


Precise medication for tumor patients in the context of mental stress

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Abstract

Cancer is the leading cause of disease-related death worldwide due to its late diagnosis and poor outcomes. Precision medicine plays an important role in the treatment of tumors. As found for many types of tumors, mental stress plays a vital role in the promotion and progression of tumors. In this paper, we briefly introduce the manifestation and effects of mental symptoms in tumor patients. We next specifically discuss the multiple roles of precision medicine in the tumor therapy. Finally, we also highlight the precision medicine strategy for psychiatric symptoms in tumor patients, which promises to enhance the efficacy of tumor therapy.

Keywords

tumor, mental stress, precise medication, treatment, target

Introduction

Tumor refers to an abnormal proliferation of cells in the body caused by a variety of carcinogenic factors, including chemicals, ionizing radiation, viruses, genetic mutations, and so on, which generally has a significant impact on patients' quality of life and may shorten their lives¹. Due to habits and customs, environmental pollution, mental stress, genetics and other factors, the incidence of tumors has continued to increase. Although there are surgical procedures, chemotherapy and radiotherapy and other treatment methods, the life quality of patients has not been significantly improved due to serious adverse reactions during the treatment of tumors². Therefore, it is of great significance to introduce the concept of precision medicine for cancer patients. Precision medicine is an emerging method of disease prevention and treatment that takes into account differences in individual variability in genes, environment, and lifestyle. Not only can it improve the drug efficacy, but also reduce the adverse reactions to a certain extent³.

The nervous system plays an important role in regulating the stability of the body. It releases neurotransmitters such as acetylcholine, epinephrine, dopamine, and participates in regulating various life activities to maintain the balance of the body environment⁴. Previous studies have indicated that psychological aspects should be considered in the

progress of breast cancer diagnosis and treatment⁵. As a crucial cancer-promoting factor, psychological factors are gradually being valued. Prior research have shown that psychological factors are closely related to the occurrence and development of malignant tumors and prognosis⁶. Appropriate psychiatric intervention can effectively improve tumor treatment, but the mechanism of antipsychotics is complex, so the applicability of patients should be fully considered⁷. Based on the recognized research,

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Table 1. The Symptoms of Mental Stress and Corresponding Treatment drugs.

Mental stress	Character	Medication
Anxiety	A disruptive feelings of uncertainty, dread, and fearfulness, exhibiting a variety of medical symptoms, including palpitations, tremors, nervousness, shortness of breath, diaphoresis, and fear.	Benzodiazepines; Alprazolam; Lorazepam
Depression	A long-term pessimistic, painful, and desperate mental state, accompanied by a wide array of symptoms affecting somatic, cognitive, affective, and social processes.	Serotonin reuptake inhibitors (SSRIs); Fluoxetine; Sertraline
Delirium	An acute confusional state that is common and costly and is associated with significant functional decline and distress	Antipsychotics; Haloperidol; Chlorpromazine
Insomnia	A state of difficulties in falling asleep, maintaining sleep, and early morning awakening, and coupled with daytime consequences such as fatigue, attention deficits, and mood instability	Nonbenzodiazepine hypnotics; Zolpidem; Benzodiazepines

precise medication for tumor patients in the context of mental stress is significant for tumor patients. It fully considers the patient's genetic makeup, lifestyle, and environmental factors, and establishes exclusive treatment strategies in accordance with individual patient differences.

The Manifestation of Mental Stress in Tumor Patients

It is inevitable that most tumor patients are accompanied by certain psychiatric symptoms, and psychiatric symptoms can significantly affect the occurrence and progression of the disease. Moreover, the mental state of tumor patients directly affects the patient's prognosis and quality of life⁸. The Institute of Medicine made specific recommendations in 2008 for the psychological care of cancer patients: Attending to psychosocial needs should be an integral part of quality cancer care. All components of the health care system involved in cancer care should explicitly incorporate attention to psychosocial needs into their policies, practices, and standards of clinical care⁹.

Tumor patients often have complex mental symptoms, manifesting as anxiety, depression, delirium, insomnia, tension, fear, and other psychology¹⁰. The psychological characteristics of tumor patients generally change in stages with the development of the disease. When they first learn of the disease, most of them have a skeptical attitude and immense stress. Some patients think that having a tumor is tantamount to being sentenced to death, and they would be anxious, depressed, and nervous. Mental symptoms such as anxiety are related to the diagnosis of the disease and the treatment of cancer. Previous studies have shown that cancer-related diagnosis can distinctly increase the patient's anxiety, thereby having a negative impact on the treatment of patients' diseases. Based on the final biopsy results, the study used a rank-sum test for analysis and concluded that the vast majority of patients experienced a remarkable increase in anxiety after cancer diagnosis¹¹. Additionally, patients may have situational anxiety, such as neurotic reactions before or after surgery or anxious while waiting for treatment. During the progress of cancer patients, anxiety usually increase and may increase abnormally after the end of cancer treatment, since without active

treatment interventions, cancer patients may be more sensitive and fearful¹². In the long course of treatment, some families have financial difficulties who are unable to afford expensive medical expenses, so they refuse to treat and have a negative attitude. Some patients cannot withstand the effects of radiotherapy, chemotherapy, and surgery, who will show tempers of irritability and rejection. With the deepening of tumor research, researchers are paying more and more attention to the relationship between negative emotions and tumor diseases, and some experts have proposed that negative emotion or major psychological shock is closely related to the occurrence, development and outcome of tumors system¹³. A secondary analysis showed that decreased depressive symptoms can obviously prolong survival in patients with metastatic breast cancer¹⁴. The survival time of tumor patients is closely related to the patient's psychological status. Properly adjusting the psychological status of cancer patients can significantly extend the patient's survival time.

Depression, anxiety and other mental symptoms tend to be characterized by chronic course and impairment of social function (Table 1). These symptoms have a negative impact on the immune function, quality of life, and tumor treatment of cancer patients. The psychological response of tumor patients can often reach a considerable degree, and affect the life quality of an individual in many ways¹⁵. It has been reported that long-term survivors of acute lymphoblastic leukemia in children and adolescents are prone to symptoms of inattention, hyperactivity and drug resistance after receiving chemotherapy alone. On top of that, the incidence of inattention symptoms, obsessive-compulsive disorder, oppositional defiant disorder, attention deficit hyperactivity disorder, and generalized anxiety disorder are higher¹⁶.

The Effects of Psychiatric Symptoms in Tumor Patients

The occurrence of psychiatric symptoms in tumor patients is a common phenomenon. Its main manifestations are changes in subjectivity, emotions, feelings, and cognition, which have a crucial impact on the life quality of patients¹⁷. The pathogenesis of psychiatric symptoms is more complex,

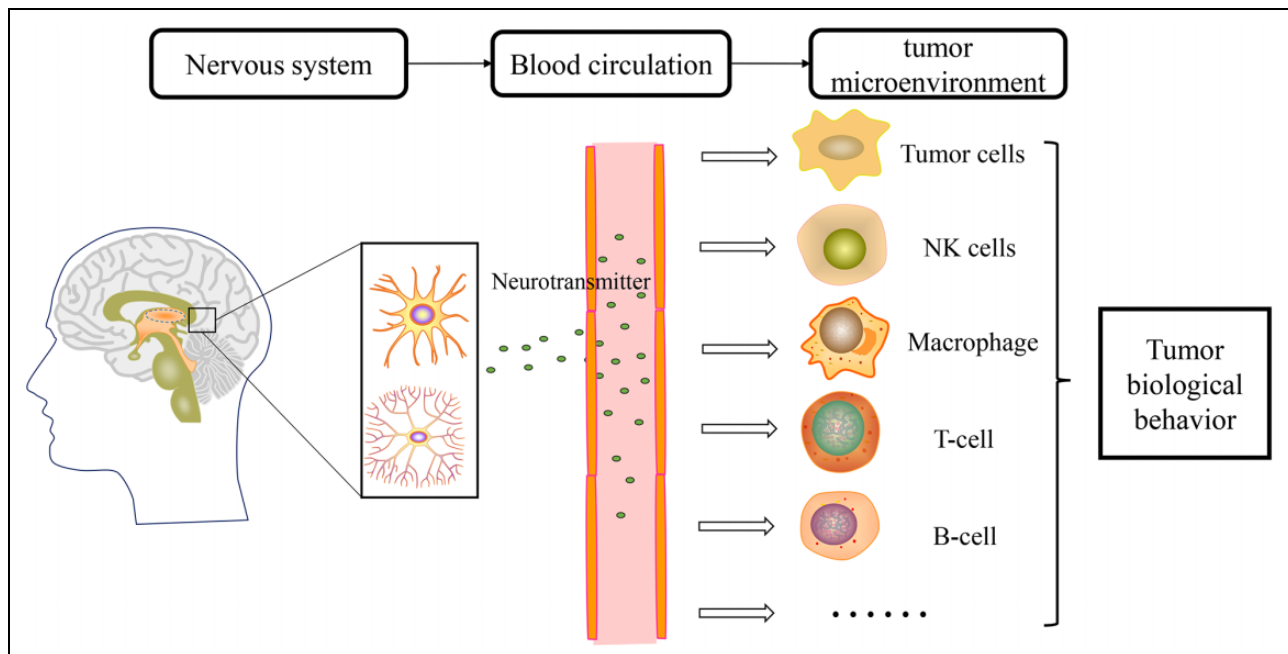


Figure 1. The influence progress of mental stress on tumor biological behavior.

which is widely acknowledged as the result of the interaction of comprehensive factors. Mental symptoms can have multiple effects on patients with tumors, mainly manifesting as immune dysfunction, enhanced tumor metastasis and invasiveness, and so on (Fig. 1).

Immune Function

Recent studies have shown that the brain and immune system have a mutual interaction. The brain can regulate peripheral immune function through the HPA axis and the direct nerves involved in governing the immune organs. The information on peripheral immune activity can also be transmitted to the brain through nerve and humoral pathways. For example, immune cells affect the central nervous system by activating the afferent vagus nerve or secreting cytokines¹⁸. Many structures in the cerebral cortex, basal forebrain, midbrain, and brainstem are related to immunity, especially the hypothalamus and limbic system as the regulatory center of the neuroendocrine and autonomic nervous system, which provide an important anatomical basis for psychological neuroimmunomodulation^{19,20}. Studies have confirmed the possible mechanism contributing to the negative psychological emotion of tumor patients to reduce their immune function is that anxiety and depression as the source of psychological response stimulate the body to produce a series of non-specific responses. The negative psychological emotions mentioned above cause the body's immune surveillance function to decline, reduce the killer cell activity and the number of T cells along the nerve-endocrine-immune axis. With the participation of carcinogens and cancer-promoting factors, they can be prone to lead to tumorigenesis and progression²¹.

The vagus nerve is a mixed nerve with a paired structure, whose motor fibers act as suspicious nuclei, parallel to the glossopharyngeal nerve. It can regulate the body's physiological response to environmental changes, injuries and infections. In the immune system, electrical stimulation of the vagus nerve inhibits the release of cytokines, thus reducing tissue damage and also relieves inflammation-mediated damage in endotoxemia, sepsis and other cytokine-dependent inflammatory disease models²². This neural circuit, called inflammatory reflex, requires action potentials in the vagus nerve, and acetylcholine interacts with the $\alpha 7$ subunit of the nicotinic acetylcholine receptor (nAChR) expressed on membrane of macrophages so as to produce cytokines in the spleen. Moreover, vagal nerve fibers terminate in the celiac ganglia, where the axons project onto the splenic nerve to dominate the nerve cell body of the spleen²³. Electrical stimulation of the vagus or splenic nerve above the celiac ganglion itself can significantly inhibit tumor necrosis factor- α (TNF- α) produced by macrophages in the red pulp and marginal regions²⁴.

Tumor Invasion and Metastasis

Tumor tissue is usually surrounded by many nerve fibers, and there are many types of neurotransmitter receptors on the surface of tumor cells. After neurotransmitters trigger the receptors, signal pathways can regulate tumor cell proliferation, angiogenesis, invasion and transfer. Psychosocial stress can affect the function of the sympathetic nervous system or the hypothalamus-pituitary-adrenal axis, changing the levels of catecholamine neurotransmitters and brain-derived neurotrophic factors, and affecting tumor growth and development²⁵.

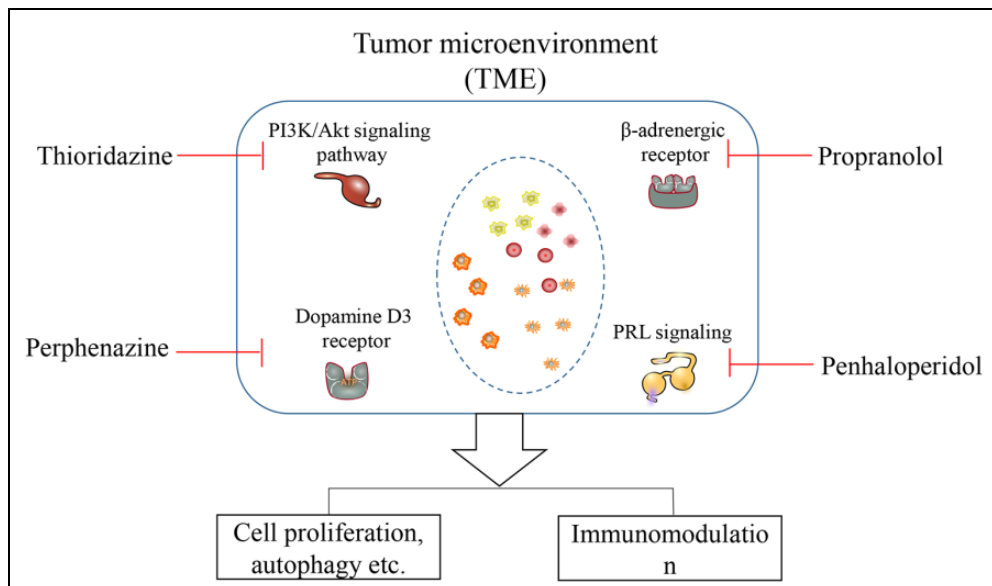


Figure 2. The mechanism of anti-psychotic drugs in tumors.

Invasion and metastasis are important characteristics of tumor cells and one of the reasons for high tumor mortality. Tumor invasion and metastasis are related to many factors and affected by many signal factors. Neurotransmitters mediate tumor invasion and metastasis by acting on tumor receptors²⁶. Stress can induce sympathetic nervous system (SNS) activation, which has no significant effect on the growth of primary tumors. However, it can enhance the metastasis and spread of tumors by affecting primary tumor metastasis and tumor cell extravasation. In addition to stress, other physiological or pharmacological substance having effect on SNS activity may also affect cancer progression²⁷. Animal experiments have shown that chronic behavioral stress leads to increased levels of catecholamines in tissues of orthotopic mouse models, increased tumor burden, and aggressive growth of ovarian cancer cells. These effects are mainly mediated by β -adrenergic receptors, activating cyclic AMP (cAMP)-protein kinase A (PKA) signaling pathway in tumor cells. A marked increase in angiogenesis and enhanced expression of VEGF, MMP2 and MMP9 is observed in tumors of stressed animals²⁸. These data indicate that mental symptoms such as stress and depression can lead to increased tumor proliferation and invasiveness.

The Effects of Antipsychotics on Tumor Patients

Cancer is not only a serious physical disease, but also a serious mental and psychological disease. Clinical studies have found that mental and psychological factors are closely related to the occurrence and development of tumor. Long-term mental stress can increase the risk of cancer, and cancer often affects the emotional and social functions of patients, thus impeding the treatment of tumor. Some studies have confirmed that long-term mental stress can promote tumor

progression and reduce the body's immune function^{29,30}. Appropriate intervention for the psychiatric symptoms of cancer patients can effectively delay the progression of the disease and improve the level of cancer treatment. Antipsychotics were originally used to control psychiatric symptoms such as Depression, anxiety and Delirium. With the deepening of research, some antipsychotic drugs have been used in the treatment of cancer³¹.

Thioridazine (TZ), an antipsychotic drug, can make multidrug resistant (MDR) cancer cells sensitive to cytotoxic agents to which they were initially resistant, and has anti-proliferation properties and apoptosis-inducing properties in various tumor cell lines³². Sokbom Kang's research also indicates that thioridazine can significantly increase the apoptosis rate of cervical cancer and endometrial cancer cells by targeting the PI3K/Akt/mTOR/p70S6K signaling pathway³³. In addition, adding perphenazine with good D3 blocking properties to current standard treatment of resection followed by temozolomide and irradiation may deprive glioblastoma of the trophic functions previously subserved by dopaminergic signaling on SVZ cells, thus prolonging survival of glioblastoma patients³⁴. Propranolol (Pro) is a non-specific β -adrenergic blocking drug that can competitively prevent catecholamines from binding to receptors. The anti-tumor activity of propranolol has been confirmed in a variety of cancers. Propranolol can be used as an effective immunomodulator, which can significantly increase the levels of IL-2, IL-4, IL-12, IL-17, and IFN- γ cytokines, and induce cellular immune responses against breast cancer³⁵. Prasad Dandawate, and so on showed that antipsychotic drugs, such as penhaloperidol, can block PRL signaling in pancreatic cancer cells to reduce their proliferation, induce autophagy, and slow the growth of mouse xenograft tumors³⁶ (Fig. 2).

Antipsychotic drugs have sedative, anti-injury, and anti-vomiting properties, as well as anti-cancer properties, which can be used as adjuvant drugs for the treatment of cancer complications, metastasis, and side effects of chemotherapy³⁷. Many in vitro and in vivo studies have shown the antipsychotic drugs have beneficial effects in anti-cancer. So Antipsychotic drugs are required for treatment purposes, but it may cause severe side effects in patients⁷. Therefore, based on precision medical strategies, the addition of effective doses of antipsychotic drugs based on the mental stress state of cancer patients and anticancer drugs can improve cancer treatment, thereby improving the quality of life of patients.

The Importance of Precision Medicine for Tumor Patients

Precision medicine is a cutting-edge medical concept and medical model based on individualized medicine, developing with the rapid progress of genome sequencing technology and the cross-application of bioinformatics and big data science³⁸. Its essence is to analyze and identify, verify, and apply biomarkers for large sample populations and specific disease types through the application of genomics, proteomics and other leading-edge medical technologies to accurately find the cause as well as target point of treatment and classify different states and stages of disease. Finally, it's supposed to realize the purpose of personalized and precise treatment for particular disease and specific patients, and improve the benefits of disease prevention, diagnosis and treatment³⁹. Cancer is the consequence of the long-term effects of environmental factors and genetic factors. After carcinogenic factors enter the body, response varies considerably in mode and intensity from individual to individual. Many tumor cells are accompanied by characteristic genetic mutations, and each cancer patient has its own genetic imprint, tumor markers, different types of mutations psychiatric symptoms age and gender⁴⁰. Based on the concept of precision medicine, we aim to find the cause of the disease from the genetic level, use the right medicine to fight the tumor precisely, and improve the survival rate of tumors.

Disease prevention and control. New tumor marker inspection technology improves early screening of tumors. Different from traditional imaging methods, endoscopy and other inspection methods, the new tumor marker test can efficiently judge the style of tumors by detecting some tumor markers in blood samples^{3,41}. Precision medicine enables the effectiveness of cancer pre-control to be improved remarkably. Compared with traditional biopsy, cancer blood test has advantages over it. The tissue used for biopsy is taken from a certain part of the tumor and therefore provide limited amount of genetic information on account of its local sampling. In contrast, blood test results can provide more comprehensive tumor DNA information. By identifying certain markers of a specific tumor in blood, including ctDNA

(tumor cell circulating DNA), miRNA (small molecule RNA), and so on, the appearance of a tumor can be judged efficiently and accurately⁴². Microscopic changes in tumor DNA often precede changes in tumor tissue growth, so blood tests can help doctors adjust treatment options in a timely manner. Liquid biopsy, especially "serum-based miRNA" detection technology, is currently mainly used for early screening of gastric, lung, and breast cancer. This shows that the traditional medicine is transitioning to precision medicine⁴³.

Previous studies also have shown that biomarkers play an important role in the differential diagnosis of various tumors. The study used mass spectrometry to identify a cell surface proteoglycan, glypican-1(GPC1). It is specifically enriched in exosomes derived from cancer cells. Researchers used flow cytometry to monitor, and isolate GPC1 (+) circulating exosomes (crExos) from cancer patients' sera. In particular, GPC1 (+) crExos was detected in the serum of patients with pancreatic cancer, with absolute specificity and sensitivity. It distinguishes healthy subjects and patients with benign pancreatic disease from patients with early or advanced pancreatic cancer. GPC1 (+) crExos levels are related to tumor burden and survival of patients before and after surgery, and they carry specific KRAS mutations. GPC1 (+) crExos can be used as a potential non-invasive diagnostic and screening tool for the detection of early pancreatic cancer to promote possible therapeutic surgical treatment⁴⁴. Exosomes contain proteins from cells of their origin and are readily available in plasma. It is considered as a promising biomarker in NSCLC. In the study, we explored the potential of exosomal protein profiles in all stages of lung cancer diagnosis and various histological subtypes. By comparing the results of labeling exosomes with corresponding antibodies in the plasma of lung cancer patients and normal people, we found that CD151, CD171, and tetraspanin 8 are the most significant distinguishing factors between patients with all histological subtypes of cancer and non-cancer patients. These findings prove that the exosomal protein profile is a promising diagnostic tool for lung cancer, independent of staging and histological subtypes^{45,46}. These data show that precision medicine can significantly strengthen the disease prevention and control of tumor patients.

Treatment and adverse reactions. Increasing evidences show that cancer is a complex and diverse disease. Patients may show similar symptoms and have the same pathological changes, but they may be caused by completely different genetic changes. It's due to heterogeneity that the response rates of patients with the same type of cancer to the currently available drugs vary greatly. For example, when treated with traditional radiotherapy and chemotherapy, patients may have several distinct responses. In summary, only a portion of cancer patients respond to a particular treatment, and the point is that we cannot predict which patients will benefit. Since the sensitivity and drug resistance of different tumor individuals to drugs cannot be judged before treatment,

many patients often suffer from unnecessary treatments and side effects^{47,48}. Most cancer treatments require chemotherapy, and chemotherapy drugs are called “cytotoxic drugs.” While killing tumors, other normal tissues are also eliminated by side effects. Before the advent of targeted drugs, the average effective rate of chemotherapeutic drugs was only 25% to 30%⁴⁹. With the development and popularization of precision medicine, the use of precision medicine to match patients with sensitive medications can avoid the side effects of other insensitive treatments, and further find sensitive and effective medicines for them, which can achieve the ideal therapeutic effect with a small amount of cost⁵⁰.

Due to individual differences in human, different patients have different tolerances to different drugs, so the use of precise treatment methods will help to formulate suitable treatment plans for different patients based on drug resistance. According to relevant research, lung cancer is classified into several different types, and the gene expression of each type is quite different. Owing to genetic, environmental and other factors, patients with the same type of cancer will have different effects and adverse reactions to the same drug. Therefore, based on the method of gene detection, finding the differentially expressed genes of each patient and selecting the corresponding targeted drugs can specifically treat the disease and reduce the adverse reactions of the drugs^{51,52}. Gefitinib is suitable for first-line treatment of advanced non-small cell lung cancer with EGFR 19 exon deletion mutation and EGFR 21 exon mutation. The objective response rate (ORRs) for EGFR-mutated NSCLC is up to 67%. However, if NSCLC patients have no mutations in EGFR 19 and EGFR 21, the efficacy of gefitinib will be significantly reduced. All patients in the study were treated with gefitinib and tested for EGFR mutations by using the direct DNA sequencing and amplified refractory mutation system (ARMS). The results showed that the median progression-free survival (PFS) of patients with EGFR mutations was obviously higher than that of patients with wild-type tumors. In terms of objective response rates and overall survival (OS), patients with EGFR mutations were also significantly different from patients with wild-type tumors⁵³.

The precision medicine strategy for psychiatric symptoms in tumor patients. Psychiatric symptom is one of the most important factors affecting tumor treatment and prognosis. Cancer-related fatigue is a typical psychiatric symptom that is common in cancer patients. It is a painful, persistent subjective feeling of fatigue, disproportionate to activity, and often accompanied by dysfunction. Studies have shown that it is closely related to the treatment of the disease and factors such as pain, depression and anxiety caused by the tumor itself⁵⁴. Under chronic psychological stress, signals from brain regions, such as blue spots and the hypothalamic ventral median nucleus, can cause disturbances in HPA axis and sympathetic nerve function, leading to the increased release of catecholamine neurotransmitters mainly including norepinephrine (NE) and adrenaline (AD). On the contrary,

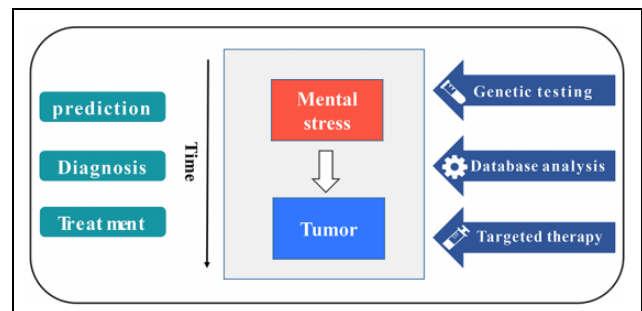


Figure 3. The precision medicine strategy for psychiatric symptoms in tumor patients.

dopamine (DA) levels decrease. AD and NE can promote tumor cell proliferation, angiogenesis, invasion and metastasis, while DA has the opposite effect⁵⁵. Epidemiological studies have also shown that psychosocial support can improve the prognosis of patients with metastatic breast cancer. During tumorigenesis and development, the release levels of correlated cytokines and chemokines in the tumor microenvironment will change⁵⁶. According to the study, interleukin 1 receptor antagonist and soluble tumor necrosis factor receptor 1 are associated with general severity and psychotic symptoms in schizophrenia and bipolar disorder⁵⁷. Therefore, based on the concept of precision medicine, we can formulate individualized treatment plans based on the types of psychiatric symptoms of tumor patients and the changes in the types and release of related neurotransmitters (Fig. 3).

Genetic testing. Genetic testing, as the name suggests, is the detection of genetic loci by sequencing or other means. Genetic testing in the past only detected abnormalities in the number of chromosomes, and new sequencing technology allowed for a clearer understanding of gene sequences. DNA sequencing can be used to determine the sequence of a single gene, a larger genetic region, a complete chromosome, or the entire genome of any organism. Cancer is the most common genetic disease, and all cancers are caused by abnormal DNA sequences. Although different cancers have different causes and symptoms, they can all be explained by genetic mutations⁵⁸. Studies have shown that mental factors, such as stress and depression, can cause tumor invasion and increase through a certain mechanism⁵⁵. Therefore, the corresponding mental factors probably related to the gene mutation. With the development of genetic testing technology, the understanding of mental stress in relation to cancer can be extended to the molecular level, which can complement traditional diagnosis. Based on the second-generation gene sequencing technology and the results of cancer gene tests, “individualized medicine” is introduced into the clinical settings, allowing doctors to conduct targeted cancer treatment on the basis of patients’ genetic information.

Database analysis. Big data analysis provides powerful technical support for precision medicine and realizes the computer-medical cross-border collaborative development. Biological big data are composed of multi-dimensional biological data such as patient medical records, diagnostic information, and lifestyle. Large amounts of data, strong heterogeneity, and high value are the characteristics of biological data set. Precision medicine is developed based on the integration of genetic data, biological samples, daily life information, and other data from large-scale populations. It brings together a large amount of data to discover its beneficial value. Big data analysis methods can effectively analyze and mine big data of biological information, which is conducive to in-depth research on the pathogenesis of diseases and promote the development of prevention and treatment methods. Through the analysis and utilization of medical big data, personalized medical solutions can be gradually implemented⁵⁹. By studying the links between susceptibility to specific diseases, genetic variation and response to specific drugs, genetic and genetic variation factors are fully taken into account in the development and use of drugs⁶⁰. With the support of medical big data, tumor patients with different mental stress can take relatively optimized treatment plans, which can help patients use more reasonable drug dosages to achieve the purpose of improving treatment effects and reducing side effects.

Targeted therapy. Targeted therapy is actually a pathophysiological treatment, which aims to block key receptors in the development of tumors and corrects their pathological processes. Because of their targeted and non-cytotoxic properties, these drugs mainly regulate and stabilize tumor cells instead of producing systemic cytotoxic effects like traditional chemotherapy drugs. Clinical practice proves that molecular targeted therapy can not only accurately “kill tumors,” but also delay tumor development and prolong the survival time of patients with tumors. Targeted therapy is the basis of precision medicine. Tumor-targeted therapy uses drugs or other substances to interfere with specific molecules (proteins) involved in tumor growth, division and spread, blocking the growth and spread of tumors⁶¹. In chronic stress, dopamine depletion creates a relaxed microenvironment for tumor growth. Reverse transcription polymerase chain reaction (reverse transcriptase-PCR) and Western blotting were used to analyze the expression of dopamine receptors (DR1-DR5). The results indicate that in this chronic stress model, compared with non-stress agonists, tumor norepinephrine levels continue to increase, while dopamine levels decrease significantly. Based on the concept of targeted therapy, the study finds that dopamine treatment can block the increase of stress-induced angiogenesis, inhibit cell viability and promote apoptosis to a great extent⁵⁵.

Targeted therapy is currently the focus of many anti-tumor drug developments. They are the cornerstone of precision

medicine, which apply human genetic and protein information to preventing, diagnosing, and treating diseases⁶². Drugs used to treat psychiatric symptoms generally have serious adverse reactions, which can easily cause symptoms such as drowsiness. Therefore, through genetic analysis of tumor patients, targeted therapy based on the patient’s psychiatric symptoms can improve efficacy and reduce adverse reactions.

Summary

There are many factors related to the occurrence and development of tumors. One of the most important factors is mental stress. Increasing evidences suggest that mental stress plays a vital role in the progression of tumor disease. Mental stress can directly affect the expression levels of genes related to proliferation, apoptosis, angiogenesis, adhesion, and metastasis, and change the biological behavior of tumors as well²⁸. Cancer patients under chronic mental stress can induce the formation of new blood vessels, laying a foundation for tumor invasion and metastasis. Under stress, the secretion levels of blood-related neurotransmitters will change, which directly affects tumor metastasis to distant organs. In addition, mental stress can affect the body’s immune system. A variety of neurotransmitter receptors are distributed on the surface of immune cells. Neurotransmitters have important regulatory effects on the maturation, differentiation, proliferation, and activation of immune cells. Psychological stress can reduce the killing ability of natural killer cells to target cells and the ability of specific immunity to recognize tumor cells through neuro-immunomodulation, which provide the relaxed environment for tumor cells to invade and migrate in the body⁶³.

Various preclinical and clinical studies have shown that targeted stress therapy may be a promising strategy that can be used along with existing immunotherapy strategies⁶⁴. Utilizing these strategies to treat tumors may lead to more breakthroughs, which can overcome the limitations of current treatments. However, these findings require a more solid research foundation before clinical application. Therefore, for tumor patients, a more in-depth exploration of the mechanism of stress in tumor tissues is needed. Precision medicine is an important method in tumor treatment, which can achieve the goal of “less medication and higher efficacy.” Precision medicine for mental stress may be more effective in the treatment of tumors. By analyzing the subject through a comprehensive epidemiological model, we fully understand the value of collecting mental stress indicators on the prognosis of patients. Further in-depth research promises to provide a more reliable foundation for targeted stress treatment of tumors.

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Author Contributions

Qishun Geng and Zhibo Shen are responsible for the acquisition, analysis and interpretation of the data, drafting of the manuscript. Others contributed to the critical revision of the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

There are no subject in this article and informed consent is not applicable.

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