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Cancer: Stress and PAI-1

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Abstract

Cancer is a group of diseases that are characterized by the development of abnormal cells, which divide almost without limit, develop, spread without control anywhere in the body, losing the cells their ability to disappear by an anti- apoptotic action, essential process for malignant transformation and tumor development. The onset and development of cancer is associated with multiple causes and predisposing factors such as stress and psychosocial factors PAI-1 is a gene regulated by stress and is paradoxicallyinteracted in close relation with uPA in the development of tumors.

Keywords: Cancer; Tumors; Genomic; Stress; Medicine

Introduction

The main cause of death of patients suffering from cancer is the presence of metastasis, a complex process that leads to the survival and growth of unique subpopulations located in areas more or less distant from their primary tumor, this being related to the problem of resistance to habitual therapy in many cases [1-3]. Cancer research over the years has shown that it is a genetic disease, not always hereditary, whose expression of cellular genomic damage lies virtually in all cells of different tissues in humans and animals [4-7]. Oncogenic mutations, as a consequence of a genetic instability, leads to an accumulation of mutations of the gene, causing the initiation of the tumor and its progression [8,9]. This process of initiation and development of cancer is associated with multiple causes and predisposing factors such as viruses, chemical mutagen, radiation, stress and psychosocial factors [10].

Cancer and stress have historically been related to medicine. Galen (130-210 B.C.) in his study "DeTumoribus" indicates that women who express melancholy was more susceptible to cancer [11]. In this line, the presence of chronic alarms or emotional stressors such as depressions, fear, anxiety is observed with certain frequency in patients affected by cancer, finding among the most frequent [12-14]. Chronic stress stimulates the hypothalamic-pituitary-adrenal (HPA) -axis systems, with the release of glucocorticoids (cortisone in humans), and the sympathetic nervous system that regulates catecholamine levels (adrenaline noradrenaline), as the most important hormones in stress, and the regulation of the inflammatory response through immune cells [10]. In the same way, chronic stress favors tumor development, increased expression of metalloproteinase of the extracellular matrix and endothelial vascular growth factor, caused high levels of catecholamines and greater tumor progression activity [15]. However, some studies find little relationship between cancer risk and stress levels [16,17].

Discussion

Oxidative stress, the product of a cluster of reactive oxygen species/ reactive nitrogen species, as a consequence of endogenous or exogenous stressors, is present in many cancer cells, generating a cellular redox disequilibrium that may be related to a stimulation oncogenic, which generates DNA mutations, critical stage and strongly inherent to the etiology of cancer [18,19]. Currently there are findings that show that cellular and molecular responses to the action of stress are related to the development of cancer progression and metastasis [20].

The acute experimental stress (survival of the animal between 1 and 4 days), after the administration of endotoxin at minimum lethal doses as a stressor, causes changes in the anatomical structure and function, leading to a marked increase of expression of the Plasminogen Activator Inhibitor (PAI-1) main inhibitor of the urokinase-type activator (uPA) and possible cause of the high frequency of vascular infarcts in different organs, including the HPA axis [21-24]. PAI-1 is a gene regulated by stress and is paradoxically interacted in close relation with uPA in the development of tumors [25]. The plasminogen system components uPA, PAI-1 are promoters in tumor growth, in invasion and metastasis, for their action on angiogenesis and cell migration and are found in high concentration in cancer cells and in plasma samples [26-31]. There is convincing clinical evidence that PAI-1 is a key factor for the invasion of tumors and metastasis [32,33]. Both the activation system (uPA) and the inhibition of the plasminogen mechanism (PAI-1) are overexpressed in many cancerous processes and are considered an indicator of poor prognosis in patients with cancer [33-39]. All the studies indicated lead to the conclusion that PAI-inhibitors could represent a field with therapeutic possibilities [40-42].

Conclusion

Cancer is a very broad field within human pathology, constituting a frequent process with a high incidence of mortality. The onset and development of cancer is associated with multiple causes and predisposing factors such as stress and psychosocial factors, stressors that are very studied at present due to their social importance. Both the activation system (uPA) and the inhibition of the plasminogen

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mechanism (PAI-1) are overexpressed in many cancerous processes and are considered an unfavorable prognostic indicator for patients with cancer. PAI-1 is a gene regulated by stress and is paradoxically interacted in close relation with uPA in the development of tumors. All the studies indicated lead to the conclusion that PAI-1 inhibitors represent a field with therapeutic possibilities.

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