Caregiving Burden, Stress, and Health Effects Among Family Caregivers of Adult Cancer Patients

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Case Study
A 56-year-old man who had myelodysplastic syndrome that transformed into acute myelogenous leukemia with cytogenetic abnormalities presented for a reduced intensity allogeneic matched unrelated donor hematopoietic stem cell transplantation (HSCT). Prior to HSCT, he had multiple unanticipated complications and adverse treatment toxic effects from his cytoreductive regimen resulting in a 3-month inpatient hospitalization. The caregiver was his 53-year-old wife of 23 years. She reported a history of arthritis and 3 years earlier had undergone coronary artery bypass graft surgery following a myocardial infarct. Currently a smoker, she reported that she was trying to quit. Despite no history of preexisting mental health conditions, the caregiver reported high levels of psychological distress, including anxiety, depression, worry, and extreme loneliness prior to her husband’s transplant.

The couple’s primary residence was in New Jersey, 143 miles from the transplant center. They were therefore required to establish a temporary residence near the transplant center. Because both the patient and caregiver were unemployed due to disability, their income was restricted. Social support was limited to a 20-year-old daughter in college and the caregiver’s sister, employed full time in New Jersey. In addition, the caregiver’s elderly mother, aunt, and father also depended on her for assistance. The caregiver’s father resided in a nursing home after becoming disabled following brain surgery.

COURSE OF TREATMENT
The HSCT initial hospitalization and immediate recovery period was difficult and prolonged, lasting approximately 2 months. The patient experienced a pericardial effusion, renal failure, pneumonia, and acute graft vs host disease. After the initial hospital discharge, the patient was readmitted twice: once for coughing, diarrhea, and...

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hematuria with clots; and a second time for acute heart failure and sepsis.

**CAREGIVING CHALLENGES**

This caregiver had multiple caregiving responsibilities, maintained 2 residences, subsisted on limited finances, and managed multiple health conditions of her own. Lacking the physical presence of a support system, she shouldered the entire burden of her husband’s brief but intense outpatient care including cleaning, driving, preparing meals, and coordinating medication, oxygen, and other treatment-related activities. She struggled to maintain hope for the transplant’s success while living with the constant uncertainty of her husband’s survival, a concern that was exacerbated by the sudden death of a close cousin. Although she complained little, when asked, she reported severe emotional distress, significant fatigue, sleep impairment, and difficulty maintaining her focus and energy throughout the transplant trajectory.

**BACKGROUND**

Family caregivers are essential partners in the delivery of complex health care services and this case exemplifies the burden and stress associated with providing care during cancer treatment. Unlike professional caregivers such as physicians and nurses, informal caregivers, typically family members or friends, provide care to individuals with a variety of conditions, most commonly advanced age, dementia, and cancer. As mounting evidence suggests that caregiving is deleterious to one’s health, increased attention is being paid to the day-to-day well-being of caregivers. Compared with noncaregivers, caregivers often experience psychological, behavioral, and physiological effects that are associated with impaired immune system function, coronary heart disease, and early death. The level of burden on caregivers of cancer patients is greater than the burden experienced by those caring for older persons and similar to that experienced by caregivers of patients with dementia. To receive a diagnosis of cancer is recognized as a significant stressor to the patient and family. However, the resultant treatment creates additional fears and challenges and frequently requires the direct support of a caregiver including assisting with activities of daily living, administering medications, providing transportation, preparing meals, managing finances, advocating for health care, and providing emotional support. Caregiving is labor intensive, with approximately one-quarter of those caring for cancer patients spending in excess of 40 hours a week providing these services to family or friends. The level of care required by the care recipient is a major factor that influences the caregiver’s life and health effects. Caregivers of cancer patients providing higher levels of support are more likely to report negative outcomes, less likely to be effective partners in the patient’s care, and are more likely to postpone their own health care needs.

Although cancer patients in general report high-symptom severity resulting in a greater need for support from the health care team, one of the most complex cancer treatments, allogeneic HSCT, is particularly burdensome. Even an uncomplicated or reduced-intensity allogeneic HSCT may require a 2- to 4-week hospitalization, followed by 3 to 4 months of intensive outpatient management. Allogeneic HSCT recipients are often debilitated and frequently experience complications and other treatment-related toxic effects that result in multiple hospital readmissions. For this reason, the caregiver in the case presented herein and her husband were required to establish a residence near the transplant center. Without a caregiver, transplant options may be limited and survival shortened. Although this potentially curative treatment provides hope, it also carries a 30% mortality rate within the first year. As a result, caregivers experience substantial stress as the burden of caring (often exclusively) for their sick loved ones, being separated from their own support systems, and balancing other life responsibilities threatens to overwhelm them.

**PRESENTING SIGNS AND SYMPTOMS OF STRESS**

As evident in the case study, the most obvious signs and symptoms of caregiving stress are often psychological problems, most commonly anxiety, depression, worry, and loneliness. These psychological reactions are related to the caregiver’s appraisal of the experience, with those reporting more benefit and deriving more meaning from the experience saying that they feel less stress and report a better quality of life. The level of distress reported by many of those caring for someone with cancer can be equal to or greater than that of the cancer patient, with adult daughters seeming to have the greatest difficulties. In addition, those reporting higher levels of emotional distress also report more problems with fatigue, sleep impairment, and unhealthy behaviors.

Caregivers of patients with cancer report having to modify their lifestyles to accommodate the care recipient’s needs including restricting leisure activity and contact with friends and family. Thus, at a time when caregivers are most in need of the restorative benefits of relaxation, they have the least amount of time and resources available. Further complicating matters, caregivers of cancer patients prioritize the needs of the patient over their own, leaving little time for maintaining good nutrition, exercising, and undertaking health evaluations. As a result, caregivers have numerous health-related problems, such as sleep disturbances and fatigue, which worsen as the patient’s physical function and symptom burden increase. The symptom burden in HSCT recipients can be significant for weeks to months following the treatment and may contribute to the symptoms reported by HSCT caregivers during the survivorship phase.
PATHOGENESIS OF HEALTH EFFECTS IN CAREGIVERS

One’s perception of an event plays a large role in the body’s response, and the experience of caring for an individual undergoing H SCT transplantation is inherently stressful. All stressors activate the hypothalamic-pituitary-adrenal axis and the adrenergic sympathetic nervous system. After exposure to stressful stimuli, the hypothalamus releases corticotropin-releasing hormone, which stimulates the pituitary gland to release adrenocorticotropic hormone, which in turn triggers the release of glucocorticoids (cortisol) from the adrenal cortex. At the same time, the sympathetic nervous system is activated with release of epinephrine (adrenal) from the adrenal medulla and norepinephrine from sympathetic nerves. In combination, the molecules released during the stress response have profound effects on the function of most cells and organs throughout the body including the brain, heart, respiratory system, muscles, skin, liver, gastrointestinal tract, and, importantly, the immune system.21

Activation of the acute stress response is life-saving and prepares the organism to avoid impending danger with enhanced vigilance, focused attention, and increased energy. In contrast, chronic stress has negative consequences on health. In chronic stress, the healthy diurnal rhythm of the hypothalamic-pituitary-adrenal axis, with a late evening nadir and a morning peak, is flattened showing instead low morning and elevated afternoon or evening cortisol levels.22 This represents a state of physiological burnout that often accompanies psychological burnout. In the early stages of burnout, hypothalamic-pituitary-adrenal axis activity is increased. Months later, hypothalamic-pituitary-adrenal axis activity decreases. One explanation for this progression may be related to changes in caregivers’ psychological coping and expectations, with active coping occurring early and loss of expectations of being able to cope successfully occurring later in the process. More recent studies indicate that dysregulation of the circadian rhythm during chronic stress also has an endocrine basis. Thus, even mild elevations in evening cortisol, as occurs in chronic stress, can disrupt the CLOCK (circadian locomotor output cycles kaput) gene mechanism of circadian regulation of the hypothalamic-pituitary-adrenal axis, resulting in functional hypercortisolism.23 Family caregivers of cancer patients also show autonomic imbalance with a shift toward the sympathetic and away from the parasympathetic tone.24,25

Although a single stressful event or multiple events with time to recovery between events may not affect health, multiple stressors without adequate recovery time or chronic stressful events as presented in the case study may increase the risk of illness. The term coined to define the load or total burden of multiple stressors similar to those to which caregivers are exposed daily is called allostatic load.26 A large allostatic load is a potential mechanism that links caregiving to adverse health outcomes.27 Chronic stress, including that experienced by caregivers of Alzheimer patients, has been shown to increase risk of infection28,29; decrease the take rate of vaccine immunization; slow wound healing20; speed cancer growth via β-adrenergic mechanisms that stimulate angiogenesis30; and speed chromosomal aging as indicated by telomere shortening.23 Stress does not cause these conditions but can foster them through the effects of stress hormones and neurotransmitters on disease processes and immune responses. On the other hand, a blunted hypothalamic-pituitary-adrenal axis response and functional glucocorticoid resistance have been associated with proinflammatory states and predispose to autoimmune/inflammatory diseases,22 cardiovascular disease,32 diabetes, and metabolic syndrome, which are characterized by central or abdominal obesity, high blood pressure, elevated cholesterol and insulin resistance,33 and depression.34

EVALUATING AND MANAGING STRESS IN CAREGIVERS OF CANCER PATIENTS

Although stressful events are inevitable, it is possible to identify a caregiver who is at increased risk of negative outcomes, assess the degree to which the caregiver’s life and health may be negatively affected, and recommend interventions that could attenuate the negative repercussions of the caregiving experience. Recognizing the psychological, behavioral, and physiological effects of caring for a loved one with cancer provides an excellent opportunity for primary prevention. A common barrier in primary prevention typically is access to pri-
mary care physicians. In this population, caregivers cross the thresholds of offices and health care agencies on a regular basis. Should a caregiver of a patient with cancer visit his/her own primary care physician, it rightly can be assumed he/she has experienced adverse health effects. However, when accompanying a cancer patient for a medical visit, the caregiver may hide or minimize these adverse effects in an effort to shield the patient and to avoid shifting attention to herself or himself. Therefore, it is imperative that the patient’s history and physical be expanded to include assessment of the caregiver. Fortunately, in the case presented herein, the interdisciplinary team, including an oncology social worker, assessed both the patient’s and the caregiver’s needs. The caregiver assessment included the knowledge level of the caregiver related to role expectations, the patient care needs or degree of burden, and the presence of competing responsibilities. The oncology social worker served as coordinator for the provision of appropriate psychological and social services in the agency and community.

Brief screening questionnaires can be helpful in a busy clinical environment (TABLE 1). Caregivers can complete the questionnaire independently and the responses are easy to interpret by a nurse, social worker, or physician who then can provide guidance regarding possible referrals for specialized care. The Distress Thermometer is a self-report measure of distress including a single-item distress rating scale from 0 to 10 and has been validated for HSCT caregivers. In addition, the American Cancer Society (AMS) developed the Caregiver Self-Assessment Questionnaire to assess caregiver stress and health, which was validated as a self-report screening measure for depression in caregivers of patients with dementia. The AMA Healthier Life Steps Program’s Personal Health Habits Questionnaire assesses key lifestyle behaviors including smoking, use of alcohol, nutrition practices, and exercise. Web-based collection systems such as the Patient Reported Outcomes Measurement Information System (PROMIS) are now available to both researchers and clinicians, allowing the collection of a large variety of outcome data including symptoms commonly prevalent in caregivers of cancer patients such as depression, anxiety, fatigue, and sleep disturbance. Two unique functions of the PROMIS program are the ability to collect patient outcomes longitudinally, making it possible to follow changes in function over time and the ability to compare patients’ outcomes against national norms.

Many well-validated psychological questionnaires are sensitive but are also subjective, indicating the need for development of more objective, quantitative measures of allostatic load. In a research setting, a comprehensive assessment of allostatic load or cumulative stress includes psychological measures of stress such as distress, anxiety, and depression; hormonal measures of the hypothalamic-pituitary-adrenal axis response (cortisol); physiological measures of the sympathetic and parasympathetic nervous system (blood pressure, heart rate, heart rate variability, and salivary amylase); and measures of end-organ effects such as immune system function and chromosomal damage. Some newer noninvasive methods include cortisol levels in hair and stress and immune biomarkers in eluates from sweat patches. Although many of these approaches show promise, they are not yet applicable in the clinical setting. More research is needed to develop and validate sensitive, noninvasive, quantitative measures of allostatic load and models that predict health outcomes.

The assessment of stress and how it affects the health of family caregivers
should be followed by guidance and individualized interventions to attenuate the health consequences. The mere act of assessing and listening to the caregivers’ needs communicates empathy, which may in itself improve outcomes.46,49 At a minimum, offering the patient and caregiver how-to information regarding patient care, maintenance of family and marital relationships, and the importance of self-care may help caregivers be more prepared and less distressed.30 Community or Web-based resources for caregivers are plentiful (http://www.cc.nih.gov/wecare/resources.html) with a select few highlighted in Table 2. A growing body of evidence supports simple stress management practices such as walking, meditating, and adopting nutritional changes such as the Mediterranean diet that may help reduce fatigue, improve sleep, and reduce the risk of some stress-related illnesses.31,32 Clinicians should remain alert to stress-related signs such as elevated blood pressure and heart rate, as well as delayed wound healing or increased frequency of infections.3,24,25

Looking toward the future, a number of questions remain. First, while a substantial body of evidence has accumulated regarding the health effects of caregiving, most of these studies have involved small sample sizes and single sites, and the translation of intervention research into practice has been slow. How preventive services such as screening, education, and referrals are systematically incorporated into our health care system is a policy issue beyond the scope of this article, but an issue clearly worthy of future attention. Although providing the level of care described herein requires some thought, the HSCT treatment. His wife then “had to go through the phases of planning his funeral, which [she] was not prepared for, feeling like there was nothing left for [her].” She “went through the grieving process like everyone else . . . just trying to survive.” She had the daunting task of explaining to her sick elderly father that her husband had passed away; 4 months later he too passed away, only 2 days before his 90th birthday. Shortly thereafter, she experienced another myocardial infarction and required the placement of a pacemaker.

More recently, financial pressures forced the caregiver to sell her house and downgrade to more affordable housing, and her cardiovascular disease continues to require careful management. On a happier note, her daughter, now 22 years old, is expecting the family’s first grandchild.

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