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Cancer related fatigue and cancer cachexia are the consequence of endocrine failure caused by persistent stress

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ABSTRACT

This study researches the cause of tumor, cancer related fatigue (CRF) and cancer cachexia (CC), and the relationship among tumor and CRF and CC.

Carcinogenesis is consequence of failure of tissue development. Tumor originates from tissue regeneration. The tumor cell is normal incomplete differentiated cell that stop in different phases of differentiation. Tumor promoter stimulates stem cell to proliferate. Carcinogen obstructs stem cell to differentiate. With tumor promoter and carcinogen, the tissue stem cells proliferate but cannot differentiate into mature cell, and form tumors. The disorder of biological signals cell proliferation and differentiation facilitates tumor development.

CRF and CC are consequence of endocrine hypofunction and failure caused by persistent stress. Nature factors and psychological factors stimulate organic stress. The significant change of stress is the activation of endocrine system. The persistent stress exhausts the capacity of endocrine glands or hormone receptors of target cells, and leads to endocrine hypofunction even failure. CRF and CC are clinical manifestation of endocrine hypofunction and failure.

Cancer is a local lesion, also is a systemic disease. As a local lesion, carcinogen obstructed stem cell to differentiate, developmental failure of local tissue forms tumor. As a systemic disease, cancer is related to natural physical, chemical, and biological factors, as well as negative spiritual factors. The material and spiritual factors induce persistent stress which eventually leads to endocrine hypofunction even failure and unbalance of homeostasis. The disorder of biological signals of cell proliferation and differentiation facilitates tumor development.

CRF and CC, as clinical manifestation of endocrine hypofunction and failure, have nothing to do with tumor size and type, but facilitate tumor development. CRF and CC are through all the course of systemic cancerous disease, and commonly precede tumorigenesis. Many patients have been found tumors because of symptoms of CRF and CC. Even if no tumor be found at that time, various tumors would be found in the follow-up.

For systemic cancerous disease, cachexia is the cause of death. Most cancer patients do not die of tumor, but of cancer cachexia. Eradicating tumor cell cannot cure systemic cancerous disease; on the contrary, the poisonous side effect of therapies usually speeds up the progress of CC and death. It is important for curing cancer cachexia and restoring the patient's constitution to prevent systemic cancer and improve the quality of life and prolong the survival.

Background

Cancer is related to natural physical, chemical, and biological factors, as well as negative emotion. Almost all cancer patients have symptoms of anorexia, fatigue, and emaciation.

Cancer related fatigue (CRF) is a kind of physical and psychological fatigue. CRF is painful experience of cancer patients. The causes of CRF are believed to be tumor, abnormality of muscle energy metabolism, parahypnosis, physiological rhythm anomaly, inflammation, stress, dysimmunity, and anomaly of hypothalamus pituitary axis hormone [1,2].

The significant feature of Cancer cachexia (CC) is progressive reduction of skeletal muscle. CC makes the patient skeletonization. CC is different from starvation. Starvation mainly reduces body fat, but CC mainly reduces skeletal muscle. Nutritional therapy cannot reverse CC. CC severely impact the quality of life and shorten the survival. Most cancer patients do not die of tumor but of CC ultimately. The therapies treating tumor usually speed up the progress of CC and death. CC is

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believed to be a primary, tumor-activated autoimmune chronic inflammatory response, and IL-6, IL-10, IL-8, TNFα, as well as other inflammatory factors play central role in CC [3,4].

Does cancer start as a small tumor and later spread, or is cancer a systemic disease with tumors only late stage symptoms, or a mixture of these. Dose tumor leads to CC, or does CC facilitate tumor development. There is no mode to explain the relationship among tumor and CRF and CC by now.

Aim

The aim of this study is to research the causes of tumor, CRF and CC, and the relationship among tumor and CRF and CC.

Theory

The cause of tumor

Carcinogenesis is consequence of failure of tissue development. Tumor originates from tissue regeneration. Tumor cell is normal incomplete differentiated cell that stops in different phases of differentiation. Tumor promoter stimulates stem cells to proliferate. Carcinogen obstructs stem cells to differentiate. With tumor promoter and carcinogen, the tissue stem cell proliferates but cannot differentiate into mature cell, and forms tumor [5]. The disorder of biological signals of cell proliferation and differentiation facilitates tumor development.

The cause of cancer related fatigue and cancer cachexia

Fatigue and cachexia are common in cancer patients, but fatigue and cachexia also appear in aged people and other diseases. CRF and CC are consequence of endocrine hypofunction and failure caused by persistent stress.

Stress is primary non-specific physiological response to various stimuli. Stress helps body to coordinate organic function to cope with internal and external changes. Nature factors and psychological factors all can stimulate organic stress. The significant feature of stress is the activation of hypothalamic pituitary adrenal axis. Proper stress helps organism to overcome pathogens and recover quickly. The intense or/and persistent stress would exhaust the capacity of the endocrine glands or hormone receptors of target cells, and leads to endocrine failure and unbalance of homeostasis.

(1) Hypoadrenocorticism makes patient debility, fatigue, inappetence, emaciation, nausea, emesis, celialgia, diarrhea, hypotension, dizziness and so on.
(2) Hypothyroidism makes patient chill, somnolence, slow response, rough skin and so on.
(3) Hypogonadism makes patient sexual hypoactivity, erectile dysfunction (ED), menstrual disorder.

Most cancer patients have the symptoms of debility, fatigue, inappetence, emaciation, nausea, emesis, celialgia, diarrhea, hypotension, dizziness, chill, somnolence, slow response, rough skin, sexual hypoactivity, erectile dysfunction (ED), and menstrual disorder. Those symptoms are consistent with that of hypoadrenocorticism, hypothyroidism and hypogonadism. CRF and CC are clinical manifestation of endocrine hypofunction and failure.

The relationship among tumor and cancer related fatigue and cancer cachexia

Cancer is a local lesion, also is a systemic disease. As a local lesion, carcinogen obstructed stem cell to differentiate, developmental failure of local tissue forms tumor. As a systemic disease, cancer is related to natural physical, chemical, and biological factors, as well as negative spiritual factors. The material and spiritual factors induce persistent stress which eventually leads to endocrine hypofunction even failure and unbalance of homeostasis. The disorder of biological signals of cell proliferation and differentiation facilitates tumor development.

CRF and Many patients have been found tumors because of the symptoms of inappetence, fatigue, and emaciation. Even if no tumor be found at that time, various tumors would be found in the follow-up.

Cancer, as a local lesion, is rarely life-threatening. Patient can survive normally with tumor, and local treatment has good effect. Cancer as systemic disease, CC is the cause of death. Most of cancer patients do not die of tumor, but of CC. Eradiating tumor cell cannot cure the systemic cancerous disease; on the contrary, the poisonous side effect of therapies can speed up the progress of CC and death. For the systemic cancerous disease, it is important for curing CC and restoring the patient's constitution to improve the quality of life and prolong the survival.

Data: The test of this theory

1. Immune cell has endocrine hormone receptors on the surface, and endocrine cell has cytokine receptors. Endocrine system can regulate the development of immune system, maturity of immune cell, and immune response by various hormones. Immune system also affects endocrine system by cytokines. For example, inflammatory factors, like IL-1, IL-6, TNFα, can activate the hypothalamic-pituitaryadrenal axis [6].
2. Cancer cachexia exist excessive inflammatory response, there are an amount of inflammatory factors, such as IL-6, IL-10, IL-8 and TNFα. It is believed that IL-6, IL-10, IL-8, and TNFα play a core role in cancer cachexia, these inflammatory factors could trigger a series of neuroendocrine changes [7].
3. The effects of chronic stress may increase incidence of cancer possibly via shortening of telomeres [8].
4. The disorder of biological signals has relationship with tumorigenesis [9].

Methods

The method to verify this theory is as below.

1. To examine the changes of endocrine function in cancer patients with cancer-related fatigue and cancer cachexia.
2. To find more biological signals of cell proliferation and differentiation.
3. To examine the changes of biological signals of cell proliferation and differentiation in cancer patients with cancer-related fatigue and cancer cachexia.

Discussion

Medical mode has transformed from biomedical mode to socio-psycho-biomedical mode. However, mainstream medicine is still accustomed to using viewpoint of biomedical mode to study the disease. Biomedical mode believes that the measurable morphological changes in organic, cellular, biomolecular level are the causes of disease. By this viewpoint, cancer is undoubtedly a molecular disease. Tumor is different from normal tissue, tumor cell is different from normal mature cell, the genetic phenotype of cancer cell is different from that of normal mature cell. There are so many measurable morphological changes in organic, tissular, cellular, biomacromolecular level, so cancer is undoubtedly a kind of genetic molecular disease. This is why the gene mutation theory is generally accepted and followed by mainstream medical community.

Socio-psycho-biomedical mode believes that health is organic functional coordination and balance, and disease is unbalance of homeostasis. By this view, we can recognize a systemic cancerous

disease. We can gain a better understanding of why cancer is related to natural physical, chemical, and biological factors, as well as negative spiritual factors, and why most cancer patients have symptoms of CRF and CC.

Cancer, as a local lesion, is rarely life-threatening. Patient can survive normally with tumor, and local treatment has good effect. Strategy of early detection and early therapy of cancer detects and treats more and more early local cancer that maybe do not need treatment. Cancer as systemic disease, systemic failure is the cause of death. Eradiating tumor cell cannot cure systemic cancerous disease; on the contrary, poisonous side effect of therapies speeds up the progress of cancer cachexia and death. This is why we query that eradiating tumor cell can cure some cancer but cannot cure all cancer, it is difficult to lengthen the survival time and improve quality of life of patient with CC by killing tumor. For the systemic cancerous patient, it is important for curing cancer cachexia and restoring the patient's constitution to prevent cancer and improve the quality of life and prolong the survival.

Declaration of interests

The author Shaoqing Lai has no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2018.12.018.

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