INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 24, no. 1, 1-5 (2011)

EDITORIAL

PSYCHOLOGICAL STRESS AND CANCER

C.M. CONTI[1], G. MACCAURO[2] and M. FULCHERI[1]

[1]Department of Clinical Psychology, University of Chieti, Chieti; [2]Department of Orthopaedics, Catholic University of Rome, Rome, Italy

Received December 9, 2010 – Accepted February 2, 2011

All the concepts reported in this editorial are based on recent literature data obtained through a PubMed search, using both Medline and manual searches, with particular reference to articles, which could be relevant to clinical practice. This paper contributes to the existing literature on depression and stress and provides important information for the development of effective strategies to manage these conditions among patients with cancer.

Stress has received a number of definitions in scientific literature, more or less accurate or complete. One of the most commonly accepted psychological definitions has been that stress occurs when demands from the environment challenge an individual's adaptive capacity and has been associated with immune system dysfunctions. Distress is a common variable in oncologic studies and is a multifactorial, unpleasant experience of an emotional, psychological, social or spiritual nature that interferes with the ability to cope with cancer. Psychological distress can worsen physical manifestation of cancer (1).

Stress and depression can influence tumor progression at a cellular level and several authors demonstrated in their articles the inter-relationships between stress, immune reactivity and tumor development (2). Once a cancer patient is affected by stress, specific pathways within the brain lead to the activation of the hypothalamic-pituitary-adrenal axis as well as the central sympathetic nervous system (3). The stress response consists in releasing key peripheral mediators such as catecholamines and glucocorticoids the role of which in the pathophysiology of chronic stress is extraordinarily complex and controversial (4). Moreover, in cancer, catecholamines can enhance carcinogenic properties of prostate, ovary, breast and colon tumor cells (5), while glucocorticoids are immune-suppressive agents (6). It has been reported that the immune system plays an important role in the development of cancer (7-9). Different immune factors, such as immune cells and various interleukins, have a significant influence on the process of tumor development and appearance of metastases (10-11). On the other hand, many studies have confirmed the influence of psychological factors on different aspects of the immune system, important in the process of tumor development (12). Cellular-mediated and humoral-mediated responses are affected in general psychiatry traumatic disorders, as is the production of cytokines (13-15). The hypothalamic-pituitary-adrenal axis responds to several compounds, such as inflammatory cytokines: tumor necrosis factor (TNF)-α, interleukin-1 (IL-1) alpha and beta, interleukin-18, interleukin-33 and interleukin-6 (16-22). Several studies proved the correlation between stress and progression of various types of

Key words: stress, cancer, psychological therapy

Mailing address:
Dr C. Conti,
Department of Clinical Psychology,
University of Chieti,
Via dei Vestini,
66013 Chieti, Italy

0394-6320 (2011)

cancer and cancer recurrence, in humans (23-25). In recent years, a number of studies have established an increasingly clear link between psychosocial or psychophysical stress, personality types and the development of cancer (26-28). Several performed clinical trials indicated a positive correlation between psychosocial stress and the severity of cancer and the high prevalence of psychiatric disorders in cancer patients is well known (29). Mental disorders, such as bio-psychosocial phenomenon and quality of life in cancer diseases, assume a specific role within the therapeutic choice (30). Physicians must give attention to the possibility of the patient's identity crises. The reconstruction of patient psycho-physical identity regarding cancer is particularly difficult. Psychological assistance acquires a relevant role in improving the patient's quality of life (31-32). In patients affected by cancer the body should be considered not only in the physical aspect but also as an expression of subjectivity and totality of the person.

Depressive disorders have frequently been encountered in cancer patients, and depressive elements have a tremendous impact on the quality of life, tolerance and compliance with anticancer treatment. Depressive disorders in cancer might be more relevant with practical clinical implications and are a major concern for cancer survivors. Therefore, clinicians and other health care providers should be aware of depression and communicate effectively with cancer patients and survivors about depression. Optimal care of these mood disorders have to be implemented and be supported by the association of pharmacological treatment and psychotherapy. It has been reported that the psychological and medical care needs of patients with tumor and an adequate structure for their cancer care have so far been only marginally considered (33). Psychotherapeutic approach is being used by patients with cancer to manage a spectrum of treatment-related symptoms and facilitate the process of psychological readjustment to the change.

There has been a great improvement in overall lifetime survival and much greater patient interest and appreciation with better follow-up and maintenance, so that we can quickly and effectively help when problems arise. Now that we have achieved an increased longevity for cancer patients, we must be able to assure them the best possible quality of life. Significant differences between medical care, psychosocial stress and the desired support were also reported in many publications (34-36). Common psychosocial difficulties experienced by cancer patients are stress, fatigue, depression, anxiety, and existential and relational concerns (37-38). Psychological therapy is one intervention being developed to address these difficulties.

The purpose of this editorial is to assess and synthesize the available research evidence for the use of psychological therapy in the management of symptoms in adults with cancer. Psychological therapy is an approach that is being used by adults with cancer to manage a spectrum of treatment-related symptoms and facilitate the process of psychological readjustment to the loss, change, and uncertainty characteristic of cancer survivorship (39-45). With advances in early diagnosis, treatment, and long-term management of cancer, the number of people living with metastatic and advanced cancers has continued to grow worldwide.

Since depression is common among patients with cancer, routine screening and prevention of depression are warranted among these people. However, depression occurs in a high percentage of cancer patients within 6 months of diagnosis, and it is correlated with the relationship between socioeconomic and clinical factors, age and quality of life. Psychological screening of patients with cancer is widely recommended as standard practice; however, standard screening measures may have limited sensitivity and specificity as demonstrated by the data reported in the literature. Development of a brief screening tool that incorporates empirically supported risk factors is recommended to improve the timely identification and support of those patients most susceptible to adverse psychological outcomes. Efficacy of psychotherapies, in cancer patients, is supported by numerous studies (46-51). However, there are currently no randomized controlled trials assessing the efficacy of psychosocial intervention in the treatment of traumatic stress disorders in cancer patients. Therefore, concepts expressed here are sources extracted from the general literature found on PubMed.

These studies suggest that stress-related psychosocial factors have an adverse effect on

cancer incidence and survival, although there is evidence that the results and ideas expressed in this article should be interpreted with caution. The effects that psychosocial stress exerted on immune suppression in patients with malignant cancer are well established; however, its exact effects are still unclear. In addition, further investigations are necessary and have to be implemented to clarify the efficacy and inter-relationship between psychological therapy and stressed cancer patients. Therefore, more research in this field is needed.

REFERENCES

1. Desaive P, Ronson A. Stress spectrum disorders in oncology. Curr Opin Oncol 2008; 20:378-85.
2. Perrella O, Cuomo O, Sbreglia C, Monaco A, Gnarini MR, Gentile B, Perrella M, Perrella A. IL-18 and interferon-γ in HCV-related hepatocellular carcinoma: a model of interplay between immune status and cancer. J Biol Regul Homeost Agents 2009; 23:251-8.
3. Li Q, Kobayashi M, Inagaki H, et al. A day trip to a forest park increases human natural killer activity and the expression of anti-cancer proteins in male subjects. J Biol Regul Homeost Agents 2010; 24: 157-65.
4. Sancini A, Tomei F, Schifano MP, et al. Stress characteristics in different work conditions: is it possible to identify specificity of risk factors by the questionnaire method? Eur J Inflamm 2010; 8:117-23.
5. Swiercz R, Grzelińska Z, Gralewicz S, Wasowicz W. Catecholamine levels in the brain of rats exposed by inhalation to benzalkonium chloride. Int J Occup Med Environ Health 2009; 22:107-13.
6. Rearte B, Maglioco A, Balboa L, et al. Mifepristone (RU486) restores humoral and T cell-mediated immune response in endotoxin immunosuppressed mice. Clin Exp Immunol 2010; 162:568-77
7. Preise D, Scherz A, Salomon Y. Antitumor immunity promoted by vascular occluding therapy: lessons from vascular-targeted photodynamic therapy (VTP). Photochem Photobiol Sci 2011; 24:Epub ahead of print.
8. Singh SS, Yadav SK, Haldar C. Effect of glucocorticoid and melatonin on immune function of an Indian tropical bird, *Perdicula Asiatica:* an *in vivo* and *in vitro* study. Eur J Inflamm 2010; 8:89-97.
9. Zhang G-H, Liu Y-F, Hu H-Y. Preparation and cytotoxicity effect of anti-hepatocellular carcinoma SCFV immunoliposome on hepatocarcinoma cell *in vitro*. Eur J Inflamm 2010; 8:75-82
10. Wang L, Yi T, Zhang W, Pardoll DM, Yu H. IL-17 enhances tumor development in carcinogen-induced skin cancer. Cancer Res 2010; 70:10112-20.
11. Boscolo P, Bellante V, Leopold K, et al. Effects of palladium nanoparticles on the cytokine release from peripheral blood mononuclear cells of non-atopic women. J Biol Regul Homeost Agents 2010; 24:207-14.
12. Deshields TL, Nanna SK. Providing care for the "whole patient" in the cancer setting: the psycho-oncology consultation model of patient care. J Clin Psychol Med Settings 2010; 17:249-57.
13. Bob P, Raboch J, Maes M, Susta M, Pavlat J, Jasova D, Vevera J, Uhrova J, Benakova H, Zima T. Depression, traumatic stress and interleukin-6. J Affect Disord 2010; 120:231-4.
14. Castellani ML, Anogeianaki A, Felaco P, et al. IL-34 a newly discovered cytokine. Eur J Inflamm 2010; 8: 63-66
15. Calabrò P, Riegler L, Limongelli G, et al. Production of serum amyloid A in response to inflammatory cytokines by human adipocytes. Eur J Inflamm 2010; 8:99-105.
16. Galliera E, Locati M, Mantovani A, Corsi MM. Chemokine system: new inflammatory markers on the horizon. Eur J Inflamm 2010; 8:1-6.
17. Castellani ML, Anogeianaki A, Toniato E, et al. Inter-relationship between chemokines and mast cells. Eur J Inflamm 2010; 8:7-14.
18. Bocchino M, Matarese A, Bellofiore B, Giacomelli P, Russo A, Signoriello G, Galati D, Sanduzzi A. Usefulness of IFN-gamma release assays in clinical management of difficult TB cases:evidence from clinical practice. Eur J Inflamm 2010; 8:43-47.
19. Yanagitani N, Shimizu Y, Kazama T, Dobashi K, Ishizuka T, Mori M. Eosinophilic bronchiolitis indicating eosinophilic airway disease with overexpression of carcinoembryonic antigen in sinus and bronchiole: case report. J Biol Regul Homeost Agents 2010; 24:99-102.

20. Su C, Picard P, Rathbone MP, Jiang S. Guanosine-induced decrease in side population of lung cancer cells: lack of correlation with ABCG2 expression. J Biol Regul Homeost Agents 2010; 24:19-25.
21. Castellani ML, Anogeianaki A, Felaco P, et al. IL-35, an anti-inflammatory cytokine which expands CD4+CD25+ Treg cells. J Biol Regul Homeost Agents 2010; 24:131-5.
22. Conti CM, Fulcheri M. Interrelationship between psychology and cytokines. J Biol Regul Homeost Agents 2010; 24:485-90.
23. Elklit A, Blum A. Psychological adjustment one year after the diagnosis of breast cancer: A prototype study of delayed post-traumatic stress disorder. Br J Clin Psychol 2010; 19:Epub ahead of print.
24. Magni P, Ruscica M, Dozio E, Passafaro L, Stefani L, Morelli P, Banfi G, Corsi MM. Plasma adiponectin and leptin concentrations in professional rugby players. J Biol Regul Homeost Agents 2010; 24:87-91.
25. Angelini A, Di Ilio C, Castellani ML, Conti P, Cuccurullo F. Modulation of multidrug resistant P-glycoprotein activity by flavonoids and honokiol in human doxorubicin-resistant sarcoma cells (MES-SA/Dx-5): implications for natural sedatives as chemosensitizing agents in cancer therapy. J Biol Regul Homeost Agents 2010; 24:197-205.
26. Velikova G. Patient benefits from psychosocial care: screening for distress and models of care. J Clin Oncol 2010; 28:4871-3
27. Tatone C, Carbone MC, Campanella G, Festuccia C, Artini PG, Talesa V, Focarelli R, Amicarelli F. Female reproductive dysfunction during ageing: role of methylglyoxal in the formation of advanced glycation end-products in ovaries of reproductively-aged mice. J Biol Regul Homeost Agents 2010; 24: 63-72.
28. Mazzoccoli G, Pazienza V, Piepoli A, Muscarella LA, Inglese M, De Cata A, Giuliani F, Tarquini R. Hypothalamus-hypophysis-thyroid axis function in healthy aging. J Biol Regul Homeost Agents 2010; 24:433-9.
29. Mendonsa RD, Appaya P. Psychiatric morbidity in outpatients of gynecological oncology clinic in a tertiary care hospital. Indian J Psychiatry 2010; 52: 327-32.
30. Costantini M, Ottonelli S, Canavacci L, Pellegrini F, Beccaro M, Randomised Italian Cluster Trial Study Group L. The effectiveness of the Liverpool Care Pathway in improving end of life care for dying cancer patients in hospital. A cluster randomised trial. BMC Health Serv Res 2011; 11:13.
31. Gigante A, Cappella M, Manzotti S, Cecconi S, Greco F, Di Primio R, Mattioli-Belmonte M. Osteoinduction properties of different growth factors on cells from non-union patients: *in vitro* study for clinical application. J Biol Regul Homeost Agents 2010; 24:51-62.
32. Printz C. Patients who die at home have better quality of life. Cancer 2011; 117:439.
33. Zhang QL, Niu Q, Niu PY, Ji XL, Zhang C, Wang L. Novel interventions targeting on apoptosis and necrosis induced by aluminum chloride in neuroblastoma cells. J Biol Regul Homeost Agents 2010; 24:137-48.
34. Kelly KM, Shedlosky-Shoemaker R, Porter K, Desimone P, Andrykowski M. Cancer recurrence worry, risk perception, and informational-coping styles among appalachian cancer survivors. J Psychosoc Oncol 2011; 29:1-18.
35. Randelli P, Randelli F, Cabitza P, Vaienti L. The effects of COX-2 anti-inflammatory drugs on soft tissue healing: a review of the literature. J Biol Regul Homeost Agents 2010; 24:107-14.
36. Garzaro M, Pecorari G, Nadalin J, Raimondo L, Palmo A, Baccega M, Giordano C. Objective and subjective assessment of digestion after ingestion of an iced dessert in healthy volunteers. J Biol Regul Homeost Agents 2010; 24:215-20.
37. Greer JA, Park ER, Prigerson HG, Safren SA. Tailoring Cognitive-Behavioral Therapy to Treat Anxiety Comorbid with Advanced Cancer. J Cogn Psychother 2010; 24:294-313.
38. Marotta F, Harada M, Dallah ED, Yadav H, Solimene U, Di Lembo S, Minelli E, Jain S, Chui DH. Protective effect of a poly-phytocompound on early stage nephropathy secondary to experimentally-induced diabetes. J Biol Regul Homeost Agents 2010; 24:41-49.
39. Hellbom M, Bergelt C, Bergenmar M, Gijsen B, Loge JH, Rautalathi M, Smaradottir A, Johansen C. Cancer rehabilitation: A Nordic and European

perspective. Acta Oncol 2011; 50:179-86.

40. Ripa C, De Tommaso G, Lisa R, Lorenzi M, Melatini MC, Mazzanti I, Abbatecola A, Antonicelli R. Pulmonary embolism with minimal D-dimer increase - disagreement between clinic and laboratory: case report. J Biol Regul Homeost Agents 2010; 24:225-8.
41. Ahangari G, Shariati GH, Asadi MR, Ostadali MR, Ahmadkhaniha HR. Novel mutation detection of regulatory molecule dopamine gene receptors (D1-D5) encoding analysis on human peripheral blood lymphocytes in schizophrenia patients. Eur J Inflamm 2010; 8:145-52.
42. Tomei G, Sancini A, Cerratti D, et al. Effects on plasmatic androstenedione in female workers exposed to urban stressors. Eur J Inflamm 2010; 8: 175-81.
43. Galliera E, Locati M, Mantovani A, Corsi MM. Chemokine system: new inflammatory markers on the horizon. Eur J Inflamm 2010; 8:1-6.
44. Preetha SP, Devaraj H. Role of sulphated polysaccharides from *Sargassum wightii* in the control of diet-induced hyperlipidemia and associated inflammatory complications in rats. Eur J Inflamm 2010; 8:23-30.
45. Frati F, Scurati S, Puccinelli P, et al. Inflammation in respiratory allergy treated by sublingual immunotherapy. Eur J Inflamm 2010; 8:121-29.
46. Boonzaier A, Pollard A, Ftanou M, Couper JW, Schofield P, Mileshkin L, Henderson M. The practical challenges of recruitment and retention when providing psychotherapy to advanced breast cancer patients. Support Care Cancer 2010; 18:1605-13.
47. Genovese T, Melani A, Esposito E, Paterniti I, Mazzon E, Di Paola R, Bramanti P, Linden J, Pedata F, Cuzzocrea S. Selective adenosine A2A receptor agonists reduce the apoptosis in an experimental model of spinal cord trauma. J Biol Regul Homeost Agents 2010; 24:73-86.
48. Ciprandi G, Cirillo I. Rupatadine improves nasal symptoms, airflow and inflammation in patients with persistent allergic rhinitis: a pilot study. J Biol Regul Homeost Agents 2010; 24:177-83
49. Pollice R, Bianchini V, Conti CM, Mazza M, Roncone R, Casacchia M. Cognitive impairment and perceived stress in schizophrenic inpatients with post-traumatic stress disorder. Eur J Inflamm 2010; 8:211-19.
50. Shekhawat N, Vijayvergia R. Investigation of anti-inflammatory, analgesic and antipyretic properties of *Madhuca indica* Gmel. Eur J Inflamm 2010; 8:165-71.
51. Shaik-Dasthagirisaheb YB, Castellani ML, Tripodi D, et al. PGD2, IL-1-family members and mast cells. Eur J Inflamm 2010; 8:137-42.