

A Case of EBV-associated Phagocytic Syndrome Treated on the Basis of the Academic Idea of Five Elements of Qi-hua Theory

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Abstract: Hemophagocytic syndrome (HPS), also known as hemophagocytic lymphohistiocytosis (HLH), is a rare and critical clinical syndrome. It is a rare and critical clinical syndrome with rapid onset, rapid progression, and a high mortality rate. At present, western medical treatment of HLH is mainly based on the diagnostic and therapeutic protocols of HLH-1994 or HLH-2004: control of excessive inflammation, delaying the progression of HLH activation; treatment of the primary cause of the disease and immunotherapy. In this paper, based on Liu Huawei's academic thought of "five elements and qi-hua theory", combined with the dialectical theory of "Wei-Qi-Ying-Blood" in Chinese medicine, we treated a case of HLH with Chinese medicine and achieved good clinical efficacy. The successful diagnosis and treatment of this patient provides some implications for the clinical use of TCM in the treatment of rare infectious diseases and hematological diseases.

1. Case Presentation

Patient, a 21-year-old female, was first diagnosed on June 13, 2020. Chief complaint: recurrent fever for more than 1 year and continued high fever for 3 months. History of present disease: The patient developed high fever on June 23, 2019 with a body temperature of 40.3 °C. The examination was unsuccessful in a grade-A hospital in Xi 'an. At the end of June, the patient was transferred to

another Grade-A hospital in Xi'an to be diagnosed with hemophagocytic syndrome combined with Epstein-Barr virus infection[1]. Three months ago, the patient suffered from high fever again, and was admitted to a hospital in Beijing. During the hospitalization, the patient received 16 times of radiotherapy and chemotherapy in addition to the conventional treatment, but the effect was still not good[2]. The fever continued to this day, accompanied by lack of consciousness. Present symptoms: fever, body temperature 39°C, fatigue, weakness in both lower limbs and inability to stand, heel pain, loose stool, twice a day, red tongue tip thin yellow, weak pulse string number. Western Medicine diagnosis: Epstein-Barr virus associated hemophagocytic syndrome. TCM syndrome differentiation: deficiency of spleen and kidney combined with liver depression and fire. Treatment: Warming the spleen and nourishing the kidney, soothing the liver and lowering the fire. Prescription: Dan Zhi easy and carefree powder combined with aconite Li soup combined with Baidi Huang soup, Danpi 10g, gardenia 10g, bupleurum 12g, Paeony 12g, Dangguo 10g, atractylodes 15g, Poria 15g, sunburned licorice 6g, peppermint 6g (bottom), ginger 15g, aconitum aconitae 10g (boiled water first decocted for half an hour), dried ginger 15g, codonopsis 15g, Zhimothe 10g, yellow cypress 10g, cooked ground 24g, yam 12g, winshan Cornus 12g, Alsea 15g, psoralea 10g, Xianling spleen 15g, Wolfberry 15g, cuscuzi 15g, 7 agents, 1 agent a day, decocted in water. Second diagnosis: On July 04, 2020, the body temperature returned to normal after 4 doses of upper dose, but the patient's spirit was improved compared to before, and loose stool was improved compared to before, once or twice a day. After eating, the stomach distension was relieved, the heel pain was relieved, the tongue was fat and the edge tip was red and the moss was thin and white, and the pulse was thin and weak, as shown in Figure 1, Table 1 and 2.

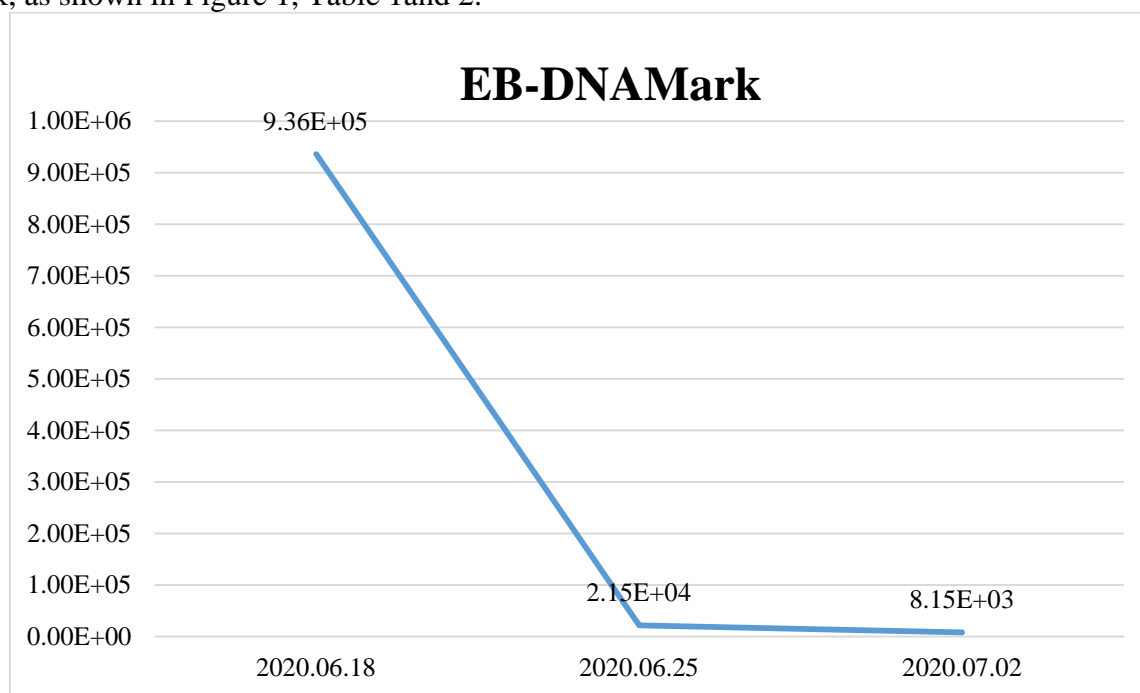


Figure 1. Quantitative changes of EB-DNA after medication

Table 1. Abnormal indicators of blood routine after first diagnosis

Date	2020.07.02
WBC	5.04×10 ⁹ /L
HB	118g/L
PLT	227×10 ⁹ /L

Table 2. Series of biochemical examinations after the first examination

Date	2020.07.02
TBIL	11.7umol/L
DBIL	5.5umol/L
IBIL	6.7umol/L
ALT	51U/L
AST	42U/L
TP	70g/L
ALB	46.8
GLB	23.2g/L
CHO	3.92mmol/L

Prescription: Chaiguilongmu Decoction and Aconiti Lizhong decoction Hezhibai Dihuang Pill, 16g bupleurum, 12g cassia twig, 15g raw keel (decocted for half an hour first), 15g raw oyster (decocted for half an hour first), 15g ginger pinellia, 15g Dangshen, 6g roasted licorice, 10g Huangshi, 12g white peony root, 15g aconiti vulgaris (boiled water decocted for half an hour first), 15g fried Baishu, 15g dried ginger, Zhimu 10g, Phellodendri 10g, Shudi 24g, yam 12g, Jiushanyu 12g, alisma 15g, Danpi 10g, Tuckaia 15g, 7 doses, 1 dose per day, decocted in water. Three diagnoses: July 11, 2020, unformed stool, 1-2 times per day, good appetite, improved heel pain, thin white red coating on the tip of tongue, weak pulse string. Prescription: Shoufang plus gardenia 6g, Danpi reduced to 6g. Fourth diagnosis: July 18, 2020, fatigue, irritability, normal eating, formed stool, 1-2 times a day, heel pain, pale tongue, thin white and smooth coating, heavy and fine pulse. Prescription: Diao Zhongyiqi + Wuling SAN + Kidney four flavor addition or subtraction, raw Astragalus 30g, Codonginseng 15g, xylopathy 6g, atractylopathy 10g, sunburned licorice 6g, Tangerine peel 15g, cohoma 10g, bupleurum 6g, pig ling 15g, Zexie 15g, Cassia twig 7g, Poria cocos 15g, Stir-fried atractylopathy 15g, psoralea 10g, Xianling Spleen 10g, Wolfberry 10g, cuscuzi 10g, 7 doses, one dose per day, decocted in water. Five diagnoses: On July 25, 2020, fatigue, irritability, heel pain, abdominal distension after eating, bowel movements taking shape, 1-2 times a day, fat tongue, moss and greasy roots, weak pulse string. Prescription: Xiaoyao powder + Kidney Siwei plus or minus, Danpi 9g, Jiaoshanzhi 9g, buplehu 12g, Paeoniae 12g, Dang Guigai 10g, Poria 15g, Stir-fried atteshu 15g, Zhilicorice 6g, mint 6g (bottom), Jiaosanxian 10g each, 7 agents, 1 agent a day, decocting in water. Six diagnosis: On August 1st, 2020, I had a cold, slightly irritated, dry and itchy throat, yellow phlegm, heel pain, poor appetite. Prescription: Small bupleurum Decoction + Stomach Ling Decoction plus or minus, bupleurum 16g, ginger pinellia 15g, Codonopsis 15g, sundried licorice 6g, Radix skullcap 10g, atractyloides 10g, Magnolia officinalis 10g, Tangerine peel 15g, Poria officinalis 15g, Atractylosan 7g, Schizonax 10g, platycodon 10g, almond 10g, ginseng 6g, Danpi 9g, Jiaoshanzhi 9g, 7 agents, day 1 agent, water decoction. 7 Diagnosis: On August 08, 2020, the pulse was weak, and the patient was able to sleep. Prescription: Chaishao Buzhong Yiqi Decoction + Wuling SAN + Kidney Siwei, Bupleurum 12g, Baishao 12g, Codonopsis 15g, Shiqi Astragalus 30g, Shiqi licorice 6g, Stir-fried atractyloides 15g, Angica 10g, Tangerine peel 15g, Shengma 10, Guiling 15g, Zexie 15g, Cassia zhi 7g, Poria cocos 15g, stir-fried atractyloides 15g, psoralea 10g, Xianling PI 10g, Wolfberry 10g, cuscuta 10g, 7 agents, 1 agent a day, decocted in water, as shown in Table 3,4.

Table 3. EB-DNA quantitation after seven visits

Date	2020.08.04
EB-DNA Mark	1.19E+04
Ferritin determination	35.000ng/ml

Table 4. Abnormal indexes of blood routine after seven examinations

Date	2020.08.04
WBC	4.59×10 ⁹ /L
HB	119g/L
PLT	228×10 ⁹ /L

Eight diagnosis: On August 15, 2020, increased intake of food, fatigue, easy to wake up, bowel movements adjusted. Prescription: Buzhongyiqi Decoction + Xiaoyao SAN + Wuling SAN + Kidney four flavors plus or minus, prepare Astragalus 30g, codonopsis 15g, prepare licorice 6g, stir-fried attekylotein 15g, Radix tangerine peel 15g, cohoma 10g, Bupleurum 12g, white peony root 12g, Poria cocos 15g, mint 6g (back), prepare aconitum 6g (fry for half an hour first), dried ginger 15g, Xianling PI 10g, Huangjing 10g, poring 15g, Alisna 15g, Cassia branch 7g, psoralea 10g, Wolfberry 10g, cuscuzi 10g, 7 agents, 1 agent a day, decocted in water. Nine diagnosis: On August 22, 2020, stool was formed, fear of cold improved, delayed menstruation, light tongue fat moss thin greasy root, heavy pulse. Supplementzhongyiqi + Chaiguilongvita + Kidney four flavor, prepare Astragalus 30g, codonopsis 15g, prepare licorice 6g, stir-fried attekchu 15g, angelica 10g, Tangerine peel 15g, cohoma 10g, bupleurum 16g, cassia twig 10g, raw keel 15g (fry for half an hour first), raw oyster 15g (fry for half an hour first), ginger pinellia 15g, Huangbaicalensis 10g, white peony 12g, Psoralea 10g, Xianling spleen 10g, Wolfberry 10g, cuscuzi 10g, 7 agents, 1 agent a day, decocted in water. Ten diagnosis: Present symptoms: late menstruation, dim tongue red moss thin white root greasy, pulse sinking thin weak. Warm Jing Soup + Kidney four flavors, Wu Zhuyu 6g, cinnamon 6g, Chuanxiong 10g, angelica 12g, Paeoniae root 12g, Danpi 10g, ginger pinellia 15g, Ophiopogon 10g, Codonginseng 15g, Zhilicorice 6g, ejiao 10g (closing), Huangjing 10g, cassia branch 10g, raw keel 15g (frying for half an hour first), raw oyster 15g (frying for half an hour first), 7 doses, one dose per day, decocted in water. After 1 year of follow-up, the disease recovered and did not recur, as shown in Table 5.

Table 5. Quantitative reexamination of Epstein-Barr virus after 10 visits

Date	2020.08.29
EB-Virus fluorescence quantification	<500
Ferritin determination	26.200ng/ml

2. Discussion

2.1 Chinese and Western Medical Pathogenesis of HPS

2.1.1 Western Medical Pathogenesis

EBV is a ubiquitous herpes virus, and it has been reported that 90% of adult individuals in China become carriers after being infected during infancy and childhood. However, the long latency period of EBV is characterized by clinical symptoms that can appear when the body's immunity decreases and can lead to a variety of life-threatening complications, including HLH and other malignancies [9]. Hemophagocytic syndromes (HPS), also known as hemophagocytic lymphohistiocytosis (HLH), is a syndrome characterized by excessive immune activation and is often characterized by fever, hepatosplenomegaly, and complete blood cell Patients with HLH are initially similar to viral colds, often with fever as the first symptom, but the disease progresses rapidly and is prone to multi-organ involvement, leading to progressive multi-organ failure, triple cytopenia and multi-organ damage to the lungs, liver and spleen in acute and severe cases, with a

high mortality [3-4]. According to the cause of onset HLH can be divided into primary HLH and secondary HLH [5], the former is characterized by early-onset and cytotoxicity-related genetic mutations, a clear family history of the disease, and a possible association with inherited genetic defects, with childhood onset more often than adult; the latter is mainly secondary to malignancies, infections, autoimmune diseases, and connective tissue diseases, among which EBV-associated HLH (EBV-HLH) is the most common type of viral secondary HLH and is a life-threatening hyperinflammatory response syndrome with an aggressive prognosis, high mortality rate, easy relapse and shorter survival time [6-8].

Treatment for EBV patients is mainly with antiviral, glucocorticoid-based immunosuppressive agents, but the efficacy is poor and recurrent even after discontinuation [9]. The currently accepted standard treatment regimen for HLH is HLH-1994 or HLH-2004, but this regimen also brings severe myelosuppression and extensive immunosuppression for patients, often leading to severe infection and death, in addition to the side effects and risk of secondary tumors associated with long-term use of etoposide chemotherapy drugs, which also bring greater suffering to patients.

2.1.2 Exploring the Pathogenesis of HLH in Chinese Medicine based on the "Five Elements of Qi-Chemistry" Theory

There is no record of the name of hemophagocytic syndrome in Chinese medicine, and there are not many reports on the use of Chinese medicine to treat this disease. Based on the clinical manifestations of EBV infection and HLH such as persistent fever and rapid disease progression, which are in accordance with the basic rule of "Qi-mechanism imbalance and Qi-transformation disorder" according to the "Five Elements and Qi-transformation theory" of Professor Liu Huawei, we have reviewed the relevant literature [10]. Therefore, this disease can be classified as a warm disease, and its pathogenesis can be understood from the perspective of the law of transmission of "Wei-Qi, Ying-Blood" in warm disease.

In the *Nei Jing*, it is said that "if winter is injured by cold, spring will be warm" and "if winter does not hide the essence, spring will be warm", emphasizing the causes of warmth from "external invasion of evil" and "deficiency of the right and evil". "It emphasizes the causes of warm diseases in two aspects. The "Five Elements Theory of Qi-Chemistry" believes that under normal physiological condition, the movement process of "lifting and lowering in and out" of human organs and qi-chemistry form of "gathering and dispersing" are complementary to each other, which together maintain the physiological function and mechanism of human organs. The physiological function of the internal organs and the vitality of the body, but also the human body itself and the premise of the exchange of Qi with nature, that is, the so-called "non-in and out, there is no to grow strong old; non-lift, there is no to grow and collect". And the process of gathering and dispersion of qi is the basic element to maintain the growth of the human body and the various life processes. As Zhuangzi said, "the human life, the collection of gas is also, gathered for life, scattered for death." Therefore, the normalization of the body's qi and qi-chemistry determines the degree of strength of the body's positive qi, and affects the body's ability to resist external evil.

According to the Five Elements Theory of Qi and Harmony, the treatment of warm-heat diseases should be based on the general idea of "facilitating the Qi mechanism and restoring Qi and Harmony", applying the "Wei-Qi-Ying-Blood Identification" method according to the characteristics of the disease mechanism at different periods of development, and focusing on regulating the Qi mechanism of the body so that there is a way out for the disease evil to penetrate and disperse. In the late stage of warm fever, when the body is deficient in vital energy and unable to resist the evil, we should focus on "supporting vital energy and preserving yin liquid", so that the vital energy of the body can be restored and promoted.

2.2 The Method of "Regulating the Flow of Qi, Regulating Qi-Chemistry"

This patient had a clear diagnosis at an outside hospital prior to consultation and had persistent fever, complete cytopenia, and persistently elevated quantitative EBV values prior to the initial consultation. The patient had gone to several hospitals for regular treatment, but his condition was still not well controlled and his condition was dangerous, so he turned to Chinese medicine.

The patient's first visit was mainly due to recurrent high fever that did not subside and lack of consciousness, which was caused by warm-heat evil Qi entering from the body and disturbing the mind. As the saying goes, "When there is excess qi, there is fire." Warm-heat evil qi is easily transformed by fire, and when there is too much qi and too much yang, high fever develops. The use of hormone therapy in the preliminary treatment aggravates the deficit of Qi and Yin, so we can see the evidence of weakness, weakness of lower limbs unable to stand, heel pain, and weak pulse. In addition, antibiotics and antivirals are also used in the preliminary treatment. According to Chinese medicine, such drugs are bitter and cold in nature, and their prolonged use is likely to cause deficiency of cold in the spleen and stomach and lead to diarrhea [11], so the patient can be seen to have dilute stools with a high frequency. Combining with the patient's tongue and pulse, we analyze that the disease mechanism of this case is complex[12-14], with a mixture of deficiency and reality, cold and heat, so the treatment should take into account both deficiency and reality, and use both cold and heat to achieve the purpose of opening up the qi mechanism and restoring qi chemistry. Therefore, the formula was selected from Dan Gardenia Prosperity San combined with Zhi Bai Di Huang Tang combined with Radix Rehmanniae Sinensis plus and minus, in which Dan Pi and Gardenia cool the camp and harmonize the blood, and the whole formula of Prosperity San dredges the liver and regulates the qi, and the formula of Peppermint penetrates and disperses the heat, so that the evil qi can have a way out and the qi can be restored[15].

3. Summary

This case is a typical case of effective control of the disease after Chinese medicine treatment, which shows that Chinese medicine can play a significant role in the treatment of acute rare infectious diseases, hematological diseases and other difficult and critical diseases. Based on the academic thought of "Five Elements Theory of Qi and Transformation", we understand the fundamental pathogenesis of this disease, which is "imbalance of the qi mechanism and loss of qi-transformation", and take "regulating the qi mechanism and promoting qi-transformation" as the fundamental principle in treatment. In the treatment, the fundamental principle of "regulating qi and promoting qi-transformation" is used, and the theory of "Wei-Qi-Ying-Blood Identification" is applied. Professor Liu Huawei's academic thought of "Five Elements and Qi Theory" has provided theoretical support and experience reference for clinical diagnosis and treatment of difficult diseases.

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Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Conflict of Interest

The author states that this article has no conflict of interest.

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