TABLE 1. MEAN SCORES FOR EACH QUESTIONNAIRE PRE- AND POSTINTERVENTION

	Preintervention	*Postintervention*	z	p *value*
FACIT-Sp	32.1 ± 6.5	33.0 ± 6.9	$z = 0.40$	$p = 0.69$
Anxiety	6.9 ± 3.6	5.1 ± 3.9	$z = -2.52$	$p = 0.01$
Depression	5.1 ± 2.9	3.5 ± 3.1	$z = -2.60$	$p = 0.009$
Total HADS	12 ± 5.3	8.6 ± 6.3	$z = -2.89$	$p = 0.004$
Growth	5.5 ± 1.1	5.7 ± 0.9	$z = 1.54$	$p = 0.12$
Appreciation	6.3 ± 1.0	6.2 ± 0.8	$z = 0.87$	$p = 0.87$
Pain	2.1 ± 2.3	2.4 ± 2.9	$z = 0.77$	$p = 0.44$
Symptom	3.2 ± 3.0	2.6 ± 3.2	$z = 0.88$	$p = 0.38$

FACIT = SP, Functional Assessment of Chronic Illness Therapy-Spiritual; HADS, Hospital Anxiety and Depression Scale.

their hands or legs to focus their attention (Fig. 1). The cyclic meditation program takes about 30 to 60 minutes per session and is conducted by nurses or a clinical psychologist who received training for at least 3 hours. The training included basic communication skills and yoga skills learned directly from a yoga specialist or using a CD or DVD. A primary physician recruited the patients and a clerk obtained informed consent and asked the patients to complete questionnaires preintervention and postintervention. In the pretherapy session, the patient learned the cyclic meditation program and it was recommended that they perform the therapy at home once per day. After 2 weeks, the patients met the interviewers in a second session to talk about their impressions.

Statistical analysis

A p value less than 0.05 was taken to indicate a significant level in all statistical analyses. All reported p values are two-tailed. The statistical procedures were conducted with SPSS 15.0 (Japanese version) for Windows (SPSS Inc., Chicago, IL, 2006). To evaluate the efficacy of mindfulness therapy on anxiety, depression and spirituality, a Wilcoxon sign rank test was conducted on the HADS and FACIT-Sp scores.

Results

Table 1 shows the scores for questionnaires pre- and post-intervention. Anxiety score of the HADS significantly decreased from 6.9 ± 3.6 to 5.1 ± 3.9 ($p = 0.01$) and Depression score of the HADS also significantly decreased from 5.1 ± 2.9 to 3.5 ± 3.1 ($p = 0.009$). Total HADS scores significantly decreased from 12 ± 5.3 to 8.6 ± 6.3 ($p = 0.004$) after the intervention, and FACIT-Sp scores increased from 32 ± 6.5 to 33 ± 6.9 ($p = 0.69$, not significant). Table 2 shows the results of correlation analyses. There were significant relationships between FACIT-Sp and HADS ($r = -0.78$, p = 000), FACIT-Sp and growth ($r = -0.35$, p = 0.04), FACIT-Sp and pain ($r = -0.41$, $p = 0.02$), and growth and appreciation ($r = 0.45$, $p = 0.009$).

Discussion

The decrease in the HADS scores after the intervention shows that mindfulness-based cyclic meditation affects anxiety and depression for Japanese cancer patients. This result is consistent with those of Tacon et al.[18,19] using the State-Trait Anxiety inventory and Garland et al.[10] using the Profile of Mood of States. Therefore, MBSR may be effective for anxiety or depression in Japanese patients as an individual and short-term therapy. Matchim and Armer[20] suggested that more research is needed to test the instruments in MBSR and establish their validity and reliability in oncology patients. Thus, the present study provides a new finding that MBSR may affect anxiety and depression in Japanese patients based on the HADS score. The increase in FACIT-Sp scores after MBSR was not significant, with a change from 32.1 to 33.0 compared to the increase in FACIT-Sp score in Garland et al.[10] from 28.43 to 32.1. These results suggest that ceiling effects may prevent a significant change in spiritual well-being.

Regarding the association among variables, the relationship of FACIT-Sp with HADS (r = −0.78) shows that

TABLE 2. CORRELATION COEFFICIENTS AMONG VARIABLES

	HADS	*Anxiety*	*Depression*	*FACIT-Sp*	*Growth*	*Appreciation*	*Pain*	*Symptom*
HADS	1							
Anxiety	—	1						
Depression	—	0.61[a]	1					
FACIT-Sp	−0.78[a]	−0.75[a]	−0.64[a]	1				
Growth	0.27	0.25	0.23	−0.35[b]	1			
Appreciation	0.22	0.21	0.19	−0.1	0.45[c]	1		
Pain	0.30	0.35[b]	0.16	−0.41[b]	0.05	−0.1	1	
Symptom	0.32	0.35[b]	0.20	−0.27	0.06	−0.3	0.30	1

[a] $p < 0.00$.
[b] $p < 0.05$.
[c] $p < 0.01$.
HADS, Hospital Anxiety and Depression Scale; FACIT = Sp, Functional Assessment of Chronic Illness Therapy = Spiritual.

spirituality is correlated with anxiety and depression. This result is also in accord with Garland et al.,[10] in which increased spirituality was related to decreased stress and reduced mood disturbance after MBSR. FACIT-Sp and growth showed a significant negative association, which is opposite to the results of Garland et al.,[10] in which a benefit finding was elicited or posttrauma growth was related to spirituality. Our results suggest that patients with high spirituality such as meaning or moderate feelings do not always experience growth. This negative association may have been influenced by other variables such as pain,[5] and self-reporting or a daily diary may be useful to examine the process of psychological change.[21,22]

Last, we note several limitations of the study, including that a control group was not established and the number of participants was small. However, the results provide a useful indication that MBSR may be effective for anxiety and depression in Japanese cancer patients, and that spiritual well-being is related to anxiety, depression, and growth. A further study including a control group may help to establish these findings more clearly.

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Author Disclosure Statement

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References

1. Lampic C, Wennberg A, Schill JE, Glimelius B, Brodin O, Sjödén PO: Coping, psychosocial well-being and anxiety in cancer patients at follow-up visits. Acta Oncol 1994;33:887–894.
2. Carlson LE, Speca M, Patel KD, Goodey E: Mindfulness-based stress reduction in relation to quality of life, mood, symptoms of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004; 29:448–474.
3. Ott MJ, Norris RL, Bauer-Wu SM: Mindfulness meditation for oncology patients: a discussion and critical review. Integrative Cancer Ther 2006;5;98–108.
4. Mytko JJ, Knight SJ: Body, mind and spirit: towards the integration of religiosity and spirituality in cancer quality of life research. Psychcooncology 1999;8:439–450.
5. Predeger E: Woman spirit: A journey into healing through art in breast cancer. Adv Nurs Sci 1996;18:48–58.
6. Kabat-Zinn J: *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain and Illness*. New York: Delacourt, 1990.
7. Speca M, Carlson LE, Goodey, E, Angen M: A randomized, wait-list controlled clinical trial: The effect of a mindfulness meditation-based stress reduction program on mood and symptoms of stress in cancer outpatients. Psychom Med 2000;62:613–622.
8. Carlson LE, Speca M, Patel KD, Goodey E: Mindfulness based stress reduction in relation to quality of life, mood, symptom, of stress and levels of cortisol, dehydroepiandrosterone sulfate (DHEAS) and melatonin in breast and prostate cancer outpatients. Psychoneuroendocrinology 2004; 29:448–474.
9. Monti DA, Peterson C, Kunkel S: A randomized, controlled trial of mindfulness-based art therapy (MBAT) for women with cancer. Psychooncology 2006;15:363–373.
10. Garland SN, Carson LE, Cook S, Lansdell L, Speca M: A non-randomized comparison of mindfulness-based stress reduction and healing arts programs for facilitating posttraumatic growth and spirituality in cancer outpatients. Support Care Cancer 2007;15:949–961.
11. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–370.
12. Kugaya A, Akechi T, Okuyama T, Okamura H, Uchitomi Y: Screening for psychological distress in Japanese cancer patients. Jpn J Clin Oncol 1998;28:333–338.
13. Peterman AH, Fitchett G, Brady MJ, Hernandez L, Cella D: Measuring spiritual well-being in people with cancer: The Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale (FACIT-Sp). Ann Behav Med 2002;24: 49–58.
14. Noguchi W, Ono T, Morita S, Aihara O, Tsuji H, Shimozuma K, Matsushima E: An investigation of reliability and validity to Japanese version of Functional Assessment of Chronic Illness Therapy-Spiritual (FACIT-sp). Jpn J Gen Hosp Psychiatry 2004;16:42–47.
15. Sanjyo M, Morita T, Hirai K: Caregiving Consequences Inventory: A measure for evaluating caregiving consequences from the bereaved family members' perspective. Psychooncology 18, 657–666.
16. Tomich PL, Helgeson VS: Five years later: A cross sectional comparison of breast cancer survivors with healthy women. Psychooncology 2002;11:154–169.
17. Nagarathna R, Monro R, Nagendra HR, Nagendra HR, Raghuram NV: Measuring the effects of yoga in rheumatoid arthritis. Br J Rheumatol 1994;33:787–788.
18. Tacon AM, Caldera YM, Ronaghan C: Mindfulness-based stress reduction in women with breast cancer. Families Systems Health 2004;22:193–203.
19. Tacon AM, Caldera YM, Ronaghan C: Mindfulness, psychosocial factors, and breast cancer. J Cancer Pain Symptom Palliat 2005;1:45–53.
20. Matchim Y, Armer J: Measuring the psychological impact of mindfulness meditation on health among patients with cancer. Oncol Nurs Forum 2007;34:1059–1066.
21. Baer RA, Smith GT, Allen KB: Assessment of mindfulness by self-report: The Kentucky Inventory of Mindfulness Skills. Assessment 2004;11:191–206.
22. Baer RA, Smith GT, Hopkins J, Krietemeyer J: Using self-report assessment methods to explore facets of mindfulness. Assessment 1996;13:27–45.

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Suicide Associated with Corticosteroid Use During Chemotherapy: Case Report

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Corticosteroids are widely known to have a variety of adverse mental effects. Although corticosteroids are frequently used to prevent vomiting induced by chemotherapeutic agent, their mental effects have received little attention in oncology settings. We report the case of a patient who experienced severe depressive symptoms after both the first and second course of treatment with a corticosteroid during chemotherapy and ultimately committed suicide. The temporal and dose–response relationships suggested a possible association between the depressive symptoms and corticosteroid. We ultimately speculated that corticosteroid withdrawal induced the depressive symptoms in this case. This case should alert clinical oncologists to pay attention to mental symptoms after prescribing a corticosteroid.

Key words: corticosteroid – mood disorder – suicide – chemotherapy

INTRODUCTION

Corticosteroids act on the hypothalamic–pituitary–adrenal (HPA) axis, which has close association with mental activity (1), and it is widely known that various adverse mental effects such as mood disorders sometimes occur following corticosteroid administration, corticoid dose reduction or discontinuance of a corticosteroid (2). Since corticosteroids are frequently used to prevent chemotherapeutic-agent-induced nausea and vomiting (3), some cancer patients develop mental symptoms as adverse effects of the corticosteroid therapy. However, corticosteroid-induced mental adverse effects after chemotherapy have received little attention and have not been elucidated by epidemiologic studies. We report the case of a patient who developed severe depressive symptoms after both the first and second course of treatment with corticosteroids during chemotherapy and ultimately committed suicide. Although we were not able to find any reports of similar cases in a search of the literature, a possible association between the depressive symptoms and the corticosteroid was suggested in this case.

CASE REPORT

The patient was a 68-year-old woman who underwent total mastectomy and axillary lymph node dissection for a diagnosis of cancer of the left breast. Histopathological examination revealed invasive ductal carcinoma and four positive lymph nodes in the axilla. The TMN classification was T2N1M0, Stage IIb. When the patient was informed of the cancer diagnosis, her negative psychological reaction was comparatively minor, because she had not felt very seriously ill and had maintained an active life, and she confronted her disease and surgical treatment positively and constructively. Four courses of doxorubicin plus cyclophosphamide combination chemotherapy (doxorubicin 90 mg, iv on day 1; cyclophosphamide 900 mg, iv on day 1) were scheduled on an outpatient basis as adjuvant chemotherapy (Fig. 1). Although dexamethasone (24 mg, iv on day 1; 8 mg, po on days 2–4), granisetron and prochlorperazine were administered for antiemesis, the patient experienced severe nausea and vomiting from days 3 to 7 after administration of the anticancer agents, and even after the vomiting stopped, it became apparent that she felt depressed. There were no other adverse effects, such as fatigue, that were likely to have been caused by the chemotherapy.

Because of the severe nausea and vomiting after the first course of chemotherapy, the second course of the chemotherapy was performed on an inpatient basis starting on day 27 after the first administration of anticancer agents. To

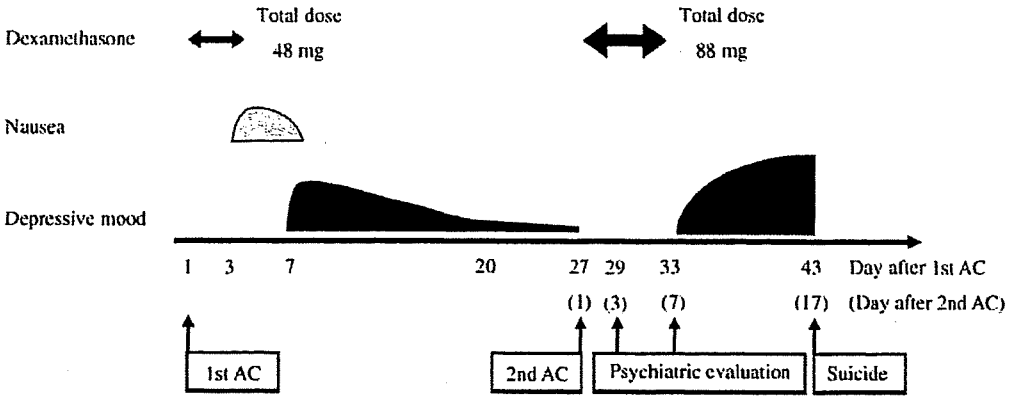

Figure 1. Procedure of the chemotherapy and symptoms. AC, combined doxorubicin plus cyclophosphamide chemotherapy; iv, intravenous administration; po, per os. The dosage of dexamethasone was 24 mg, iv on day 1; 8 mg, po on days 2–4 on the first course, and 24 mg, iv on day 1; 16 mg, po on days 2–4; 8 mg, po on days 5–6 on the second course.

reduce the nausea and vomiting, the dose of dexamethasone was increased and it was administered for a longer period than during the first course (24 mg, iv on day 1; 16 mg, po on days 2–4; 8 mg, po on days 5–6). In addition, the patient was referred to the psycho-oncology division on day 3 of the second course for her depressive symptoms. A psychiatric evaluation was performed and the course of her depressive symptoms was reviewed the same day. The results showed that from days 7 to 20 of the first course of chemotherapy, she had experienced severe symptoms of depression, including depressed mood, markedly diminished interest or pleasure at all, decreased appetite, hypersomnia and fatigue but had not had recurrent thoughts of death, and that her symptoms met the criteria for major depressive episode in DSM-IV-TR. Since then her depressive symptoms had gradually decreased, and after administration of the second course, she had rapidly recovered and had no depressive symptoms by the time of the psychiatric evaluation. She was not sure what caused her depressive symptoms. Because the patient had no past history or family history of psychiatric disorders, including mood disorders, addiction or suicidal ideation, no health problems other than cancer, no addictions and no financial problems, and her psychological reaction to the cancer diagnosis had been minor, we considered the possibility that the episode was associated with corticosteroid administration, but the evidence was not conclusive at that point.

The patient experienced little nausea during the second course of chemotherapy, and she was discharged on day 7 with no physical or psychiatric problems. We examined the patient immediately before discharge on day 7 of the second course, since she had developed corticosteroid-induced depressive symptoms on day 7 of the first course. Thinking that she might develop depressive symptoms again, we scheduled the first outpatient clinic visit for day 21 of the second course, but instructed the patient to contact us anytime she experienced any emotional problems.

Despite our measures to detect depressive symptoms early, the patient committed suicide by hanging on day 17 of the second course. Her family told us that after discharge she had appeared to have gradually become more severely depressed than after the first course, and that she had a gloomy facial expression and had stayed in a dark room all day long at home doing nothing.

DISCUSSION

We have reported the case of a breast cancer patient who developed depressive symptoms after both courses of chemotherapy. During the second course, she was treated with a higher dose of dexamethasone and experienced severer depressive symptoms that led to her suicide. Doxorubicin or cyclophosphamide was administered concurrently, but neither drug is known to induce mental symptoms. The temporal and dose–response relationships between the corticosteroid administration and the depressive symptoms in our patient suggest possible induction of severe depressive symptoms by the corticosteroid.

Corticosteroids are generally used as effective drugs to control chemotherapeutic-agent-induced nausea and vomiting (3), but, as is well known, they sometimes induce various adverse mental effects such as mood disorders, delirium and psychotic disorders (2). Incidences of corticosteroid-induced adverse mental effects from 1.8% to 57% have been reported (4). Naber et al. (5) found that 36% of ophthalmologic patients developed a mood disorder during steroid therapy and 10% of the patients in their study developed a depressed mood. The corticosteroid dose is an important risk factor for the development of mental symptoms (4), and the severity of the symptoms appears to be dose-dependent (6). The higher dose of the corticosteroid used to control our patient's intolerable vomiting may have led to the exacerbation of her mental symptoms.

There was a lag between the administration of the corticosteroid and the onset of the depressive symptoms in our

patient. She experienced depressive symptoms a few days after the final dose of dexamethasone during the first course. Her depressive symptoms rapidly improved soon after the start of the second course, but they flared up again after dexamethasone was stopped on day 7, and she ultimately committed suicide on day 17. A direct pharmacological action of corticosteroids causes depressive symptoms (2), and we initially suspected that the corticosteroid had induced the depressive symptoms, but we ultimately speculated that corticosteroid withdrawal induced the depressive symptoms in this case. Some case reports (7,8) have shown that corticosteroid withdrawal symptoms commonly take the form of depression, anxiety and fatigue, but the incidence of corticosteroid withdrawal symptoms have never been revealed in previous reports. They are sometimes associated with evidence of HPA axis suppression, and withdrawal syndromes can occur during both acute and long-term corticosteroid therapy (6,9). Therefore, caution should be exercised with regard to adverse mental effects after even a brief course of corticosteroid therapy.

Although this may be a rare case of the worst outcome, i.e. with the patient committing suicide, patients who receive chemotherapy may be at risk for depressive symptoms when treated with a corticosteroid. This case should alert clinical oncologists and psychiatrists to pay attention to the mental symptoms, especially depressive mood, during the relatively long-term care of their patients undergoing chemotherapy who are treated with a corticosteroid concurrently. Physicians should screen their patients for depressive symptoms and, if any are found, conduct a careful follow-up in view of the possibility of a suicide attempt. Further observational research is necessary to see the picture.

Finally, we were careful to protect the patient's anonymity in this report. More specifically, we have not included any information that could be used to identify the patient, such as her name, department where she was treated or date of admission.

Conflict of interest statement

None declared.

References

1. Musselman DL, Nemeroff CB. Depression and endocrine disorders: focus on the thyroid and adrenal system. *Br J Psychiatry Suppl* 1996;30:123–8.
2. Patten SB, Neutel CI. Corticosteroid-induced adverse psychiatric effects: incidence, diagnosis and management. *Drug Saf* 2000;22:111–22.
3. Kris MG, Hesketh PJ, Somerfield MR, Feyer P, Clark-Snow R, Koeller JM, et al. American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006. *J Clin Oncol* 2006;24:2932–47.
4. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. *Mayo Clin Proc* 2006;81:1361–7.
5. Naber D, Sand P, Heigl B. Psycopathological and neuropsychological effects of 8-days' corticosteroid treatment. A prospective study. *Psychoneuroendocrinology* 1996;21:25–31.
6. Brown ES, Khan DA, Nejtek VA. The psychiatric side effects of corticosteroids. *Ann Allergy Asthma Immunol* 1999;83:495–503.
7. Fricchione G, Ayyala M, Holmes VF. Steroid withdrawal psychiatric syndromes. *Ann Clin Psychiatry* 1989;159:99–108.
8. Hassanyeh F, Murray RB, Rodgers H. Adenocortical suppression presenting with agitated depression, morbid jealousy, and a dementia-like state. *Br J Psychiatry* 1991;1:870–2.
9. Naumovski J, Bozinovska C, Kovkarova E, Petkovska L. Single-dose dexamethasone-induced adenocortical suppression in an intentional self-poisoning-case report. *J Toxicol Clin Toxicol* 2003;41:895.