Clinical Report 2 (Kampo Medicine)

A Case of Recurrent Intestinal Bleeding due to Radiation-induced Enterocolitis Successfully Treated with Kyukikyogaito

Takahito Saito[1)2)]
1) Medical Corporation Tomidahama Hospital
2) Yokkaichi Medical Association, Kampo Medicine Study Group

Abstract

An 88-year-old woman suffered from recurrent intestinal bleeding because of radiation-induced enterocolitis after radiation therapy for cervical cancer of uterus about ten years ago. Recently, she was diagnosed renal anemia and chronic heart failure, and accepted iron, vitamin B and erythropoietin therapy simultaneously.

On March 13th in 2015, she was admitted to the hospital due to exacerbation of anemia. On her admission course, dark bloody stool was sometimes detected. Blood transfusion was done three times within about a month, but anemia was not recovered. Judged that venous bleeding, "oozing", repeatedly continued and there are no indication to endoscopic and surgical procedures, *kyukikyogaito*, Kampo medicine, was started under this poor condition ("yin deficiency") just after fourth blood transfusion. After then, anemia was recovered sooner and bloody stool was not detected. She was successfully treated with *kyukikyogaito* and discharged on April 22th. One month after her discharge, anemia was recovery, so *kyukikyogaito* was stopped.

Radiation-induced enterocolitis is well-known to hematochezia. There are several strategies for this disease such as hemostatics, blood transfusion, drug's enema, endoscopic and surgical procedures. According to experience of this case, *kyukikyogaito* is effective to radiation-induced enterocolitis repeating intestinal hemorrhage.

Keyword: radiation-induced enterocolitis, venous bleeding, Kyukikyogaito

Introduction

Lower gastrointestinal bleeding is commonly known to be caused by radiation-induced enterocolitis after radiation therapy for prostatic cancer or cervical cancer. Generally if the bleeding is not remarkable, and can be expected to stop naturally by itself in most cases. However, in cases with continuing bleeding, a hemostatic may be administered, or blood transfusion may be given. Endoscopic treatment and surgical resection are also attempted, but resection may be difficult in some cases[1)].

Kyukikyogaito is made from seven types of crude drugs: *Rehmanniae* Radix, *Paeoniae* Radix, *Angelicae Acutilobae* Radix, *Glycyrrhizae* Radix, *Cnidii* Rhizoma, *Asini* Corii Collas and *Artemisiae* Folium. It is known as a type of hemostatic that is effective for gynecological bleeding, urologic bleeding, hemorrhoidal bleeding, and other venous bleeding in the lower body. It is a prescription that acts against yin deficiency (poor complexion, pallid complexion, ectomorphism, sensitivity to cold), and has been used for female genital bleeding, as written in the section on gynecological and pregnancy illnesses in the *Kinkiyoryaku* (Essential Prescriptions from the Golden Cabinet)[2)]. It is said to be effective to symptoms of anemia in patients who are sensitive to the coldness and experienced longer bleeding, such as hemorrhoidal bleeding, post-traumatic internal bleeding, postpartum bleeding or anemia.

In this particular case, the patient's anemia advanced despite of receiving blood transfusions three times. Though chronic, persisting venous bleeding was suspected, and natural hemostasis was judged to be difficult. Thus, *kyukikyogaito* was chosen as a hemostatic, and good progress was achieved, as reported below, in reference to relevant literatures.

Case study

Subject: 88-year-old woman

Chief complaint: General malaise and fatigue

Past medical history:

Age 40: Appendectomy

Age 75: Cervical cancer (radiation therapy), adhesive intestinal obstruction

Age 81: Cataract

Age 85: Lumbar compression fracture

Age 87: Gouty arthritis, adhesive intestinal obstruction, lower-leg cellulitis

Family medical history: NA

Clinical course 1 (history of present illness):

The patient had been receiving medical care at a hospital nearby for high blood pressure and hyperuricemia. In 2002, she received radiation therapy for cervical cancer. Thereafter, she occasionally developed adhesive intestinal obstruction and venous intestinal bleeding caused by chronic ischemic entero colitis (radiation enteritis) after irradiation. Each time she developed these illnesses, she received therapy in hospital under a gastroenterologist. In June 2011, she was diagnosed with atrial fibrillation and chronic heart failure, and was given anticoagulant therapy, but the therapy was discontinued due to exacerbation of gastrointestinal bleeding. Thereafter, she was diagnosed with chronic heart failure, chronic renal failure and renal anemia, and was treated with an erythropoietin preparation in addition to an iron preparation, on a continuous basis. From around March 10th, 2015, she began to experience a sense of malaise and fatigue when walking. On March 13th, she visited our clinic. She was found to be anemic (Hb 5.6g/dl), and was admitted for blood transfusion. Because she was taking iron, she continued to pass black stool intermittently.

Physical findings from the perspective of Western medicine:

Normal body temperature; SpO2: 95%; pulse 45/minute, irregular, blood pressure 96/60mmHg; body weight 42kg; anemia in palpebral conjunctiva; cardiopulmonary functions: nothing abnormal detected; abdomen: flat, soft

Examination findings from the Eastern medicine perspective:

Subjective symptoms: Sense of malaise and fatigue when walking

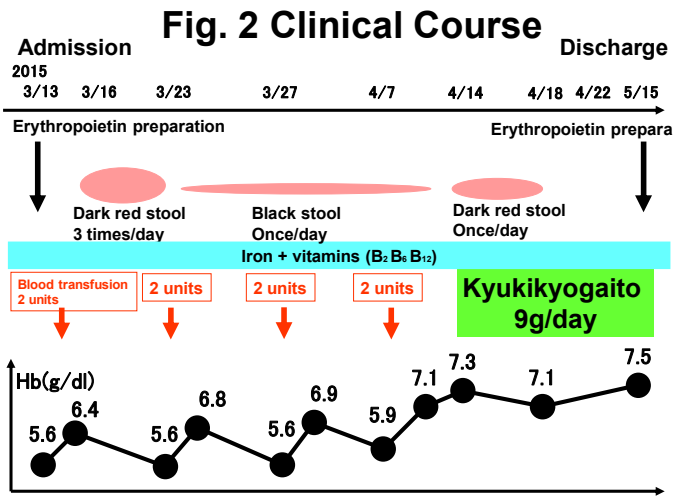
Objective findings: Poor, sallow complexion upon inspection. Ectomorphic. Sunken, thin and weak pulse. Thin white coating on tongue. Sublingual venous dilatation. Weak abdominal strength and weakness of the lower abdominal region.

Examination results:

Blood exam: White blood cell count 2800dl, red blood cell count 1.67million, hemoglobin 5.6g/dl, hematocrit 17.9%, urea nitrogen 51mg/dl, creatinine 3.14mg/dl, uric acid 12.1mg/dl

Abdominal CT: Change in pelvic (ileum and adnexa) adhesions (Fig. 1)

Fig. 1 Abdominal CT findings
An adhesion is seen in the pelvic organs.



Clinical course 2 (course after hospital admission): Fig. 2

After being admitted to the hospital, the patient received blood transfusion three times while receiving an iron and vitamin B preparation, but dark red stool occasionally appeared in addition to black stool (due to the iron preparation), and her anemia did not improve. Due to persistent venous intestinal bleeding caused by chronic ischemic enterocolitis, natural hemostasis was considered difficult. Judging from signs of renal deficiency, blood deficiency and blood stasis, a prescription of *kyukikyogaito* (9g/day) was begun after her fourth blood transfusion. Thereafter, no advancement of anemia was seen, so the patient was discharged on April 22th. On May 15th, a month after administering *kyukikyogaito*, the prescription was stopped, because the anemia was found to have improved.

The iron, vitamin B and erythropoietin preparations were continued after the termination of *kyukikyogaito*, but no longer intestinal bleeding or advancement of anemia were detected.

Observations

Radiation enterocolistis is well known as a disorder of the pelvic tissue and particularly the gastrointestinal tract, caused by radiation therapy for prostate cancer or cervical cancer. There are early effects and late effects, and may take more than ten years for the effects to occur. It causes hemorrhagic transformations such as inflammation and ulcers in the rectum, sigmoid colon, or small intestine. Radiation enteritis can be classified by progress, severity and pathology, and requires an efficient treatment strategy, but treatment guidelines have yet to be established. Normally, the bleeding is expected to stop on its own, and either a hemostatic drug is administered or conservative treatment through blood transfusion is chosen in most cases. At the same time, in cases of frequency bleeding, endoscopic hemostasis or drug infusion therapy is chosen, and in cases of stenosis or perforation, hyperbaric oxygen therapy or surgical therapy are chosen[1]. In this particular case, the patient experienced both early and late effects, and received inpatient treatment each time, such that the pattern of her daily life was sometimes disrupted.

Kyukikyogaito is regarded as an effective hemostatic for venous bleeding that does not accompany febrile symptoms in the lower body. This is understandable when considering that licorice is added to Shimotsuto, a representative prescription for blood deficiency, in addition to the Artemisia princeps leaf and donkey hide gelatin, which also have a hemostatic effect[2]. Today, it is considered effective against hemorrhagic anemia in people with a weak constitution, like the patient in this case study. With regard to literature, there are reports mainly in reference to bleeding in the lower body, such as radiation enteritis[3], hemorrhoidal bleeding[4], diverticular bleeding[5], Crohn's disease[6], ulcerative colitis[7, 8], uterine bleeding[9, 10], and hematuria and urinary tract bleeding[11, 12]. Among them, Kobayashi's report[5] indicates a hemostatic effect against diverticular bleeding, but the subject had been taking an anticoagulant and an antiplatelet drug, so it is difficult to clearly determine whether the effect was a result of a cessation of medication or the administration of *kyukikyogaito*. Other case reports also include the administration of Western hemostatics in addition to *kyukikyogaito*, and do not distinctly present the sole effect of *kyukikyogaito*. However, it is worth noting that Iwabuchi's report[9] compares *kyukikyogaito* with Western hemostatics, and discusses the efficacy of *kyukikyogaito*. Also, in Matsumoto's report[12], which focuses on bleeding caused by bladder cancer, *kyukikyogaito* is used with the expectation of temporarily stopping the bleeding, and certainly not as a fundamental treatment, but it is considered important for avoiding psychological stress and blood transfusion.

Meanwhile, there have also been experiential cases where *kyukikyogaito* was effectively used to stop venous bleeding in the upper body, such as

upper gastrointestinal bleeding (lower esophageal bleeding, so-called the Mallory-Weiss syndrome) that does not accompany decrease in blood pressure hypotension, respiratory tract bleeding, or hematobilia (hemorrhagic cholecystitis). There is also a report[13] that discusses the efficacy of *kyukikyogaito* against chronic subdural hematoma including an upper body illness.

Furthermore, cases have been experienced where *kyukikyogaito* stopped the bleeding after a colon polyp biopsy, post-resection bleeding, melena caused by ischemic colitis, and tumor bleeding caused by advanced colon cancer. In all cases, the bleeding clinically disappeared within two days, and no anemia or blood pressure drop was observed, but because other Western hemostatics were also used at the same time, it is difficult to determine the sole effect of *kyukikyogaito*.

Thus, this particular case is very significant in that it proved the efficacy of using only *kyukikyogaito*. *Kyukikyogaito* was applied, because the patient also displayed a yin deficiency pattern, such as blood deficiency and blood stasis in addition to renal ischemia. It had a more immediate effect than expected, and was found to be effective against repeating radiation enterocolistis like this case, at the least.

Based on this case study, literature reports and experimental cases, there was a renewed awareness that the selection target for *kyukikyogaito* is not active bleeding (bleeding that has surgical indications, such as arterial bleeding and varicose vein ruptures), but rather a bleeding pattern like this case study with oozing (venous bleeding), or chronic bleeding (continuously runny bleeding) that is not so fresh blood.

It should be noted that no reports on *kyukikyogaito* exist in the PubMed database, so international evaluations have yet to be made.

References

1. Masako Chino, Takanori Suganuma, Naoyuki Urakami et al.: "Radiation Enteritis," *Gastroenterological Endoscopy*, 2010, 52: 1381-1392.
2. Kazumoto Inaki: "Basics and guide to practice – Manual of important Kampo medicine prescriptions: *Kyukikyogaito*," *Kampo Shinryo*, 1996, 15: 10-13.
3. Ryusuke Obi, Kentaro Tezuka, Yoko Tamagawa: "A case in which *kyukikyogaito* was effective against bleeding caused by radiation enteritis," *Kampo Medicine*, 2014, 65: 248.
4. Kiyoshi Ishida: "Kampo therapy for hemorrhoidal bleeding – *kyukikyogaito* usage experience," *Prog. Med.*, 1989, 9: 590-596.
5. Ataru Kobayashi: "Five cases in which *kyukikyogaito* was effective against internal hemorrhoidal bleeding and diverticulular bleeding of colon under treatment by an anticoagulant and antiplatelet drug," *Science of Kampo Medicine*, 2015, 39: 128-131.
6. Satoshi Utsumi, Noboru Arai, Hiroshi Sato et al.: "A case in which *kyukikyogaito* with *senkinnaitakusan* was effective against Crohn's disease associated with colon cancer," *Kampo Medicine*, 2004, 55 (separate issue): 242.
7. Tsuneo Ozeki, Shuichi Mizuno: "About ulcerative colitis – Centered on differential diagnosis and treatment," *Jpn. J. Med. Pharm. Sci.*, 1987, 18: 1723-1726.
8. Takatoshi Noguchi: "Kampo therapy for ulcerative colitis – Polypharmacy and combined usage with Western drugs," *Kampo Shinryo*, 1996, 15: 23-25.
9. Shinsuke Iwabuchi: "Hemostatic effect of *kyukikyogaito* on functional uterine bleeding – Comparison with Western hemostatics," *Kampo Medicine*, 2000, 50: 883-890.
10. Naohisa Ushiroyama, Wataru Sakuma, Sakura Nosaka et al.: "Clinical effect of *kyukikyogaito* against threatened miscarriage," *Recent*

progress of kampo medicine in obstetrics and gynecology, 2006, 23: 100-103.

11. Hiroyasu Yoshikawa, Takao Ikeuchi, Shoki Kai: "Clinical effect of *kyukikyogaito* and *saireito* against idiopathic microhematuria," *Kampo & the Newest Therapy*, 1997, 6: 55-58.
12. Kazuo Matsumoto: "*Kyukikyogaito* for hematuria from bladder cancer," *Journal of Kampo Medicine*, 2013, 60: 1855-1857.
13. Shinichiro Yoshihara, Katsuyuki Hirakawa, Toru Inoue: "Experience in using *kyukikyogaito* against chronic subdural hematoma," *Proceedings of the 20th Scientific Meeting of the Japanese Society for Kampo Medicine and Neurological Surgery*, 2011, 33-35.