

Theoretical basis and clinical application of tumors due to spleen deficiency and dampness

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Abstract: Spleen deficiency and dampness is one of the pathogenesis of tumor. Spleen is the source of Qi and blood biochemistry. Spleen deficiency leads to the imbalance of Ying and Wei, which is a prerequisite for the development of tumors. Dampness causes illness and disease and is the key to the development of tumors. Both spleen deficiency and dampness promote the development of disease. From a modern medical perspective, spleen deficiency and dampness are associated with immune dysregulation, angiogenesis, hypoxia, dysbiosis of the intestinal flora, and the production of adhesion molecules, which are factors in tumor formation and metastasis. The clinical case of tumor caused by spleen deficiency and dampness is analysed and applied.

Keywords: spleen deficiency, dampness, tumor

1. Introduction

Malignant tumor is the biggest killer of human beings and poses a serious threat to human health. In recent years, the survival rate of malignant tumors has gradually increased worldwide, and in China, although the survival rate has improved, there is still a gap with developed countries [1-2]. The understanding of tumor in traditional Chinese medicine has a long history. As early as Yin ruins, there was a record of the word "tumor"^[3] in oracle bones. In the pre-Qin calendar, there is a record of "ulcerative doctor tube swelling, tube ulcer, tube ulcer rupture". This shows that the treatment of the disease at that time was multidisciplinary, and the tumor was treated by the ulcer doctors. In the period of Spring and Autumn and Warring States, the Huang Di Nei Jing had a deeper understanding of the name, symptoms and etiology of tumors. The recorded diseases such as "intestinal bacteria", "obstruction", "accumulation" and "choking diaphragm" were all related to tumors to some extent. As in the Ling Shu Water Distension, "What about stone evidence? When it is born in the uterus, cold qi is born in the female from the Zi Men and can be guided down", similar to tumors and fibroids in the uterus. According to Hua Tuo's "Zhong Zang Jing" of the Han Dynasty, "All carbuncles, gangrene, sores and swellings are caused by the five internal organs and six internal organs", carbuncles, gangrene, sores and swellings are caused by internal toxins not flowing from the five internal organs and their causes have been divided into external and internal causes. For example, Tian Daofa et al. attributed the pathogenesis of malignant tumors to internal deficiency of the middle qi, the absence of a biochemical source of Ying qi, and the lack of moistening of Ying Liao, followed by the onset of phlegm and fire stagnation^[4]. Shang Jing et al. believed that the root cause of tumor formation was lack of positive qi, and the disease itself was lack^[5]. We believe that spleen deficiency dampness also plays an important role in the development of tumors. The spleen deficiency and dampness is gradually formed on the basis of spleen deficiency, which is mainly due to the weakness of spleen deficiency and the failure of the spleen to rise and clear, leading to the loss of water and grain, the abnormal rise and fall of qi, and the dampness and stagnation of water, thus blocking Yang qi, blocking qi, and prolonged stagnation and heat, which are combined into poison, and the stagnation of qi leads to blood stasis, and the intermingling of phlegm and blood stasis with poison, forming "polyps"^[6]. The main clinical manifestations are abdominal distension and filling, heavy limbs, short red urine, headache and fever, fatigue, itching skin, nausea and vomiting, sweet mouth mucosa, red tongue and yellow coating, and slippery pulse. The treatment method should be mainly to strengthen the spleen and remove dampness.

Research into the pathogenesis of tumors is increasing and understanding is becoming more advanced. This paper discusses the influence of spleen deficiency and dampness syndrome on the development of tumors and the theoretical basis of spleen deficiency and dampness syndrome. On this basis, the clinical application of spleen deficiency and dampness syndrome in tumors was analyzed. This study provides a new idea for Chinese medicine treatment of malignant tumors and a new perspective for clinical application.

2. Exploring tumors from a TCM perspective of spleen deficiency and dampness

2.1 Spleen deficiency and tumor

Modern medical practitioners have confirmed the close relationship between spleen deficiency and tumors from different angles. It is written in the "Difficult Classic Forty-three Difficulties" that "Those who have a good grain, but no grains, will die; when the water is gone Ying will be scattered, and when the grains are gone Wei will perish." Yin and Wei are derived from water and grain, produced in the spleen and stomach of the middle coke, and Wei Qi and Yin blood are the important material basis for human life activities [7]. Li Dongyuan of Jin Yuan believed that "internal injury of the spleen and stomach, all diseases born", weak spleen and stomach, insufficient qi, disease prevention, and evil ability weakened, evil invasion, all diseases born. Song Zhuo et al. summarized the causes of tumors and various therapeutic approaches, such as radiotherapy, surgery, targeted therapy, and immunotherapy. The pathogenesis of gastrointestinal malignancies is mainly due to spleen deficiency, which is evidenced by the efficacy of three stages of tumor prevention, treatment, and rehabilitation [8]. Guo Yong believed that the occurrence of tumors is related to the deficiency of positive energy and the weakness of the spleen and stomach [9-10]. The spleen-strengthening method can improve immunity, inhibit the proliferation, invasion, and migration of cancer cells, and reduce the side effects of radiotherapy. A trial found that gastrointestinal anxiety-based spleen-strengthening herbs combined with palliative chemotherapy prolonged survival in advanced gastric cancer [11].

2.2 Dampness and tumor

Dampness is a yin evil, which by its nature is sticky and causes many illnesses, leading to longer, difficult to heal, longer duration, and recurrent attacks. The formation of a tumor is a long process, and its "body yin" nature has the characteristic of being insidious in its onset. The overuse of the organs causes internal deficiency and localized poor flow of Qi and blood, resulting in the breeding of yin and evil [12]. Modern medical practitioners have also noticed the importance of dampness in the progression and evolution of tumors. According to Professor Li Yan, the pathogenesis of bladder cancer is originally deficient and its development is related to dampness, while the San Jiao and the bladder interact in the metabolism of water and dampness [13]. Therefore, Professor Li uses the draining method in the treatment of bladder cancer to promote the release of the San Jiao. The study found that ovarian cancer resistance relapse is consistent with the characteristics of wet stagnation. The treatment of ovarian cancer mainly uses the combination of invigorating spleen and dampening drugs to correct the moist environment in the body, and plays a multi-channel, multi-level and multi-target way [14].

2.3 Spleen deficiency and dampness and tumor

Spleen qi is the main rising, rising clear that is to spread water and grain essence, lifting the internal organs in two aspects; dampness is easy to trap the spleen qi, blocking its dissemination of the machine. Spleen deficiency and dampness are mutually influential. Spleen deficiency is the cause of dampness and dampness is the result of spleen deficiency. Wang Dong et al. identified a total of 19 potential biomarkers, such as glutathione and levyneglutamate, in the blood samples of liver cancer patients with spleen deficiency and dampness. In the control group, 6 indexes showed an increasing trend and 13 indexes showed a decreasing trend, and 17 of the indexes had a modulating effect after oral administration of Si Jun Zi Tang. These indicators could regulate the metabolic pathways of d-glutamine and glutamate in patients with spleen deficiency liver cancer [15].

3. Exploring spleen deficiency and dampness and tumor from Western medicine

During tumor progression, spleen deficiency and dampness can interact to make the disease worse. Immune dysregulation, angiogenesis, hypoxia, dysbiosis of the intestinal flora, and production of

adhesion molecules manifested by spleen deficiency and dampness may be factored in tumor formation and metastasis.

3.1 Immune dysregulation

Ling Shu - Shi Chuan" cloud: "the spleen, the main for the guard", "Ling Shu - five infirmity fluid other" said: "the heart for the main, spleen for the guard". The guard is the internal organs of the guard. The spleen is not only the main transport transformation, but also the main control blood, its essence is always "guard". Guard means to protect the surface of a muscle, similar to the body's immune system. Zhang Shuqiao et al. found that mouse spleen-specific/non-specific immunodeficiency affected the immune function of hepatocellular carcinoma, especially abnormal immune recognition of T-cell receptors, leading to survival, invasion and metastasis of hepatocellular carcinoma evading recognition and attack by the body's immune system^[16]. Deng Yu et al. investigated that after the administration of tonifying Zhong Yi Qi Tang to spleen-deficient mice, the production of cytokine IL-2 was enhanced and T-cell immune activity was restored to normal levels^[17]. Wang Yongdan et al. established a liver cancer model of spleen deficiency to study the effects of spleen deficiency on the proliferation, apoptosis and invasion and metastasis of liver cancer cells^[18]. It has been found that cytotoxic T lymphocyte antigen 4 (CTLA4) is up-regulated in the exosomes of hepatocellular carcinoma with spleen deficiency and is more aggressive. CTLA4 promotes the proliferation, self-renewal and metastasis of hepatocellular carcinoma by regulating the PTEN/CD44 pathway.

3.2 Angiogenesis

The Spleen is the master of blood control and it regulates the normal circulation of blood in the veins. When the spleen loses its function of regulating blood, blood does not follow the meridians, and blood that leaves the meridians is stagnant blood. Blood stasis will further affect the production of new blood. Tobias Kratzsch et al. established a mouse model of spinal cord metastasis, and by immunohistochemical analysis, the treatment group (axitinib) showed reduced metastasis formation and a reduced number of CD31-positive endothelial cells compared to the control group (placebo). The results suggest that the VEGFR inhibitor axitinib has an anti-angiogenic effect in preventing and delaying the formation of symptomatic spinal metastases^[19].

3.3 Hypoxia

There is a close relationship between the spleen and the lung, which is a mother-child relationship in the Five Elements theory. The spleen is the mother of the lung, and the lung is the son of the spleen. The spleen is responsible for transporting water and grain essence, while the lungs are responsible for breathing and inhaling the natural clear air. The qi of water grain essence and natural clear qi converge as zong qi, and the two interact with each other. When the spleen is deficient, resulting in chronic hypoxia, the body can be induced to produce hypoxia-inducing factors (including HIF-1 and HIF-2), which can promote tumor tissue vascular regeneration, tumor cell extravasation and tumor metastasis. The HIF promotes gastric cancer cell proliferation by activating the PI3K/alkaline phosphatase pathway, and HIF upregulation promotes VEGF to promote gastric cancer cell metastasis, among other responses^[20].

3.4 Dysbiosis of intestinal flora

The spleen is the source of Qi and blood biochemistry and has the function of transporting water and grain essence to protect the skin against external evil. The intestinal flora provides nutrients to the body, regulates metabolism, intestinal epithelial development and immunity, and functions similarly to the physiological functions of the spleen^[21]. Spleen deficiency, on the other hand, has been shown to be caused by dysbiosis of the intestinal flora, which causes mucosal damage and chronic inflammation, followed by the production of harmful substances that lead to the development of tumors. It was found^[22-23] that *Clostridium perfringens*, the dominant colorectal cancer flora, has been shown to be associated with the development and pathogenicity of colon and is abundant in the tumor tissues of patients with MSI-H (high microsatellite instability) and CIMP-H (high CpG island methylator phenotype). Zhang Hui et al. found that *E. coli* produced a genotoxic toxin in mice^[24] that promoted colon carcinogenesis and accelerated metastasis^[24].

3.5 Adhesion molecule production

Combined with modern medical research on dampness, dampness is related to local circulatory disorders and impaired immune function. The changes caused by dampness are closely associated with tumors. Malignant tumors metastasize and spread in a variety of ways and can extend throughout the body with characteristics similar to wet adhesions. Adhesion molecules are involved in the process of infiltration and metastasis of tumors and regulate the killing effect of killer cells on tumor cells. Liu Xiping et al. found that the expression of phagocyte membrane glycoprotein (CD44) and soluble adhesion molecule p-selectin (CD62p) was higher than that of the blank group in the spleen deficiency rat model [25]. The expression of soluble intercellular adhesion molecule-1 (CD54) was not significantly down-regulated. The CD44 is an extremely widely distributed transmembrane adhesion protein on cell surface, which is mainly involved in heterogeneous adhesion, that is, the adhesion of tumor cells to host cells and host matrix, which promotes the invasion and metastasis of tumor cells in patients with cholangiocarcinoma [26]. Data analysis showed that the overall survival (OS) of patients with high CD44 expression was significantly shorter than those with low CD44 expression, and the prognosis of the high CD44 expression group was worse than that of the low CD44 expression group. The strong adhesion of intestinal tumor platelet aggregates to tumor cells occurs through the cell adhesion molecule P-selectin (CD62p). P-selectin (CD62p) gene deletion was found to inhibit the growth and metastasis of intestinal tumors [27].

4. Application to tumors with spleen deficiency and dampness

According to Chinese medicine, the etiology of tumors is the deficiency of the root cause, i.e. the deficiency of the positive and the negative. Treatment is carried out by eliminating evil and supporting the positive and harmonizing yin and yang. Chinese medicine can improve the body's immunity and reduce the toxic side effects of radiotherapy, which can be applied to the patient's symptoms, improve the quality of survival and prolong the survival cycle.

Case: Shi, a female, 51 years old, was first diagnosed on June 22, 2021. The patient is postoperative for an endometrial malignant tumor. Her symptoms include clear consciousness, mental clarity, bilateral shoulder pain, numbness and discomfort in hands and feet, obvious emaciation, poor food intake, nocturnal rest, and bowel regulation. The tongue is red with a white greasy coating and the pulse is sunken and thin. Western medicine diagnosed as endometrial malignancy. The TCM diagnosis was obstruction (spleen deficiency and dampness syndrome). Treatment is to strengthen the spleen and resolve dampness. The formulae prescribed are Radix Codonopsis pilosulae 15g, Atractylodes macrocephala 15g, Poria cocos 15g, Glycyrrhiza glabra 6g, Pericarpium chenopodium 10g, Radix et Rhizoma pseudostellariae 10g, Fructus mucronatae 10g, Fructus saxifraga 10g, Fructus beehive 10g, Fructus scorpion 10g, Fructus coix lacrymae 30g, Fructus yam 30g, Fructus roxellanae 15g, Fructus laxis 15g, Fructus roxellanae 30g, Fructus roxellanae 3g, Fructus centipede 3, Fructus astragali 30g, Fructus angelicae 10g, Fructus salt Boneset 15g, Hot Boneset 15g, 14 doses in total, decoction in water, taken warm in the morning and evening.

The second consultation was held on July 06, 2021. After taking the medicine, the symptoms improved significantly and the pain in the shoulder was relieved. The first dose was added with 15g of Salt Eucommia and 15g of Salt Niubizi. The next 14 doses were taken in the same way as before.

Third consultation on August 17, 2021. Bilateral shoulder pain improved without weight loss. 15g of Wu Jia Pi and 15g of Gentiana Macrophylla were added in front, followed by 14 doses, taken as before.

After endometrial cancer surgery, the patient's physical condition is poor, the function of the internal organs is dysfunctional, the spleen and stomach are weak, the transportation and transformation are out of order, the production of water and grain essence is reduced, the Ying Qi is insufficient, the spleen is unable to ascend and clear, the Qi flow is obstructed, resulting in the stagnation of dampness and turbidity, resulting in numbness in the hands and feet, bilateral shoulder pain, poor appetite, etc.

The formula uses Xiang Sha Liu Jun Zi Tang plus reduction to tonify the Qi, strengthen the spleen, and move the Qi to resolve phlegm. The study found that after taking Xiang Sha Liu Jun Zi Tang, the blood CD3+ and CD4+ were significantly higher than the original, which effectively improved the patient's spleen and stomach qi deficiency and significantly improved the patient's immunity [28]; beehive and whole scorpion [29] belong to the worm group of drugs, which have the nature of attacking

and rushing, and can attack and remove evil toxins, with the efficacy of dispelling evil and inducing menstruation, relieving pain, dispelling toxins and dispersing nodules, which are strong and powerful, and have a better effect on the symptoms and quality of life of patients with malignant tumors, and are Coix seed oil, one of the main components of Coix seed, can stop the growth cycle of cancer cells, down-regulate the expression level of VEGFR, and thus inhibit the spread of cancer cells^[30]; yam strengthens the spleen and relieves dampness and was found to significantly reduce the expression of IL-17A and IL23p19, inhibit the differentiation of Th17 cells and reduce the production of IL -17A production to counteract inflammatory factors and play an immunomodulatory role^[31-32]; fried hen's inner gold and fried six shengqu are used to strengthen the spleen and eliminate food, salt boneset and scalded boneset are used to strengthen the kidneys and bones, and chicken blood vine and centipede are used to soothe tendons and relieve pain. *F Rhodiola rosea* can regulate immune function and also enhance the therapeutic effect of tumors, and pharmacological studies have shown that rhodioloside, a component of *rhodiola rosea*, promotes HIF-1 α descent, and also inhibits tumor cell proliferation and affects the tumor cell cycle^[33-34]; the combination of *Astragalus* and *Radix Angelicae Sinensis* benefits qi and replenishes blood, induces apoptosis and inhibits tumor cell proliferation^[35]. In the second diagnosis, we added *Eucommia* and *Niubizi* to tonify the liver and kidney and strengthen the tendons and bones. At the third diagnosis, symptoms were significantly relieved, and *Wujiapi* and *Gentiana macrophylla* were added to enhance the dispelling of wind-dampness.

5. Conclusion

The spleen is an earth in the five elements, and is known as the "source of the afterlife" and the "source of qi and blood biochemistry". The spleen transports water and grain essences is a source of nutrients needed to sustain vital activities, and provides adequate nourishment for other organs, meridians, limbs, tendons, skin, and other tissues. Spleen deficiency is a prerequisite for the development of tumor, and dampness causes disease. All things are born on earth and should be transformed from it. Tumors are caused by spleen deficiency and dampness, so they should also be treated by strengthening the spleen and dispelling dampness.

From modern medical analysis, spleen deficiency and dampness are associated with immune dysregulation, angiogenesis, hypoxia, dysbiosis of intestinal flora, and the production of adhesion molecules as factors in tumor formation and metastasis. In clinical practice, it is important to clarify the type of evidence and to integrate TCM evidence on spleen deficiency and dampness with clinical symptoms, disease pathology and physiological states. It also needs to be combined with research on the mechanism of action of Chinese medicine to fully explore its potential effects, to make therapeutic use more accurate, and to provide new ideas for the treatment of spleen deficiency dampness tumors.

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