

The Use of Gui-Pi-Tang in Small Animals with Immune-Mediated Blood Disorders

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Abstract : Immune-mediated hemolytic anemia (IMHA) is one of the most common causes of anemia in small animals and immune-mediate thrombocytopenia (IMT) is also an immune mediated disease that affects small animals. The initial treatment for IMHA and IMT is medical suppression of the immune system with glucocorticoids and other immunosuppressive drugs. However, even with appropriate treatments, some animals are not responsive to the treatment and may need further immunosuppressive therapies or some alternative medicines. An eight-year-old spayed female Siamese cat with IMHA and an eight-year-old castrated male King Charles Spaniel dog with IMT were referred to the traditional medical service of the veterinary medical center. Both animals were unresponsive to steroids or other immunosuppressive treatments. Gui-Pi-Tang, one of the traditional herbal medicines, was administered to the animals. After 1-month of Gui-Pi-Tang administration, the packed cell volume (PCV) of the cat and platelets count of the dog had showed remarkable improvement. After four months of follow up in the cat, and 18 months of follow up in the dog, the improved PCV and platelet counts of the animals were maintained normally. Therefore, Gui-Pi-Tang might be considered as an alternative treatment in small animals with immune-mediated blood disorders.

Key Words : Cat, dog, Gui-Pi-Tang, immune-mediated hemolytic anemia, immune-mediate thrombocytopenia.

Introduction

Numerous immune-mediated disorders have been identified in dogs and cats. Immune-mediated hemolytic anemia (IMHA) and immune-mediated thrombocytopenia (IMT) are among the commonly diagnosed immune disorders in small animals. IMHA and IMT are diseases that result from a type II hypersensitivity reaction (9-11). Most cases of IMHA and IMT are idiopathic. However, some cases have been identified as secondary to the effects of toxic agents, certain drugs, and underlying disease states (5). The clinical signs associated with IMHA are low RBC count and an inflammatory response. IMT is characterized by the clinical signs of hemorrhages into the skin and tissues, prolonged bleeding times, decreased platelet counts and anemia (15). The primary treatment for IMHA and IMT is immune suppression with glucocorticoids (11). Furthermore, if necessary, blood transfusion, splenectomy and more speculative immunosuppressive agents are options for therapy (1,7). Despite of the appropriate glucocorticoid treatment, some animals are not response to the standard treatments and occasionally the out-

come can be life threatening. Hence, the limited success of conventional treatments involved with corticotherapy has led to seek alternative treatments. Gui-Pi-Tang is one of traditional herbal medicines used in Asian countries. It has been reported to be useful in the treatment of chronic immune-mediated thrombocytopenia in humans (17). Gui-Pi-Tang as the *Xue* tonic formula has been useful for the treatment of severe blood deficiency in traditional medicine (12,16).

Case

This report described the use of Gui-Pi-Tang for the treatment of a cat with IMHA and a dog with IMT. An eight-year-old spayed female Siamese and an eight-year-old castrated male King Charles Spaniel were referred to the traditional service of the veterinary medical center. The cat presented with a history of lethargy, poor appetite, petechia on caudal neck and ear pinnae for 2 weeks. Because of the petechia sign the cat also was examined whether IMT or not. The cat did not have thrombocytopenia. After the work up, the cat was diagnosed with IMHA with 11% PCV. For the rule out the different diseases shown similar histories, infectious diseases such as mycoplasma, FeLV, FIV, and Coomb's test were examined and all results were negative. The cat was

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treated with intravenous dexamethasone (1 mg/kg, 12h), a 60 ml whole blood transfusion on the day in addition to one week of prednisone (5 mg/kg, 12h). One week later after the treatment, the PCV was 12%. Next, a cyclosporine was added as an immunosuppressant. However, the PCV did not recover to normal values. The owner wanted to try traditional Chinese medicine (TCM) as alternative treatment.

The dog was diagnosed with chronic immune-mediated thrombocytopenia with a platelet count of 55,000/ μ l 2 years previously. The size of platelet in King Charles spaniel varies and is relatively large compared to that of other breed dog. To rule out this concerning, both manual calculator and auto-calculator were used for the diagnosis of dog. The dog had the clinical signs of lethargy, weakness and multiple collapses. Though the dog was started an immunosuppressive therapy with prednisone (5 mg/kg, 12h), the dog was unresponsive to this treatment. The owner decided to treat the dog with traditional medicine 1.5 years ago.

TCM treatment with Gui-Pi-Tang was administered in both animals. The dose was 0.5 g per 10 to 20 lb body weight twice daily. One month after the administration of Gui-Pi-Tang, the PCV of cat increased by 36 %. After four months of follow up the improved PCV was maintained normally. The PCV was 36% by one month and 30% after four months of treatment (Fig 1). In the case of the dog, the platelet counts were significantly increased after the administration of Gui-Pi-Tang. The Platelet counts were 140,000/ μ l at six months, 174,000/ μ l after 12 months, and 161,000/ μ l after 18 months after treatment was started. At 18 months of follow up the platelet counts were maintained in normal range (Fig 2).

Discussion

Recently, the popularity of TCM has increased around the world because of the minimal side effects when compared with western medicine (14). According to TCM, the energy (*Qi*) homeostasis, of negative and positive forces in the body, is thought to be essential for good health. Disease occurs when an energy imbalance is established (3). Blood (*Xue*) in

TCM is a red colored liquid that contains a special form of *Qi*. The *Xue* that circulates throughout our body contained within the blood vessels bestows nourishment and moisture to the body itself and the Zang Fu organs. *Xue* is the carrier and transporter of *Qi*, in addition, *Xue* also stores Qi. Qi controls the way *Xue* is created, circulated and held in place inside vessels. Qi and *Xue* are not only closely related with each other in health but also in disease. If Qi becomes imbalanced it caused imbalances in *Xue* (16).

While western medicine explains IMHA and IMT as autoimmune disorders, TCM has a different explanation. The diagnosis for both clinical abnormalities is a “deficient *Qi* failing to maintain *Xue*.” The clinical signs of “deficient *Qi* failing to maintain *Xue*” include fatigue, shortness of breath, exercise intolerance, and general weakness. Aging, chronic illness and constitutional weakness lead to *Qi* deficiency. If left untreated, the *Qi* deficiency may be exacerbated and result in a *Qi* that is too weak to maintain and secure the *Xue* inside the blood vessels; this can result in the development of hemorrhaging.

TCM is a system of medicine that is comprised of five branches: acupuncture, Chinese herbal medicine, food therapy, Tui-na, and Tai-chi or Qi-gong. Among the branches herbal medicine is widely accepted as a treatment for imbalances in the body. Herbal medicine has unique synthetic and synergistic effects that result from the interactions among the herbal components (2,14). Hence one herbal formula may have a wide range of therapeutic applications.

Gui-Pi-Tang is a Chinese herbal formula that is a made up of several different herbs that together treat anemia and IMT by tonification of *Qi* and *Xue*. It has been used to treat anemia, palpitation, several neuroses, and insomnia. From scientific researches, it has been reported that platelet counts increased after oral administration of the herbal formula Gui-Pi-Tang in human patients without any side effects (17). It has been studied that Gui-Pi-Tang had effects of immunological control function. As examples, the transformation of lymphocyte in Gui-Pi-Tang treated group was not increased, but the production of nitric oxide was significantly increased in Gui-Pi-Tang treated group. In addition, the Gui-Pi-Tang treated group increased the population of helper T cell and macrophage (8). Gui-Pi-Tang has been known to have a pro-

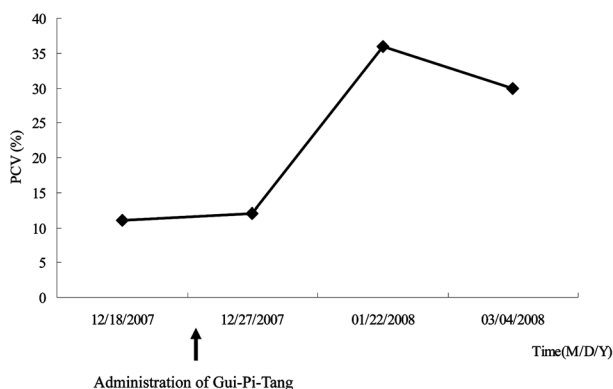


Fig 1. PCV before and after the administration of Gui-Pi-Tang in the cat.

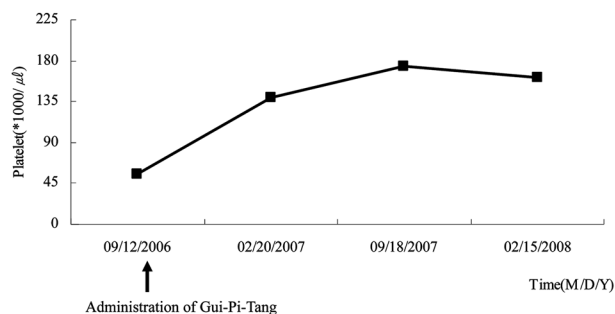


Fig 2. Platelet counts before and after the administration of Gui-Pi-Tang in the dog.

duction of interferon- γ in the blood mononuclear cells (13).

Gui-Pi-Tang consists of Ginseng 6g (*Ren Shen*), Atractylodes 6g (*Bai Zhu*), Astragalus 6g (*Huang Qi*), Poria 6g (*Fu Ling*), Angelica 6g (*Dang Gui*), Longan 6g (*Long Yan Rou*), Saussurea 6g (*Mu Xiang*), Polygala 6g (*Yuan Zhi*), Ziziphus 6g (*Suan Zao Ren*), Zingibery 12g (*Sheng Jiang*), Jujube 12g (*Da Zao*), and Licorice 6g (*Zhi Gan Cao*) (6). Among these herbs, Ginseng, Astragalus, Atractylodes, and Angelica have been described to improve and transport *Xue*, as well as *Qi* and *Xue* (4). It has been studied that Ginseng and Atractylodes increase the total count of IgM and the function of the reticuloendothelial system (4). The administration of Astragalus has reported to increase white blood cells and multinuclear leukocytes in mice (4).

Although Gui-Pi-Tang may have the therapeutic effect on immune mediated disorders, further basic research is recommended to reveal a precise scientific evidence of the therapeutic effect.

Conclusion

In conclusion, we report two cases that improved after the administration of Gui-Pi-Tang. The small animals had improved clinical signs of IMHA and IMT as well as favorable changes in their blood values with an increased PCV and platelet counts. Our results suggest that TCM with Gui-Pi-Tang is a safe and effective alternative treatment option to western immunosuppressive therapies.

References

- Balch A, Mackin A. Canine immune-mediated hemolytic anemia: treatment and prognosis. *Compend Contin Educ Vet* 2007; 29: 230-238.
- Borchers AT, Sakai S, Henderson GL, Harkey MR, Keen CL, Stern JS, Terasawa K, Gershwin ME. Shosaiko-to and other Kampo (Japanese herbal) medicines: a review of their immunomodulatory activities. *J Ethnopharmacol* 2007; 73: 1-13.
- Carneiro ER, Carneiro CR, Castro MA, Yamamura Y, Silveira VL. Effect of electroacupuncture on bronchial asthma induced by ovalbumin in rats. *J Altern Complement Med* 2005; 11: 127-134.
- Chen JK, Chen TT. Tonic herbs. In: *Chinese medical herbology and pharmacology*. California: Art of medicine press. 2004: 834-980.
- Dodds WJ. Animal model: canine and equine immune-mediated thrombocytopenia, and idiopathic thrombocytopenic purpura. *Am J Pathol* 1977; 86: 489-491.
- Hayashi AM, Matera JM, da Silva TS, Pinto AC. Electroacupuncture and Chinese herbs for treatment of cervical intervertebral disk disease in a dog. *J Vet Sci* 2007; 8: 95-98.
- Kohn B, Weingart C, Eckmann V, Ottenjann M, Leibold W. Primary immune-mediated hemolytic anemia in 19 cats: diagnosis, therapy, and outcome (1998-2004). *J Vet Intern Med* 2006; 20: 159-166.
- Lim DW, Kim DH, You DY. Effect of Kamiguitang on immunologic control function. *The journal of Oriental Gynecology* 1999; 151: 253-280
- Balch A, Mackin A. Canine immune-mediated hemolytic anemia: pathophysiology, clinical signs, and diagnosis. *Compend Contin Educ Vet* 2007; 29: 217-225.
- Werner LL, Gorman NT. Immune-mediated disorders of cats. *Vet Clin North Am Small Anim Pract* 1984; 14: 1039-1064.
- Mccullough S. Immune-mediated hemolytic anemia: understanding the nemesis. *Vet Clin North Am Small Anim Pract* 2003; 33: 1295-1315.
- Nishizawa K, Saito H, Nishiyama N. Effects of Kamikihito, a traditional Chinese medicine, on passive and conditioned avoidance performance impairment in senescence accelerated mouse (SAM). *Jpn J Pharmacol* 1990; 54: 375-382.
- Oh MS, Huh Y, Bae H, Ahn DK, Park SK. The multi-herbal formula Guibi-tang enhances memory and increases cell proliferation in the rat hippocampus. *Neurosci Lett* 2005; 379: 205-208.
- Qin B, Nagasaki M, Ren M, Bajotto G, Oshida Y, Sato Y. Effects of keishi-ka-jutsu-to (traditional herbal medicine: Gui-zhi-jia-shu-fu-tang) on in vivo insulin action in streptozotocin-induced diabetic rats. *Life Sci* 2003; 73: 2687-2701.
- Thompson JP. Systemic immune-mediated diseases. In: *Saunders manual of small animal practice*, 2nd ed. Philadelphia: Saunders. 1994: 181-188.
- Xie H. Acupuncture for internal medicine. In: *Xie's veterinary acupuncture*. Australia: Blackwell. 2007: 267-327.
- Yamaguchi K, Kido H, Kawakatsu T, Fukuroi T, Suzuki M, Yanabu M, Nomura S, Kokawa T, Yasunaga K. Effects of kami-kihito (jia-wei-gui-pi-tang) on autoantibodies in patients with chronic immune thrombocytopenic purpura. *Am J Chin Med* 1993; 21: 251-255.

면역매개성 혈액장애를 가진 소동물에서 귀비탕의 사용

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요 약 : 면역 매개 용혈성 빈혈(IMHA)은 소동물의 빈혈을 일으키는 가장 흔한 원인 중의 하나이고, 면역매개 혈소판 감소증(IMT) 또한 소동물에 영향을 줄 수 있는 면역관련 질환이다. 스테로이드제나 다른 면역억제제를 이용한 면역억압이 IMHA와 IMT의 일차적인 치료법이다. 그러나 적절한 약물의 적용에도 불구하고, 몇몇 동물은 치료에 반응이 없어 다른 면역억제제나 대체의학적 치료에 필요하다. IMHA로 진단된 8살의 중성화한 삼 고양이와 IMT로 진단된 8살의 킹찰스 스파니엘이 전통수의학진료를 위해 동물병원에 의뢰되었다. 두 동물 모두 스테로이드제나 다른 면역억제제에 반응이 없었다. 그래서 전통한약요법으로 귀비탕을 두 동물에게 적용하였다. 귀비탕 적용 한달 후 고양이의 농축적혈구용적과 개의 혈소판 수치에 현저한 변화가 나타나기 시작하였다. 귀비탕을 먹이기 시작한 후 4개월 후에도 고양이의 농축 적혈구 용적이 정상으로 유지되었으며, 18개월 후에 측정된 개의 혈소판 수 또한 정상으로 유지되었다. 이 증례로부터 면역혈액질환이 있는 소동물에 있어 귀비탕은 대체요법으로 사용될 수 있다는 것을 알 수 있다.

주요어 : 고양이, 개, 귀비탕, 면역계 용혈성 빈혈, 면역매개 혈소판 감소증.