Integrating Kampo and Evidence-Based Medicine (6) – Type 5 Cases

Is There a Type 5?

Hiromichi Yasui
Japan Institute of TCM Research

Introduction

In this series, I define four types of use of Kampo medicine in daily clinical practices within Japan's unified medical system, and discuss the diseases that fall under each of these types, by giving relevant case examples. In the previous issue of this journal, I introduced four episodes, and explained that they fall under the four types of use of Kampo medicine in daily clinical practices. Let me recount them below.

Type 1: Kampo treatment is better than standard modern medical treatment

Type 2: The effects of standard modern medical treatment and Kampo treatment are both strengthened when the two are used in combination

Type 3: The side effects of standard modern medical treatment can be mitigated in combination with Kampo treatment

Type 4: Circumstances prevent the application of standard modern medical treatment, but treatment is needed

☆ ☆

I introduced the aforementioned four types of Kampo use at a certain academic society. Among the members was Dr. Masayuki Kashima, a young friend of mine whom I respect (a physician in the internal department at Japanese Red Cross Kumamoto Hospital). After listening quietly to my presentation, he surprised me, saying "Doctor, I think there is a fifth type." He said that medicine is steadily advancing, and good drugs and new treatment methods are being developed one after the other. However, Kampo medicine is extremely useful to patients who cannot receive such expensive treatment. There are patients who are suited to Kampo not from medical reasons, but from economic ones. These patients do not fall under any of the four types that have so far been introduced, so Dr. Kashima noted that a Type 5 category should be created. As an explanation, he then introduced a case example from among a number of cases he has personally experienced.

Episode 1

A 37-year-old male patient began to complain of malaise, headaches, and joint aches from around August 3, 2014. On August 16, he came down with a fever of more than 39°C. As this continued for the next days, he consulted a local doctor. The results of a blood test showed aberrant values, with a WBC count of 1900/mm^3, Plt of 118 × 10^3/mm^3, and an LDH of 942 U/l. Therefore, on August 26, the patient visited the hospital where Dr. Kashia works, with a referral letter from the local doctor.

Height: 165cm; Weight: 72kg (-4kg in 2 weeks)

Temperature: 38.4°C, with alternating chills and fever and high temperatures from early evening. The lowering of body temperature is accompanied by perspiration.

Blood pressure: 145/90mmHg; Pulse: 94/min.; Respiratory rate: 16/min.

Slight hyperemia in the bulbar conjunctiva; No swelling of the cervical lymph node; Swollen spleen

Pulse examination: String-like and smooth

Tongue inspection: Slightly yellow tongue coating; slightly red tongue body

Abdominal examination: Intermediate abdominal strength; discomfort and distension in hypochondrium region

Examination findings were as follows.

WBC:1870/mm3; Hb13.7g/dl; Plt120,000; GOT: 111U/L; GPT: 90U/; LDH: 1346U/L;

CRP: 4.77mg/dL; TG: 146mg/dL; Ferritin: 4420ng/mL; Soluble IL-2 receptor: 2030U/ml;

Nyelogram (8/29): M/E3.80; Megakaryocyte count: 16/c.mm; Nucleated cell count: 37950/c.mm;

Hemophagocytosis caused by histiocyte was observed in places.

Abdominal echo: Hepatosplenomegaly

General appearance indicated the patient was not in acute distress.

From the first visit, Dr. Kashima strongly suspected hemophagocytic syndrome or leukemia, and recommended inpatient examination and treatment. However, the patient did not have health insurance, and said hospitalization would pose a large economic burden and is therefore impossible.

Dr. Kashima forewent the use of a steroid, as using it before diagnosis would make accurate diagnosis and the prospect of prognosis difficult later on. Yet, the patient's symptoms were strong, and close observation was required, so based on Kampo diagnosis, Dr. Kashima administered Shosaikoto and had the patient continue to come in as an outpatient.

The patient began taking Shosaikoto from August 26, and was relieved of his fever by the morning of the 28th. A myelogram taken on the 29th affirmed the diagnosis of hemophagocytic syndrome, but because the patient's fever had already subsided and his CRP improved to 1.30 mg/dl on the same day, the same Kampo medicine was continued to be prescribed on an outpatient basis. Thereafter, the patient's cytopenia and liver disorder also gradually improved, and treatment was deemed complete on September 9 upon confirming normalization in various examinations. Regular follow-ups were performed thereafter, but no recurrence was observed over a year, so the patient was allowed to terminate his visits.

Dr. Kashima also said as follows.

"Hemophagocytic syndrome is a life-threatening disease that frequently runs a rapid course and leads to multiple organ failure. It could be caused by virus infection, drug allergy, a connective tissue disease such as SLE, or a malignant disease, but it is known to be caused mostly by intravascular malignant lymphoma. There is no single method of treatment, but normally, chemotherapy against malignant lymphoma, administration of a large dose of immunosuppressant, or plasma exchange therapy is attempted in cases of poor reaction to massive steroid. I administered Shosaikoto in this case based on Kampo medicine diagnosis. The effect was dramatic, but even more worthy of mention is that the patient's economic burden was largely minimized."

The patient did not have health insurance for reasons unknown. If he had been hospitalized to receive standard treatment, it would have cost him an enormous amount of medical fee.

Thanks to Dr. Kashima's appropriate judgment, the patient's symptoms were ameliorated by taking Kampo, and his medical fee was able to be minimized. In sum, the patient improved owing to an inexpensive treatment method, without depending on expensive standard treatment. For reference, the price of a day's dose of Shosaikoto is approximately 230 yen. The patient took the prescription for 15 days, so it cost him 3,450 yen in total.

Such cases are not necessarily few, but they are hardly taken up, because most are simply reported as an isolated case. For treatment of serious diseases, many people do not believe there are any cases in which inexpensive Kampo medicine can be superior to expensive standard medicine. However, this is not necessarily true in all cases.

Shosaikoto will not always improve the symptoms of hemophagocytic syndrome. Dr. Kashima was able to prescribe it in this case, because he has abundant experience in the emergency outpatient and outpatient internal medicine departments, as well as deep knowledge of Kampo medicine theory.

It is sufficiently worth discussing whether or not this represents a case in which treatment by inexpensive Kampo medicine due to economic reasons improved the patient's symptoms compared to standard treatment. In a sense, it does, but as there are too many uncertainty factors, it might be somewhat too early to conclude that this case

represents Type 5. In terms of the four conventional types, this case would fall under Type 4.

Episode 2

Let us look at another case, the "Case of Mediastinal Lymphangioma Successfully Treated with Kampo Medicine"[1], which was published in the *Journal of Alternative and Complementary Medicine* by Dr. Keiko Ogawa, a discussion partner of mine who is in charge of outpatient Kampo medicine at Kanazawa University Hospital.

The patient is a two-year-old boy who was born with a tumors mass in his left axillary fossa. At an age of 1 year and 9 months, he was referred to a children's hospital in the region, and was diagnosed with a mixed type of lymphangioma in the region from his left axillary fossa and left mediastinum to his pleural cavity. He was treated at the hospital by OK-432 sclerotherapy, but to no effect.

The patient's parents thus requested Kampo treatment, and took the patient to see Dr. Ogawa as an outpatient when he was 2 years and 10 months old.

An MRI examination of the chest performed immediately before the first visit to Dr. Ogawa indicated a partly cavernous to mixed polycystic lymphangioma from the left cervix to the mediastinum. The MRI findings were as follows.
The left mediastinum was almost wholly affected by lymphangioma, causing a displacement of the liver and trachea and a deviation of the trachea.

The clinical course was as follows. First, marked sweating was interpreted as an exterior pattern, and the patient was prescribed Eppikajyutsuto. The MRI taken three months after the first visit did not show any reduction in the size of the lymphangioma. Five months later, the patient developed repeated bronchial asthma triggered by an infection and accompanied by hives, and sweated, so Ogikenchuto was also administered along with Eppikajyutsuto. A reduction in the lymphangioma was observed in the MRI that was taken after 9 months, and further reduction after 15 months. The cyst in the cervix almost wholly disappeared, and a clear reduction in size of the polycystic area, in particular, was observed (Figure 1). The cross section also showed a reduction of the tumor mass, as well as a return of the displacement of the trachea to normal condition (Figure 2). The number of coughing and frequency of asthma attacks declined, and the same prescription is still being continued at present.

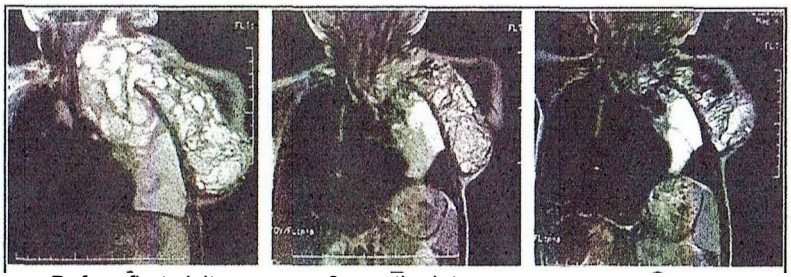


Figure 1: Changes in MRI findings (1)

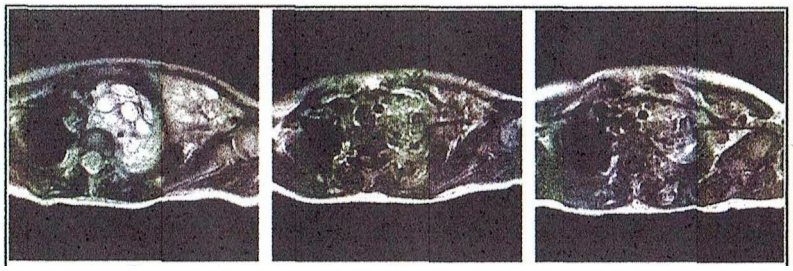


Figure 2: Changes in MRI findings (2)

This case report was written in English. Thus, people around the world were able to read it. A while after the journal was published, Dr. Ogawa received an email written in English. It was from the U.K. A father of a child with the same disease wrote to inquire how he could acquire the drug, because although Japan's Kampo prescriptions for medical use are highly superior, they are not approved as medicinal drugs in countries other than Japan.

Infantile lymphangioma is caused by a congenital anomaly of a lymphatic vessel. It is a benign tumor, but it develops by indistinctly infiltrating the surrounding organs, and displaces the surrounding organs. There is no known standard treatment, and treatment by sclerotherapy using various drugs has become the first choice of treatment today. Depending on the nature of the lesion, sclerotherapy is not effective, and surgical treatment is then considered. However, because its boundary is unclear, as mentioned above, removal by surgery runs the risk of damaging normal tissues around it. For this reason, it is difficult to completely remove the tumor in such cases, and treatment runs into a brick wall, so to speak, in many cases.

In this case, sclerotherapy using OK-432 was already performed, without effect. There was still a number of possible Western medical treatment methods, but Dr. Ogawa succeeded in dramatically ameliorating the young patient's lymphangioma using Kampo medicine.

After Dr. Ogawa's report was published, a number of pediatricians and pediatric surgeons submitted additional reports one after the other to the effect that the disease was ameliorated by using Eppikajyutsuto. Representative of these is the "Clinical Efficacy of Herbal Medicine for Pediatric Lymphatic Malformations: A Pilot Study"[2] by Dr. Naoki Hashizume et al. of Kurume University Hospital, published in *Pediatric Dermatology*.

Pilot Study by Dr. Hashizume et al.

Dr. Hashizume et al. monitored the progress of eight children (four boys and four girls) with lymphatic malformations after applying Eppikajyutsuto (TJ-28; Tsumura, Tokyo, Japan).

The result was as follows.

Four of the eight patients had a macrocystic type of lymphatic malformation, and the other four had a micro-macrocystic mixed type. They were observed over a period of 75 months, from January 2009 to May 2014, and were administered the drug over 7.2±2.9 months (a scope of 5±12 months). After administering Eppikajyutsuto to these patients, their magnetic resonance imaging (MRI) results showed a reduction ratio of 54.5±38.3% (73.6±27.0% among macrocystic types, 35.4±41.5% among micro-macrocystic mixed types). Among the four patients with a macrocystic lymphatic malformation, a considerable reduction was observed in one patient, and a moderate degree of reduction was observed in two patients. Among the four patients with a micro-macrocystic mixed lymphatic malformation, a noticeable improvement was observed in three patients. No reaction was observed in the other patient. There were no advanced adverse events.

The presentation of this paper after Dr. Ogawa's case report further demonstrated that Eppikajyutsuto is effective against lymphatic malformations in a significant number of patients. Other case reports presented at a number of academic societies held in Japanese also conspicuously show the drug's effectiveness against lymphatic malformations.

In the case of this disease, pediatricians and pediatric surgeons who possess accurate knowledge of modern medicine can use this prescription under their own supervision and obtain results relatively easily, without making a precise Kampo medicine diagnosis as in the previous case example. Kampo medicine is inexpensive. A single day's dose of Eppikajyutsuto is around 85 yen, so even a year's

worth costs only approximately 31,000 yen. It is far more inexpensive and easier to use compared to sclerotherapy and operative treatment.

When focusing on the fact that in these examples Kampo was able to ameliorate the patient's symptoms at a lower cost to the patient than standard treatment, they could perhaps be classified under Type 5. However, with regard to the fact that Kampo provided effective treatment without standard treatment, many might say that they rather fall under Type 1.

☆ ☆

The episodes by Dr. Kashima and Dr. Ogawa, and the pilot study by Dr. Hashizume associated with Dr. Ogawa all characteristically demonstrate that Kampo medicine was able to ameliorate patients' diseases in an inexpensive manner, where Western standard treatment would have cost a large amount of medical fee. Kampo medicine is taken orally, so it is non-invasive, and is simple and easy for the patient to take.

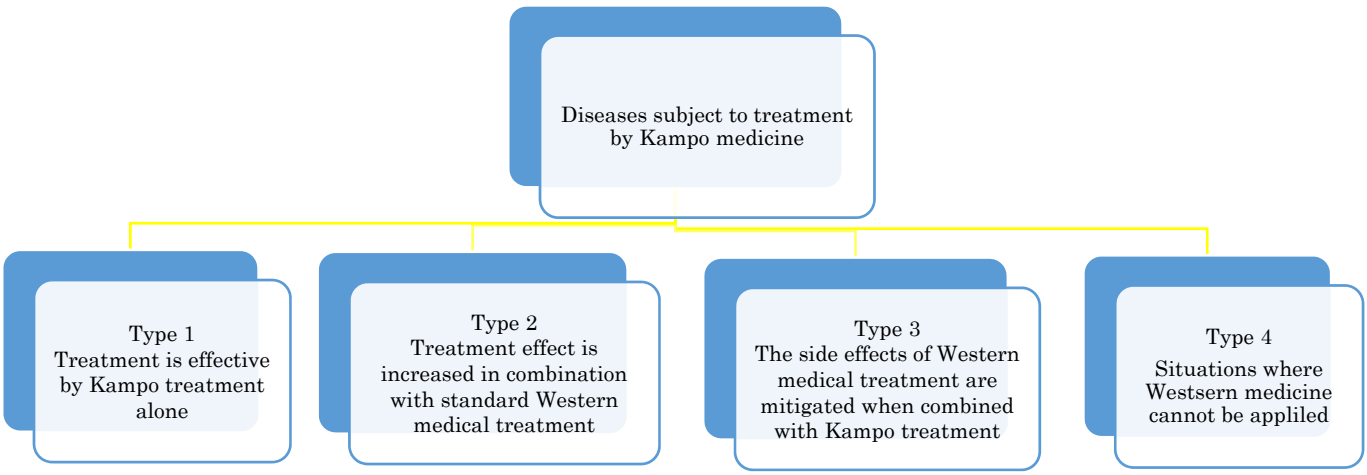
Ogawa's experience as a pediatric surgeon and outstanding capabilities as a Kampo doctor led her to prescribe Eppikajyutsuto and Ogikenchuto. Furthermore, Dr. Ogawa's case report led to the study by Dr. Hashizume et al., and generated an even larger number of case reports.

These case reports and studies show that Kampo medicine, under certain conditions, is extremely cost-effective. However, it is too early yet to decide whether a Type 5 category should be created, based on their data alone. The views of an even greater number of people shall be obtained before making a decision.

References

1) Keiko Ogawa-Ochiai et al.: Case of Mediastinal Lymphangioma Successfully Treated with Kampo Medicine, THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE, Volvme17, Number6, 2011, 563-565
2) Naoki Hashizume, et al.: Clinical Efficacy of Herbal Medicine for Pediatric Lymphatic malformations: A Pilot Study, Pediatric Dermatology, 2016;33(2):191-5

The four types and their characteristics



In the case in Episode 1, Dr. Kashima's advanced diagnostic capability regarding Kampo medicine led him to prescribe Shosaikoto. In Episode 2, Dr.