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LETTER TO THE EDITOR

Stress resilience and survival among cancer patients: is there any absolute truth?

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Chronic stress has been reported to have an impact on cancer progression [1]. Recently, stress resilience in late adolescence has been connected with survival among patients suffering from cancer [1]. Low compared with high stress resilience has been linked to increased mortality in cancer patients [1]. It has been observed that individual variations in stress resilience may influence survival among men with some types of cancer [1]. It has been indicated that there is a significant relationship between low stress resilience and mortality among men suffering from cancer, particularly oropharyngeal cancer, upper respiratory tract cancers, prostate cancer, and Hodgkin lymphoma [1]. To date, the potential influence of stress susceptibility on cancer progression still remains unknown [1]. Formerly, chronic stress has been described to trigger tumor growth and angiogenesis in a mouse model of ovarian cancer through activation of the tumor cell cyclic AMP(cAMP)–protein kinase A (PKA)-signaling pathway by the β2 adrenergic receptor [2]. It has been speculated that β2-adrenergic activation of the cAMP–PKA-signaling pathway represents a major mechanism by which behavioral stress can increase tumor angiogenesis in vivo, thereby inducing malignant cell growth [2]. Later, it has been verified that across the occurrence of a wide range of adverse life events, mammalian immune cells show a conserved transcriptional response to adversity (CTRA) involving increased expression of a number of proinflammatory genes including interleukin-6 (IL-6) gene [3]. β2-adrenergic up-regulation has been recognized as one molecular mechanism by which chronic stress appears to promote the proinflammatory component of the leukocyte CTRA gene expression dynamic [3]. Concordantly, β2-adrenergic receptor antagonism has been documented to inhibit IL-6 expression [4]. Increased levels of the proinflammatory cytokine IL-6 have been detected in several types of cancer [5]. Increased levels of IL-6 have been connected with depression, fatigue, and disability in ovarian cancer patients [4]. Patients with ovarian cancer who had not developed recurrent disease by 1 year have been revealed to have more normalized levels of IL-6 [5]. It has been highlighted that the normalization of IL-6 is associated with improvements in fatigue, vegetative depression, and disability [5]. An important link has emerged between plasma IL-6 response to acute stress and early life adversity in healthy adults [6]. IL-6 represents a proinflammatory cytokine which has been found to be significantly linked to post-traumatic stress disorder [6]. IL-6 appears to be not a factor only implicated in the immune response, but in major physiological systems including the nervous system [7]. IL-6 has been demonstrated to be an integral part of the innate inflammatory response to a physical stressor [6]. IL-6 has been established to contribute to neurogenesis and in the response of mature neurons and glial cells in normal conditions and following a wide range of injury models [7]. An intricate interplay has been proposed to exist between stress and neuroimmune regulation in the neuropathology [6]. Greater acute IL-6 release and higher IL-6 concentrations over time have been shown in individuals with adverse experiences in early life than in controls without early life adversity [6]. Elevated IL-6 levels have been detected to precede classical Hodgkin Lymphoma (cHL) at least up to 4 years preceding diagnosis in presumably immunocompetent individuals [8]. The constant elevation in cHL risk with elevated levels IL6 across 4 or more years prior to diagnosis appears to suggest a B-cell-stimulatory environment that triggers the genesis of cHL [8]. IL-6 has been recognized to promote prostate cancer cell proliferation and inhibit apoptosis in vitro and in vivo [9]. Increased IL-6 levels have been identified in patients with untreated metastatic or castration-resistant prostate cancer and relate negatively to tumor survival and response to chemotherapy [9]. IL-6 has also been proved to be a gender-independent factor, serum

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levels of which appears to be higher in patients affected by laryngeal cancer than normal subjects [10]. Serum levels of IL-6 have been significantly related to progression of this type of cancer [10]. Taken together, low stress resilience may contribute to increased mortality among cancer patients by up-regulation of IL-6 expression. Stress resilience may influence cancer survival through various pathways, and in this contest, IL-6 appears to have a crucial role in the functional leukocyte CTRA network-linking stress resilience and cancer survival. In this light, IL-6 might be utilized as a biomarker for risk stratification, screening, and early diagnosis of cancer in future clinical prediction models. Strategies aimed to support cancer patients with emotional resilience and stress management should be inserted among tailored interventions designed to promote well-being and psychological resilience in people living with cancer.`

Compliance with ethical standards

Conflict of interest The author declares no potential conflicts of interest.

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