening in the morning, and what is it after feeding and dressing the children?" These activities exhausted her, and Mrs. L expressed shame because she believed she was not being a good wife and mother. She admitted to being tearful every day and crying when she feels anxious and tired because she cannot manage all of her household chores. After further questioning, Mrs. L stated that her job entailed managing the household and childcare duties; as a result, she did not expect help from her husband. She said, "It is my fault for getting this cancer. I probably would not have it if I had not been so stressed since we moved to the United States." Appearing anxious she asked, "How am I going to have this radiation treatment?"

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### Clinical Problem Solving

Responding to this clinical interview by Associate Editor Nancy Jo Bush, RN, MN, MA, AOCN®, is Grace Cherry, RN, MSN, OCN®, oncology nurse practitioner at the University of California, Los Angeles.

### How is the fatigue experienced in the healthy populations differentiated from cancer-related fatigue (CRF)?

Fatigue can be categorized as physiologic, acute, or chronic (Desai, 2001; Morrison &

Keating, 2001; Rodriguez, 2000). Physiologic fatigue develops in healthy individuals when one of the following occurs: inadequate sleep, not enough rest, over activity, poor physical conditioning, stress, or a change in diet. Correction of these factors usually leads to rapid improvement. Acute fatigue is unexplained by a physiologic process, less than six months in duration, and not relieved with bed rest. Chronic fatigue is not partially or completely resolved by rest or sleep, but it is persistent and lasts for more than six months.

On the other hand, CRF has numerous definitions, including "a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning" (Mock et al., 2004, p. FT1). This is a distressing symptom characterized by diminished energy and impairment in concentration, memory, activities of daily living, psychological stability, and motivation (Portenoy & Itri, 1999). CRF can be acute or chronic and, unlike physiologic fatigue or fatigue experienced by healthy individuals, is more distressing, more severe, and not relieved by rest or sleep (Mock et al.; National Cancer Institute [NCI], 2004). CRF is the most common symptom in patients experiencing cancer and reportedly causes the most distress (Curt et al., 2000).

### Which etiologies should be considered when evaluating CRF and why?

CRF is a multidimensional phenomenon, but its exact mechanism is unknown (NCI, 2004). However, a neuropsychological model of the central nervous system (CNS) and peripheral nervous system (PNS) has been proposed (NCI). Impairment of the CNS and PNS may be caused by chemotherapy and biologic therapy. In addition, medications that act on the CNS may compound fatigue.

*The solutions offered to the clinical problems posed in this column are the opinions of the authors and do not represent the opinions or recommendations of the Oncology Nursing Society, the Oncology Nursing Forum, or the editorial staff.*

Digital Object Identifier: 10.1188/05.ONF.237-240

CNS damage prevents transmission in the spinal cord and malfunction of the brain cells in the hypothalamic region, which may affect motivation. PNS damage may prevent transmission in the neuromuscular junction and negatively influence fiber activation. Because inflammatory mediators are believed to affect complex CNS and behavioral processes such as affective, motivation, and cognitive functions (Bower, Ganz, Azis, Fahey, & Cole, 2003), an inflammatory model also has been suggested. Several studies have examined the role of different inflammatory mediators such as circulating T lymphocytes and cytokines.

Major etiologies for CRF that should be considered during assessment include uncontrolled pain, infection, emotional disturbance, sleep deprivation, anemia, inadequate or excessive nutritional intake, and inactivity (Mock et al., 2004). Evaluation of CRF must include assessment of specific treatment side effects that can directly cause fatigue such as heart failure secondary to anthracycline therapy or anemia related to bone marrow suppression. Comorbid conditions such as hypothyroidism and cardiopulmonary insufficiency may compound the degree of CRF and also must be considered. A thorough medication profile will identify whether specific drugs (e.g., antihypertensives, anxiolytics) are contributing factors. CRF also may be indicative of recurrence or progression of disease.

#### **At which time in the disease trajectory should CRF become a focus of clinical assessment and treatment?**

Because of the high prevalence of CRF, patients should be screened for fatigue at diagnosis, treatment initiation, and appropriate intervals as needed (Mock et al., 2004) using a 0 (no fatigue) to 10 (worst fatigue imaginable) rating scale. Healthcare providers also should illicit information from caregivers and family members because the patient may not be aware of the full impact of fatigue. When patients report moderate (4–6) or severe (7–10) levels of fatigue, a focused history and physical to determine causative and contributing factors are warranted (Mock et al.).

Numerous side effects related to treatment contribute to fatigue, which may be present prior to the start of chemotherapy or radiation treatments, with severity increasing as treatment progresses (Jacobsen et al., 1999). Treatment-related fatigue is most common in women experiencing therapy-induced menopausal symptoms or anemia (Tchen et al., 2003). Chemotherapy-induced fatigue also should be expected, but severity depends on patient status and treatment regimens. For example, fatigue has been reported to be less severe in new treatment regimens with drugs such as doxorubicin and paclitaxel compared to doxorubicin and cyclophosphamide (Bottomley et al., 2004). In addition, radiation-induced fatigue can occur and tends to increase as treatment progresses. Healthcare

providers should continue to assess fatigue at follow-up appointments and throughout survivorship. The impact of fatigue on quality of life should be evaluated after treatment and managed symptomatically. Persistent or unexplained fatigue always must be assessed to eliminate the possibility of disease recurrence and progression, which are primary concerns for any patient with a history of cancer.

#### **Which biobehavioral dimensions are important to consider when assessing and treating CRF?**

A patient's psychological status has been shown to correlate with his or her report of fatigue. For example, anxiety and depression were related to fatigue during and long after treatment ended (Bower et al., 2000; Jacobsen et al., 1999; Okuyama et al., 2000; Servaes, Verhagen, & Bleijenbergh, 2002). Psychological distress and anxiety prior to the start of adjuvant radiation contributed to fatigue that continued years after patients completed treatment (Genitz et al., 2004). Patients who lacked confidence and expected negative outcomes, a cognitive process known as catastrophizing, have reported more fatigue when undergoing radiation for breast cancer (Jacobsen, Andrykowski, & Thors, 2004). Pessimism also has been associated with heightened levels of fatigue and greater disruption in participation in everyday activities (Carver, Lehman, & Michael, 2003). Patients with an external locus of control have been found to experience more fatigue (Servaes et al.).

According to Holley (2000), CRF is akin to a form of suffering. The intensity, duration, rapid onset, and energy drain that occur with CRF can diminish patients' ability to experience satisfaction and meaning in life. Physical, cognitive, spiritual, social, and psychological domains are affected negatively, and patients may experience disengagement from life (Holley).

#### **Which sociocultural dimensions are important when assessing and treating CRF?**

Research among women with breast cancer has identified certain demographic variables associated with CRF. Younger women with lower annual incomes and women who are not married were more likely to experience fatigue (Bower et al., 2000). However, in a study of women with breast cancer receiving adjuvant chemotherapy, no relationship was found between these variables and fatigue (Jacobsen et al., 1999). Women with poorer health status, including arthritis, headaches, and heart disease, also experienced more fatigue than healthy women (Berger & Higginbotham, 2000; Bower et al., 2000). Furthermore, women with lowered physical activity rates have been found to suffer more fatigue (Berger & Higginbotham).

Mrs. L's case study is one example of the sociocultural dimension of CRF. The strongly patriarchal Korean culture may affect a Korean woman's experience with breast cancer (Im, Lee, & Park, 2002). Traditionally, the Korean husband, father, or eldest son is the spokesperson or decision maker for all family members, including family members' illness-related circumstances. Many Koreans are raised to believe that illness is the result of bad luck or punishment for wrongdoing. The tendency to blame the victim may have caused Mrs. L to believe she was at fault for the development of her breast cancer. Koreans generally believe that negative emotions rather than risk factors cause illness, compounding the woman's fears of accountability for her disease. In addition, removal of a breast is believed to bring bad luck to Korean women and their family members. These negative perceptions have been found to contribute to feelings of depression and helplessness among Korean women; as a result, this psychological distress can lead to fatigue (Lee, 2001). Korean culture places emphasis on the family as an essential social unit where the woman's status is low and her health status is trivial. In a traditional Korean household, the woman is expected to sacrifice herself for her family and is responsible for all household tasks, even when she is employed. In the past, family members, including husbands, did not help with any household chores despite the woman's health status. Inability to do all expected household and childcare tasks leads to feelings of guilt and despair. Again, in this context, the vicious cycle of increased shame causes more fatigue. Moreover, lack of social support can lead to higher mood disturbance and higher levels of fatigue (Lee, Chung, Park, & Chun, 2004). Lastly, because depression commonly is perceived as shameful, Korean women may not admit their emotional and subsequent physical symptoms (e.g., fatigue) to their healthcare providers. This case study highlights the complexity of CRF and the biobehavioral and sociocultural dimensions that affect the severity and response to the experience.

#### **Which interventions can be most helpful in identifying the causative factors of CRF, managing symptoms, and supporting patients' response to treatment and quality of life?**

Laboratory tests infrequently reveal the cause of chronic fatigue (Seller, 2000), although some tests should be ordered to eliminate other disease processes. A complete blood count with differential can quickly test for anemia. Other tests such as vitamin B<sub>12</sub>, folate, serum iron, transferrin, ferritin, and erythropoietin levels and direct and indirect Coombs can be ordered to determine the type of anemia and appropriate treatment. Comorbidities in all major organ systems should be evaluated with a metabolic panel, fluid and

electrolyte status, and thyroid function tests. Nutritional and activity status also must be evaluated. By the end of a thorough history and physical examination, including assessment for symptoms such as fatigue and pain, the nurse can begin to plan treatment based on clinical findings. For example, underlying physiologic causes such as anemia must be corrected first and then fatigue can be reevaluated accordingly. Disease- and treatment-related symptoms (e.g., nausea, vomiting, pain, constipation, diarrhea, mucositis, dyspnea) must be managed appropriately because uncontrolled symptoms can increase fatigue.

Interventions for CRF include education and nonpharmacologic and pharmacologic measures. In addition, the nurse should implement preventive techniques before high levels of fatigue occur, compromising the patient's ability to function and quality of life (Mock, 2003). Education should begin at diagnosis and the initial assessment. The nurse should discuss the impact of treatment-related fatigue with the patient and family, review preventive interventions such as nutrition and exercise, and assist the patient in evaluating fatigue as treatment progresses. Nurses play a vital role in using cognitive behavioral approaches to help patients and their families explore and reframe the meaning of cancer and fatigue related to their cultural beliefs, values, and life goals. For a young Korean mother such as Mrs. L, giving her permission to schedule rest periods and seek out social support for household and

childcare needs can normalize the experience and provide assurance that the fatigue can be managed.

Nonpharmacologic interventions include relaxation, exercise, and nutritional support. Patients can be taught to use distraction techniques such as listening to music, reading, and socializing to manage symptom distress and prevent fatigue. Energy-conservation techniques (e.g., setting priorities, pacing, delegating, taking naps that do not interrupt nighttime sleep) help patients prioritize the activities that are most important to them to complete (Holley, 2000). Exercise should be individualized to the patient's condition, age, and cancer therapy (Mock, 2003). Adequate nutrition and fluid intake also are vital for fatigue prevention. Nurses should seek out interdisciplinary support staff (e.g., social services, physical therapy, nutritionists) to help plan and monitor the patient's fatigue treatment plan. Psychological support (e.g., support groups, counseling) may be beneficial for patients at high risk for anxiety or depression.

Pharmacologic interventions are prescribed to treat underlying causes of CRF. For example, erythropoietin injections are given to help alleviate anemia. Healthcare providers can review the National Comprehensive Cancer Network practice guidelines when managing patients' anemia (Sabbatini, 2004) and prescribing pain medications (Panchal & Grossman, 2004). Antidepressants and anxiolytics can be prescribed to alleviate depression and anxiety and insomnia,

respectively. Interestingly, fatigue related to depression or anxiety most often resolves after the medications take effect. Treating depression appropriately provides patients with the energy needed to eat well, exercise, and address other factors that may contribute to fatigue. Psychostimulants such as methylphenidate and exercise have been found to be helpful combating fatigue in patients with advanced cancer (Schwartz, Thompson, & Masood, 2002).

In conclusion, interventions should be based on a thorough physical and psychosocial assessment and individualized to alleviate patients' symptoms and enhance their quality of life.

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## Clinical Highlights: Cancer-Related Fatigue

**Definition:** Cancer-related fatigue (CRF) is “a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning” (Mock et al., 2004, p. FT1).

**Pathophysiology:** The exact pathophysiological mechanisms underlying CRF are unknown. A neuropsychological model addresses the role of toxic substances such as medications on the central nervous system and peripheral nervous system causing fatigue. An inflammatory model has suggested the role of different inflammatory mediators such as circulating T lymphocytes and cytokines.

**Risk factors:** The morbidity and mortality related to CRF are influenced by disease state, treatment regimens, comorbidities, and psychological status. Risk factors for CRF are increased if patients experience the following comorbid conditions: uncontrolled pain, infection, emotional distress, sleep deprivation, anemia, inadequate or excessive nutritional intake, and inactivity (Mock et al., 2004).

**Prevention:** Healthcare providers can prevent CRF by identifying high-risk patients; assessing fatigue at diagnosis, treatment initiation, and follow-up through survivorship; educating patients about CRF and self-care management strategies such as nutrition, exercise, and relaxation; and prescribing pharmacologic support when appropriate (e.g., erythropoietin for anemia).

**Clinical findings:** Signs and symptoms of fatigue are multifaceted and include physical (e.g., dyspnea), emotional (e.g., depression), cognitive (e.g., memory loss), and behavioral (e.g., lethargy) components. Focused assessment of CRF must include evaluation of the five most common clinical conditions that cause fatigue in patients experiencing cancer and treatment: pain, emotional distress, sleep disturbance, anemia, and hypothyroidism (Mock, 2001).

**Differential diagnosis:** Differential diagnosis for CRF includes, but is not limited to, identification of undiagnosed or unmanaged comorbidities (e.g., cardiopulmonary, renal, neurologic, endocrine dysfunction); under-

lying metabolic, hematologic, or fluid or electrolyte imbalances; malnutrition; immobility; and psychological distress (Mock, 2001).

**Treatment:** Identifying and treating underlying mechanisms contributing to CRF (e.g., anemia) are of primary importance. Management of symptoms contributing to CRF (e.g., uncontrolled pain) is secondary. Education and nonpharmacologic and pharmacologic interventions should be included in a comprehensive, interdisciplinary treatment plan.

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