Introduction

Muscle cramp is a rare adverse event observed in the treatment of cancer with chemotherapy. Its incidence was reported only 0.2% in the treatment with S-1. For the measure of this adverse event, it is reported that Shakuyaku-kanzo-to (SKT), a Kampo medicine could be effective. In this report, we show the experience of the patient who was effective by the administration of Goshajinkigan (GJG), a different Kampo medicine to improve muscle cramp arose by using S-1 for the treatment of pancreatic cancer.

Case report

Eighty-year-old female was introduced to our hospital with chief complaints of body weight loss and anorexia by home doctor on March 2015. Since father examination was performed, she was diagnosed as having unresectable pancreatic cancer invaded to the duodenum and bile duct and suspected lung metastasis (Fig. 1a, 1b). After bile duct stenting (Fig. 1c), chemotherapy with S-1 and gemcitabine was initiated. After 4th course, gemcitabine had been discontinued by the toxicity, and then single administration for two weeks of a dose of 80 mg of S-1 was continued every three weeks. She often experienced muscle cramp at low legs, and she visited the emergency room with complaint of gait disturbance due to worse of muscle cramp. Her biochemical study showed almost normal electrolytes levels. Then a Kampo formulation Shakuyaku-kanzo-to (SKT), which was thought to be rapid-acting for these symptoms, was administered because of her sustained marked symptoms. No effect of SKT on these symptoms was observed; therefore, GJG was selected by Kampo medicine physician in combination with her complaints and body status. The administration of GJG was started 2.5 g once a day and then dose escalation was scheduled because it might induce gastrointestinal disorders. Since dose was escalated 5 g twice a day 2 weeks after initiation, incidence of muscle cramp was reduced three times a week. After 7 weeks, symptoms were disappeared. At this moment, she can continue the chemotherapy with S-1 under control of adverse event by the administration of 5 g of GJG twice a day.

Key Words: Goshajinkigan, S-1, muscle cramps, Kampo medicines

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Gosha-jinki-gan for S-1 related muscle cramps
Fig. 1 A white arrow shows an unresectable pancreatic cancer invaded to duodenum (a), and suspected lung metastasis (b). Bile duct stenting was performed (c).
Gosha-jinki-gan for S-1 related muscle cramps

The administration of GJG was started 2.5 g once a day and then dose escalation was scheduled because it might induce gastrointestinal disorders by Rehmannia (Jiou) a component of GJG for the elderly or Kyo-sho patients. Since dose was escalated 5 g twice a day 2 weeks after initiation, incidence of muscle cramp was reduced three times a week. She was instructed that she could take 7.5 g three times a day without adverse events and should decrease to 2.5 g once a day if the adverse events were occurred. After 7 weeks, symptoms were disappeared without dose escalation to 7.5g/day, so she continued chemotherapy with S-1 under control of adverse event by the administration of 5 g of GJG twice a day and obtained stable disease (Fig. 2a, 2b) in 18 months.

Discussion

Kampo formulations have been proven useful for the treatment of chronic illnesses. They are intended not only to help recover the natural balance of the human body, but also treat the body’s impairments, such as indigestion and fatigue. Based on this concept, several kinds of Kampo formula have been widely used for palliative care including cancer associated symptoms and adverse effect of chemotherapy in Japan.

SKT, a Kampo formulation with anticholinergic and prostaglandin inhibitory effect has been reported to be effective in reducing muscle pain, muscle spasms, joint pain and numbness. So, we first tried SKT for the treatment for the muscle cramps induced by S-1 administration. However no effect of SKT on these symptoms was found. Since KM physician diagnosed that GJG was suitable for her present status, it was initiated. Seven
weeks after initiation of GJG, symptoms were disappeared.

GJG, an aqueous extract of a combination of 10 herbs, is widely used in Japan for the treatment of lumbago, edema of the lower extremities, numbness, lower urinary tract symptoms, diabetic neuropathy and pain in people with diminished physical strength. Recently, preventive effects of oral GJG on oxaliplatin-induced hypoesthesia and paclitaxel induced allodynia in animal models were reported. Clinically, GJG could show the preventive effect of paclitaxel induced peripheral neuropathy for patients with ovarian or endometrial cancer who underwent chemotherapy by a multicenter study. Additionally, retrospective study showed the preventive effect of GJG on oxaliplatin induced peripheral neuropathy. However, there is no report that GJG improves on the muscle cramp. In this case, her muscle cramps probably occurred by the administration of S-1. Because the mechanism of induction of muscle camps was considered to be unusual, SKT might not work for the muscle cramps. GJG selected in consideration of her body imbalance by Kampo physician might show effect on muscle cramps in this case. Because the intestinal adverse events using GJG were often observed in the elderly or Kyo-sho patients, the administration of GJG was started 2.5 g once a day and then dose escalation was scheduled. Fortunately, she was obtained the effect on muscle cramp without dose escalation to the dose of usual use. For the select of Kampo medicine, it is important that her body status has been diagnosed accurately by the Kampo physician.

Conclusion

A Kampo formulation SKT selected for the muscle cramps arose by using S-1 for the treatment of pancreatic cancer was not effective. In contrast, GJG selected by KM physician in combination with her complaints and body status improved the symptoms and made it possible to continue the chemotherapy.

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