Clinical application of shiunko for dermal complications related to cancer treatment

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Abstract

【PURPOSE】To estimate clinical application of shiunko for reducing complications related to cancer treatment, such as radiation-induced dermatitis and hand-foot syndrome induced by molecular target drugs.

【METHODS】Patients involved in this study were as follows: 1. Thirty-one patients with simple scalp dermatitis induced by radiotherapy for brain tumors; 2. Nine patients with severe dermatitis from concurrent treatment with chemotherapy and radiotherapy for cancers including nasopharyngeal cancer; 3. Prophylactic usage of shiunko in four patients with radiation-induced scalp dermatitis; and 4. Six patients with dermal complications caused by molecular target drugs including hand-foot syndrome. Shiunko was applied in the same manner as in the treatment with standard ointment. The efficacy was evaluated with the improvement rate of the symptoms: excellent (more than 80%), good (more than 50%), fair (less than 50%), and no effect (less than 30%).

【RESULTS】Favorable therapeutic effects were observed in all patients. Shiunko not only showed prominent analgesic effects in all cases, which were not achieved in corticosteroid treatment, but also promoted healing in areas eroded by radiation. The patients with hand-foot syndrome gave the highest evaluations for moisturizing and analgesic effects.

【CONCLUSION】Shiunko is expected to be an effective ointment for treating scalp dermatitis caused by radiation and dermal complications induced by molecular target drugs.

Key words shiunko, radiation-induced dermatitis, molecular target drugs, hand-foot syndrome, decubitus.

Introduction

Radiotherapy and chemotherapy cause several complications that impair quality-of-life (QOL) of cancer patients. In this paper, the author estimated the usefulness of shiunko] for two kinds of dermal complications: radiation-induced dermatitis (simple radiation dermatitis, radiation dermatitis complicated by chemotherapy, and a prophylactic usage of shiunko to radia-
tion-induced dermatitis), and dermatitis induced by molecular-targeted drugs such as hand-foot syndrome.

1. Radiation-induced dermatitis

a) Simple radiation dermatitis

Radiation-induced scalp dermatitis is a type of burn caused by radiotherapy for brain tumors, and often impairs QOL of cancer patients. In this study, we evaluated the efficacy of shiunko in treating radiation-induced scalp dermatitis.
Thirty-one patients (15 male and 16 female patients; ages range from 51 to 79 years-old, mean 64.0) with malignant brain tumors were involved in this study. The histological diagnoses were: malignant glioma (18 cases), primary central nervous system malignant lymphoma (8 cases), metastatic brain tumor (4 cases), and atypical meningioma (1 case). Performed radiotherapies were as follows: whole brain (11 cases) and focal (20 cases). Symptoms were as follows: redness (29 cases), burning pain (19 cases), itching (15 cases), and erosion (8 cases). Shiunko was applied in the same manner as in the treatment with standard ointment. The efficacy was evaluated with the improvement rate of symptoms: excellent (more than 80%), good (more than 50%), fair (less than 50%), and poor (less than 30%).

Favorable therapeutic effects were observed in all patients (excellent: 21 cases, good: 10 cases). The efficacy was confirmed within a few hours in patients who showed a quick response to the treatment. In some cases, reepithelialization was observed even during the period of radiotherapy.

**Representative case 1: 69 year-old male with glioblastoma**
He had focal brain radiotherapy up to 60 Gy. He had complained burning scalp pain since the beginning of hair loss. Betamethasone lotion was effective in the earlier phase, but the patient could no longer tolerate the pain on the last day of radiotherapy. Thus, shiunko was applied and good efficacy was observed. The symptom was resolved in a few hours.

**Representative case 2: 46 year-old male with malignant astrocytoma**
He had focal brain radiotherapy up to 60 Gy. He had complained burning scalp pain with itching since the radiation dose of over 30 Gy. Shiunko was applied and showed good efficacy. Shiunko enabled the patient to discontinue the steroid lotion used in the early stage.

In conclusion, shiunko is expected to be more effective than steroids in treating radiation-induced scalp dermatitis.

Prophylactic usage of shiunko is described in the latter chapter.

**b) Radiation dermatitis complicated by chemotherapy**

In the treatment of nasopharyngeal cancer and esophageal cancer, combination of radiotherapy and chemotherapy, so-called chemoradiation, yield better outcome. However, this combined therapy also worsens radiation-induced dermal complications.

Based on the good outcomes of the shiunko treatment to radiation-induced scalp dermatitis, the author evaluated the efficacy of shiunko as treatment for severe dermatitis induced by chemoradiation.

Nine patients involved in this study are as follows: 7 patients with head and neck carcinomas (two cases each of oropharyngeal, hypopharyngeal, and laryngeal carcinomas, and one case of parotid carcinoma), and one case of each esophagus cancer and vulvar carcinomas. Seven male and two female patients were involved in this study. Ages range from 54 to 73 years-old (mean 66). Types of chemotherapy performed were as follows: 7 patients with 5-FU (fluorouracil) and CDDP (Cisplatin), one patient with CDDP and TS-1 (Tegafur, gimestat and otastat potassium). Severe erosions and intolerable burning pain were observed in all cases but steroid-based treatments did not sufficiently relieve these symptoms.

Shiunko was applied after radiotherapy in the same manner as in the treatment with standard ointment. The efficacy was evaluated in the same manner as that of simple radiation dermatitis.

Excellent therapeutic effects were observed in all patients.

**Representative case 1: 73 year-old female with laryngeal cancer (fig.1)**

She had radiotherapy up to 66 Gy and chemotherapy of CDDP and 5-FU. Her irradiated neck was reddened, eroded and caused intractable pain, and did not respond even to steroid treatment. Then, shiunko was applied and showed good efficacy.

![Fig. 1 73 Year-old female with laryngeal cancer](image)

Left: Shiunko was applied from the day the irradiation dose reached to 54 Gy.
Right: 11 Days after 66 Gy irradiation.
She said that the intractable neck pain was resolved soon after shiunko was applied.

**Representative case 2: 69 year-old male with parotid carcinoma**

He had radiotherapy up to 70 Gy and chemotherapy of CDDP and 5-FU. His irradiated neck was extensively eroded and he had complained of intractable pain and did not respond even to steroid treatment. Then, shiunko was applied and showed good efficacy. The restored skin was also in good condition.

In conclusion, shiunko showed an excellent pain-relief effect for chemoradiation-induced complex scalp dermatitis. Shiunko also showed early and good recovery of those eroded skin. Shiunko was considered a much more effective ointment than steroids.

c) **Prophylactic usage of shiunko to radiation-induced dermatitis**

In this study, the author evaluated if shiunko can prevent or alleviate radiation-induced scalp dermatitis.

Four patients (2 male and 2 female patients; ages range from 58 to 79 years-old, mean 67.8) with malignant brain tumors were involved in this study. The histological diagnoses were: one case each of glioblastoma, primary central nervous system malignant lymphoma, cerebellar metastasis of rectal cancer, and atypical meningioma. Performed radiotherapies were as follows: whole brain (1 case) and focal (3 cases). Irradiated doses range from 49 to 60 Gy (mean 54.8 Gy). Shiunko was applied from the first day of radiotherapy.

Favorable therapeutic effects were observed in all patients. The scalp conditions were maintained well until the end of radiotherapy.

**Representative case 1: 70 year-old female with cerebellar metastasis of rectal cancer (fig.2)**

She had focal radiotherapy of 50 Gy on the right posterior fossa. The scalp condition was extremely good with only a few blisters around the auricle.

**Representative case 2: 79-year-old female with glioblastoma**

She had radiotherapy of 60 Gy on the right frontal lobe. The scalp condition remained good with only small abrasions. The auricle, which is relatively delicate to radiation, remained good.

In conclusion, shiunko may alleviate radiation-induced scalp dermatitis. Prophylactic use of shiunko requires further verification.

2. **Dermatitis induced by molecular target drugs**

New anti-cancer agents, molecular target drugs, brought about new type of dermatitis, which is so-called hand-foot syndrome.4 No appropriate treatment for this syndrome has been established yet.

Based on the shiunko's wound-healing properties: vascular endothelial growth factor (VEGF) production, apoptosis induction and moisturizing wounds,7 the author used shiunko for the hand-foot syndrome.

Six patients (all female) treated with molecular target drugs were involved in this study. Ages range from 54 to 70 years-old (mean age 61.8). Types of molecular target drugs were as follows: 2 cases each of cetuximab and bevacizumab, 1 case each of gefitinib and panitumumab. All patients complained of intolerable pain in fingers with thinned and weakened skins. Steroid-based treatments did not sufficiently relieve these symptoms.

Shiunko was applied to the entire hands and the patients wore cotton gloves at night. The efficacy was evaluated in the same manner as mentioned above.

Favorable therapeutic effects (excellent and good in 3 cases respectively) were observed.

![Fig. 2](image-url) 70 Year-old female with cerebellar metastasis of rectal cancer
Left: The irradiation field in the right posterior fossa.
Middle & Right: The skin condition was extremely good with only a few blisters around the auricles.
Representative case: 70 year-old female with colon cancer

She received a combination of FOLFOX6 therapy and cetuximab. Dermal complication such as reddening, thinning, and weakening of skin, and pain from cracked skin were observed. Skin patches and other ointments were not effective. The skincare-specialized nurse tried shiunko on her. Shiunko was applied to the entire hands and the patient wore cotton gloves before going to bed.

Cracked skins healed within 1 month in spite of ongoing chemotherapy. According to the patient, she felt happy when applying shiunko and sleeping with the cotton gloves because she is pain-free.

Shiunko showed a favorable pain-relief effect, especially for perionychia, and kept skin moist. Shiunko was considered as one of the effective ointments.

Discussion

Shiunko, covered by the Japanese Health-Insurance System, is an ointment invented by Seishu Hanaoka in the early 19th century and is a well-known ointment for treating burns.

Shiunko is composed of only five natural remedies, that is, lithospermi radix, angelicae radix, sesame oil, beeswax, and lard. But, it has several unique activities, such as anti-bacterial activity,9) detoxification, anti-histamine activity,10) and moist wound healing. Furthermore, recent studies demonstrated vascular endothelial growth factor (VEGF) production and apoptosis induction,5,6) which promote wound healing.

To treat radiation-induced dermatitis, we must control intolerable dermal pain, protect the skin from dermal damage such as erosion, and promote dermal healing and recovery. Shiunko has prominent properties: 1) mitigation of skin redness and itching by inhibiting immediate type of inflammation through anti-histamine activity; 2) prevention of skin damage from infection through anti-bacterial activity; 3) promotion of reepithelialization and angiogenesis6) of damaged skin through moist wound healing.7) Steroid ointments, however, lack the latter activity.

Those three properties of shiunko also contribute to alleviate the dermal complications caused by molecular target drugs. Furthermore, decubitus is thought to be a good candidate for these properties of shiunko.

Conclusion

Shiunko is an effective ointment for treating radiation-induced dermatitis and the dermal complications caused by molecular target drugs. In addition, shiunko is expected to excel steroid ointments in these treatments.

References