

Diagnosis and Treatment Exploration of NF1-Related Malignant Peripheral Schwannoma Based on "Life Gate Theory"

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Abstract: More than 50% of malignant peripheral schwannomas originate from neurofibroma, with very poor prognosis. Currently, there is a lack of treatment guidelines and the effect is not ideal. Based on the views of Life Gate Theory including that "life gate is hub of nature" and "the fire of the life gate should be supplemented with water", supplementing the fire of the life gate applies both "radix rehmanniae preparata and astragalus" to nourish Yin and Qi, which has formed a new approach to diagnose and treat NF1 malignant peripheral neurofibroma with traditional Chinese medicine. Case 1 is attached for proof.

Keywords: Fire and water of life gate; Malignant peripheral schwannoma; supplement in water

1. Introduction

Be advised that papers in a technically unsuitable form will be returned for retyping. After returned the manuscript must be appropriately modified. Malignant peripheral nerve sheath tumor (MPNSTs) usually originates from neurofibroma, half of which happen in the Neurofibromatosis Type 1 (NF1) patients. Among the NF1 patients, the MPNST morbidity is about 1/3500, and the morbidity among the common people is 1/100 thousand. According to the statistics, the MPNST risk of NF1 patients is 8% to 13%, and 30% NF1 related MPNST are developed from neurofibroma. MPNST is the main death reason of the NF1 patients. At present, it is considered that NF1 is the neural ectodermal abnormality caused by aberrant dominant gene, leading to the multiple neoplastic hyperplasia of peripheral nerve and the connective tissue hyperplasia in nerve sheath and nerve fibers. The current NF1 related MPNST diagnosis are the combination of imaging evaluation, Positron Emission Tomography -Computed Tomography (PET-CT) or Magnetic Resonance Imaging (MRI) and Computed Tomography (CT). The pathological examination of infection focus is still the diagnosis "golden standard". The characteristics of MPNST are high risk of recrudescence, poor prognosis and high malignancy grade. The treatment currently needs the wide surgical resection, but it is easy to transfer after surgery and the recurrence rate is obviously higher than other malignant tumors. The result of the analysis to more than 1800 MPNST patients is very terrible. The survival rate after five years of prognosis is about 45%. In the latest research, the local recurrence rate of MPNST is among 25% to 37%, depending on the tumor grade. The NF1 related MPNST hasn't well respond to the chemotherapy, and the chemotherapy also obviously increases the death rate of the patients. In history, sarcoma is the first tumor model taken immunotherapy as the relative treatment strategy. The main way of tumor blocking immune control is the interaction of immune cells, but the experimental effect is not good. The process of the present therapeutic schedule is only for delay management, which is for the further exploration.

The traditional Chinese medicine recognition and verification of the NF1 related MPNST should be distinctive with the general "pneumocele" and "sarcoma", which belongs to the consuming disease because of infiltrating growth and viscera oppression. Although there is no detailed description to this disease in the textbook, due to the cancer scope and its feature of the abnormal lump in the viscera organs, the reasons of this disease include the lack of innate endowment and weakness of postnatal positive Qi. Pathological factors are mostly the Qi accumulation, phlegm coagulation, dampness stagnation, blood stasis and toxin accumulation, which become a tangible mass over time. The key of pathology is cancer toxin, and the deficiency of positive Qi is the internal cause and result of the disease. Patients with this disease are mostly deficient, and cancer lesions affect their operation of Qi and blood. Therefore, patients in the middle and late stage often have pathogenesis changes such as deficiency of Qi and blood, Yin and Yang, etc. The prognosis is very poor if the body is excessively wasted. Due to the low incidence rate of

the disease, there is no specific classification or treatment reports in the literature on this disease treatment with traditional Chinese medicine.

During the exploration of Life Gate Theory, we have found that treatment based on the Life Gate Theory has important significance on the malignant tumor and the complication. Now the traditional Chinese medicine treatment is explored with the method of Life Gate Theory, in order to explore the new clinical thinking.

2. Shadow description of the Life Gate Theory

The word "life gate" originated in *Lingshu · Root Knot*. For the human body, its important value is recorded in the *Classic on 81 Medical Problems*, which puts forward that the life gate is "the place storing the nerve and spirits, and combines the original Qi", meaning that the life gate is the place where the primordial spirit, nerve and Qi exist together. Primordial spirit is the innate essence, which plays an important role in transforming the acquired form. The Ming doctor Sun Yikui said that "life gate is the vital energy of the two kidneys, not water or fire, but the hub of nature", "nature" refers to creation and cultivation, "the birth of things comes from nature" (*Huangdi Neijing · Su Wen · Six Micro Purports*), which reflects the important role of life gate in the formation process of human tangible materials. In *Apocrypha Sublime Words*, Chen Shiduo proposes that "the acquired fire is within the twelve functions, and the acquired fire can only be eliminated by the innate fire. The life gate lives in the water and fire, which complement each other, positive and infinite", revealing the role of the innate Qi hidden in the life gate in dominating and commanding the functions of various organs, promoting the rise and fall of Qi, blood and body fluid, and maintaining the coordination of the functions of internal organs. The Qi mechanism of the viscera all depend on the life gate and rely on it as the foundation. If the life gate is coordinated and vigorous, the Qi, blood and body fluid are accessible and smooth, and the Qi to resist evil is cultivated. The positive Qi is stored in the body, and evil won't exist. The life gate contains the meaning of water and fire, and actually means that life gate includes not only the basis of material metagenesis, but also the basis of functional operation. According to the *Internal Classic*, "water and fire are the signs of Yin and Yang; Yin and Yang are the principles of all creatures, the parents of change, and the house of gods. Treatment must pursue the foundation." Then water and fire can also represent Yin and Yang. Only when the Yin and Yang of the human body are peaceful, the spirit is prosperous, and can be transformed into fine substances to nourish the viscera and meridians.

There are many deficiency syndromes related to life gate. The essence of parental reproduction condenses and combines to form the initial embryo of the human body, which is called the innate essence. Essence can turn into Qi, which is the Yuan Qi in the embryo. The function of Yuan Qi is the fundamental Qi of body activity, development and metabolism. *Classic on 81 Medical Problems* says that "moving Qi between the kidneys is the source of vitality", and the life gate is the place to maintain the vitality of the original Qi. Therefore, the root of congenital is the life gate, which is the root of human nature. So people are often afraid of its shortcomings, and the life gate diseases are usually the deficiency diseases. The long delay and consumption of malignance diseases are deficiency, even the real symptoms are recognized as the true deficiency and false reality. True Yin and true Yang are out of balance for a long time, and serious losses lead to spiritual extinction. The life gate determines the root of the twelve meridians. If the fire of the life gate declines, the twelve meridians will not operate smoothly, and it is difficult for Qi and blood to reach and nourish meridians, leading to multiple diseases. The balance of the rising, falling and transformation of the fire of life gate in the body is the core source and power of life gate. The basic pathogenesis of cancer is the dysfunction of organs, the damage of true Yin and true Yang, and the decline of positive Qi. Its pathogenesis is closely related to the theory of life gate.

3. Recognize and verify the etiology and pathogenesis of NF1 related MPNST from Life Gate Theory

The malignant nature and lifelong risk of NF1 related MPNST makes modern medicine committed to studying the characteristics of gene mutation and immunohistochemistry. Although the molecular mechanism of NF1 leading to the malignant transformation of MPNST is unclear, the signal path changes of rat sarcoma protein (RAS) / Raf protein kinase (RAF) / mitogen activated protein kinase (MAPK) / phosphatidylinositol 3 kinase (PI3K) / protein kinase B (AKT) / rapamycin target of rapamycin (mTOR). Compared with benign nerve sheath tumors, the expression of PTEN gene (gene of phosphate and tension homology deleted on chromosome ten) in PI3K / AKT / mTOR signal path of MPNSTs is reduced, and it is not regulated by NF1.

In the experiment of MPNSTs genetic engineering mouse model, it is further found that the immunohistochemical expression of epidermal growth factor receptor (EGFR) has increased. Genome research relies on advanced technical support, and the disease is still being explored. Genes and immunity are important factors to maintain the normal function of the human body and realize the complex regulation to the internal organs of the body, which corresponds to the functions of "true Yin, true Yang" and "essence Qi Theory" in traditional Chinese medicine. There has been the discussion that "Qi, blood and body fluid" and "Yin and yang theory" are closely related to modern immunology. Immune surveillance and immune defense are contained in the theory of Qi, blood and body fluid, and Qi, blood and body fluid are the important parts of the immune system. The theory of Yin-Yang balance is closely related to immune function and pathological changes. The treatment principles of adjusting Yin and Yang used in the clinical treatment of diseases in traditional Chinese medicine include immune regulation therapy. Considering that the process of immune response is closely related to the operation of human spirit and Qi, the regulation balance of true Yin and true Yang maintains normal activities of viscera organs.

If the body is weak, it is difficult for the positive Qi to resist after being infected by the external evil, which produces pathological products blocking the operation of body fluid. When the true Yang and true Yin lose balance or the true Yang is damaged for a long time, it is difficult to transport the essence to the five organs and twelve meridians to resist the invasion of disease and evil, making the body produce ineffective immune response or immune damage, which leads to the continuous invasion of evil Qi and miscellaneous diseases. Evil is attached to the meridians, then the meridians loses the nourishment of essence and Qi, resulting in Qi-stagnation and blood stasis producing mass, which is difficult to dissipate. For a long time, it will oppress the viscera, impair the function, and further consume the true Yin and true Yang, which can be seen that the body is in the consumptive status to produce foul disease, such as MPNST and other refractory diseases. Once MPNST is diagnosed, whether there is surgical intervention or not, the focus is to reduce the tumor, cultivate the positive Qi and prevent recurrence. According to the recognition and verification of traditional Chinese medicine, it is the deficiency of true Yang of life gate, the Qi, blood and body fluid are difficult to reach the place of disease, which can't nourish meridians. The positive Qi is difficult to fight against disease and evil, accumulating foreign matters. If the evil is in the body for a long time, there will be an imbalance between Yin and Yang, and the damaged Yang will influence Yin. The unhealing will cause the deficiency of Yin and Yang. The waste of fire in the life gate will lead to weight loss and sleepiness. This theory is similar to the sleepy symptoms caused by other cancer diseases. The imbalance of Yin and Yang in the body mechanism and the loss of Qi, blood and body fluid will lead to the wanton malignant growth of pathogenic foreign bodies with local nutrients. After multiple cases, they will oppress the meridians and viscera to damage the normal function of viscera. Therefore, the pathogenesis belongs to the deficiency of true Yang of life gate. In the category of "origin deficiency", if life gate is not straightened and supplemented in time to treat the root, it is easy to get sick repeatedly. "Thorough Knowledge of Medicine" has said: the strong fire of life gate makes the life prosperous, and the weak fire makes the body vulnerable. The kidney stores essence and is close to the life gate. Chen Xinsheng, Zhao Lihua and Shao Nianfang describe the correlation between the "life gate theory" of traditional Chinese medicine and the physiological function of kidney in western medicine, and they believe that the life gate is similar to adrenal cortex, hypothalamus pituitary adrenal cortex system and its function; The material basis of life gate is cyclic nucleotide. It is proposed that the foundation of continuous life circle is the vigorous water and fire of the life gate between the kidneys. Evil Qi is easy to damage the physiology of the kidney first, suggesting that kidney is the organ strengthening the root and foundation.

4. Discussion on treating NF1 related MPNST based on Life Gate Theory

4.1. Life gate supplementation starting from kidneys

Tonifying the water and fire of life gate is the fundamental treatment for MPNST. *Classic on 81 Medical Problems* said: "the gate of life. Its Qi is connected with the kidney." It has pointed out that the left kidney and the right life gate are connected with the kidney. When tonifying the fire of the life gate, take the kidney as the basis to balance Yin and Yang and positive Qi. Doctors such as Sun Yikui and Zhao Xianke believe that the kidney and the life gate are an inseparable whole, which is generally called the mansion of water and fire and the house of Yin and Yang, meaning that the kidney and life gate are born homologous, so the tonic is positioned as the kidney. The drugs should nourish Yin and kidney, such as radix rehmanniae, asparagus, ophiopogon japonicus, radix scrophulariae, etc. And the medicine to replenish Qi and warm Yang is often used. According to *Truth-seeking Herbal Foundation*, astragalus

membranaceous is suitable for water deficiency but Qi cannot be released, and it is more suitable for fire decline but Qi cannot reach the upper. It can not only promote the movement of Qi, blood and body fluid to reach the whole body, but also prevent the retention of Yin fluid. Based on these two, the prescription is combined to cultivate and protect the life gate and bring out the best in each other.

4.2. Sympathetic application of Yin and Yang, treatment of Yang in Yin

Therefore, for patients with NF1 related MPNST, the treatment should be "replenishing it in water and seeking Yang in Yin". The principles of mutual use of life gate Yin and Yang is applied to replenish the Yin of life gate to generate Yang. In the book *Thorough Knowledge of Medicine*, Zhao Xianke points out that "the monarch fire of life gate is the fire in the water, which depends on each other and never separate." It means that the powerful tonification cannot be applied for tonify the life gate water and fire, but is necessary to "nourish the life gate" and "warm the life gate" to replenish from the "water". Water and fire in life gate belong to true Yin and true Yang, which are inseparable. They are rooted and used each other, rather than the relationship of "Yin and Yang opposing each other". Tonifying Yang must seek Yang in Yin, tonifying Yin must seek Yin in Yang. Nourishing Yin and generating Yang is based on the "attribute" selection of disease. When the four Qi, five flavors and four seasons alternate, the principles of Yin and Yang complementing each other is adopted, that is, "deficiency makes up for deficiency" and "Yang disease cures Yin". Although people are born in fire, they are raised in water. Invisible fire and invisible water interact with each other and hide each other to nourish true Yin and generate true Yang, replenish the positive Qi of the life gate, and reach the meridians to prevent the recurrence of evil diseases. Surgery can be used to relieve the symptoms in the early stage of the disease, but due to its high recurrence rate, the focus is to prevent recurrence and take tonifying the life gate as the method, in order to provide new prevention and treatment thinking.

5. Typical cases

The patient was a 13-year-old male, was treated 1 month after operation of MPNST. At the age of 2, the patient had the surgery in the local hospital due to chest wall mass. The postoperative pathology was neurofibroma. At the age of 7, the left chest wall mass recurred. Neurofibroma mass resection was conducted on July 26, 2006. Postoperative pathology: neurofibroma on the left chest wall, with rich cells and active growth. In July 2013, mass was found again on the left chest wall without treatment. On October 9, 2013, the left chest wall mass resection and partial rib resection were conducted in another hospital. Postoperative pathology: neurogenic tumor with highly active tumor cell culture and invasive growth in surrounding tissues. The proliferation of tuberculosis focus was highly active and grew aggressively in the surrounding tissues with the characteristics of low-grade malignant tumor biological characteristics, which was considered as the local progression. Diagnosis: MPNST. Radiotherapy has been performed 3 times in other hospitals, with 25 times totally (not after radiotherapy). He came to our hospital on November 14, 2013 for further treatment of integrated traditional Chinese and Western medicine. There was no obvious discomfort at the initial diagnosis. The night rest, daily diet and the stools were normal. The tongue was light red, the moss was thin and white, and the pulse was late. Physical examination: young male, conscious, old surgical scars could be seen on the left chest wall, without local red swollen. The respiratory sounds of both lungs were clear, and the pathological murmur after operation and chemotherapy can be heard through auscultation. Regional lymph nodes showed no obvious swelling.

Western medicine diagnosis: MPNST. Traditional Chinese medicine diagnosis: cancer disease. Traditional Chinese medicine syndrome type: deficiency of true Yang, fire failure of the life gate, Qi accumulation and phlegm coagulation. The treatment should be nourishing Yin and latent Yang, warming and tonifying kidney Qi to balance true Yin and true Yang. Ginseng and astragalus, Dihuang decoction were given. Prescription: dangshen 15g, roasted Astragalus 30g, radix rehmanniae preparata 9g, radix paeoniae alba 30g, common macrocarpium fruit 15g, cortex moutan 12g, Alisma orientalis 12g, Poria cocos 15g, subprostrate sophora 5g, scorpion 5g, centipede 1, black snake 6g, raw oyster 30g. Take in water twice in the morning and evening respectively, with one dose per day.

On January 27, 2014, reexamination of magnetic resonance imaging (MRI): 1 "Postoperative reexamination of fibroma on the left chest wall" is about 9.10 thoracic vertebrae level. Space occupying lesions under the left chest wall and above the diaphragm were considered as tumor diseases. The diameter was 4.1cm; 2. The shape of left chest wall and soft tissue signal changed, which was considered as the postoperative changes and suggested to re-exam. MR reexamination on February 25, 2014:

compared with October 29, 2013, the inflammatory absorption of the lower lobe of the right lung was more, and the effusion in the left pleural cavity was more. MR reexamination on January 8, 2019: "left chest wall tumor post operation" change. Compared with January 17, 2018: at about T9 and T10, there was no significant change in the lesions above the diaphragm of the horizontal left chest wall, and in the adjacent subcutaneous tissue. MR reexamination on January 7, 2020: "left chest wall tumor post operation" change. Compared with January 8, 2019: About T9 and T10, the diaphragm of the horizontal left chest wall was stable disease (SD), and the near subcutaneous was SD.

During the 9-year from the follow-up visit to August 26, 2021, this treatment was continuously applied, with ginseng and astragalus and Dihuang decoction as the main formula, which increased and decreased with climate and symptoms. At the stage of youth development, the three supplements should be especially used without three discharges to strengthen and promote growth. Dangshen and astragalus membranaceus are still measured in medium dose to nourish the positive qi of life gate. The patient had high quality of life, without obvious recurrent lesions, and can take food normally.

Note: after the diagnosis of MPNST on the chest wall, the adolescent took traditional Chinese medicine for 9 years, and the chest wall mass still had the recurrence after resection for 2 times. Initial diagnosis: ginseng and satragalus Dihuang decoction is the pill of six ingredients with rehmannia plus Dangshen and Astragalus to nourish the spleen and kidney, replenish Qi and nourish Yin. Compatible with scorpion, centipede and black snake to dredge collaterals, attack poison and disperse knot; Raw oysters to strengthen soft and solid loos knot. The whole prescription combines connection and nourishment, strengthens the right and resists evil, with obvious effect to resist the recurrence. After chemotherapy, there was still a tendency of recurrence in January 2014 (one year after left chest wall mass and partial rib resection were excised), without radiotherapy or chemotherapy. Adjust the measurement of traditional Chinese medicine composition meant adding part of the tonifying life gate drugs: dangshen 30g, roasted Astragalus 45g, radix rehmanniae preparata 20g, Epimedium 20g and Festuca 6g. The inflammatory pleural effusion was absorbed without obvious recurrent lesions or obvious oppression and discomfort, and the life quality was high.

6. Conclusion

In conclusion, Life Gate Theory provides a new diagnosis and treatment idea for NF1 related MPNST, focusing on preventing disease recurrence and improving the survival time of patients. Nourish true Yin to produce true Yang, and help Yang to transform Qi. The life gate and the two kidneys nourish each other. If they are distributed in the twelve meridians, there will be no harm. Only when water and fire are combined, can infinite biochemistry and self-healing of diseases occur. When the internal organs are calm, the Qi can be strengthen, the tri-jiao can be connected, blood can reach the meridians, the tumor can be dissipated, and the five internal organs and the meridians can be reconciled.

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