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Psycho-oncology

Treatment of cancer patients with both interleukin-2 (IL-2) and interferon-α (INF) is associated with increased likelihood of depression, as well as other psy-
Psychological symptoms, including reduced energy, diminished appetite, poor concentration, impaired confidence, and confusion. Cytokines have been noted to cause chemical changes in the brain that are similar to those seen in depressed patients, and it is thought that this may be the process that produces the side effect of depression. IL-2 influences noradrenergic activity, while INF affects serotonin levels by causing a depletion of its precursor, tryptophan. Thus, patients undergoing cytokine treatment for renal cell cancer should be monitored for signs of depression and receive appropriate therapy. Depression in cancer patients in general is seriously underdiagnosed, and the likelihood of this symptom with cytokine treatment means that clinicians should be even more alert for signs of depressive mood. This note will describe briefly some less frequently discussed considerations on the management of depression, a potential symptom for the renal cell cancer patient who is the focus of this Tumor Board.

At the Block Center for Integrative Cancer Care, an outpatient clinic offering conventional cancer treatment integrated with a fully individualized program of therapeutic nutrition, tailored supplement regimens, fitness training, and mind-spirit strategies, all patients undergoing treatment receive regular monitoring with the Hospital Anxiety and Depression Scale (HADS) along with other standardized instruments that indicate adjustment to cancer or impaired quality of life. Using these assessments helps to identify those who could benefit from clinical intervention and can indicate specific, personal issues of distress. Thus, if the present patient, with advanced and rather rapidly progressing renal cell carcinoma, were to present at the Block Center for cytokine treatment (most likely with IL-2), she would undergo an initial evaluation with the HADS (as well as quality-of-life scales) before beginning treatment and subsequently on at least a bimonthly basis during treatment. We have found that using regular psychological testing to detect the presence of depression, other adjustment disorders, and quality-of-life impairment in patients undergoing cancer treatment adds significantly to our ability to detect problems and intervene in a timely manner.

For a number of reasons (eg, perhaps heeding a well-intentioned imperative of family and friends to maintain a “positive attitude”), many cancer patients will not easily acknowledge “negative” feelings with even the most sensitive physicians or psychologists but might be more willing to indicate emotional symptoms when encouraged to do so privately with a simple pen-and-paper questionnaire. Careful evaluation of the responses to our psychosocial assessments has frequently allowed us to detect significant emotional-spiritual distress among patients that they might not have reported to us verbally and to intervene appropriately to match that individual’s needs with psychotherapeutic or medical treatments.

This patient’s lack of prior psychological disorders indicates that she may not react to cytokine treatment with a depressive episode since patients with higher initial scores on variables such as neuroticism seem to be more likely to become depressed during cytokine treatment. However, because she has no prior experience with psychological disorders, if she does encounter depression as a consequence of her treatment, she might feel both anxious and distressed about the very presence of this surprising mood disturbance. Should depression emerge as a side effect, in counseling this woman we would provide her with information explaining the probable source of her depression. Doing so should help to reassure her that the depressive symptoms accompanying cytokine treatment (along with hyperfatiguability, confusion, and any other psychological side effects) are a probable effect of treatment, that it is not a manifestation of long-term psychopathology nor does it bode a permanent change in her psyche. To some patients who experience psychological symptoms for the first time during cancer treatment, it can feel as though their emotions are betraying them by shifting so unexpectedly, mirroring the betrayal of their bodies in producing a life-threatening cancer. Even at this introductory phase of counseling, explaining the likely transient nature of her depression and describing specific strategies that we will develop collaboratively with her to help manage difficult emotions on her own should provide her some degree of comfort and foundational confidence in the process. In addition to speaking with a therapist, if this patient is receptive to the possibility, arranging for her to talk with another patient who has undergone the same treatment and suffered similar painful emotions and who has successfully recovered from the depression may provide a hopeful model for own eventual improvement.

Based on a new model of human reactions to stress—which may be more descriptive of the female response to stressors than simply “fight-or-flight”—as postulated by Shelley Taylor and colleagues, we are now beginning to understand a biobehavioral pattern labeled tend-and-befriend, which involves nurturing (protecting) and forming supportive alliances when vulnerable and threatened. This tendency among women has been linked with the neuroendocrine release of oxytocin enhanced by estrogen output, which affects endogenous opioids, reducing the sympathetic and hypothalamic-pituitary-adrenocortical physiology of stressors. The very positive benefit of tend-and-befriend is its potential to calm both psyche and soma. Therefore, even though this patient has the
support of her husband and adult children, connecting her to others who are experiencing or who have experienced comparable medical and emotional circumstances might afford this understandably distressed woman with additional physiological and psychological relief.

Techniques for self-management of milder levels of depression also serve to relieve patients enduring such symptoms by helping them to reassert some sense of control over their situation since distress over loss of control is common among cancer patients. We would attempt to intervene in a multidisciplinary fashion with this patient should we find that she was showing depressive symptoms. Adequate nutrition and exercise are basic to management of depression at our facility. Since this patient does not have a personal exercise routine at this time, our physical care staff would be working with her to develop such a regimen for reasons of general health and improvement of performance status. They would also emphasize the ability of exercise to alleviate depression and that adherence to her exercise recommendations might to some extent relieve her depression as well as increase her energy levels if she is experiencing the severe fatigue often noted among patients undergoing cytokine treatment.

Among the self-management techniques that might be recommended to this patient are those involving self-suggestion and imagery, eliciting specific sensory details (visual, auditory, olfactory, and tactile) from her that would thus be consonant with her own sense of comfort and safety. Accumulating clinical and observational evidence suggests that the more specific and detailed such images are, the more effective they will be in helping to induce physiological and psychological ease. Training patients in self-hypnosis, self-suggestion, and imagery can engender an enhanced sense of emotional control over an unfamiliar intensity of emotional distress. (Because some patients hold strong convictions against hypnosis due to religious beliefs or personal distrust, we would not automatically introduce this strategy to this woman but would explain documented benefits of hypnotherapy and speak with her about her receptiveness or objections to this technique.) However, certainly imagery and positive self-suggestion are safe and effective in most situations.

Another factor that may affect the severity of depression and other symptoms in cancer patients undergoing treatment is lack of sleep, a difficulty widely reported in this population. Conversely, depressive feelings may contribute to sleep difficulty, which may then exacerbate daytime fatigue. In patients with metastatic breast cancer, sleep problems were significantly associated with depression, including problems falling asleep, waking during the night, fewer hours of sleep per night, and use of sleeping pills. A simple and efficient technique, expressive writing or expressive disclosure, which has been gaining psychological and medical attention, might be helpful if this patient is troubled by sleep disturbance exacerbating or exacerbated by depressive feelings. Expressive writing was found to decrease the severity of sleep problems in patients undergoing vaccine treatment for metastatic renal cell carcinoma in a small controlled trial, and this might be recommended to our patient should she develop sleep difficulties alongside a depressed mood (or independently of it).

Expressive writing, a brief, structured psychological intervention, involves writing 20 minutes daily for 3 or 4 consecutive days about profoundly painful thoughts and feelings associated with their cancer experience. While writing about personal angst seems associated with physical and psychological benefits, writing about emotionally neutral topics does not produce the same effect. The patient should be encouraged to disclose through this writing process, which can take place in the total confidentiality and comfort of her home, her most private, personally distressing thoughts and feelings. Writing in privacy may provide a more comfortable forum for emotional expression, particularly for those who find it embarrassing or awkward to openly discuss personal feelings in a public setting. Thorough but straightforward written and verbal instructions should explain the background and step-by-step procedure of expressive writing and emphasize that no one need ever read what she writes and that this process is not about writing per se but about disclosing. Primary directions should guide her to write freely for the prescribed 20 minutes each day, ignoring syntax, word choice, and punctuation, that is, to just let the “flood gates open” and express without any concern for mechanics.

Since the history for this patient reveals that discovering the recurrence and progression of her cancer has been deeply upsetting, she might reasonably be encouraged to focus on all of her most distressing, not easily resolvable thoughts and feelings resulting from her current medical findings. When finished with the 3- or 4-day process, she can dispose of what she has written (some patients have reported personal rituals for burning or shredding what they have written, which seems to provide them with some closure) or, of course, she has the option of placing what she has written in a secure location if she does choose to retain the outpouring of her expressive writing. It needs to be pointed out to the patient that the expressive writing exercise is different from keeping an ongoing journal, in which events and thoughts are simply recorded and.
kept and in which the most personally difficult or traumatic emotional events are not the primary focus.

Since some patients could feel apprehensive about the expressive writing exercise because of concern that they might feel emotionally overwhelmed if they open up to dark or depressive thoughts and feelings, we do make sure that the patient has access to the therapist/counselor, by telephone if necessary. The availability of the therapist seems to calm any initial uneasiness of these patients, and neither reports after follow-up inquiry with patients nor calls from patients due to distress in conjunction to this process of emotional expression have yet occurred. It is very important to provide this woman with phone and/or pager numbers of trained professionals for readily accessed personal support and emotional backup in the slight likelihood that she might feel troubled as a consequence of this disclosure exercise.

Finally, it is wise to keep in mind that symptoms closely resembling major depressive disorder can be seen in patients undergoing treatment with cytokines. Suicidal risk has been noted in some patients. Thus, pharmacological options should be kept in mind for patients being treated with cytokines in case of the development of more severe depression, or depression that does not resolve with reassurance, lifestyle, or self-help interventions. For milder cases, St. John’s Wort could be considered during IL-2 monotherapy, as IL-2 metabolism appears not to be affected by cytochrome P450 metabolism, the source of herb-drug interactions with this botanical. For more severe cases, treatment with selective serotonin reuptake inhibitors (SSRIs) would be considered. And certainly, preventative treatment with an SSRI should be part of a full treatment plan for this patient if she had a prior history of depression.

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Integrative Physician’s Perspective

Medical Oncology

It is a privilege to be able to feature a contribution to this Tumor Board by Drs Supriya Gupta and Nicholas Vogelzang of the University of Chicago Section of Hematology/Oncology. Under Vogelzang’s leadership, the research team at this institution has made a very significant contribution to our knowledge of this disease, which is, as discussed in this Tumor Board, remarkably worrisome for patients and physicians alike.

With 25% to 50% of patients exhibiting distant metastases at initial diagnosis with renal cancer, and with 40% of patients developing metastases after surgery for primary disease, renal cell carcinoma (RCC) can be extremely lethal. The availability of immunotherapies that can produce fairly durable remissions, such as IL-2, as discussed by Gupta and Vogelzang, relieves the concerns raised by the fact that RCC appears to be resistant to cytotoxic chemotherapies. They point out that none of the single-agent chemotherapies currently available have shown effectiveness in...